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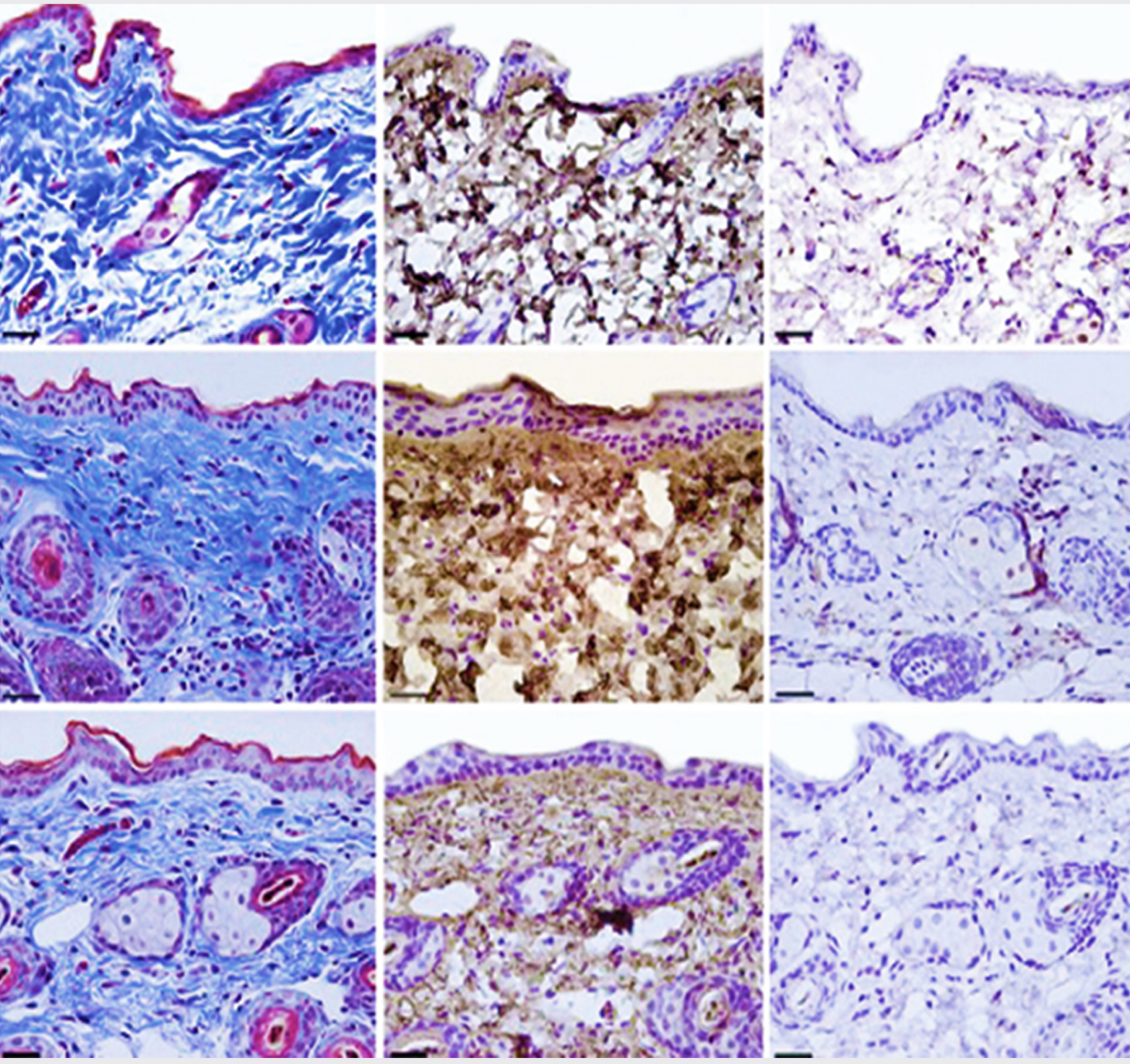

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Plastic and Aesthetic Research

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Editorial Plastic and Aesthetic Research

Fifty-six years of plastic surgery

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Evolution is the natural state of all things and certainly our field of plastic surgery is not exempt. The appearance on the scene of a new journal dedicated to the pursuit of excellence is no exception. It is my distinct pleasure to become the Editor-in-Chief of Plastic and Aesthetic Research and to help guide it into the evolutionary process so it can play its role in the advancement of methods to make people's lives better.

Plastic surgery is an exceptional field. It is not regionally-based or system-based. It is not cardiovascular surgery; it is not genitourinary surgery; it is not ear, nose, and throatsurgery. Then what is it?

We know in ancient India forehead flaps were being used to reconstruct noses, which had been amputated as punishment for adultery. This was surgery necessitating familiarity with random flaps. Therefore, it is reasonable to assume that random flaps were probably being employed in other reconstructive problems; however, we have no credible proof of this. We do have proof of skin grafts, rhinoplasties, face lifts and a variety of other aesthetic and reconstructive procedures being done in 19th century Europe, but not by surgeons who were organized and worked collectively to promote the spread of common knowledge. This did not occur until the advent of World War I.

During World War I, medicine advanced. Individual military personnel with injuries of massive degree, which heretofore had been fatal, were being saved. However, resulting traumatic sequelae were well-beyond the knowledge of contemporary treatment modalities.

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To deal with these problems the allied forces organized a unit under the direction of Sir Harold Gillies (in private life an otolaryngologist) and surgeons working in this unit were treating many of the problems previously deemed irreparable. After the war, the body of knowledge and experiences achieved from these efforts were disseminated to all parts of the world giving birth to organizations of like-minded surgical adventurers who called themselves "plastic surgeons"… from the Greek word "plastikos" or to form, mold, or make new. It was impossible to limit themselves to one system or to one region. The description that best identified their specialty was innovation… and that is what we plastic surgeons are… innovational surgeons.

The evolutionary process moved rapidly after World War I and even more rapidly during World War II and the years succeeding it. My personal observation of the process began during my residency in 1958. We were doing cleft lips by the Tennison technique as Ralph Millard had not yet become well-known. The full understanding of fluid and electrolyte physiology in burn patients, as well as today's commonly known knowledge of burn wound care, had not come on the scene. The rare face lift was a simple skin stretch technique as Mitz and Peyronie were still in training and the superficial musculoaponeurotic system was unrecognized. The open rhinoplasty was reserved for nasal reconstruction with cleft lip. Open aesthetic rhinoplasty was generally unheard or were mere fantasies. Illous and liposuction were decades away as was Uebel and Barrera's single follicle method of hair restoration.

The list of operative evolution goes on and on; but, plastic surgery advanced in other skills as well as in techniques. Our anesthesia was ether, with cyclopropane coming in a bit later; but, both of these were explosive; therefore, ruling out use of an electro-cautery. It was all clamp and tie for hemostasis (a big problem as we were not aware of aspirin's effect on coagulation) or local. The only sedation we had with local was an assortment of barbiturates.

Lighting for surgery was one overhead light, then a movable light stand… and the endoscope was unheard of ("take a deep breath" became my mantra).

Management of postoperative pain in the early years now seems near barbaric and penicillin (a Godsend) had just become well-known.

Current evolutionary excitement seems focused on the use of fat. Whereas Guerro Santos and Chachir were extolling the miracle of fat grafting before the turn of the century, it was not until Coleman described the importance of the fat's being grafted in very small droplets that most plastic surgeons took an interest in fat grafting. Then, with Khouri's introduction of the BRAVA system, large volume fat grafting became a reality. Now, the woman wishing breast augmentation without a foreign material put into her body can be accommodated. Now, immediate breast reconstruction can be carried out with no expander, no silicone implant, and no distal flap, with a sensitive breast the usual expectation.

Yes, the evolution in plastic surgery has been remarkable… change, change, change… constant and unremitting… but one thing has not changed: our sole purpose in all our efforts remains the same. Our identity as plastic surgeons… as innovational surgeons… implies that we use special techniques as surgeons to fulfill our single and primary goal… to make our patients' lives longer, better, or both. To this we remain dedicated… and with this new journal we hope the make the path straighter and more direct for all our colleagues.

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Editorial Plastic and Aesthetic Research

In consideration of a career in research

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Research is to see what everybody else has seen and to think what nobody else has thought.

-Albert Szent-Györgyi

Research is creating new knowledge. If you have a thirst for knowledge, an inquiring mind, and the skill to seek answers, then a research career may be for you. Research professionals are on the cutting edge of scientific and technological developments, and their work leads to new medicines, consumer products, industrial processes, and numerous other developments. Research careers span virtually all areas of life, from business and economics to computer science and biotechnology.

Careers in research are evolving at a rapid pace globally. During recent times, there has been remarkable progress in the medical and dental field sowing to the development of newer technologies with regard to materials, pharmacological products, and diagnostic materials. However, the status of research in developing countries, when compared with many western countries, remains restricted to paper and publications. Research that is limited to the laboratory is not beneficial to the general public or patients, in particular. This kind of research has no clinical significance.

If you steal from one author, it's plagiarism; if you steal from many, it's research.

-Wilson Mizner

Despite the fact that there are sufficient sponsors and funding agencies available, only a small number of medical and dental professionals opt for a full-time research career, especially in India.

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Many researchers work for pharmaceutical or biotechnology companies, while others work in universities or government research laboratories. University researchers may also work as professors in their academic discipline. Researchers working in applied research and development often work for a specific company's R and D division, conducting research for new products and conducting development activities for existing ones.

Most research positions require the postholder to have a doctoral degree, especially for research jobs in universities or in the biological and medical sciences. In addition, research professionals must continually update their knowledge so as to remain on the cutting edge of their research area or specialism.

In postgraduate programs, a dissertation is a required, the main purpose of which is to expose students to the research environment. Occasionally, the subject or area of study selected by a student may not be practically possible to carry out in their parent institution – even though many colleges delivering postgraduate programs include "research center" or "research institute" as part of their institution's name. These postgraduate students then have to run from pillar to post to seek permission to undertake their study in other places, or otherwise spend huge amounts of money to finish their research work.

Undergraduate (or graduate) researchers learn tolerance for obstacles faced in the research process, how knowledge is constructed, independence, increased self-confidence, and readiness for more demanding research.[1]

As noted above, there are nonetheless numerous benefits for students who get involved in research. Research experience allows graduate students to better understand published works, learn to balance collaborative and individual work, determine an area of interest, and ultimately, jump-start their careers as researchers. Through exposure to research as undergraduates or graduates, many students discover their passion for research and continue on to graduate studies and faculty positions.

First and foremost, a direct benefit of research starts in the classroom. When investigating any phenomenon in class, it is useful to know how the original study was performed. By engaging in research first hand, students find it easier to understand the rationale underlying others' research. For example, only after forming your own hypotheses do you truly understand the nuances of research designs and better conceptualize course material. In addition, undergraduate research can provide students with an ongoing source of one-on-one mentorship that is otherwise unheard of in the broader undergraduate curriculum.

Exposure to an area of research undoubtedly also helps students explore career fields. If you are considering research as a career path, experience in a research setting is invaluable. Exposure to research guides some students toward research after graduation, as well as allowing other students to make informed decisions not to pursue careers in research. In addition, the earlier that students become involved more experience they attain, which, in turn, enhances their career choices. For example, students considering careers in medicine will also benefit greatly from exposure to research. Many medical schools value research experience for admissions. Perhaps more importantly, a solid basis in hypothesis-driven research is what evidence-based medical practice is built upon. Experience in this area can enhance an understanding of both the medical curriculum and the medical literature.

Exposure to research as graduates can also increase the likelihood of becoming successful researchers in the future. Some undergraduates, unsure what to do upon degree completion, proceed to graduate school with the ill-fated idea that it is the next logical step after undergraduate studies. If they have undergraduate experience in research, they are more likely to know if they actually enjoy research. Usually, however, undergraduate students discover a passion for research they did not know existed. Institutions of higher education have a way of attracting the most curious minds, but asking questions and finding answers is a calling that many discover only after they first test the research waters.

Due to focus and importance of research at PhD level, it is often believed that creating new knowledge is the main goal of postgraduate academic degrees. The main objective of completing a doctoral degree is to become a competent researcher who can conduct independent research in his or her chosen area. If we accept the premise that the purpose of a PhD program is to produce competent researchers, then the research completed during such programs is primarily undertaken as a contribution toward this goal, and the nature and sophistication of the research output is less important.

What is important is to learn to properly formulate a problem and apply suitable techniques to produce results that further the state of understanding about that problem. Hence, while doing a PhD, the scholar should be self-motivated and committed to working hard and over extended periods of time on problems. Research is often a lonely business (except, of course, in disciplines where group activity is more common), and a PhD program is an incisive preparation for a career in it. Research is a tough career; but, with the development of these skills by doing a PhD, it can become easier and more satisfying.

Learn from yesterday, live for today, hope for tomorrow. The important thing is to not stop questioning.

-Albert Einstein

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Review Article Plastic and Aesthetic Research

Nanotechnology applications in osteodistraction

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ABSTRACT

Most current strategies for bone regeneration have relatively satisfactory results. However, there are drawbacks and limitations associated with their use and availability, and even controversial reports about their efficacy and cost-effectiveness. The induction of new bone formation through distraction osteogenesis (DO) is widespread clinical application in the treatment of bone defects, limb deformities, and fracture nonunions. However, a lengthy period of external fixation is usually needed to allow the new bone to consolidate, and complications such as refracture at the distraction gap often occur. Although various biomaterials have been used as injectable delivery systems in DO models, little has been reported on the use of nanobiomaterials as carrier materials for the sustained release of growth factors in bone regeneration. One area of focus in nanotechnology is the delivery of osteogenic factors in an attempt to modulate the formation of bone. This review article seeks to demonstrate the potential of nanobiomaterials to improve biological applications pertinent to osteodistraction.

Key words:

Bone regeneration, distraction osteogenesis, nanobiomaterials, nanoparticles, nanotechnology

INTRODUCTION

The most common form of bone regeneration is fracture healing, during which the pathway of normal fetal skeletogenesis is reactivated.[1] However, with substantial loss of bone tissue the regenerative process is compromised, as is seen in cases of avascular necrosis and osteoporosis. These challenging situations often necessitate the augmentation of natural bone repair.

Distraction osteogenesis (DO) is a method of producing large quantities of bone using local host tissues stimulated by mechanical distraction forces. After an osteotomy the continuously enlarging gap is filled with living bone via intramembranous ossification of the newly built bone.[2] The main advantage of DO is that it can achieve regeneration of living bone with the same strength and width as that of the native bone. Peripheral nerves, vessels, muscles, tendons, ligaments, and skin are also gradually lengthened in proportion to the lengthening bone.[3] DO has been widely used for the treatment of leg-length discrepancy, nonunion, traumatic bone defect, deformity, musculoskeletal tumor and osteomyelitis.[4]

Recent discoveries have highlighted that nanotechnology may universally augment all materials used for regrowing bone.[5] Nanotechnology, a new focus in the area of biomedical research, involves the visualization, manipulation, and fabrication of materials on the smallest scales, in dimensions of 1 μm down to 10 Å. The unique feature of this nanotechnological approach is that it enables

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consideration of the spatial and temporal levels of material organization in order to develop appropriate hierarchical structures. These nanomaterials have shown superior properties over their conventional counterparts owing to their distinctive nanoscale features and novel physical properties.[6-8] Currently, applications of nanomaterials in osteodistraction include the use of nanofilms and nanoparticles to protect against infection in surgical implants, and the use of engineered surfaces to improve bone healing and formation and to assist in osteogenesis via the distribution of osteogenic factors. This review seeks to demonstrate the potential of nanobiomaterials to augment biological applications pertinent to osteodistraction.

NANOFEATURES INFLUENCE CELL BEHAVIOR

The topography of nanomaterials (e.g. pores, ridges, grooves, fibers, nodes, and combinations of these features) is known to significantly influence cell behavior.[9]

Furthermore, implant surface chemistry plays a critical role in deciding the performance and success of these devices. The interaction of four proteins – fibronectin, vitronectin, laminin, and collagen – is known to enhance osteoblast function on nanomaterials compared to conventional materials.[10] Proteins and other biomolecules that dynamically adsorb to biomaterial surfaces upon implantation can trigger nonspecific inflammatory responses, which can limit integration of the device and influence *in vivo* performance.

The wettability of a nanomaterial can significantly alter cell behavior. The surface composition, surface treatment, surface roughness, immobilization of various chemical agents to the surface of the implant or biomaterial, and the presence of nanofeatures on the surface, alter surface wettability and affect cell behavior.[9] Increased surface wettability, or hydrophilicity, has been associated with enhanced protein adsorption, and consequently, cell adhesion on biomaterials. The ability to synthesize and process nanomaterials with tailored structures and topographies to direct subsequent functions of specific cell lines provides potential for the design of novel proactive biomaterials that could improve the efficacy of bone implants.

OSTEODISTRACTION AND NANOTECHNOLOGY

Although DO with an external fixator has become a popular method of treating cases with substantial bone loss, it is not without complications [Figure 1]. One of the major drawbacks of this method is that it is time-consuming and the ring fixator must be maintained *in situ* until full consolidation of the bone. This is inconvenient and even uncomfortable for the patient.[11]

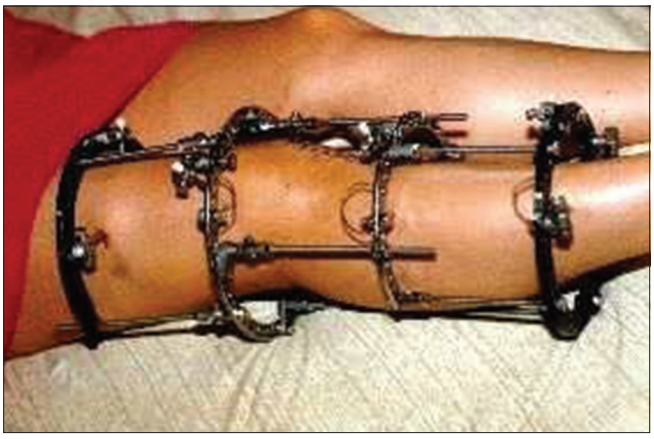

Figure 1: Ilizarov's external ring fixator for limb lengthening

Further, Paley[12] reported pin tract infections in 36% of patients, and Karger *et al*.[13] noted joint contractures in 65% of patients when the limb was lengthened by 24% (7 cm) of its initial length.

Advances in nanotechnology have stimulated investigations into cell-substrate interactions from the microscale to the nanoscale. Using this technique, it is now possible to fabricate advanced materials with more favorable properties for orthopedic applications. There have been quite a few reports in the literature investigating the usefulness of various nanomaterials for reducing the risk of implant-associated infections and accelerating the bone healing process.

NANOCOMPOSITES FOR BONE TISSUE REGENERATION

The introduction of polymer nanocomposites into bone tissue engineering allows the complex architecture of native bone tissue to be mimicked, providing a novel and practical approach to the massive production of materials for bone tissue engineering.[8] Synthetic or natural polymer matrices offer a wide range of mechanical properties and exhibit different biodegradation features, whereas various inorganic nanoparticles provide bioactivity. Furthermore, their integration makes it possible to fabricate materials that mimic the structural and morphological organization of native bone. Although there is great potential to improve current biomaterials and develop advanced nanocomposite scaffolds for bone regeneration, each of these materials has specific drawbacks.

Bioceramic/synthetic polymer nanocomposites for bone regeneration

Nanocomposites based on bioceramics and biodegradable polymers (e.g. calcium phosphate, calcium sulfate, beta-tricalcium phosphate [β-TCP], hydroxyapatite [HA], poly-lactic acid [PLA], poly-glycolic acid, and poly-lactide-co-glycolide) have attracted much attention

for bone tissue regeneration because of the excellent combination of bioactivity and osteoconductivity of bioceramics with the flexibility and shape controllability of polymers. Such nanocomposites are also able to closely mimic the microstructure of bone. These composites have shown a better cell response than conventional composites, depending on different factors, such as material composition, fabrication method, microstructure and mechanical properties of the composites, among others. Nonbiodegradable polymers have been used in bone tissue engineering for their better mechanical properties and chemical stability than biodegradable polymers. However, some of these polymers, such as polyethylene, polypropylene and poly (etherether ketone), demonstrate severe immune responses.

Bioceramic/natural polymer nanocomposites for bone regeneration

Natural biopolymers (e.g. chitosan, collagen, HA, silk fibroin, and calcium phosphate) are currently of interest in tissue engineering because their biological recognition may positively support cell adhesion and function. However, these polymers have poor mechanical properties. HA-reinforced natural polymers exhibit much better mechanical and biological properties, and thus may resolve many of these difficulties.

Carbon nanotube/polymer nanocomposites for bone regeneration

Carbon nanotubes (CNTs) have excellent mechanical properties, a highly specific surface area and a low density, which makes them ideal for the fabrication of tissue engineering scaffolds with polymers. The addition of CNTs to a polymer helps cell growth and promotes cell attachment, proliferation and differentiation. The cytotoxicity of CNTs is still obscure, but their toxicity can be reduced when incorporated into a polymeric matrix, thus making it possible to fabricate CNT – polymer nanocomposites for bone tissue engineering. However, the long-term toxicity of CNTs in human tissue and their influence on bone remodeling need further investigation.

IMPLANT-ASSOCIATED INFECTION AND NANOTECHNOLOGY

Implant-associated infection is one of the most serious complications in orthopedic surgery. Bone infections associated with foreign body materials are especially difficult to treat. Removal of the infected implants, long-term systemic antibiotic therapy, and multiple revisions with radical debridement are frequently required.[14-16] The consequences of infection can be devastating and may lead to prolonged hospitalization, poor functional outcome, sepsis, and even amputation.[17]

Implant-associated infections are the result of bacterial adhesion to an implant surface and subsequent biofilm formation at the implantation site.[18] The formation of biofilm takes place in several stages, starting with rapid surface attachment, followed by multilayered cellular proliferation and intercellular adhesion in an extracellular polysaccharide matrix.[19] Biofilms are resistant to both the immune response and systemic antibiotic therapies.

Different surface modification strategies for orthopedic implants have been investigated, including (a) the addition of materials with desired functions to the surface; (b) the conversion of the existing surface into more desirable chemistries and/or topographies; and (c) the removal of material from the existing surface to create new relevant topographies.[20] The latter, which was tested during *in vitro* studies, provides the surface with a specific roughness to promote osteoblast proliferation and cell adhesion.

Coating metal implants with a bactericidal film would inhibit bacteria from colonizing implant surfaces and provide a high antibiotic concentration in a local region commonly known as a nidus for bacterial infection.[21] Different surface modifications and coating techniques can be used, such as direct impregnation with antibiotics and immobilization of an antimicrobial agent in a matrix capable of binding to different surfaces,[22] as well as coating with antimicrobial, active metals such as copper and silver,[23] nitric oxide-releasing materials[24] and titanium dioxide films.[25]

Ainslie *et al*.[26] have shown *in vitro* that nanostructured surfaces display reduced inflammation in comparison with a respective flat control. Controlled drug release from the surfaces of implanted medical devices coated with nanostructured films is expected to yield additional advantages over conventional coatings. However, so far this approach has gained limited clinical use for orthopedic coatings.

Li *et al*.[21] developed biodegradable polypeptide multilayer nanofilms to potentially serve as antibiotic carriers at the implant–tissue interface. They demonstrated that polypeptide multilayer nanofilms, with or without cefazolin, have antibacterial activity against organisms frequently associated with osteomyelitis, and may improve bone healing through improving osteoblast cell adhesion, viability, and proliferation.

Etienne *et al*.[27] developed a strategy based on the insertion of an antimicrobial peptide (defensin) into polyelectrolyte multilayer films built by the alternate deposition of polyanions and polycations. Examination of *Escherichia coli* D22 growth at the surface of defensin-functionalized films revealed 98% inhibition when positively charged poly (l-lysine) was the outermost layer of the film, owing to the interaction of the bacteria with the positively charged ends of the film.

Diamond nanoparticles or nanodiamonds (ND) have recently gained significant attention for local drug release

in the form of coatings. Recent studies of cell viability, such as the production of luminescent adenosine 5' triphosphate, have shown that ND are not toxic to a variety of cell types.[28] Huang *et al*.[29] have examined the cytotoxicity and anti-inflammatory response of dexamethasone-loaded ND nanofilms *in vivo* and found that the nanofilms are non-apoptotic and non-cytotoxic, with efficient drug-eluting characteristics, thus being of great interest as novel implant coatings.

Rauschmann *et al*.[30] have developed a bioresorbable composite of calcium sulfate and nanoparticulate HA for the local delivery of antibiotics to tackle bone infection. No *in vitro* cytotoxicity was noticed, and the composite material exhibited better biocompatibility than pure calcium phosphate. Owing to its high porosity, it revealed initial high antibiotic release followed by a subsequent decline, ensuring concentrations well above the respective minimal inhibition concentrations of gentamicin- and vancomyin-susceptible bacteria within the first 3–4 days.

Adams *et al*.[31] have examined the release of vancomycin from thin sol-gel films deposited on titanium alloy surfaces implanted in an animal model. The coatings exhibited a significant inhibiting effect against the adhesion and biofilm formation of *Staphylococcus aureus*.

Active coatings for the delivery of therapeutic molecules using the advantages of nanotechnology have a bright future. Implant-related microbial infection is a serious threat after orthopedic surgery. The literature review has revealed that an increasing volume of research is focusing on developing antimicrobial agents with high efficiency and controlled-release ability. This method is very efficient because it reduces systemic toxicity and the side-effects of parenteral antibiotics, while also yielding higher drug concentrations in the relevant tissues.

THE BONE HEALING PROCESS AND NANOTECHNOLOGY

Surfaces that contain micro- and nanoscale features in a well-controlled, "engineered" manner significantly affect cellular and subcellular function. The optimal micro/nanostructure for desired osseointegration is still a subject of debate.

A number of novel approaches have been developed for the fabrication of biomaterial-based three-dimensional scaffolds.[32] The electrospinning method has been actively explored recently and offers ultrafine polymer fibers, a high specific surface area, and the possibility of various modifications, including mineralization of scaffolding with HA, which has been shown to reduce cellular cytotoxicity *in vitro*.[33,34] The features of nanofiber mats are morphologically similar to those of the extracellular matrix of natural tissue.

The development of nanofibers has enhanced the scope of fabricating scaffolds to mimic the architecture of natural human tissues at nanoscale. The high porosity of nanofiber scaffolds provides more structural space for cell accommodation and facilitates the efficient exchange of nutrients and metabolic waste between a scaffold and its environment.

A crucial point for the success of a scaffold, especially in bone tissue engineering, is a combination of the structural/mechanical properties of a polymer structure and biological activity, both of which play a critical role in cell seeding, proliferation, and new tissue formation. The interest in temporary substitutes is that they provide mechanical support until the tissue has regenerated and remodeled itself naturally.

Kikuchi *et al*.[35] fabricated an artificial bone material having a bone-like nanostructure and chemical composition. Composed of HA and collagen, the bone material was synthesized under biomimetic conditions through self-organization mechanisms between HA and collagen. The nanofibrous architecture improved the features of protein adsorption, including serum fibronectin and vitronectin, which may mediate cell interactions with scaffolds.[36]

Recombinant human bone morphogenetic protein (rhBMP) is used to induce ectopic bone formation in skeletal and nonskeletal sites.[37] Many other carriers have already been reported: β-TCP, biphasic calcium phosphate, ceramics, insoluble bone matrix, collagen, PLA-polyglycolic acid copolymer, tantalum, and titanium.[38-42] Most carriers loaded with BMP-2 show an early burst of BMP-2 release with a reduction in retained BMP-2 to less than 10% within the first 5 days.

Previous studies, using the rabbit model of DO, have shown that the optimal rate of lengthening is 0.7 mm/day, twice-daily lengthening;[43] when lengthened faster (>1.3 mm/day) the quality of the regenerated bone is poor. Al Ruhaimi[44] suggested that shortening the duration of osteodistraction by increasing the distraction rate is unsuccessful and results in nonunion. Increasing the distraction rate together with the local application of drugs to the distraction site is an evolving area.[45] Local application of osteogenic mediators such as BMPs into the distraction site is useful;[45] however, targeting and transcutaneous injections are current problems after initiation of the distraction.

Wang *et al*.[46] used a rabbit model of a 1 cm tibial bone defect to study biomaterials in DO, to determine whether this could reduce the treatment time and enhance the quality of bone formation. According to their results, the combination of biomaterials with a DO technique could be a new and cost-effective means to reduce treatment time and enhance bone consolidation in the management of larger bone defects.

BMP-2 and BMP-7 have also been reported to promote bone consolidation during DO.[47] Therefore, exogenous administration of BMP may enhance DO both temporally and spatially and enable rapid distraction, thereby shortening the time to repair the bone defect. Although various biomaterials have been used as injectable delivery systems in DO models, little has been reported on the use of nanobiomaterials as carrier materials for the sustained release of growth factors in bone regeneration.

The most widely explored osteogenic factors are the members of the transforming BMP-2 family, which have all been shown to augment the bone-forming capacity of osteoblastic cell populations when delivered at the appropriate times in the wound-healing cascade.[48] Unfortunately, these factors have been shown to be a challenge to formulate and deliver, owing to their complex tertiary structures, short biological half-lives, and possible systemic toxicity.

Efficient delivery of the osteogenic molecules *in vivo* can be achieved by incorporating them into a carrier, which can be implanted directly into the defect site. This method results in localized drug delivery and reduces possible toxic systemic effects. Synthetic polymers are attractive for this application as they can be fabricated to exact specifications, allowing for the fine-tuning of the physical properties that influence drug release, as well as their rate of degradation. For controlled release, osteogenic factors can be incorporated directly into the polymer component of poly-hydroxy acid matrices through a number of techniques,[49] and their final release can be modulated by parameters such as pore size and protein loading of the matrix.[50]

Haidar *et al*.[50] studied the effect of an early single injection of biodegradable core-shell nanoparticles loaded with various low doses of recombinant human BMP-7 (rhBMP-7/rhOP-1) on new bone regeneration and consolidation in a rabbit model of tibial DO. According to their results, the use of nanoparticles maintains the bioactivity of the encapsulant, minimizes the therapeutic doses of rhOP-1, and accelerates DO via its localized release-controlled osteogenic, and naturally biocompatible polymeric properties.

Elimination of the external frame distraction device can itself improve the results of osteodistraction [Figures 2-5]. Konaş *et al*.[51] developed an internal distractor that allows local intermittent BMP-2-containing chitosan hydrogel infusion to the distraction site during distraction. According to their results, distraction with an osteoinductive drug-releasing distractor can increase ossification in DO. Moreover, chitosan is biocompatible, and its particles act as bony extracellular matrix elements and integrate with the tissue. In the authors' own experience, chitosan–alginate scaffolds were superior to

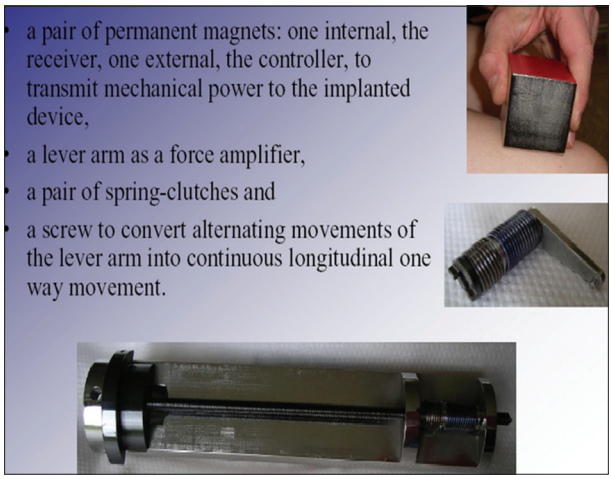

Figure 2: The Phenix M-Bone device consists of a pair of permanent magnets (one external, the controller, and one internal, the receiver, which transmit mechanical power to the implanted device) upper figure: the controller magnet; middle figure: a lever arm as a force amplifier; lower figure: a screw to convert alternating movements of the lever arm into continuous longitudinal one-way movements

Figure 3: Photograph of the Phenix-M bone transport rod (above). Close-up of bone transport mechanism, with threaded core used to transfix the bone transport segment (below)

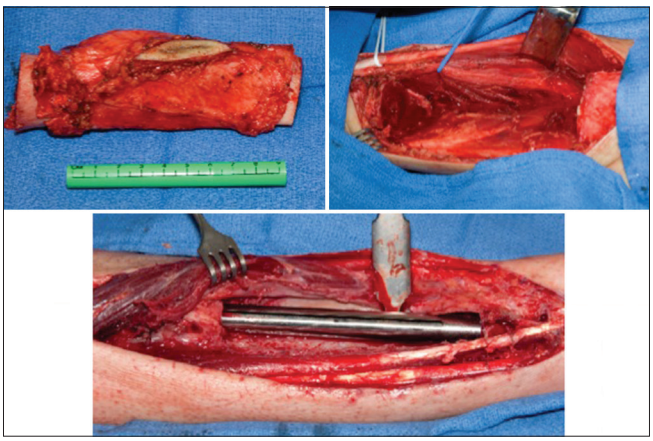

Figure 4: A 15-year-old boy presented with osteosarcoma of the distal tibia. Surgical resection specimen (above, left). Surgical defect after resection (above, right). Bone transport device, after implantation (below). The bone transport segment can be identified in the left of the figure

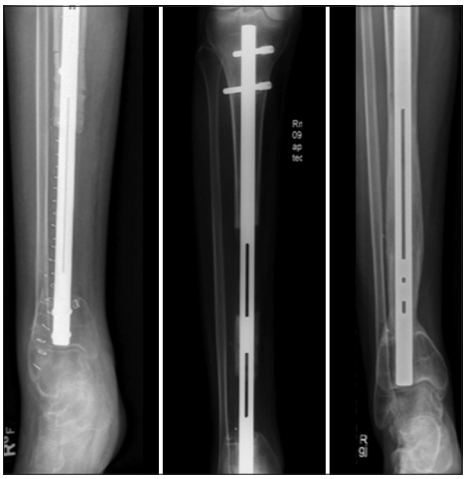

Figure 5: A 15-year-old boy presented with osteosarcoma of the distal tibia. Radiographs demonstrate initial resection and the placing of the bone transport device (left), midpoint of transport (middle), and after bony consolidation (right)

no treatment for the healing of critical calvarial defects in a rat model. Adding BMP-2 to these scaffolds further improved bone regeneration, in both a rat and a clinical model (data not shown).

OSTEODISTRACTION AND NANOTECHNOLOGY DRUG-RELEASE SYSTEMS

One area of focus in nanotechnology is the delivery of osteogenic factors in an attempt to modulate the formation of bone. Research has focused on the use of biodegradable materials as scaffolds for cellular ingrowth, cell transplantation, or the delivery of therapeutic molecules as methods for regenerating osseous tissue.

Since Urist *et al*.[52] demonstrated that glycoproteins extracted from demineralized rabbit could induce bone formation in ectopic sites in tibia matrix from rabbits and mice, tremendous advances have been made in the development of recombinant growth factors, proteins, and peptides for the regeneration of bone tissue. These factors have been shown to induce bone formation within a defect without the use of a carrier, but their relatively short half-lives necessitate the use of significant amounts of protein.

To increase the *in vivo* efficacy as well as reduce the quantities needed, the development of carriers capable of controlled, sustained delivery of proteins and peptides is desirable. In order to minimize surgical intervention for the implantation of controlled-release scaffolds, the development of materials that can be injected and cross-linked *in situ* would be desirable.

DO is characterized by the formation of new bone between two osteotomized bone segments, which are separated by gradual traction. The consolidation period represents the time needed for a complete bridging of the distraction gap by bone and a further maturation of this bone. In general, the bone consolidation phase takes approximately 6–12 weeks in the craniomaxillofacial region and 3–6 months in long bones.[53]

Various methods have been tested to promote bone formation in the distraction gap, e.g. electrical and mechanical stimulation,[54] transplantation of osteoblast-like cells,[55] administration of growth factors such as bone morphogenetic proteins, or fibroblast growth factor 2.[56] Another procedure to accelerate bone regeneration involves the application of osteogenic proteins in the distraction gap using nanotechnology-fabricated drug-release systems.[57]

Much research effort has been committed to the investigation of ordered mesoporous silica materials in the biomedical field for two main reasons: their ability to regenerate bone tissue[58] and their drug delivery possibilities.[59] When these silica-based ordered mesoporous materials are exposed to the physiological environment, a series of chemical reactions take place in the material–living tissue interface, which lead to incorporation of the material into the living tissue.

Available pore volume and surface play a key role in the protein-loading capacity of silica-based ordered mesoporous materials. If large biomolecules, such as certain proteins, are targeted to be adsorbed in ordered mesoporous materials, these matrices should present several characteristics: (1) a large size pore size to allow diffusion; (2) a large surface area to allow a large retention percentage; (3) and a high pore volume to offer available space into the mesopores to be filled by the protein.

Several natural and synthetic polymers have been explored for use as delivery vehicles for bone-inductive molecules. The poly (α-hydroxy acid) family of polymers, including PLA, poly (lactic-co-glycolic acid) (PLGA), and their copolymers, have been the focus of much of this research as they are biocompatible, undergo controllable hydrolytic degradation into natural metabolites, and can be processed into many forms.[60] In addition, microparticles of PLA and PLGA have been used to deliver many factors, including transforming growth factor 1 and BMP-2, into osseous defects.[61] Finally, porous PLGA scaffolds have also been developed to provide support for cellular migration. Some of this work focused on the adsorption of therapeutic agents onto prefabricated scaffolds, but control of the factor's release kinetics was found to be limited with this technique.

FUTURE CHALLENGES

Bone growth and remodeling involves a plethora of growth factors, recruitment of mesenchymal stem cells, and the action of three different mature cell types (osteoblasts,

osteocytes and osteoclasts) as well other factors that are yet to be revealed. To move to the next developmental phase of nanobiomaterials science, it is critical to understand the cellular and molecular basis governing the interaction between nanostructure and cells.

It has become more apparent that nanomaterials hold much promise for bone regeneration applications, and this warrants further exploration. The endpoint is limited only by the extent of our imaginations.

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Original Article | Plastic and Aesthetic Research

Auricular seroma: a new concept in management

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ABSTRACT

Aim: Auricular seroma is a cystic swelling with a collection of serous fluid between the perichondrium and cartilage. The successful treatment of auricular seromas remains a challenge because this disease has a high propensity for recurrence. **Methods:** A total of 20 patients with auricular seromas were treated by remodeling a corrugated rubber drain. **Results:** All patients tolerated the procedure well. No patient had any collection of fluid after the removal of the splint. No patient experienced pain, fever, or edema after treatment. The seroma disappeared without disfigurement. There were no recurrences on further follow-up. **Conclusion:** Aspiration and splint application by remodeling a corrugated rubber drain provides very simple, minimally invasive, and effective management of seromas. It is a cost-effective treatment that prevents patient distress from fluid recollection and social embarrassment.

Key words:

Auricular seroma, remodeling, corrugated rubber drain

INTRODUCTION

Auricular seroma is a cystic swelling with a collection of serous fluid between the perichondrium and cartilage. It is usually in the upper part of the auricle. Seromas can develop spontaneously or after surgery or trauma (primarily blunt trauma) to the ear. An amber or straw-colored fluid is sometimes aspirated. Depending on the nature of the swelling and symptoms, auricular seromas can be distinguished from other lesions of the pinna.[1] Successful treatment of auricular seromas is challenging because of their high propensity for recurrence. We propose a very simple, effective management of seromas by remodeling a corrugated rubber drain.

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METHODS

Between May 2010 and August 2013, we treated 20 cases of auricular seromas at the Mahatma Gandhi Institute of Medical Sciences (Sevagram, India). No patient had any history of insect bites or any other medical illness. One patient had a definite history of blunt trauma to the ear; it was a nontender fluctuant swelling.

All seromas were drained by aspiration using all aseptic precautions [Figure 1]. The corrugated rubber drain was cut and shaped in accordance with the site of the seroma. Using 3-0 silk, the remodeled piece of corrugated rubber drain was fixed through the cartilage using a single suture [Figure 2]. Antibiotic ointment was topically applied, but no dressing was applied. The patient was administered with oral antibiotics and oral anti-inflammatory drugs. After 3 days, the patients were reviewed and the splint was removed. For the next 7 days, the patients were followed-up for any recurrence.

RESULTS

Of the 20 patients, 18 patients were males and 2 patients were females. Thirteen patients had swelling in the right

ear and seven patients had swelling in the left ear. The mean age of the patients at presentation was 23.9 years. The most common complaint was external deformity, followed by pain (2 patients). Table 1 lists the sites of the seromas.

Of the 20 patients, 2 patients had already been treated with aspiration and bandage, but they presented with recollection. The exact cause of the seromas was unknown, except for 1 patient in whom there was a definite history of blunt trauma to the ear while playing.

All patients tolerated the procedure well. They were followed-up every 7 days up to 21 days. After 3 days, the splint was removed. None of the patients had any collection of fluid or experienced any pain, fever, or edema. The seroma disappeared without disfigurement. Further follow-up showed no recurrences. The patients were reviewed subjectively for the cosmetic impact of the treatment. We found that they were satisfied with the treatment since there were no dressings, which prevented social embarrassment. It was cosmetically acceptable [Figure 3].

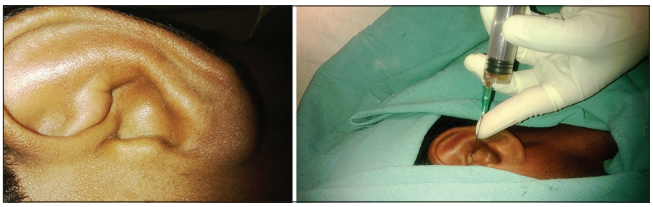

Figure 1: Aspiration and drainage of the seroma

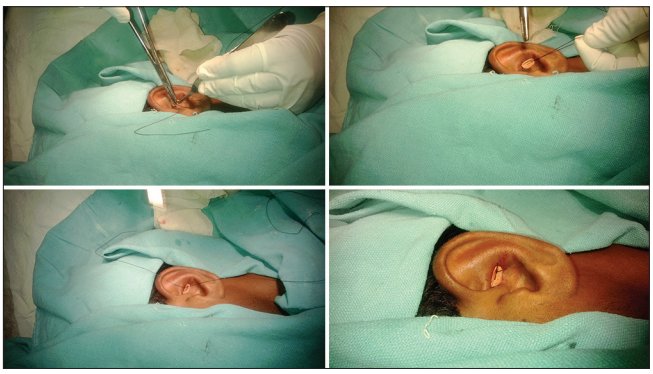

Figure 2: Placement of the corrugated rubber drain

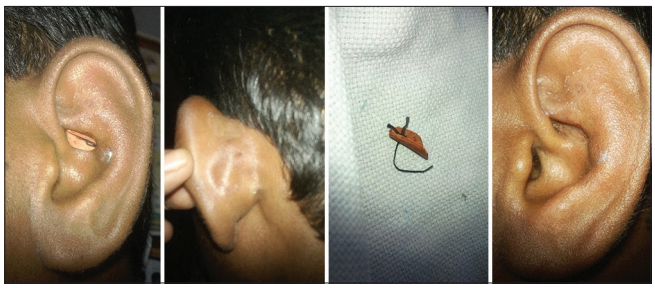

Figure 3: The pinna on follow-up

DISCUSSION

The successful treatment of auricular seromas remains a challenge because this disease has a high propensity for recurrence. Seromas are usually drained by aspiration and a compression bandage is applied. It is difficult to maintain molded pressure bandages on both sides of the pinna in place long enough to effectively prevent recollection. Many patients have a recollection and the bandage causes social embarrassment. Ghanem *et al*.[2] found recurrence of seromas after aspiration and bandage. Various other treatment modalities have been practiced such as applying pressure splints using coat buttons, achieving compression using cotton wool bolsters, and using silicone rubber splints. The limitations of these modalities include their availability and pliability. O'Donnell and Eliezri[3] suggest excising a disc of cartilage and perichondrium to cure recurrent seromas. Placement of a continuous portable suction drain that remains at the incision site is a treatment option that has been advocated.[4] Mattress or quilting sutures are applied in anatomical grooves to achieve compression more evenly after primary aspiration.[5] The intralesional injection of triamcinolone as a treatment option for auricular seromas has also proven useful.[6] A review of the literature suggests that 19-gauze stainless steel wire and chemically cured resin have been used to fabricate a pressure appliance to prevent recurrence.[7]

We have proposed a very simple and effective management of seromas using aspiration and applying a splint formed by remodeling a corrugated rubber drain. A corrugated rubber drain has many advantages. A corrugated rubber drain is firm and easily available. It can be remodeled so that it fits into the small depressions of the pinna. It is pliable and can be shaped in accordance with the site of the seroma. This drain is fixed with a single suture, which splints adequately. No dressings are required and no complications have been noticed. This method is a minimally invasive procedure that is simple and effective. It also prevents patient distress from recollection, treatment, and social embarrassment. It is also cost-effective. This treatment can be administered to large seromas by using a single suture. A corrugated rubber drain is a treatment option in a rural setting where the availability of resources limits the treatment options. Most patients prefer not to make repeated visits to an outpatient department. This type

Table 1: Site distribution of the seromas

Site	Number
Between the antihelix and cymba concha	11
Concha	5
Between the helix and antihelix	3
Multiple	1

of treatment is simple and effective. To prevent auricular cartilage infections, it has been suggested that seromas should not be aspirated in an outpatient department. However, our simple procedure can be performed with no complications in an out-patient department, provided it is performed under aseptic conditions and precautions are maintained.

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Original Article Plastic and Aesthetic Research

A modified bilobed flap design for nasal tip defects

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ABSTRAC

Aim: The correction of nasal tip defects presents many challenges. Zitelli's bilobed flap has been widely used for such repairing defects, but may be complicated by interrupted scars on the nasal dorsum. Our study evaluates the design principles, results, and advantages of a modified bilobed flap for repairing nasal tip defects. **Methods:** The primary lobe was located between the defect and the cheek, and the second lobe was located in the cheek. The width of the primary lobe was equal to that of the primary defect. The length of the primary lobe was 10% longer than the distance of the distal defect edge to the pivot point of the flap. The length of the second lobe was 30% longer than the distance of the distal defect edge to the pivot point of the flap. The width of the second lobe was 90-100% of that of the primary lobe. The ability to close the defect under minimal tension, the cosmetic appearance, and any complications were evaluated. **Results:** This technique was performed in 34 cases; defect size ranged from 0.8 cm × 0.9 cm to 1.2 cm × 1.8 cm. All defects were closed under minimal wound tension, all scars were inconspicuous, no obvious complications occurred, and the aesthetic outcomes were considered favorable. **Conclusion:** The modified bilobed flap can provide satisfying outcomes with lower morbidity and inconspicuous scarring. It is simple and suitable for repairing small- to medium-sized defects in the nasal tip.

Key words:

Bilobed flap, nasal reconstruction, nasal tip defect

INTRODUCTION

Resection of benign lesions is a common cause of nasal defects in young patients. The conventional bilobed flap (Zitelli's design) used for reconstruction of defects of the lower third of the nose traditionally utilizes skin from the mid dorsum and the sidewall of the nose.[1] However, the conspicuous scarring and loss of conformity in the cosmetic subunits of the nose might be unacceptable to young patients, particularly in individuals with darker skin tones. Herein, we describe a modified bilobed flap that utilizes skin from the nose and cheek, and review the advantages of this technique's use in nasal tip reconstruction.

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METHODS

Our study comprised 34 patients who had defects of the nasal tip. We conducted a retrospective review of all patients who had undergone defect reconstruction with the modified bilobed flap by a single surgeon at the Department of Plastic Surgery, Affiliated Hospital of Medical College, Qingdao University, from July 2008 to July 2013. The review board of our Affiliated Hospital approved this study and all patients involved in this article agreed to have their pictures published and signed the consent form. Outcome measures included the ability to close the defect with minimal tension, cosmetic appearance, any complications, and any need for further repair.

Flap design

Based on the designs of Zitelli and Baker,[1] Xue *et al*.[2] planned a superiorly based bilobed flap obtained from the nasolabial region. First, two arcs were marked to define the boundaries of the flap and its proper angulations. The radius and diameter of the nasal defect were measured with calipers. A pivot point was placed in the nasal sidewall and was located one radius from the free edge of the defect. The center line of the defect was marked. The radius of the center arc was equal to the diameter of the nasal defect. The radius of the distal arc was equal to the distance between the distal edge of the defect and the pivot point. Based on the pivot point, the two arcs were marked with a standard geometry compass.

Second, the two lobes of the flap were configured. The primary lobe was located between the defect and the cheek and was slightly larger than the primary defect. The width of the primary lobe was equal to that of the primary defect. The length of the primary lobe was 10% longer than the distance of the distal defect edge to the pivot point of the flap. The second lobe was located in the cheek and was slightly smaller than the primary lobe. The length of the second lobe was 30% longer than the distance of the distal defect edge to the pivot point of the flap. The width of the second lobe was 90-100% of that of the primary lobe. The two flaps rotated a total of 90°-100°. Based on the two arcs, the two lobes of the flap were marked.

Surgical technique

The lesions were removed below the nasal superficial musculoaponeurotic system. The specimens were sent for histopathological examination to ensure clearance of the margins.

Incisions were made along the previously described markings. The primary lobe was undermined above the perichondrium of the nasal cartilage to promote adequate tissue perfusion of the flap. Once this layer was reached, the flap was easily elevated. The second lobe was elevated in the plane of the superficial fascia, and the pedicle portion was separated with blunt dissection to preserve the blood supply to the deep tissue. It is important that the thickness of the primary lobe is equal to that of the second lobe.

The two lobes were transposed to their desired locations. The primary and secondary defects were repaired by rotation of the two lobes. Hemostasis was performed. A 5-0 absorbable monofilament suture was used to close the deep layer, which allowed the skin layer to be closed under minimal tension. The redundant distal portions of the lobes were removed with regard to the state of the closure tension. The tertiary wound was closed directly in a side-to-side manner. A 6-0 nylon suture was used to close the skin layer. Rubber drainage was applied to prevent subcutaneous hemorrhage and was removed1 day later. The stitches were removed from the skin 5-7 days later [Figures 1 and 2].

RESULTS

Reconstruction procedures using the modified bilobed flaps were performed in 34 cases with tissue defects of the nasal tip. The study sample included 5 male and 29 female patients, with an average age of 27.14 ± 7.79 years. Twenty patients presented with nevus, 8 with granuloma, and 6 with fibroma. The size of the defects ranged from 0.8 cm × 0.9 cm to 1.2 cm × 1.8 cm. All defects were closed successfully without difficulty using this technique. The defects were repaired under minimal closure tension as a single-stage procedure. The patients were then followed for 3 months and 18 months. No severe complications were found to have occurred after any of the operations. There were no dissymmetry deformities or retraction deformities of the nasal ala in any of the cases.

We did not find any patient with nasal valve collapse,

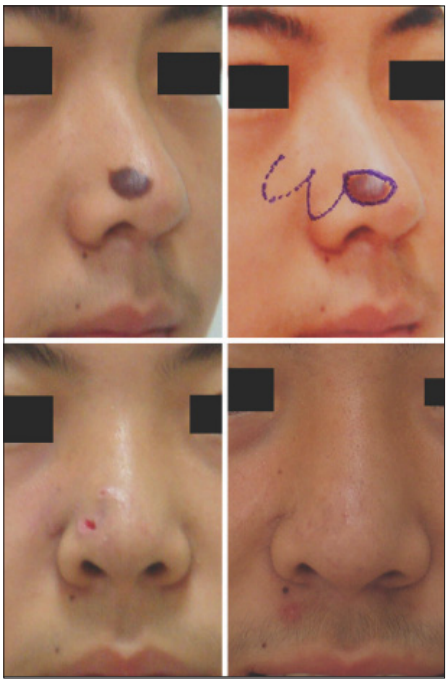

Figure 1: Modified bilobed flap reconstruction of a nasal tip defect in a 19-year-old man: before the operation (upper left); the bilobed flap design (upper right); incision infection 1 week after the operation (lower left); at the 13 months follow-up (lower right)

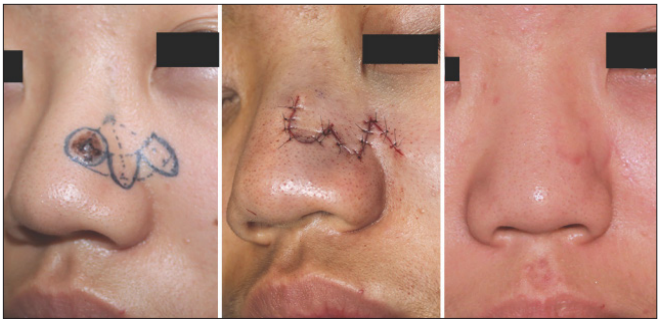

Figure 2: Modified bilobed flap reconstruction of nasal tip defect in a 20-year-old woman: the bilobed flap design (left); immediately after the operation (center); at the 1-year follow-up (right)

and no patients complained of ventilation barriers. Three patients presented with an obscure alar crease and did not require further repair. There was incision infection in one patient 3 days after the operation owing to the exudation of a sebaceous gland. The wound healed well 10 days later [Figure 1]. There was mild trapdoor deformity in one patient 1 month after the operation; however, the deformity disappeared after two steroid injections. All of the flaps survived completely with ideal color and texture matching. All of the scars healed well and were inconspicuous. All 34 patients were satisfied with the results.

DISCUSSION

Before the techniques for nasal reconstruction being discussed, some general comments regarding the nature of nasal skin are warranted. The nasal skin is typically divided into three zones.[3] Zone I, the upper half of the nose, is the thin, loose, compliant, and non-sebaceous skin of the dorsum and sidewalls. In contrast, Zone II includes the thick, taut, non-compliant, and sebaceous skin of the nasal supratip, tip, and alae. It readily reforms to its previous shape, and thus it is difficult to contour and reconstruct. Due the thickness and stiffness of the sebaceous skin, even small defects cannot be closed in a linear manner, as the surgical tension might cause obvious nasal deformation. Zone III encompasses the areas of the triangles, columella, and nasal infratip lobule, where the skin again becomes thin, loose, and nonsebaceous. Consideration of such categories is critical in the nasal reconstruction of small- to medium-sized defects as the type, color, and texture of the skin surrounding the nasal defect play a critical role in ultimately determining the optimal method for reconstruction.

In conventional algorithms for nasal reconstruction, classic options for the repair of defects in Zone II include the bilobed flap, nasolabial flap, dorsal nasal flap, forehead flap, and full-thickness skin graft. These reconstruction options are time-tested and reliable, although none is without disadvantages.

The nasolabial flap is a good reconstructive option for lateral nasal defects such as defects in the sidewall and alae. The transposition design can be performed as a single-stage procedure, and can provide excellent color and texture matching. However, for central defects in the nasal supratip and tip, an interpolated design should be performed. The pedicle has to be divided 3 weeks later, and the flap has to be reshaped 2-3 months later.

The bilobed flap is also known as the "workhorse flap" for the reconstruction of defects of the lower third of the nose.[1] It was first described by the Dutch surgeon Esser in 1918.[4] Esser's initial flap design described two equally sized transposition flaps transferred to cover defects of the distal nasal tip. The primary lobe transposes 90° to cover the primary tissue defect. The second lobe also transposes 90°, to cover the surgical defect produced by the displacement of the primary lobe. The primary lobe is located on the nasal dorsum adjacent to the primary defect. The second lobe is located on the more proximal nasal dorsum. Due to the large transposition arc, the flap rotation has to be accomplished with significant surgical effort and high wound-closure tension. It is inevitable that numerous significant standing deformities are produced after this operation, including "dog ear", alar displacement, and alar asymmetry. A second repair procedure is necessary for some patients.

In 1989, Zitelli[5] modified the bilobed flap to include a total transposition arc of 90°-110° and an approximately 45° pivotal arc between each lobe. Zitelli's bilobed flap uses skin from the mid dorsum and the sidewall. Smaller angles of flap transposition produce less severe "dog ear" deformities along the border of the flap. Furthermore, smaller angles of flap transposition allow the surgeon to transfer the flap more easily. The flap can be rotated with lower wound tension, which produces less alar displacement. This design clearly decreases the likelihood of complications. It is especially suitable for the reconstruction of defects of the lower third of the nose.

However, vertical scarring on the mid dorsum and interrupted scarring on the tip occurs after using Zitelli's bilobed flap. The wound might heal well and be inconspicuous in older patients or patients with compliant nasal skin. However, the scar can be conspicuous in younger patients, particularly in individuals with darker skin tones. Most of the patients in our study could not accept the predicted outcomes of using Zitelli's bilobed flap. A modified bilobed flap utilizing skin from the lower dorsum and cheek was therefore recommended to these patients, and they agreed with the plan.

This technique combines the advantages of the nasolabial flap and Zitelli's bilobed flap, and thus offers more advantages. First, it is a single-stage procedure and is less technically complex. The two flaps (the primary and secondary lobes) are transposed with a total arc no more than 90°-100°. The flaps can be rotated easily due to the smaller angles. Although the skin beside the defect is thick and noncompliant, the primary lobe can be transposed to the correct location with small closure tension. The surgeon can repair the second defect easily with a nasolabial flap (the second lobe).

Second, this technique has lower morbidity. Any degree of alar asymmetry can be quite noticeable since the nose is the most prominent part of the center of the face. Accordingly, one of the most important principles of nasal reconstruction is that asymmetry deformity should be avoided. As described above, the skin on the nasal dorsum and sidewall is thin, loose, compliant, and

nonsebaceous, and the skin on the distal nose is thick, taut, noncomplaint, and sebaceous. Improper wound tension could not only lead to hypertrophic scarring, but also alar displacement. Therefore, it is not recommended that defects of distal nose be treated primarily with adjacent undermining when the defect is small. The surgeon must be acutely aware of the influence of the size of the lobes when using the bilobed flap, as both the width and the length of the lobes can affect the final incomes of reconstruction.

Moy *et al*.[6] suggested that the diameter of the primary lobe should be 90-100% of that of the primary defect and that the diameter of the second lobe should be 80-85% of that of the primary lobe. In our study, the diameter of the primary lobe was equal to that of the primary defect, which can ensure lower closure tension for repair of the primary defect. Alar displacement may result if the diameter of the primary lobe is even slightly smaller. In contrast to techniques described in previous reports, in our study, the second lobe was taken from the cheek and had a diameter of 90-100% of that of the primary lobe. In fact, the second lobe is a nasolabial flap. The size of the second lobe is chosen on a case-by-case basis. The cheek has more abundant and lax skin than the nasal sidewall; therefore, the cheek can provide a larger flap than can the nasal sidewall. Tertiary defects on the cheek can also be more easily closed in a linear manner.

In 1987, Dzubow discussed the effect of pivotal restraint on flap rotation and transposition.[7] He stated that the flap was restrained by the tissue located around the pivotal point (the base of the flap), when any flap of tissue was either rotated or transposed around a pivotal point. Thus, the bilobed flap is shortened after it is transposed to a new site. The greater degree of flap movement around the pivotal point, the more the flap shortens.

The main reported disadvantage of Zitelli's bilobed flap is alar retraction resulted from distal flap tension. Cho and Kim stated that this distal tissue retraction and distortion is a result of pivotal restraint.[8] The rotation of the bilobed flap causes the flap to shorten, thereby creating a gap that must be spanned by the distal edge of the defect. Their study in human cadavers demonstrated that lengthening the primary lobe in Zitelli's design could compensate for this expected gap and allow for less tension at the distal wound edge. Such a closure would prevent distal retraction and reduce anatomic distal distortion.

Given this concept of pivotal restraint, the loss of flap length must be accounted for during the bilobed flap design. Some researchers proposed to lengthen the flap.[2,7-9] In our study, the length of the primary lobe was slightly longer than the distance of the distal defect edge to the pivot point of the flap, and the length of the second lobe was slightly longer than that of the primary lobe. The redundant distal portions of the flaps are removed as needed after the two lobes are transposed into their desired locations. Neither undersized nor oversized flaps are recommended as the former might lead to alar elevation, while the latter can push the alar rim inferiorly and result in trapdoor deformation. The ideally sized lobe of the bilobed flap should neatly cover the defect under minimal closure tension.

Third, the scars are less obvious. As already noted, the nose is the most prominent part of the face; therefore, interrupted scars on their nose might not be acceptable to many younger patients in Asia.[10] Mature scars are more visible in individuals with darker skin tones than in those with lighter skin tones. Surgeons should therefore aim to decrease the number of scars and control hypertrophic scars on the nose. In contrast to previous designs, there were no noticeable scars on the mid-dorsum in patients in our study. Most incisions were placed in the natural lines such as the alar crease and the nasolabial groove. As described above, all defects were closed under minimal tension; therefore, less hypertrophic scarring occurred.

Lastly, this technique can provide better texture matching than is available through the conventional bilobed flap. The skin of the distal nose is thick and dense with sebaceous glands, similar to the skin of the nasolabial region. In contrast, the skin of the nasal dorsum and sidewall is thin and non-sebaceous. Particular attention should be paid to ensuring that the exudation of the sebaceous glands is removed in time to prevent incision infection.

The disadvantage of our design is that the primary lobe might destroy the anatomy of the alar crease and result in an obscure alar crease-a complication that can be avoided through careful suturing. In addition, the technique is only suitable for small- to medium-sized defect repair, due to the limited size of the primary lobe.

In conclusion, the modified bilobed flap can provide satisfying outcomes with lower morbidity and inconspicuous scarring. It is simple and suitable for repairing small- to medium-sized defects in the particular area of nasal tip.

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Conficts of interest
None declared.

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Comparison between four treatment modalities for active myofascial triggers points

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ABSTRACT

Aim: The study aimed at the painful trigger points (TrPs) for the purpose of ablating muscle spasms and restoring normal muscle length to find the most effective treatment for alleviating pain and improving mouth range of motion in patients with myofascial pain dysfunction. **Methods:** We enrolled 72 patients with pain and reduced mouth opening due to temporomandibular joint dysfunction. Patients assigned to four groups and four treatment modalities used to treat myofascial TrPs pain. We used mean and standard deviation values. The Mann–Whitney *U*-test was used to compare the two groups. The Wilcoxon signed-rank test was used to study the changes by the time in mean pain scores. The Student's *t*-test was used to compare maximum mouth opening (MMO) groups. Then paired *t*-test was also used to study the changes of time in an MMO. **Results:** The results showed that pulsed electromagnetic field (PEMF) therapy is the most effective treatment modality regarding for pain relief. Both the anesthesia and PEMF groups showed a reduction in mean pain scores throughout all follow-up periods, and a statistically significant increase in mean MMO. **Conclusion:** The findings suggest that PEMF is the most effective treatment for alleviating pain and improving mouth range of motion in patients with myofascial pain.

Key words:

Low-level laser therapy, myofascial pain, pulsed electromagnetic field, temporomandibular joint dysfunction, trigger points

INTRODUCTION

Myofascial pain dysfunction syndrome (MPDS) is the most common cause of facial pain. Patients with MPDS experience pain, restricted jaw movements, and masticatory muscle tenderness.[1] Psychological factors, occlusion imbalance, and parafunctional habits have been cited as its most important underlying causes.[2]

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Myofascial pain dysfunction syndrome is a regional muscular pain syndrome characterized by the presence of hypersensitive points known as "trigger points" (TrPs) in one or more muscle and/or connective tissue. The masseter muscles and to a lesser extent temporalis muscles are frequently involved in MPDS.[3]

It has been suggested that certain nerve endings in the muscle tissue become sensitized by allergenic substances, which create a localized zone of hypersensitivity.[4-6]

Trigger points are discrete, focal, hyperirritable areas located in taut bands of skeletal muscle. The TrPs are painful upon compression and can induce referred pain, referred tenderness, motor dysfunction, and autonomic phenomena.[7]

Myofascial trigger points (MTrPs) are classified as being active or latent, according to their clinical characteristics.

An active TrPs causes pain at rest, while a latent TrPs does not cause spontaneous pain, but may restrict movement or cause muscle weakness.[8]

Thus, a typical TrPs is characterized by the presence of discrete focal tenderness within a palpable taut band of skeletal muscle, which generates both referred regional pain and a local twitch response (LTR). TrPs are associated with referred pain in MPDS, while tender points in comparison are associated with pain at the site of palpation only and occur in the insertion zones of muscles, not in the taut bands in the muscle belly.[9]

Several histopathologic mechanisms have been proposed to account for the development of TrPs and subsequent pain patterns. Many researchers concur that acute trauma or repeated microtrauma may lead to the development of a TrPs.[10]

In the head and neck regions, MPDS presents as tension headaches, tinnitus, temporomandibular joint pain, and in rare cases visual symptoms.[11]

Palpation of a hypersensitive bundle or nodule of muscle fiber of harder than normal consistency is the physical finding most often associated with a TrPs. Localization of a TrPs is based on the physician's sense of feel, assisted by patient expressions of pain and by visual and palpable observations of LTR.[7]

The diagnosis of temporomandibular joint dysfunction (TMJD) requires a skilled clinician with training and experience in recording a patient's histories, conducting thorough examinations, and identifying MTrPs. Diagnosis confirmed by the occurrence, at least of a taut band, and pain felt by the patient when pressure is applied to a tender nodule.[12]

Most treatment methods for myofascial pain are empirical and aim to identify painful TrPs for the purpose of ablating muscle spasm and restoring normal muscle length, function and strength.

Both psychological and physical treatments are necessary to overcome MPDS.[1] Conservative treatments are generally useful for alleviating pain and preventing dysfunction. Dentists use different therapies such as pharmacologic treatments, which include analgesics, muscle relaxants, antidepressants, neuroleptics, or nonsteroidal anti-inflammatory drugs.[13]

Alternative treatment modalities include acupuncture, massage, acupressure, ultrasonography, application of heat or ice, diathermy, transcutaneous electrical nerve stimulation, ethyl chloride spray, and stretching techniques.

Other methods of treatment include: dry needling; TrPs injections with local anesthetic, saline, or steroid; occlusal splints; biofeedback; and physiotherapy.[2]

Treatment modalities that have been used to inactivate of MTrPs include: interrupting the pain cycle by penetrating the MTrPs with a needle; injecting local anesthetic or saline; and applying a cooled spray to the skin, followed by muscle stretching.[11]

Low-level laser therapy (LLLT), ultrasound and electro galvanic stimulation can also be useful in managing MTrPs.[14,15]

Modern dental practice encompasses low-level lasers therapy to accelerate tissue healing, alleviate pain, reduce inflammation and physiotherapy in the orofacial region. Low-level laser application plays an important role in the treatment of most musculofacial disorders and facial pain.[16-19]

Laser light is energy that results from stimulated emission of radiation. The laser light biostimulation of structural tissue can be increased to an energy level that creates chemical reactions. It stimulates protein synthesis, phagocytic activities and aerobic energy to induce anti-inflammatory, analgesic, and tissue repair effects.[20] The laser type is determined by the wavelength of the light based on the solid state aggregation of the energized material. Many types of lasers have been used, e.g., helium: neon, gallium-aluminum-arsenide (Ga-Al-As), neodymium-doped yttrium aluminum garnet, and carbon dioxide.[21]

Gallium-aluminum-arsenide is a diode laser with a wavelength of 780 nm. Some studies have shown that Ga-Al-As lasers have positive effects,[22,23] including acceleration of wound healing and pain reduction,[24,25] although many studies have shown no positive effect.[26,27]

Laser photobiomodulation is a low-cost, noninvasive treatment that has been widely used for treating a diverse range of conditions, including muscle/joint conditions. It has been used frequently in physical therapy practice for pain relief and tissue regeneration, and has been proven as beneficial in treating TMJD. Various studies have confirmed therapeutic effects including are anti-inflammatory, analgesic and cell activity modulating actions.[28-30]

Dry needling has been found to be as effective as drug injection for the relief of pain in muscles and connective tissue. In the treatment of TrPs for persons with myofascial pain syndrome, in which an acupuncture needle is inserted into the skin and muscle directly into a MTrPs.[31]

A MTrPs consists of multiple contraction knots, which are related to the production and maintenance of the pain cycle. Accurate dry needling of a MTrPs elicits a LTR, which is an involuntary spinal cord reflex in which the muscle fibers in a taut band of skeletal muscle contraction. An LTR indicates the proper placement of the needle in a TrPs. Research has shown that dry needling

that elicits LTRs improves treatment outcomes. It has been suggested that A-delta nerve fibers are activated, as the needle pierces the skin, resulting in inhibition of muscular C-nerve fibers that transmit pain from the TrPs.[32]

Injection of a local anesthetic is one of the most effective treatment options available and is cited repeatedly as a way of achieving optimal results. The use of a local anesthetic is more comfortable for many patients and results in a longer lasting reduction in MTrP pain.[10]

Pulsed electromagnetic field (PEMF) stimulation is a form of alternative therapy that claims to treat disease by applying electromagnetic energy to the body.[33] Among the reported therapeutic methods, the use of biophysical interventions, such as PEMF therapy, has attracted the attention of clinicians in recent years, because of their noninvasive characteristics.[34,35] It was observed that PEMF may affect tissue healing through a primary effect on vascular growth therefore has a role in stimulation of the healing process.[36-38]

Although MTrPs are a widely recognized phenomenon in clinical practice, much remains to be elucidated with regarding their pathophysiology, mechanisms of pain referral, and treatment of choice. Hence, this study aimed to examine the effect of the four most common treatment modalities used to treat pain associated with MPDS through their direct effect on MTrPs.

PATIENTS AND METHODS

Patients

We enrolled 72 patients, from the outpatient clinic of the Oral and Maxillofacial Surgery Department, Faculty of Oral and Dental Medicine, Cairo University, Egypt. They were 57 females and 15 males aged 18–42 years (average 30 years), all with active MTrPs of the masseter muscle. The review board of Cario University approved this study.

General inclusion criteria were:

- Diagnosis of temporomandibular disorder
- Aged >18 years
- Musculoskeletal dysfunction
- Pain impairment
- The presence of a TrPs characterized by spontaneous pain of the right or left masseter muscle
- Restricted range of mouth opening
- No previous surgery in the temporomandibular region
- No other morbid conditions in the temporomandibular region as rheumatic diseases, or neurological diseases.

In addition, each patient had to fulfill the following criteria (according to the Helkimo index)[39]

- Slightly impairment of movement (index DiI)
- Moderate dysfunction = DiII
- Muscle pain sensitivity to pressure in four places (severe disorder)
- Pain associated with two or more movements (severe disorder)
- Sensitivity to posterior pressure (severe disorder).

Methods

The patients were divided randomly into four groups with each comprising 18 patients.

Treatments

Group I (low-level laser)

After locating of MTrP LLLT (wavelength 980 nm, power 0.2 W, total energy 12 J) was applied using a fiber probe over the TrPs in a circular movement for 50 s. In this group, each patient received LLLT 3 times per week for 4 weeks.

Group II (dry needling)

Each TrPs was marked clearly and the skin prepared and cleansed. The overlying skin was held between the thumb and index finger. It was then punctured with a dry needle. In this group, each patient received three sessions per week for 4 weeks, each session lasting 50 s.

Group III (anesthesia)

Each TrPs was injected with 0.5 ml mepivacaine 3% local anesthetic solution. In this group, the injections were given 3 times per week for 4 weeks, using a standard dental syringe and 27-gauge needle.

Group IV: (pulsed electromagnetic field)

Each TrPs was exposed to (PEMF) stimulation. In this group, each patient received three sessions per week for 4 weeks, each session lasting 50 min.

Clinical examination

The masseter muscle was located by a flat palpation technique, using one index finger. The masseter muscle was examined by means of palpation to determine:

- A palpable taut band
- A hypersensitive area within the taut band
- Pain felt by the patient when pressure was applied to the sensitive area (identifying an active TrPs)
- Repetition of a referred pain sensation upon stimulation of the area
- The occurrence of a LTR upon sharp palpation of the taut band.

Each patient pointed to the exact location of the pain and rated the pain (on a visual analog scale [VAS]) from 0 to 10 with 0 corresponding to no pain and 10 correspond to the worst pain. This information was recorded on the patient's chart. The pain was evaluated preoperatively and after 1 month, 2 months, and 3 months respectively from the start of treatment.

Assessment of painless maximum mouth opening (MMO) was performed by measuring the distance (in mm) between the edges of the upper and lower central incisors using a Vernier graduated caliper.

No other therapies were used. The patients were asked to stop taking other pain medications and receiving other therapies. Cetal (paracetmol 500 mg [micronized] tablets, Egyptian International Pharmaceutical Industries Co., Cairo, Egypt) was prescribed as a pain killer only as required.

Evaluation of four groups was performed at six stages: prior to the treatment, after 2 weeks (mid-treatment), after 4 weeks (end of treatment), and monthly thereafter for 3 months.

The data regarding the pain scores were presented as mean ± standard deviation values. For the pain scores and percentage changes in different variables, the data showed a nonparametric distribution; therefore, the Mann–Whitney *U*-test (a nonparametric alternative to the Student's *t*-test) was used to compare the two groups. The Wilcoxon signed-rank test (a nonparametric alternative to the paired *t*-test) was used to study the changes in mean pain scores over time.

The MMO data showed parametric distribution; therefore, the Student's *t*-test was used to compare the two groups. In addition, the paired *t*-test was also used to study the changes in MMO observations over time.

The significance level was set at $P \leq 0.05$. Statistical analysis was performed using IBM® SPSS® statistics version 20 (IBM Corporation, NY, USA).

RESULTS

Pain

Preoperatively: there was no statistically significant difference between pain scores in Groups I and II; although both showed statistically significantly lower mean scores. Furthermore, there was no statistically significant difference between pain scores in Groups III and IV, both showed statistically significant higher mean scores.

After 2 weeks, Group I showed a statistically significant higher mean score. There was no statistically significant difference between pain scores in Groups II and III; both showed lower mean scores. Group IV showed a statistically significantly lowest mean score.

After 3 months, Group I showed a statistically significantly highest mean score, followed by Group II and then Group III. Group IV showed a statistically significantly lowest mean score [Table 1].

For all time periods: in Groups I and II, there was nonstatistically significant decrease in mean pain scores. In Groups III and IV, there was a statistically significant lower mean pain scores [Table 2].

The percentage change was calculated as:

$$\frac{(\text{Preoperative score}) - (\text{Postoperative score})}{\text{Preoperative score}} \times 100$$

After 2 weeks and after 3 months: there was no statistically significant difference between percentage reduction in pain scores of Groups III and IV; both showed a statistically significantly highest mean percentage reduction in pain scores. There was no statistically significant difference between percentage reduction in pain scores of Groups I and II; both showed a statistically significantly lowest mean percentage reduction in pain scores [Table 3].

For all time periods: there was no statistically significant difference between pain scores in Groups I and II; both showed statistically significant higher mean scores. There was no statistically significant difference between pain scores in Groups III and IV; both showed statistically significant lowest mean scores [Table 4].

In Group I, there was nonstatistically significant reduction in mean pain scores for all time periods.

In Group II, there was nonsignificant reduction in mean pain scores after 2 weeks, and a statistically significant reduction in mean pain scores after 3 months.

In Groups III and IV, there was a statistically significant reduction in mean pain scores for all time periods [Table 5].

The percentage change was calculated as before.

After 2 weeks and after 3 months: there was no statistically significant difference between percentage reduction in

Table 1: The mean, SD values and results of Kruskal–Wallis test for comparison between pain scores (at rest) in the four groups

Time period	Group I		Group II		Group III		Group IV		*P* value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Preoperative	4.7[b]	3.3	3.7[b]	2.7	6.6[a]	2.5	6.4[a]	2.7	0.008*
2 weeks	4.4[a]	1.7	3.4[b]	3	2.8[b]	2.8	1.8[c]	2	0.034*
3 months	4.1[a]	2.9	2.9[b]	3.1	1.8[c]	2.2	1[c]	1.7	0.008*

*Significant at $P \leq 0.05$, different letters are statistically significantly different according to Mann–Whitney U-test. SD: Standard deviation

Table 2: The mean differences, SD values and results of Wilcoxon signed-rank test for the changes by time in mean pain scores (at rest) of each group

Group	Time period	Mean difference	SD	*P* value
I	Preoperative to 2 weeks	−0.3	3.4	0.574
	Preoperative to 3 months	−0.6	3.9	0.607
II	Preoperative to 2 weeks	−0.3	2.4	0.623
	Preoperative to 3 months	−0.9	3.9	0.327
III	Preoperative to 2 weeks	−3.8	2.4	0.003*
	Preoperative to 3 months	−4.8	2.4	0.003*
IV	Preoperative to 2 weeks	−4.6	2.9	0.001*
	Preoperative to 3 months	−5.4	3.2	0.001*

*Significant at $P \leq 0.05$. SD: Standard deviation

Table 3: The mean percentage, SD values and results of Kruskal–Wallis test for comparison between percentage decrease in pain scores (at rest) in the four groups

Time period	Group I		Group II		Group III		Group IV		*P* value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Preoperative to 2 weeks	−8.2[b]	13.5	−7.3[b]	5.9	−56.6[a]	38.8	−62.2[a]	37.8	0.001*
Preoperative to 3 months	−4.9[b]	19.7	−5.8[b]	13.4	−69.3[a]	35.5	−72.8[a]	40.2	0.004*

*Significant at $P \leq 0.05$, different letters are statistically significantly different according to Mann–Whitney *U*-test. SD: Standard deviation

Table 4: The mean, SD values and results of Kruskal–Wallis test for comparison between pain scores (PPT) in the four groups

Time period	Group I		Group II		Group III		Group IV		*P* value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Preoperative	9.1[a]	0.9	8.9[a]	1.3	7.8[b]	1.2	7.9[b]	1.2	0.008*
2 weeks	7.4[a]	2.4	8.1[a]	2	3.4[b]	2.9	3.2[b]	2.3	<0.001*
3 months	8[a]	2.3	6.4[a]	2.8	2.1[b]	2.4	1.2[b]	1.9	<0.001*

*Significant at $P \leq 0.05$, different letters are statistically significantly different according to Mann–Whitney *U*-test. SD: Standard deviation, PPT: Pain-pressure threshold

Table 5: The mean differences, SD values and results of Wilcoxon signed-rank test for the changes by time in mean pain scores (PPT) of each group

Group	Time period	Mean difference	SD	*P* value
I	Preoperative to 2 weeks	−1.6	2.6	0.055
	Preoperative to 3 months	−1.1	2.2	0.095
II	Preoperative to 2 weeks	−0.7	1.8	0.131
	Preoperative to 3 months	−2.4	2.5	0.008*
III	Preoperative to 2 weeks	−4.3	2.6	0.002*
	Preoperative to 3 months	−5.7	2.3	0.002*
IV	Preoperative to 2 weeks	−4.7	2.6	<0.001*
	Preoperative to 3 months	−6.7	2.4	<0.001*

*Significant at $P \leq 0.05$. SD: Standard deviation, PPT: Pain-pressure threshold

pain scores of Groups III and IV; both showed a statistically significantly highest mean percentage reduction in pain scores. There was no statistically significant difference between percentage reduction in pain scores of Groups I and II; both showed a statistically significant mean percentage reduction in pain scores [Table 6].

Maximum mouth opening

Preoperatively and after 2 weeks: there was no statistically significant difference in MMO between the four groups.

After 3 months: Group IV showed a statistically significant highest mean MMO. There was no statistically significant difference between Groups I-III; all showed the statistically significantly lowest mean scores [Table 7].

In Groups I and II, there was no statistically significant change in mean MMO for all the time periods.

In Groups III and IV, there was a statistically significant increase in mean MMO for all time periods [Table 8].

The percentage change was calculated before.

For all time periods: there was no statistically significant difference between the four groups [Table 9].

DISCUSSION

Temporomandibular pain of myofascial origin is a condition that is often referred to outpatient clinics of Oral and Maxillofacial Surgery Department. In this study, the highest proportion of patients with TMJD is among women aged 21–30 years. One explanation for higher prevalence is that women have lower levels of muscle strength under stress than men.

The use of noninvasive and costless methods of treatment with reduced morbidity is our aim. The standard way of treating temporomandibular myofascial pain in our hospital is to use a combination of pharmacologic and splint therapy, which produces temporary relief. However, pharmacologic treatments quickly reach the limit of therapeutic efficacy and they are also associated with side effects (e.g., gastrointestinal disorders, drug interactions, and adverse reactions), so research is currently focused on the search for alternative treatments.

Active exercise, manual therapy, postural training, and relaxation techniques, may decrease pain and increase overall vertical mouth opening. The characteristics of TMJD, however, remain highly debated as its hallmark findings of taut bands (localized areas of increased muscle tone and tenderness) and TrPs (smaller areas of increased tenderness within the bands that produce referred pain on pressure) depend on the clinician's skills at identification.

The identification of taut bands and TrPs is important not only for diagnosis, but also for potential treatment. We believe that pain from TMJD is better expressed by the participant themself, so patients are required to self-evaluate their pain as: nonexistent, mild, moderate, severe and very severe, using a VAS.

Trigger points also appear to have a positive effect on pain, releasing a TrPs through ischemic spots reduction, which results in reduced pain. Active MTrPs act as major peripheral pain generators for regional and generalized musculoskeletal pain conditions.

Table 6: The mean percentage, SD values and results of Kruskal–Wallis test for comparison between percentage decrease in pain scores (PPT) in the four groups

Time period	Group I		Group II		Group III		Group IV		*P* value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Preoperative to 2 weeks	−17[b]	27.7	−7.3[b]	14.1	−57.6[a]	35.1	−58.7[a]	30.9	<0.001*
Preoperative to 3 months	−11.6[b]	25.6	−27.8[b]	29.7	−74.1[a]	30.5	−83.3[a]	28.2	<0.001*

*Significant at *P*≤0.05, different letters are statistically significantly different according to Mann–Whitney U-test. SD: Standard deviation, PPT: Pressure-pain threshold

Table 7: The mean, SD values and results of one-way ANOVA test for comparison between (MMO) in the four groups

Time period	Group I		Group II		Group III		Group IV		*P* value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Preoperative	36.2	6.8	35.6	5.5	34.6	2.4	35.7	9.4	0.958
2 weeks	37.6	4.9	37.1	4.4	36.6	1.4	40	5.6	0.376
3 months	35[b]	3.8	36[b]	4.2	36.8[b]	1.2	40.1[a]	5.3	0.050*

*Significant at *P*≤0.05, different letters are statistically significantly different according to Tukey's test. SD: Standard deviation, ANOVA: Analysis of variance, MMO: Maximum mouth opening

Table 8: The mean differences, SD values and results of paired *t*-test for the changes by time in mean (MMO) of each group

Group	Time period	Mean difference	SD	*P* value
I	Preoperative to 2 weeks	1.3	4.6	0.413
	Preoperative to 3 months	−1.2	6.7	0.598
II	Preoperative to 2 weeks	1.6	6.9	0.518
	Preoperative to 3 months	0.4	7.1	0.857
III	Preoperative to 2 weeks	2	1.9	0.015*
	Preoperative to 3 months	2.2	1.8	0.007*
IV	Preoperative to 2 weeks	4.3	7	<0.001*
	Preoperative to 3 months	4.4	7.2	<0.001*

*Significant at *P*≤0.05. SD: Standard deviation, MMO: Maximum mouth opening

Masseter muscle was selected a model for testing therapeutic modalities in our study, because masseter muscle taut bands are more superficial making them easily distinguishable and subsequently more sensitive to the external effects of PEMF therapy.

As hypertonic shortened mandible elevators (masseter) limit temporomandibular range of motion, therefore this hypothetically allows for greater range of motion to decrease tension in these muscles.

Recent evidence in understanding the pathophysiology of MTrPs agree that local pain and tenderness at MTrPs may be intrinsic part of muscle ischemia associated with sustained focal muscle contraction and/or muscle cramps. Massage techniques seem to be more effective when applied to superficial muscles than when applied to masseter muscles. Similar results were found in the study by Thomas *et al*.[40] who reported that a reduction in muscular pain could be achieved using a portable PEMF device. We believe that direct applications of PEMFs lead to masseter muscle massage (focal muscle fiber contraction), which aside from a heating effect have had the greatest impact on pain relief.

The results indicate that exposure to a specific low-frequency PEMF appears to exert some beneficial analgesic effects, particularly in patients with TMJD and should be used as an adjunctive treatment with other therapies.

Laser therapy induced a reduction in pain symptoms after application and increased patient's range of mouth opening. The reduction in muscle pain between the first and last session in this study; showed the difference between laser and PEMF therapies, with PEMF treatment controlling pain more efficiently. Laser treatment is a supportive therapy that is effective at treating patients with TMJD and relieving pain symptoms without changing the etiology of the disorder, so that successful treatment can be achieved in the long term.

For MTrPs injection is an effective technique for providing high pressure stimulation. High pressure stimulates mechanoceptors to modulate pain. One injection is often not sufficient to relieve pain, so several injections may be required. TrPs muscle injection provides an immediate way to relieve pain at its source, although it has a short-term effect; however in conjunction with supporting therapies, it is considered to be an effective, inexpensive and easy treatment option.

In this study, the technique used was to quickly insert, the needle tip into a point within the MTrP region, the rapid movement of the tiny tipped needle can provoke strong stimulation. Strong stimuli applied to the sensitive nociceptors can generate strong impulses, and these impulses are transmitted to the spinal cord. It is likely that these impulses can subsequently break the negative cycle in which the neural circuit is responsible for the MTrPs (the hypothetical "MTrP circuit")[38] in a manner similar to hyperstimulation analgesia. This is probably the mechanism for remote pain control as described in this study.

Table 9: The mean percentage, SD values and results of Kruskal–Wallis test for comparison between percentage changes in (MMO) in the four groups

Time period	Group I		Group II		Group III		Group IV		*P* value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Preoperative to 2 weeks	5.7	15.7	7.1	11.7	6.1	6.1	18.1	32.4	0.736
Preoperative to 3 months	−0.3	3.4	4	5.2	6.7	5.9	18.7	33.6	0.132

SD: Standard deviation, MMO: Maximum mouth opening

CONCLUSION

Our findings suggest that PEMF is the most effective treatment for alleviating pain and improving mouth range of motion in patients with myofascial pain dysfunction. However, in spite of its effect on reducing pain and improving range of mouth opening, we couldn't rely on this treatment method alone for patients with TMJD. Rather it should be used as an adjunctive treatment with other therapies, such as splint therapy or arthrocentesis.

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Original Article Plastic and Aesthetic Research

Internal derangement of temporomandibular joint: role of arthocentesis with steriod

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ABSTRACT

Aim: The aim of this study was to compare the efficacy of arthrocentesis with arthrocentesis plus steroid in the treatment of temporomandibular joint (TMJ) internal derangements. **Methods:** Nine males and 11 females aged 17–39 years were enrolled in the study. The patients were complaining of limited mouth opening and TMJ pain. Arthrocentesis was performed under aseptic conditions. All patients were clinically evaluated before the procedure, and 1 week and 6 months after the procedure. Intensity of TMJ pain and maximal mouth opening was recorded at each follow-up visit. **Results:** Both groups showed significant improvement in mouth opening and a reduction in pain scores in the postoperative period; however, the addition of steroid did not improve the overall outcome of the procedure. **Conclusion:** Arthrocentesis is a simple and safe procedure for patients with internal derangement of the TMJ with closed lock. However, the outcome was not improved by the addition of steroid.

Key words:

Arthrocentesis, internal derangement, steroid, temporomandibular joint

INTRODUCTION

The temporomandibular joint (TMJ) is subject to many disorders commonly known as temporomandibular joint disorders (TMD). These disorders are accompanied by pain, limitation, and deviation in mandibular range of motion, TMJ sounds, headache, and facial pain. Among these, internal derangement and TMJ osteoarthritis are the most common disorders, ranging from normal mouth opening and clicking to varying degrees of pain, restricted mouth opening, and loss of functional activity. The term "internal derangement" was introduced by Hey in 1814 as a general orthopedic term for a localized mechanical fault in a joint, but was later used more specifically to describe displacement of the TMJ disc.[1] Arthrocentesis for the TMJ was introduced by Nitzan *et al.* in 1991[2] and bridged the gap between surgical and nonsurgical treatment.[3] It involved irrigation of the upper joint compartment with a therapeutic substance, releasing adhesions, and flushing out inflammatory substrates, thereby relieving pain and improving function. TMJ arthrocentesis signifies the lavage of the upper joint compartment with physiological saline or Hartmann's solution (Ringer's lactate) using a needle for in- and out-flow.[4] Arthrocentesis can be performed either under low pressure using an elevated infusion bag or under normal pressure using a syringe.[1] This technique was first introduced at the beginning of the 1990s and was derived directly from TMJ arthroscopy, based on the hypothesis that the most effective successful component of TMJ arthroscopy was merely that the patient was submitted to an intervention, and not based on all the complicated maneuvers intended to recapture the disc, fix the disc, and remove the adherences within the joint using tiny and sophisticated instruments.[2] Arthrocentesis, as originally proposed, employed a technique involving the use of two needles that were inserted into the superior joint space at certain

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points; these points were termed "McCain's points" and were marked on a line drawn from the middle of the tragus to the lateral canthus. The entry points were marked along this canthotragal line. The first point, corresponding to the glenoid fossa, was marked 10 mm from the mid-tragus and 2 mm below the line, and the second point, corresponding to articular eminence, was marked 10 mm from the first point and 10 mm below the line. The simple flushing action in the joint may eliminate or reduce the effect of biochemical factors that contribute to inflammation and pain. Intra-articular corticosteroid injections are occasionally administered to alleviate inflammation. Intra-articular corticosteroid injection has an unpredictable prognosis and can also lead to local side-effects on the joint.

METHODS

A total of 20 patients (11 females and 9 males) aged 17–39 years were enrolled in this study. The review board of University of Kashmir approved this study. The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki declaration. A detailed clinical examination was performed, along with any necessary investigations. All the patients selected for the study had been diagnosed with TMJ internal derangement with closed lock through clinical and radiographic examination (magnetic resonance imaging). Only such patients were taken for study in which all the conservative measures had failed. A written and verbal consent was obtained from the patients for treatment and associated complications, after the treatment outcome were fully explained to them. A visual analog scale (VAS) was used to score pain (range 1–10), where 1 denoted no pain at all, and 10 denoted very severe pain. These values were recorded at 1-week preoperatively, and at 6 months postoperatively. The maximal mouth opening (MMO) was evaluated and recorded (in mm) pre- and post-operatively. The patients were divided into two groups, with 10 patients per group. One group underwent only arthrocentesis while the other group underwent arthrocentesis followed by a single injection of triamcinolone acetonide (20 mg) into the joint. The results were compared both pre- and post-operatively. The entire procedure was performed by one surgeon and conducted under local anesthesia [Figure 1]. About 100 ml of Ringer's lactate was used for arthrocentesis. After the lavage was completed, the needles were removed, and the patient's jaw was gently manipulated by the clinician in the vertical, protrusive and lateral excursions to help further release the disc and break the adhesions. The patients were then followed up at 1 week and 6 months. The results were then analyzed using an SPSS Statistics software package manufactured by IBM Corporation (Armonk, New York, U.S.). Postoperative changes in pain, lateral movements, and range of mouth opening were compared with the preoperative values using the Mann–Whitney *U*-test.

RESULTS

Before treatment, the mean VAS score was 6.6 and the mean MMO was 23 mm. Posttreatment, the mean VAS pain score decreased to a mean value of 2.7 at 1 week and then to 1.2 at 6 months in the arthrocentesis-only group [Table 1], whereas the MMO increased to a mean value of 34 mm at 1 week and 42.1 mm at 6 months in the steroid group [Table 1], which indicates significant improvement in patient symptoms and complaints. However, the mean MMO after steroid injection increased from 23.9 to 42.2 mm [Table 1], and the mean pain score decreased from 6.7 to 1.11 [Table 2], though the difference between the two groups was not significant.

DISCUSSION

Temporomandibular disorders comprise a wide variety of disorders of the TMJ, masticatory muscles, or both,[5,6] with the main symptoms presenting as pain and dysfunction. Pain associated with TMJ disorders may be due to vasoconstriction and release of nitric oxide, reactive oxygen species (ROS), and thiobarbituric acid. Elevated ROS levels in synovial fluid may result from mechanical stress and high pressures directed to the upper compartment during clenching and jaw movement.[7] Lavage of the upper compartment by TMJ arthrocentesis forces apart the flexible disc from the fossa, washes away degraded particles containing inflammatory components and decreases intra-articular pressure. Furthermore, the elimination of nitric oxide and ROS relieves the pain.

The concept of TMJ arthrocentesis and lavage was first borne out of the successful use of TMJ arthroscopy

Table 1: Comparison of MMO between the two groups

Group	Mean preoperative MMO (mm)	Mean postoperative MMO (mm)		*P* value
		At 1-week	At 6 months	
Arthrocentesis only (*n*=10)	23	34	42.1	1.000
Arthrocentesis plus steroid (*n*=10)	23.9	33.3	42.2	

MMO: Maximum mouth opening; *n*: Number of patients

Table 2: Comparison of pain between the two groups using a VAS

Group	Mean preoperative pain	Mean postoperative pain		*P* value
		At 1-week	At 6 months	
Arthrocentesis only (*n*=10)	6.6	2.7	1.2	1.000
Arthrocentesis plus steroid (*n*=10)	6.7	2.4	1.11	

VAS: Visual analog scale

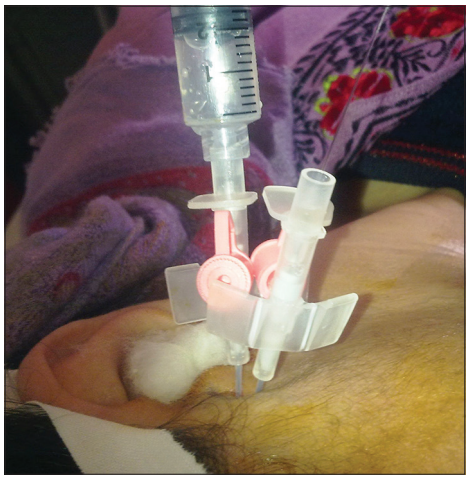

Figure 1: Arthrocentesis in progress

not only as a diagnostic tool, but also as a therapeutic technique, resulting in remarkable improvement in pain, jaw opening and function in selected patients simply by lavage of the superior joint space.[4] The hydraulic distension provoked by the lavage pressure under the upper joint compartment with a large volume of saline has been considered the reason for the positive clinical outcomes in patients with sudden-onset closed lock.[8] A single-session arthrocentesis procedure was then proven effective also in improving pain and dysfunction in subjects affected by TMJ osteoarthritis, likely due to a thorough removal of catabolytes from the joint space.[6] In the case of the closed lock, the central portion of healthy disc indeed separates from the fossa, leaving rims fastened to the surface of the eminence, which leads to increased negative pressure in the closed space between the fossa and disc. This pressure difference constitutes a force sufficient to keep the disc compressed against the fossa (the "suction cup effect").[9]

In our study, the maximum mouth opening increased from 23 to 42.1 mm in the arthrocentesis-only group, whereas it increased from 23.9 to 42.2 mm in the steroid group [Table 1]. The VAS score decreased from 6.6 to 1.2 in the arthrocentesis group, whereas it decreased from 6.7 to 1.11 in the steroid group [Table 2]. The results did not support the clear superiority of one treatment protocol over the others to achieve pain management in TMJ inflammatory-degenerative joint disease over a short-term, namely a 6-month follow-up period. Findings suggested that neither statistically nor clinically significant differences existed between the treatment groups. This concurs with the study conducted by Manfredini who compared six different treatment protocols. All protocols were associated with positive outcomes, in line with the TMD literature highlighting improvements, at least to some extent.[10] Murakami *et al.* compared arthrocentesis, arthroscopic surgery, and nonsurgical treatments in TMJ closed lock and found similar values for pain level and jaw dysfunction.[11] They concluded that arthrocentesis, rather than being an alternative to arthroscopic surgery, would be indicated for patients with acute TMJ closed lock refractory to medication and mandibular manipulation. In their review, Al-Belasy and Dolwick have reported that no medication was used for intra-articular injection in 4 studies, steroid was used in 14 studies, and hyaluronic acid was used in 2 studies.[9]

Complications are rare in arthrocentesis and occur more often with arthroscopy.[12] Nevertheless, potential complications may develop with arthrocentesis, such as damage to capsular tissues and discal tissue, increased risk of the facial nerve injury, preauricular hematoma, middle ear injury, and intra-articular instrument breakage. Redundant injury of the capsule by needles can also aggravate inflammation in the joint and increase the incidence of solution extravasation to neighboring tissues when the arthrocentesis is finally performed.[13-16] A rare case of extradural hematoma has also been reported with the conventional technique of arthrocentesis, which could have occurred because of blind triangulation of the needle. Arthrocentesis and arthroscopy are the primary treatments for patients who fail conservative methods of management of TMJ pain, restriction, and locking. An improvement in mouth opening is observed irrespective of the Wilkes score. There is a clear improvement in pain score based on this intervention, and as such, this management should be offered routinely.[17] Our results concur with the study conducted by Xu *et al.*, who showed that lavage and arthrocentesis helped to improve range of mouth opening and lateral movements, and reduce patient complaints.[18] In the absence of a clear history of trauma, arthrocentesis should be the first-line treatment in patients aged under 25 years.[15]

The results of this study concur with those of other studies, which show that arthrocentesis improves range of mouth opening and relieves pain, but the addition of steroids does not help to alleviate the symptoms of TMJ derangements.

CONCLUSION

Temporomandibular joint arthrocentesis and lavage with manipulation is a simple, less invasive and less expensive technique than TMJ arthroscopy with low morbidity rates. It should be considered as an effective and efficient alternative to more invasive surgical procedures for a selected group of patients and as a minimally invasive, highly effective procedure in the treatment of patients with internal derangement of the TMJ with closed lock.

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Case Report Plastic and Aesthetic Research

Management of extensive intraparotid vascular malformation: a case report

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ABSTRACT

Treatment of large soft tissue vascular lesions remains one of the greatest challenges in modern plastic surgery. The extent of the disease and the involved structures, but also the expectations of the patients are important in determining the way of treatment. The effective management of hemangiomas and vascular malformations of the head and neck requires a team approach, in order to understand the biologic behavior of the lesion, complete the diagnostic studies necessary to define the area of involvement, and understand the benefits and limitations of interventional radiologic and surgical procedures. The synthesis of this knowledge can help determine the best treatment. The strategic plan and subsequent management of a 34-year-old Maori man with an extensive arteriovenous intraparotid malformation is presented.

Key words:

Embolization, hemangiomas and vascular malformations, intraparotid malformation, vascular lesions

INTRODUCTION

Treatment of large soft tissue vascular lesions remains one of the greatest challenges in modern plastic surgery. The extent of the disease and the involved structures, but also the expectations of the patients are important in determining the way of treatment.[1]

The biologic classification of hemangiomas and vascular malformations (VMs) by Mulliken and Glowacki in the early 1980s has not only simplified the terminology, but has also clarified their clinical behavior and treatment options.[2] In most instances, a hemangioma can be differentiated from a VM by the history.[3]

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CASE REPORT

A 34-year-old Maori man presented with an extensive arteriovenous malformation over his left face. The patient first noted small cherry-sized nodules behind his left ear at 8 years of age. His main symptom was recurrent and spontaneous bleeding, which he controlled with direct pressure. The lesion remained quiescent until 10 years later, when he noticed progressive enlargement of the mass. In addition to the frequent bleeding, he began experiencing increasing pain, skin tightness and troublesome pulsation at night [Figures 1-3]. The patient agreed to publish his facial pictures and signed the form.

Magnetic resonance imaging (MRI) demonstrated a large VM, which predominantly filled the superficial aspect of the left parotid gland and extended posteriorly into the left external ear [Figure 4]. Its blood supply was derived from the left external carotid artery [Figure 5].

In preparation for surgical resection, patient underwent embolization 1 week prior to operation. The left occipital artery was embolized with 3 Guglielmi Detachable Coils (Target Therapeutics, Fremont, California, USA) and

the superficial temporal artery with Onyx Liquid Embolic System (Onyx® HD-500) [Figure 6].[4,5] This resulted in reduction in lesion size and its vascularity. The planned excision included the skin directly overlying the parotid as well as the lower half of the ear [Figure 7] and extended down into the neck, to allow for closure of the defect as a cervicofacial rotation advancement flap. Careful dissection allowed for retrograde identification of the facial nerve branches. The tumor was circumscribed and simultaneous dissection performed in all directions [Figure 8]. It was possible through this approach to then remove the entire tumor superficial and deep to the facial nerve, including the lower part of the ear [Figures 9 and 10]. It was decided at the end of the procedure not to remove the remaining components of the pinna as these are quite asymptomatic and removing them wound mean probably having to use a temporal parietal fascia and covering it with a skin graft, which is considered unnecessary at present. However, this would be an easy procedure to do as a second stage should the pinna component become problematic.

There were no complications related to either the preoperative angiography or embolization procedure. The patient was discharged on day 5 after the procedure. Histology confirmed arteriovenous malformation involving the subcutaneous tissue and parotid gland without any atypia or malignancy present. There has been no recurrence to our knowledge so far.

DISCUSSION

Maxillofacial VMs are formed due to an error of vascular morphogenesis. They may correspond to a defective remodeling process at the final stages of vessel formation. Although no hereditary VM exist, the defect might be genetically based and secondarily expressed in the first few years of life. VM generally grow in proportion to the growth of the affected child, but may increase in size secondary to various triggering factors such as increased

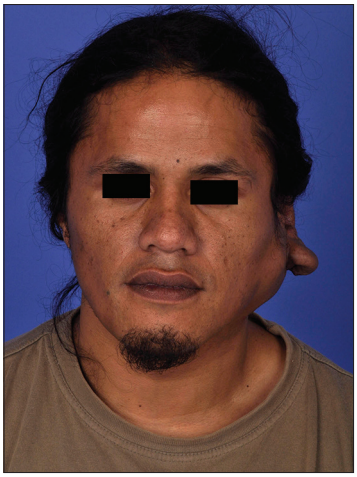

Figure 1: Preoperative anteroposterior view of the patient with large vascular malformation. A 6 cm by 8 cm pulsatile mass over the left parotid region, down to the angle of the jaw, and involving the left earlobe with resultant macrotia, with multiple raised nodules form underlying ectatic vessels are seen throughout. The overlying skin is discolored and taut

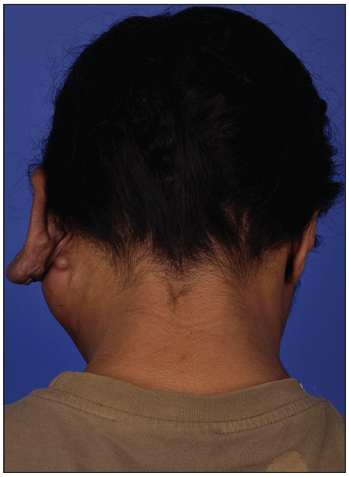

Figure 3: Posterior view

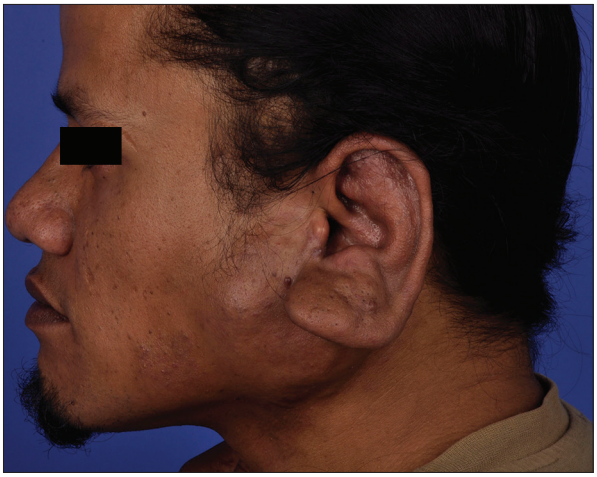

Figure 2: Lateral view of the same patient

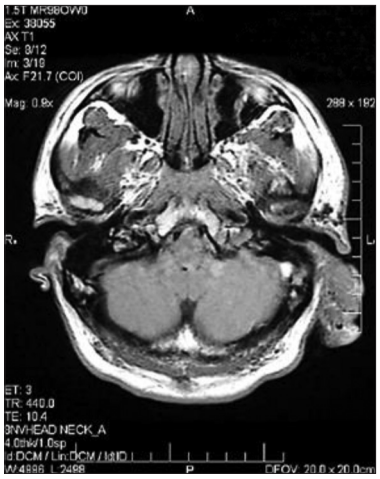

Figure 4: Magnetic resonance imaging confirmed the presence of a vascular malformation of the left external carotid artery supplying in and around the scalp and the left ear

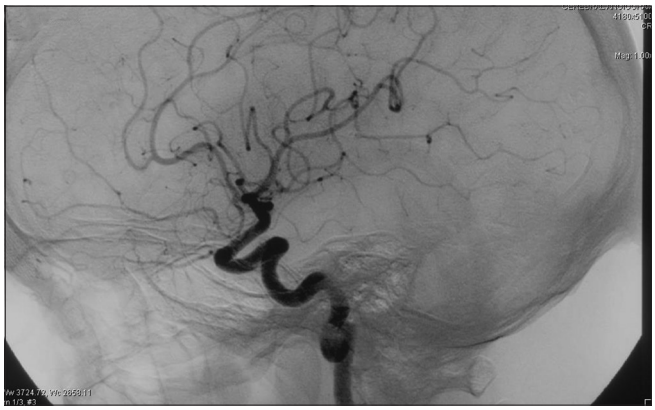

Figure 5: Digital subtraction angiography identified an arteriovenous malformation around the left ear

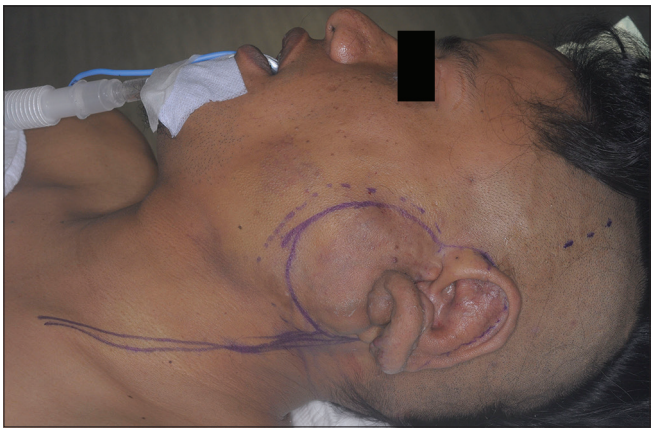

Figure 7: Preoperative design and marking of the cervicofacial rotation flap

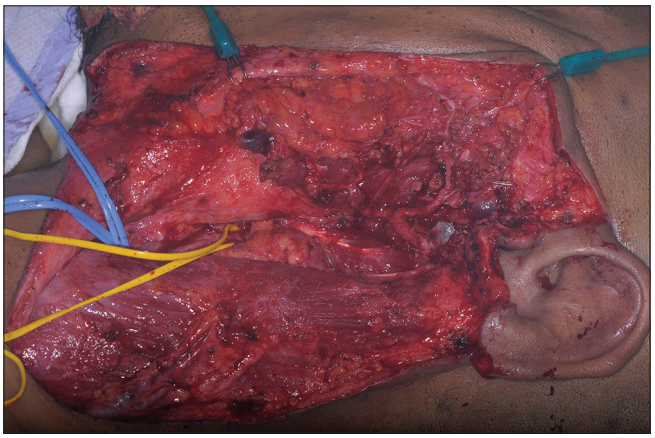

Figure 9: Intraoperative view following excision of the vascular malformation

blood flow, arterial occlusion and venous thrombosis, endocrine, trauma, or iatrogenic insults such as incomplete surgery and proximal embolization, and infection.

High flow in an existing VM can induce arteriovenous shunting, which, in turn, increases flow demand, cascading enlargement of the malformation.

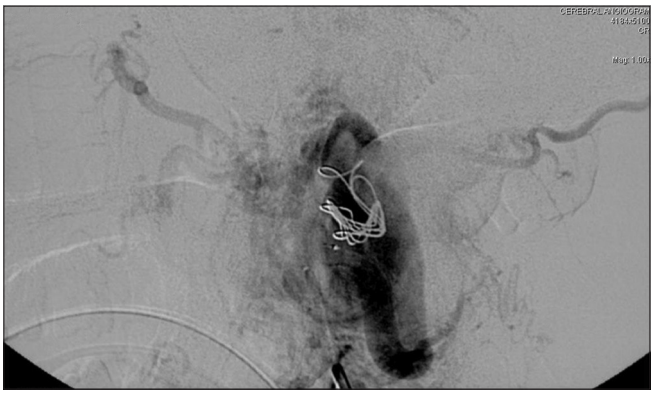

Figure 6: Digital subtraction angiography postembolization: The hypertrophic left occipital artery feeding the main A-V fistula was occluded by 3 Guglielmi Detachable Coils (Target Therapeutics, Fremont, California, USA). Anterior auricular artery branches supplying the vascular nidus was embolized with Onyx Liquid Embolic System (Onyx® HD-500)

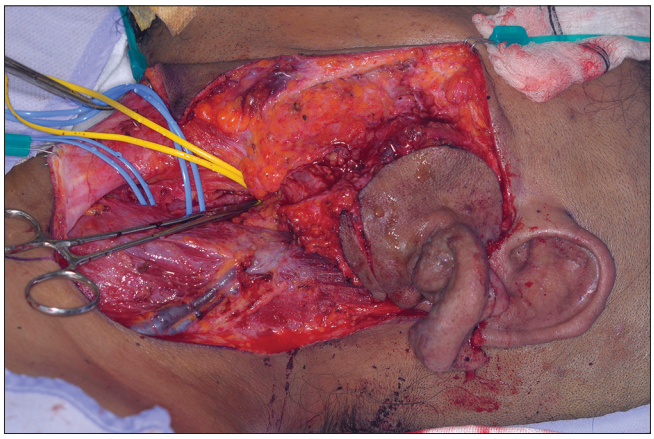

Figure 8: Intraoperative view after careful dissection of the facial nerve and control of the neck vessels

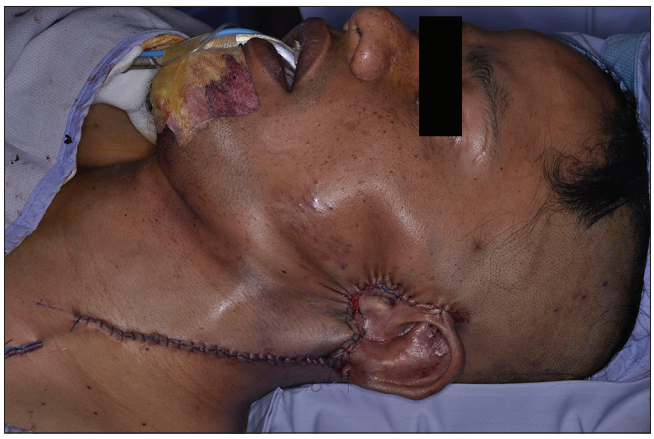

Figure 10: Postoperative view after skin closure

Increased understanding of these additional physiologic variants may help to define their clinical presentation and evolution and assist in designing therapeutic strategies.[6] The diagnosis is usually made based on clinical history and physical examination. Cross section

noninvasive imaging such as computed tomography (CT) or MRI is helpful for assessment of the extent of the disease, associated lesions, or multifocal involvement. MRI is the most useful single imaging modality in the investigation of VMs. The combination of multiplanar spin echo imaging and flow-sensitive sequences permits characterization of the nature and extent of most lesions. Angiography is reserved for patients in whom a decision has been made to intervene and is generally performed at the same time as embolization. VM are challenging to treat and require the skills of multiple disciplines.

Management of these lesions is best achieved by a specialist who understands the various clinical expressions of the problem, the natural history of the lesion, and the patient's needs. The primary goal of treatment is to restore and preserve function, stop bleeding, and improve or restore cosmesis.

Vascular malformation in children under 10 years of age may interfere with natural growth and maturation of the maxillomandibular frame, causing malocclusion of the mouth or modeling defects owing to external pressure on the forming bones or sinuses. Early intervention can arrest or even reverse such changes.[6]

The use of sclerosing and/or embolic agents in the treatment of hemagiomas was first described by Brooks in 1931,[7] documented by Edgerton in 1976.[8] Since then, preoperative embolization of soft tissue vascular lesions became almost the standard of care in the surgical management of these lesions.

The selection of an appropriate agent depends on the type of lesion, the method of embolization, and the experience of the interventional radiologist. The embolization procedure not only decreases the operative bleeding, but also facilitates the identification of a safe tissue plane for surgical excision.

Total resection is the gold standard. Three-dimensional (3D) CT scans facilitate both a better understanding of their complex 3D configuration and their relations with other anatomic structures such as bones and vessels. In addition, postoperative visualization demonstrates the volume of tissue removed.[9] Conventional imaging modalities, such as MRI and angiography, are good for understanding both the extent and the flow characteristics of the disease.

CONCLUSION

Effective management of hemangiomas and VMs of the head and neck requires a team approach, in order to understand the biologic behavior of the lesion, complete the diagnostic studies necessary to define the area of involvement, and understand the benefits and limitations of interventional radiologic[10] and surgical procedures. The synthesis of this knowledge can help determine the best treatment.[11]

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Case Report | Plastic and Aesthetic Research

Options for thumb revascularization: our experience and literature review

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ABSTRACT

Traumatic injuries to the thumb resulting in segmental loss of a digital artery are not uncommon. To bridge the gap and repair a transacted digital artery, the superficial palmar arch or the radial digital artery of the index finger can be used to reconstruct the ulnar digital artery of thumb for revascularization. Revascularization following segmental loss resulting from a crushed ulnar digital artery of the thumb can be performed based on the superficial palmar arch or the radial digital artery of the index finger, avoiding anastomosis at two sites and hence providing better results. The digital vein from the index finger can also be used to enhance the venous return of the injured thumb. However, because of known variability in the palmar arch, intraoperative verification is needed to ensure the safe transfer of the arch or the radial digital artery of the index finger. The aim of this article is to discuss the possibilities for thumb revascularization, using a case report in which the injured thumb was revascularized with a superficial palmar arch.

Key words:

Radial digital artery index finger, superficial palmar arch, thumb revascularization, ulnar digital artery thumb

INTRODUCTION

The decision whether to proceed with revascularizing the thumb following a crush injury depends on several factors, including the mechanism of injury, the patient's age, occupation and hand dominance, and overall medical condition and intraoperative assessment of the injured structures. Crush injuries at the base of the thumb involving loss of digital artery segments can present a challenge to the reconstructive surgeon. Primary repair of the digital artery may be difficult and may be achieved by shortening the proximal phalangeal bone if there are associated fractures. Repair of the digital artery is likely to require vein grafting, as significant segmental loss of the digital artery often results from injuries in this area. To bridge the gap and repair a transected digital artery, the palmar arch or radial digital artery of the index finger can be used to reach the ulnar digital artery of the thumb without a vein graft. In addition, a vein from the index finger can be used to achieve venous drainage of the thumb.

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CASE REPORT

A 60-year-old male sustained a mutilating injury to his dominant right thumb [Figures 1-3]. A radiograph of the right hand in the anteroposterior view showed a fracture

at the level of the shaft of the proximal phalanx of the thumb [Figure 4]. Intraoperatively, transection of the ulnar digital artery was at the level of the base of the thumb. The thumb was ischemic. Skeletal fixation was achieved using Kirschner wires [Figure 5]. Dissection of the digital nerve revealed contused nerve fibers, although the fibers were intact. The ulnar digital artery was found to be transected at the shaft level with segmental loss; this segmental loss made primary repair difficult. The radial digital artery and the nerve of the thumb were contused but intact. The dorsal veins were contused.

To bridge the gap, the superficial palmar arch was dissected until its ulnar end where the branch to the common digital artery to the index and middle fingers arising from the palmar arch. A digital clamp was placed over the ulnar end of the palmar arch and the radial digital artery of the index finger. The tourniquet was released and the vascularity of the index finger was confirmed, before reapplying the tourniquet. A Vascular clip was used to ligate the superficial palmar arch just before the division of common digital artery to the index and middle fingers. To obtain additional length, the radial digital artery to the index finger was also ligated and divided. The palmar arch was turned to reach the ulnar digital artery of the thumb, facilitating end-to-end repair without a vein graft. The digital vein of the index finger was also utilized to allow venous drainage of the thumb [Figure 6]. On release of the tourniquet, there was good blood flow into the thumb and fingers [Figure 7]. Postoperatively, the patient received six sessions of hyperbaric oxygen therapy. After an uneventful hospital course, the patient was discharged on the tenth postoperative day.

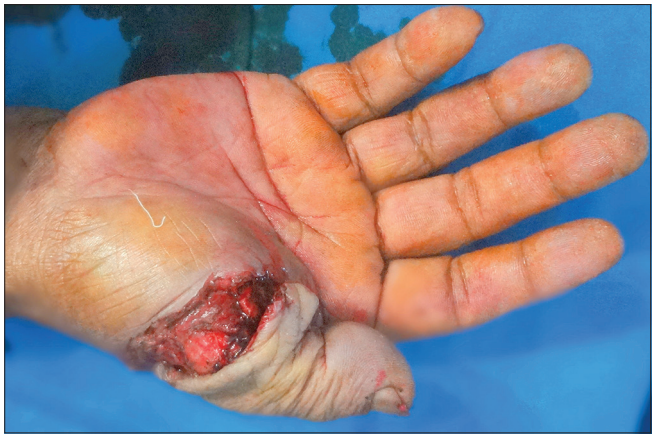

Figure 1: Crush injury to the base of the right thumb, volar aspect

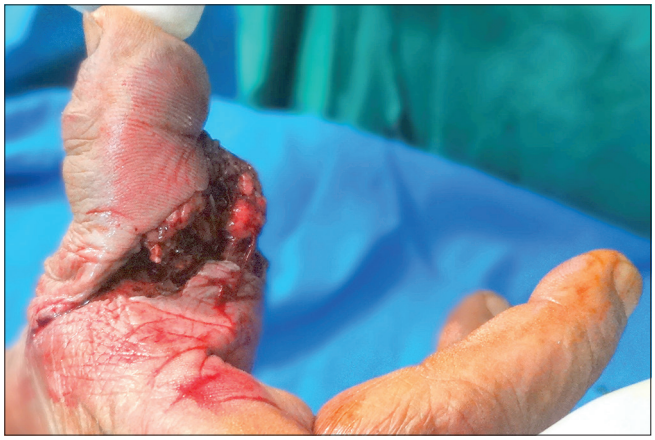

Figure 3: Ulnar aspect of the injured thumb

DISCUSSION

Avulsion injuries to the thumb can result in extensive damage to long segments of vessels, which makes direct suturing of the structures difficult. The decision to proceed with revascularizing an avulsed thumb depends on several factors, including the mechanism of injury, the patient's age, occupation and hand dominance, and overall medical condition and intraoperative assessment of the injured structures. When the decision is taken to retain the thumb by revascularization, the options available are to use a vein graft to reconstruct the segmental loss or to transfer nearby vessels to adequately bridge the gap of the injured

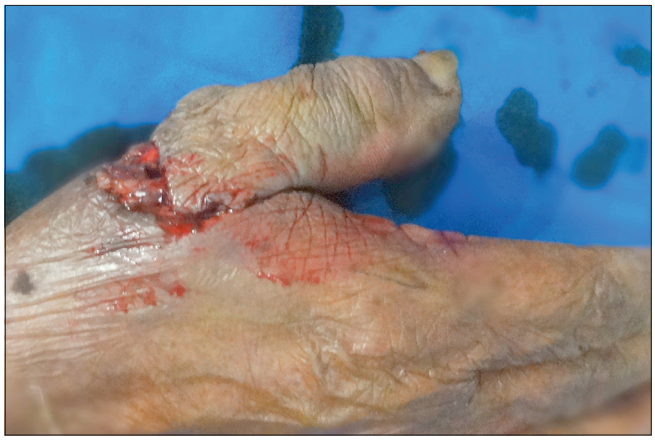

Figure 2: Dorsal aspect of the injured thumb

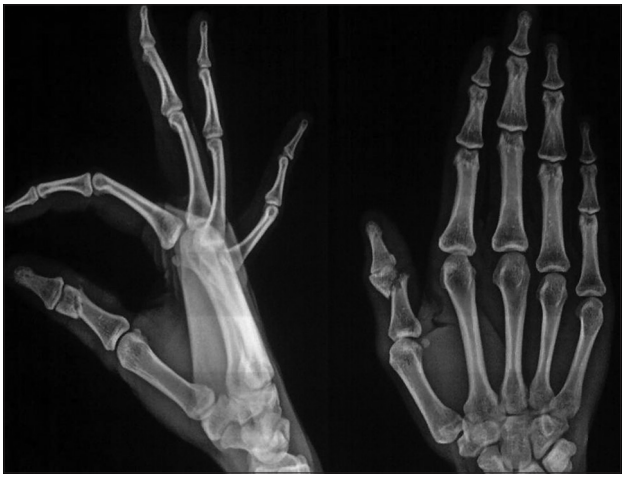

Figure 4: Radiograph of the right hand in the antero-posterior view, showing a fracture at the level of shaft of the proximal phalanx of the thumb

segment. Ideally, a single end-to-end primary arterial repair of the ulnar digital artery can obviate the need for two anastomotic sites, as in the case of vein grafting.

A classic morphology of the complete superficial palmar arch is formed by the superficial palmar branch of the ulnar artery and the superficial palmar branch of the radial artery.[1] Superficial and deep palmar arches of the hand, formed by the radial and ulnar arteries, provide the dominant blood supply to the hand, with an intricate network of collateral flow. The superficial palmar arch is classified into two categories: complete or incomplete. The latter is formed when the anastomoses between the radial and ulnar superficial vessels constituting the arch are absent.[2]

It is important for surgeons dealing with reconstructive hand surgeries and restoration of the functional anatomy of hand to understand how the pattern of the superficial palmar arch can vary. Several cadaveric and radiographic studies have revealed enormous variability in the vascular anatomy of the deep and superficial palmar arches.[3] Conventionally, the superficial palmar branches of the ulnar and radial arteries form the superficial palmar arch. The ulnar artery appears to be the main feeding vessel.[1] The ability to reconstitute the arterial flow when revascularizing the thumb using the palmar arch or radial digital artery of the index finger depends on the anatomic configuration of the superficial palmar arch. The surgeon should always be aware of the variations in the superficial palmar arch before proceeding, and the expendability of the superficial palmar arch or the radial digital artery branch must be established to avoid ischemia of adjacent digits. If the anatomy of the superficial palmar arch is normal [Figure 8], then the palmar arch or the radial digital artery of the index finger can be safely transferred distally to the ulnar digital artery to revascularize the thumb [Figure 9]; however, the possibility of using a reverse radial forearm flap to resurface the palmar or dorsal defect associated with these types of injury may be compromised. Richard and Goldner have discussed transposing the digital neurovascular bundle in patients who have experienced a crush injury of the digits.[4]

Other methods used to revascularize such injuries, include reconstructing the injured segment with vein grafts harvested from the distal third of the forearm,

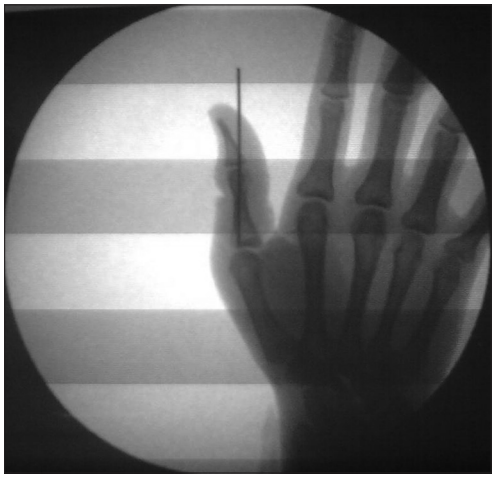

Figure 5: C-arm picture demonstrating skeletal fixation with Kirschner wires

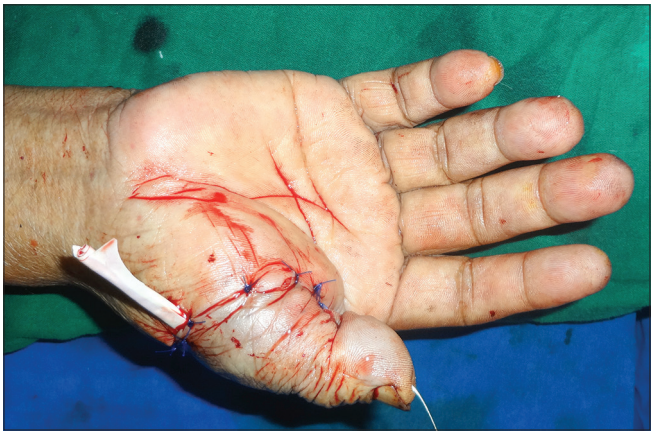

Figure 7: Postoperative picture following revascularization

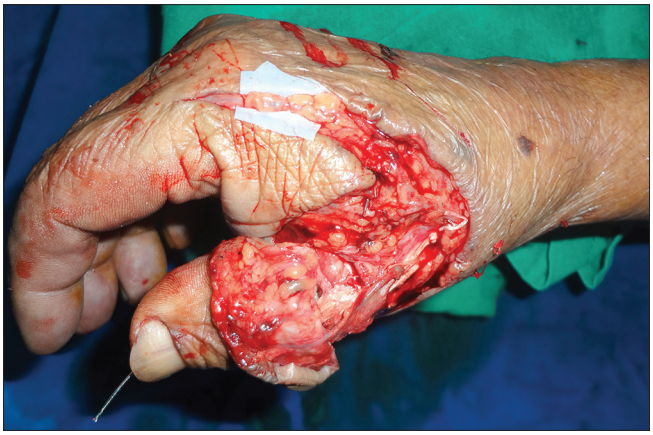

Figure 6: The superficial palmar arch and digital vein from the index finger were used to revascularize the thumb

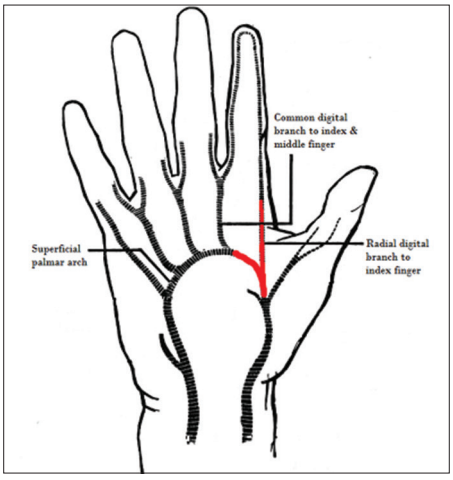

Figure 8: Schematic depicting the normal superficial palmar arch anatomy

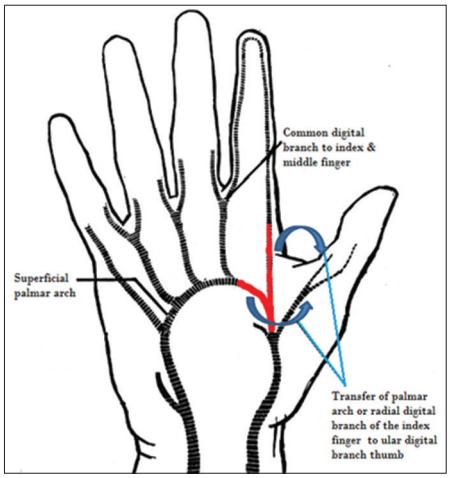

Figure 9: Schematic representing transfer of the palmar arch or radial digital artery of the index finger for revascularization of the thumb

vessel shift of the radial or ulnar arteries, and forming an arteriovenous fistula [Figure 10].

The advantage of the vein graft procedures is that there is no need to sacrifice the palmar arch. The disadvantages are the need for two anastomoses, and that the proximal part of the injured artery can be in spasm since it is near to the zone of trauma. This can result in an unfavorable outcome following anastomosis, with the need for further revision procedures and additional incisions for vein graft harvest. The advantages of the transfer of superficial palmar arch or radial digital artery for thumb revascularization over vein grafts are the need for just one anastomosis, which reduces the incidence of thrombosis, and that the artery borrowed for anastomosis is out of the zone of trauma, resulting in better outcomes. The disadvantage of this procedure is the possibility of loss of the index finger, although the chance of this is low as one vascular bundle is retained and there are additional arterial perforators from the metacarpal arteries.

Another method with which to salvage the thumb following crush or avulsion injuries is to shift the undamaged arteries (radial or ulnar).[4] Disadvantages of this method are scar contracture, size mismatch of the vessels, and concomitant damage to the utilized vessel.

Some authors have suggested creating an arteriovenous fistula.[5] This method is usually used when there is no suitable artery in the devascularized part. Better results are obtained when the volar veins are used for anastomosis and when there is less tension on the anastomosis between the proximal volar digital artery and the dorsal vein.[6] Morris *et al.* have suggested that the presence or absence of venous valves appears to be an

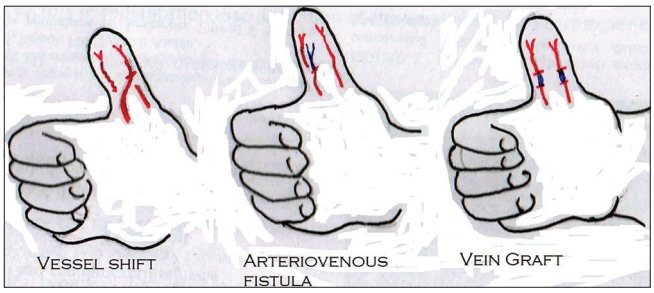

Figure 10: Options for thumb revascularization

important consideration[7] and warrants further evaluation before attempting a clinical transfer.

The principle of transposing the radial digital artery or superficial palmar arch could very well be used in cases of amputation at the level of the base of the thumb, where venous grafts may be avoided for establishing the circulation.

CONCLUSION

Revascularizing the thumb is a challenging and rewarding experience for the plastic surgeon. Knowledge of the superficial palmar arch and its anatomical variability are critical for successful revascularization. Therefore, bridging the vascular gap to repair the transected ulnar digital artery of the thumb, superficial palmar arch or the radial digital artery of the index finger could be safely transferred distally for revascularisation.

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Progressive drain withdrawal without suture removal: a technical note

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Sir,

Drains are traditionally used in a variety of surgical procedures;[1,2] although there is limited evidence of their usefulness.[3] Drains are classified based on various characteristics: as open or closed systems, as active versus passive, as prophylactic versus therapeutic; or by composition (e.g. polyurethane, silicone, or rubber).[2,4] Closed vacuum drains apply negative suction (60-80 kPa) in a sealed environment.[5] Drains are often secured using a single suture or adhesive tape to prevent inadvertent removal. Complications from drains include pain, hemorrhage, drain entrapment, and retrograde bacterial migration that can result in postoperative infections.[1,2]

We routinely use drains after flap reconstructions. For example, we place two or three vacuum suction drains in the gluteal myocutaneous rotation flaps that are used to cover sacral pressure sores. The drains are sutured for security and are completely removed if drainage is less than 30 mL/day.[1,2] If fluid production from the wound exceeds 30 mL/day for 5 days and is serous in nature, we progressively remove the drain in 3 cm steps until removal is complete.

The present report describes a method of progressive removal of an external drain without suture release. Specifically, we suture a loop through the skin and fix the drain by a double-loop through the first loop. One or two additional loops can be added if necessary. The suture is tied with multiple knots, and a simple dressing over the drain is used for wound closure.

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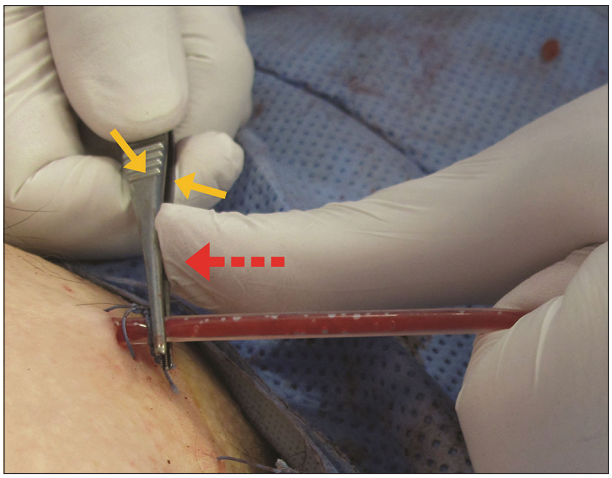

Figure 1: Progressive drain removal without suture release. Gentle traction on the drain with the forceps in place permits withdrawal of drain

For drain withdrawal, the drain suture is soaked with disinfectant spray (Bode Cutasept®F, Hamburg, Germany), to facilitate passage of the drain. The vacuum is then released to prevent the drain from adhering to the tissue. The forceps are positioned directly proximal to the securing suture and closed firmly. The drain is compressed and slid through the suture with gentle traction. If toothed forceps are used, the drain must be positioned proximal to the teeth to avoid tearing. This technique is applicable to drains of various diameters and materials.

We have used this technique to gradually extract drains during 7 years of high-volume plastic surgery [Figure 1]. Our patients have reported no discomfort or pain. The technique is safe and useful in situations where gradual drain withdrawal is advantageous, such as high-output seromas, postflap harvests, and groin dissections. It

avoids the need for re-suturing and permits healing from the wound base. This method requires a certain level of training and caution when performing the retrieval. The drain's security must be checked after each withdrawal as it can loosen, resulting in premature drain removal.

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Review Article Plastic and Aesthetic Research

Current and future applications of nanotechnology in plastic and reconstructive surgery

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ABSTRACT

Although nanotechnology is a relatively young field, there are countless biomedical applications in use or under investigation. Many specialties have benefitted from nanoscale refinements of diagnostic and therapeutic techniques. Plastic and reconstructive surgery is an incredibly diverse specialty, encompassing craniofacial and hand surgery; trauma, oncologic and congenital reconstruction; burn care, and aesthetic surgery. Advances in nanotechnology have significantly impacted wound management, topical skin care, implant and prosthetic design, tissue engineering, and drug delivery systems. Currently, plastic surgeons are researching the utility of nanoscale tools for bone regeneration, bone prosthetics, and drug delivery. Nanotechnology will continue to build upon preceding discoveries, and its biomedical applications in the field of plastic and reconstructive surgery will expand significantly.

Key words:

Bone graft, burns, drug delivery, implants, nanotechnology, tissue engineering, wound care

INTRODUCTION

Nanotechnology can be defined as the science of design, synthesis, characterization and application of materials and extremely small devices. The smallest functional unit of this technology, in at least one dimension, is on the nanometer scale, which is one billionth of a meter.[1-3] Nanotechnology is the design and engineering of novel products that interact with biological, electrical and chemical systems on the atomic level, thus yielding a level of specificity and specialization that was not feasible in the past. In the 1950's, European researchers discovered formation of an active biological field from the oxidation of titanium when exposed to air. They identified that this promotes living tissue ingrowth.[4] This phenomenon was used to take a tremendous leap in medical technology, specifically in bone implant applications. Nanomedicine is a subdivision of nanotechnology that employs highly specific molecular interventions for both the diagnosis and treatment of disease processes. Currently, nanomedicine has allowed advancement in the fields of drug delivery systems, gene therapies, body and organ imaging, surgical tools, and diagnostic procedures.

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SOFT TISSUE REPAIR AND HEALING

Wound and burn care are two areas of clinical care that are already benefitting from developments in nanotechnology.[5] Wound dressings constructed using nanoscale fabrication techniques can greatly improve wound healing. Nanofibers may be created from various

materials using manufacturing techniques on a nanoscale. The nanofibers provide a three-dimensional structure that mimics the native extracellular matrix (ECM) while the host tissue regeneration replaces the scaffold. Nanofiber scaffolds provide several properties that are essential for tissue repair: mechanical integrity, temperature control, fluid absorption, and gas exchange.

In rat models, scaffolds made of collagen nanofibers accelerate acute wound healing by enhancing capillary and fibroblast proliferation.[6] In a study by Choi *et al.*,[6] recombinant human epidermal growth factor (EGF) was immobilized on electrospun biodegradable nanofibers to treat diabetic ulcers in a rat model. Human primary keratinocytes were cultivated on the nanofiber matrix to investigate the effect of EGF nanofibers on their differentiation. Wound healing effect of the EGF nanofibers was confirmed in diabetic animals with dorsal wounds. In *in vivo* wound healing studies, the EGF-nanofibers group was superior to control groups (conventional dressing, nanofibers alone, or EGF solutions). This study showed that EGF-conjugated nanofibers could potentially be employed as a novel wound healing material by increasing proliferation and phenotypic expression of keratinocytes in diabetic wounds.

Chitin and chitosan nanofibrils are nanocrystals of natural polysaccharides derived from the exoskeletons of crustaceans. These fibrils have been used in a variety of formulations to aid wound healing. Muzzarelli *et al.*[7] showed in murine models that different formulations of chitin nanofibrils almost lead to normal physiologic repair of wounds. They subjected various formulations of dibutyryl chitin (DBC), a modified chitin carrying butyryl group at the three and six positions, to a battery of *in vitro* and *in vivo* tests. The DBC's were then incorporated into a 5-methylpyrrolidinone chitosan solution and submitted to freeze-drying to produce a reinforced wound dressing material, which was then tested *in vivo* in full thickness wounds in rats. The rats had full thickness dorsal wounds bilaterally and treated with the experimental agent on one side, and control on the contralateral side. The animals were studied at either 7 or 14 days and the skin of each surgical wound was excised. The use of 4 mm × 4 mm pieces as wound dressings resulted in significantly less cutaneous scarring, as measured by collagen I/collagen III rations, and as measured clinically.

Chitin nanofibrils/chitosan glycolate can be manufactured into a spray, gel or impregnated onto a dressing for wound care. Using a rat model, Mattioli-Belmonte *et al.*[8] demonstrated that each of these delivery systems has a specific application: use for superficial abrasions, shallow wounds in aesthetic areas, and slow healing dermo-epidermal wounds, respectively. Enhanced tissue repair and reduced scarring was seen in all the applications. Although the results from all of these studies are impressive, they have not been examined in human clinical trials.

Silver has long been heralded for its antimicrobial properties and has demonstrated efficacy against multi-drug resistant organisms as well as exhibiting antiinflammatory properties.[9,10] Nanoscale fabrication techniques have allowed manufacturing silver into nanoparticles, which markedly increases the rate of silver ion release, and thus increasing its clinical utility.[10,11] A nanocrystalline silver dressing was recently evaluated in chronic wounds by Sibbald *et al.*[9] In a prospective, uncontrolled study, a variety of chronic, nonhealing wounds (foot, pressure, and venous stasis ulcers, and miscellaneous wounds) were treated with a nanocrystalline sliver dressing [Figure 1]. Surface bacterial counts were found on semi-quantitative swabs to be significantly diminished in those wounds treated with nanocrystalline dressing. Since bacteria contribute to tissue damage leading to poor wound healing, the decreased bacterial load from silver nanocrystalline dressing facilitates wound healing. In addition, growth factors have been shown to play a critical role in the proliferative phase of wound healing. Growth factors serve to attract the cells necessary for fibroblast and epithelial cell growth and migration, as well as initiating the formation of new blood vessels into the area of injury. Novel polymerized nanocarriers have been produced, which can provide for consistent and significant dosages of growth factors. The growth factors are embedded into the polymerized nanocarriers that allow sustained release of these bioactive molecules. The nanocarrier drug delivery system has been successful in treating wounds in a clinical setting.[10]

The cosmetic and topical skin care industries have also benefited from advances in nanotechnology. For example, micronized zinc oxide and titanium dioxide (TiO_2) are used in sunscreen manufacturing by functioning as ultraviolet blockers in these products. Their nanoscale fabrication increases their transparency on skin and allows increased user compliance. In addition, it also increases their refractive index, resulting in a "stronger" sunscreen.[12] Lipid nanoparticles have been added to various cosmetic and dermal products to increase contact with the stratum corneum. Therefore, it allows increased drug penetration into the skin, improved hydration through their occlusive properties, and provide controlled release of active ingredients.[13] In an open clinical trial, fullerene gel applied to patients with acne vulgaris showed a significant reduction cutaneous inflammation and infection, suggesting yet another application of nanotechnology in skin care.[14]

IMPLANTS AND PROSTHESES

In 2012, breast augmentation and implant-based breast reconstruction after mastectomy were the most common plastic surgery procedures. Breast implants that contain nanofiber coatings for the delivery of tumor-specific anticancer drugs are currently being evaluated.[15] This technology has the potential to revolutionize cancer care, by facilitating area-specific chemotherapy to the tumor bed while alleviating some of the undesirable effects of current systemic chemotherapy regimens. In addition,

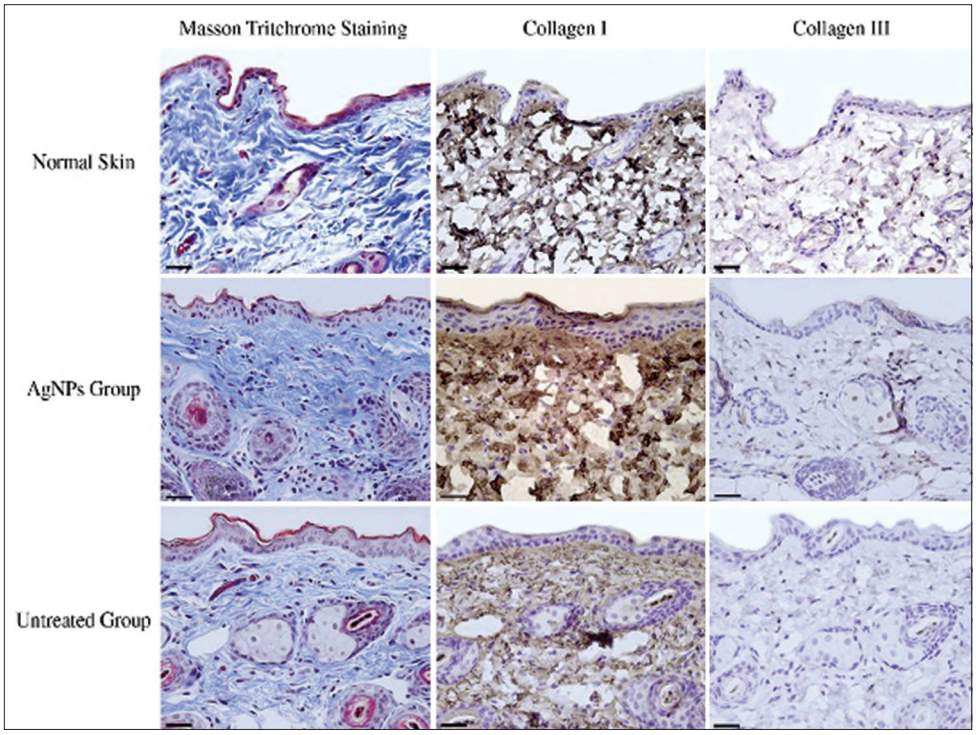

Figure 1: Histological staining of healed skin in each experimental group. Masson trichome staining shows the distribution and density of collagen protein in healed skin in various groups. Collagen protein was stained blue, nuclei are stained black and the background (muscle, cytoplasm and keratin) are stained red. Immunohistochemistry staining shows the expression of collagen Type I and Type III of healed skin in normal skin, silver treated, and untreated groups, respectively (scale bar: 20 μm)[9] (used with permission)

utilizing nanoscale technology in manufacturing can improve the strength of breast implants. The shell of silicone breast implants is made up of cross-linked and reinforced silicone rubber nanocomposite. The silicone rubber is weak and, therefore, must be reinforced, most commonly with nanosized SiO_2. Finally, even with modern breast implants, capsular contracture continues to be one of the significant long-term complications of long-term breast implant placement. It has been demonstrated in a rat model that surface modification of implants with antifibrotic drugs (e.g. halofuginone) can decrease capsule formation.[16]

TISSUE AND ORGAN ENGINEERING

Nanotechnology has been used to construct and repair various tissues utilized in plastic surgery. Electrospun nanofiber matrices have been developed for skeletal muscle regeneration in both *in vitro* and *in vivo* experimental models.[17] Reconstructive plastic surgeons are currently using cartilage engineering that has been utilized in orthopedic surgery for many years. The engineering of auricular cartilage for ear reconstruction is an established technique. Additionally, nasal cartilage is being examined for complex nasal reconstruction after cancer, trauma, or congenital defects.[18] Artificial skin has long been used for the treatment of skin defects. Currently, the use of scaffolds composed of polylactic and polyglycolic acids embedded with various growth factors are used to improve skin healing.[19,20] With precise manufacturing techniques and the utilization of novel biomaterials, the development of these products can provide enhanced aesthetic appearance after reconstruction. This has been proven to be safe, reliable, and reproducible.

NERVE TUBULIZATION

Nerve regeneration is an area of particular interest to both plastic surgeons and nanotechnology researchers. Plastic surgeons perform the majority of the peripheral nerve surgeries involving the hands, face, and trunk.[21,22] Traumatic nerve injuries resulting in loss of nerve tissue over 5 mm frequently require nerve grafting, often from an autologous source. Donor sites for this procedure, however, are limited. To avoid the morbidity of autologous nerve grafting, nanoscale manufacturing techniques have been employed to develop new approaches in peripheral nerve repair. Tubular and porous nanostructured conduits, using various natural materials, have been developed to guide regenerating nerves. These structures have been loaded with various biomaterials or cell types (e.g. embryonic stem cells, Schwann cells, neural stem cells) to aid regeneration. Chitosan nanofiber mesh tubes were studied in sciatic nerve injuries in a rat model by Wang *et al.*,[23] in which they noted partial recovery of sensory function as the nerves elongated through the tubes. Biodegradeable micropatterned scaffolds that mimic the extracellular membrane can also be coated with laminin and seeded with Schwann cells to guide neuron alignment and promote axon regeneration after injury.[19] Currently, researchers are designing neural interfaces between the peripheral and central nervous system, and limb prostheses for patients with traumatic amputations and spinal cord injuries.[24,25]

NANOTECHNOLOGY IN BONE BIOLOGY AND REPAIR

Current developments in bone matrix depend on the understanding that the bone microenvironment is made up of progenitor cells, mineralized ECM scaffold, soluble chemical signals (such as cytokines), and mechanical stimuli.[26] Nanoscale fabrication techniques can improve each of these components. Scaffolds made of nanomaterials provide a geometric porous structure that allows osteoblastic differentiation.[27] Such techniques are conceptually simple, yet were not technically possible until the development of modern nanoscale fabrication techniques. Advances in fabrication and manufacturing make nanotechnology an exciting and powerful tool in the development of bone reconstruction.

BONE PROSTHESES

Nanotechnology can be used to manipulate the surfaces of standard bone replacement implants to maximize tissue ingrowth, while minimizing inflammation. Raimondo *et al.*[28] recently investigated the use of electron beam absorption to resurface standard titanium and polyethylene (PE) implant surfaces. Then, they evaluated them for surface characterization, surface energy and contact angles, and osteoblast and endothelial cell adhesion [Figure 2]. They found that the nano-roughened surfaces were more favorable in each category. While unmodified titanium surfaces demonstrated excellent adhesion of both osteoblasts and endothelial cells, once modified, the PE surface showed significantly increased osteoblast adhesion and showed similar endothelial cell adhesion. This study introduces a novel process to efficiently nano-roughen materials and provides an additional example of nanotechnology use to enhance the performance of standard synthetic materials.

Liu and Webster[29] re-emphasizing the importance of the homogenous dispersion of poly-DL-lactic-co-glycolic acid (PLGA) nanoparticles for optimal enhancement of cell adhesion. They demonstrated that PLGA prosthetics enhanced with a well-dispersed nanoceramic coating had improved load-bearing limitations. This improved mechanical strength was most likely due to the strong bonds between nanoparticles and PGLA, as conveyed by the fine ultrastructure of the particles. This enhancement of mechanical strength, through the application of nanoparticles, is a previously underappreciated finding in nanomaterials. Finally, this work highlights that the three-dimensional structure of nanoparticles and its interactions can increase their applications.

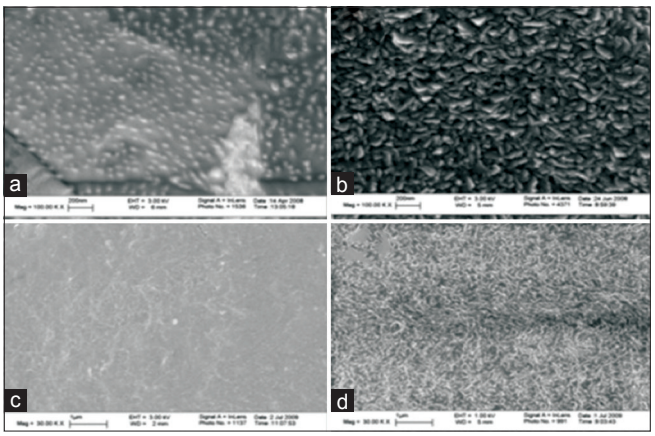

Figure 2: Scanning electron microscopy images of (a) conventional titanium (Ti), (b) nanorough Ti, (c) conventional polyethylene (PE), and (d) nanorough PE. Scale bars in (a) and (b) are 200 nm while (c) and (d) are 1 μm[28] (used with permission)

Hydroxyapatite (HA) is currently used to fill bone defects by itself or as a prosthetic coating. While HA has advantages over other bioceramics, such as creating strong bonds with native tissues, it lacks a homogeneous degradation phase. Given the nanoscale architecture of native bone crystals, manufacturing HA on a nanoscale would theoretically improve its utility. Poinern *et al.*[30] investigated the effects of thermal and ultrasonic techniques for the development of these particles and demonstrated that either technique can generate particles of similar consistency. Abd El-Fattah *et al.*[31] histomorphometrically analyzed the tissue by growth and scaffold degradation in three groups of rats with identical bone defects: one filled with mirco-HA, one with nano-HA and one control group without filler. They found increased reactive bone formation and biocompatibility in nano-HA group compared with other groups. These findings have immediate implications for improving the utility of HA for craniofacial, hand, extremity, and truncal bone reconstructive applications.

BONE REGENERATION

In addition to aiding the development of bone prosthetics, nanotechnology also provides many inroads to improve bone regeneration. The induction of progenitor cells into osteoblasts is an important component of bone regeneration. A novel application of nanotechnology to achieve this goal is the application of specific nanoscale surfaces to produce specific cellular responses, such as osteoblastic differentiation. Oh *et al.*[27] investigated the effect of culturing human mesenchymal stem cells (hMSC) on TiO_2 nanotubes ranging in size from 30 nm to 100 nm. They found that the larger nanotubes forced the elongation of the hMSCs and consequently encouraged differentiation into osteoblastic cell lines. They proposed that smaller nanotubes capture local proteins easily and establish an ECM-like environment allowing for easy hMSC adhesion. In larger nanotubes, there is less capture of local proteins, and the hMSCs require to stretch and develop filopodia to elongate across the surface and establish adequate adhesion [Figure 3]. This geometrical manipulation provides the cytoskeletal stress theorized to induce osteoblastic differentiation. This technique could feasibly improve previous methods of osteoinduction that involve gene therapy.[32]

NANOTECHNOLOGY IN MAXILLOFACIAL SURGERY

Nanotechnology has the potential to bring enormous changes to the fields of maxillofacial surgery and

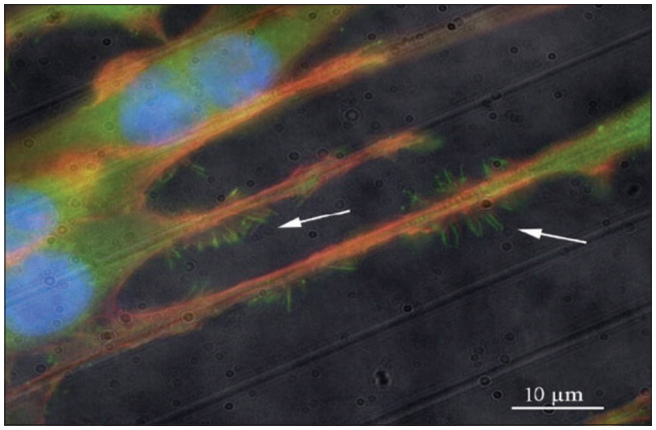

Figure 3: Filopodia of endothelial cells induced by nanotopography[27] (used with permission)

dentistry through the aid of nanorobotics, nanomaterials, and biotechnology.[33] Nanorobots have a diameter of 0.5–3 µm and are made of components sized from 1 nm to 100 nm. They can be programmed, thus enabling clinicians to execute accurate procedures at the cellular and molecular levels. Specifically, they have roles in local anesthesia, diagnostics, therapeutics, dental and maxillofacial hard tissue repositioning, and dentifrice. In maxillofacial surgery, nanomaterials can be used as bone replacement materials, prosthetic implants, dental fillers, dental restorative materials, impression materials, and even for orthodontic wires exhibiting very high strength and excellent deformability, corrosion resistance, and surface finish. Finally, tissue engineering with natural nanomaterials holds the potential to completely reconstruct a patient's dentition and craniofacial skeleton.

DRUG DELIVERY

Nanoscale technologies have numerous applications in drug delivery [Table 1]. Bone infections can be catastrophic and are difficult to manage even in the age of modern antibiotics and best surgical techniques.[34] Plastic surgeons are frequently involved in the management of these problems because they provide technical expertise with vascularized tissue transfer and soft tissue reconstruction. Deep tissue infection with multiple drug resistant organisms coupled with the morbidity of serial operations and potentially toxic systemic therapies begs for the introduction of new approaches. The antimicrobial properties of silver have long been appreciated, and current nanotechnological techniques have allowed the production of nanoscaled silver particles with a very high surface to mass ratio. Zheng *et al*.[35] examined PLGA composite grafts treated with nanosilver compared with PLGA controls [Figure 4]. They were able to demonstrate that this composite had strong antimicrobial properties and that the presence of the nanosilver did not affect the osteoinductive properties of PLGA in the presence of bone morphogenic protein-2. In a rat model, nanosilver-PLGA composite grafts demonstrated complete healing without residual bacteria, while control animals had residual bacterial contamination. This study

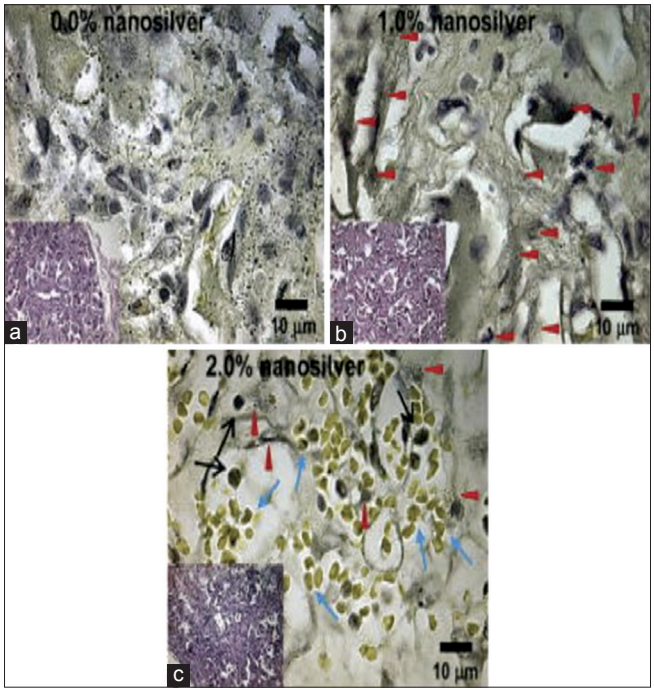

Figure 4: *In vivo* antibacterial activity of nanosilver particle-poly-DL-lactic-co-glycolic acid (PLGA) composite grafts. After 2-week contamination with 108 CFU *Staphylococcus aureus* Mu50, rat femoral segmental defects with implanted grafts were harvested, fixed, decalcified, embedded, sectioned and stained with Taylor modified Brown and Brenn Gram-stain as well as H and E. (a) Compared to serious bacterial infection (black dots) found in control PLGA grafts, (b) 1.0% nanosilver-PLGA composite grafts significantly reduced bacterial survival to colonized collation (red arrows). (c) On the other hand, only limited bacterial colonies (red arrows) were observed in 2.0% nanosilver particle-PLGA composite grafts *in vivo*, and more red blood cells (blue arrows) were found in the grafts instead of phagocytes (black arrows)[35] (used with permission)

Table 1: Nanoscale drug delivery technologies[1] (used with permission)

Drug delivery technology	Materials	Nanostructure forms
Biologic	Lipids Peptides Nucleic acids Polysaccharides Viruses	Vesicles, nanotubes, rings, nanoparticles
Polymeric	Poly (lactic acid) Poly (glycolic acid) Poly (alkylcyanoacrylate) Poly (3-hydroxybutanoic acid) Poly (organophosphazene) Poly (ethylene glycol) Poly (caprolactone) Poly (ethylene oxide) Poly (amidoamine) Poly (L-glutamic acid) Poly (ethyleneimine) Poly (propylene imine)	Vesicles, spheres, nanoparticles, micelles, dendrimers
Silicon based	Silicon Silicon dioxide	Porous, nanoparticles, nanoneedles
Carbon based metallic	Carbon Gold Silver Palladium Platinum	Nanotubes, fullerness, nanoparticles, nanoshells

shows that silver can be used as an antimicrobial agent in grafts while previous studies showed its topical use.

Kose *et al.*[36] examined silica-based mesoporous materials to characterize the features that determine the loading capacity and delivery of medications integrated into these devices. They specifically focused on silica-based mesoporous materials because they can be manufactured with a high degree of homogeneity with a tunable pore size. Their work highlights the importance of pore size, volume, and surface area in both drug adsorption and drug elution from the device.

Nanotechnology has further applications beyond the fabrication of devices and materials on the nanoscale. Nanotechnology also allows us to study and quantify biological processes at this level using various techniques. Differences of regional bone on the nanoscale may allow for improved or novel harvesting techniques in addition to infrequently used donor sites for graft harvest. Through this knowledge, we can improvise the architecture of materials to increase success rate in tissue reconstruction. Leong *et al.*[37] have utilized tissue characterization on the nanoscale to categorize the various tissues present during bone callus formation. Understanding bone healing biology at the nanoscale will help us develop ways to improve this process for reconstructive purposes.

CANCER TREATMENT

Cancer treatment often involves multiple modalities, including surgery, chemotherapy, and radiation therapy. The single most important predictor of patient survival for cancer is complete surgical resection. Nanometer-sized particles such as quantum dots and colloidal gold have novel size-tunable properties that neither discrete molecules nor bulk materials can provide.[38] These particles have the potential for tumor localization, tumor margin detection, identification of important adjacent structures, mapping of sentinel lymph nodes, and detection of residual tumor cells or micrometastases. Contrast agents containing such particles can be accumulated in solid tumors through passive and active targeting mechanisms. In addition, intraoperative imaging can be used to overcome problems with tissue penetration of traditional optical methods [Figure 5]. Such agents include quantum dots, and surface-enhanced Raman scattering nanoparticles. Evaluating the long-term fate and toxicity of nanoparticles remains a challenge. Finally, it is important to design agents that are accumulated in tumors, but are cleared from other organs and tissues.

In conclusion, nanotechnology has a vast array of applications in plastic and reconstructive surgery [Table 2].

Table 2: Summary of nanotechnology applications in plastic and reconstructive surgery

Material	Device	Application
Lipids, peptides, nucleic acids, polysaccharides, viruses	Vesicles, nanotubes, nanoparticles	Drug delivery
Peptides, antibodies	Activatable probes, tumor paints	Tumor targeting, theranostics
Polymers (poly-lactic acid, glycolic acid, caprolactone, propylene, *etc.*,)	Vesicles, spheres, nanoparticles, micelles, dendrimers	Drug delivery
Silicone, silicone dioxide	Nanoparticles, nanoneedles	Drug delivery
Carbon	Nanotubes, fullerenes	Drug delivery
Carbon	Semiconductor quantum dots	Tumor targeting
Gold, silver, palladium, platinum	Nanoparticles, nanoshells	Drug delivery, quantum dots, tumor detection
Gold	Surface-enhanced Raman scattering	Tumor targeting
Poly lactate, poly glycolic acid	Layered scaffolds	Composite skin grafts, chronic wounds, burn wounds, skin diseases
Poly lactate, poly glycolic acid	Contoured scaffolds	Customized fat grafts, breast reconstruction
Poly lactate, poly glycolic acid	Flexible scaffolds, bioreactors	Functional muscle grafts, solid organ transplants
Poly lactate, poly glycolic acid	Hydrogel scaffolds	Moldable cartilage scaffolds, craniofacial and skeletal reconstruction, dental restoration and reconstruction
Poly lactate, poly glycolic acid	Rigid scaffolds, mineralized substrates	Bone grafts
Collagen	Nanofibers	Wound care
Chitosan	Nanofibrils	Wound, burn care
Silver	Nanoparticles	Wound and burn care
Zinc oxide, titanium dioxide	Nanoparticles	Sunscreen
Fullerene, lipids	Vesicles, nanotubes, nanoparticles	Skin care products
Silicone, silicone dioxide	Nanofiber, nanoparticle	Breast implants
Peptides, collagen, PLGA, chitosan	Flexible scaffolds, nanofibers	Nerve conduits
PLGA, titanium, polyethylene	Nanoscale surfacing	Bone prostheses and implants
Hydroxyapatite	Nanoparticles, implant coating	Bone replacement, implant coating
Titanium, carbon	Nanotubes	Bone regeneration scaffolds
Carbon, metal colloids	Nanorobots	Tissue healing, bone replacement, tumor theronostics, anesthesia
Ceramics (nonorgainic, nonmetallic compounds)	Nanocoating, nanofibers, nanocomposites	Bone restoration, reconstruction

PLGA: Poly-DL-lactic-co-glycolic acid

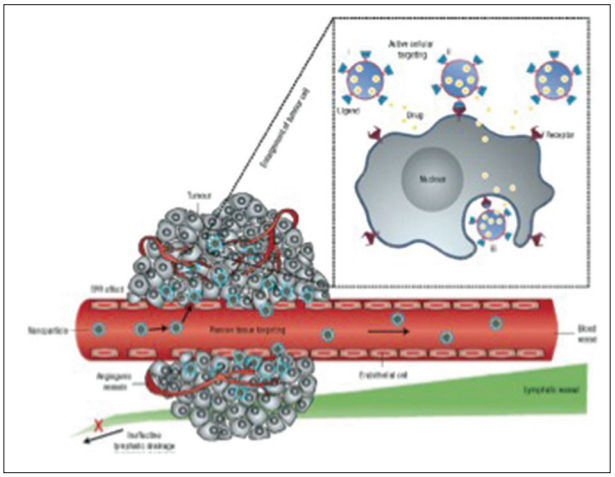

Figure 5: Active versus passive targeting of cancerous tissue. Nanoparticles passively diffuse through the highly permeable endothelial layer of blood vessels in cancer tissue. In addition, decreased lymphatic drainage from solid cancer tissue prevents the nanodrug from returning to the systemic circulation. Active nanodrugs target the tumor tissue with engineered tissue-specific ligands on the surface of the nanodrug[2] (used with permission)

Specifically, wound management, topical skin care, implant and prosthetic design, tissue engineering, and drug delivery systems have each been influenced by advances in nanotechnology. As our understanding of biology on the nanolevel progresses, the use of this technology will increase exponentially. These characteristics make nanotechnology a powerful tool when applied to all aspects of tissue reconstruction.

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Original Article | Plastic and Aesthetic Research

Management of isolated zygomaticomaxillary complex fractures with an individualized approach: a retrospective study

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ABSTRACT

Aim: Fractures of the zygomatico maxillary complex (ZMC) are commonly seen after traumatic injuries to the facial skeleton. The aim of the study was to review the outcome of individualized treatment approach in the management of isolated ZMC fractures. **Methods:** A retrospective analysis of 25 patients was conducted to assess the outcomes of isolated ZMC (iZMC) fracture treatment at a multi specialty hospital (Punjab, India) over a 3–year period. **Results:** Out of the 25 patients reviewed, 4 patients required no surgical intervention and 21 patients underwent surgical reduction via the buccal sulcus approach. An individualized treatment plan was formulated for each patient to decide mini plate fixation at one– two– or three–point with or without orbital rim exploration. Two patients required removal of mini plates from the buttress area on postoperative follow up. **Conclusion:** Our review shows that an individualized treatment approach produces the most favorable results in the management of iZMC fractures.

Key words:

Fixation, fractures, reduction, zygomatic complex

INTRODUCTION

The zygoma is a prominent bone in the facial skeleton and contributes to structural and functional stability of the craniofacial complex. Due to its location, the zygoma and its associated processes are easily fractured in a trauma.[1] As the zygoma is usually associated with adjacent bones, fractures to this region are termed as zygomatico-maxillary complex (ZMC) fractures. Fractures of the ZMC may occur alone known as isolated ZMC (iZMC) fracture or in association with fractures of other bones of the craniofacial complex.[2]

Since the first description of surgical management of a ZMC fracture, many authors have proposed a variety of surgical approaches for reduction of the bone. In addition, after the evolution of bone plating systems, a large number of recommendations have been made for stabilization or fixation of these fracture segments.[2] This study presents a retrospective review of iZMC fractures, managed with an individualized approach.

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METHODS

A retrospective analysis of available records over a 3-year period (from January 2011 to January 2014) was conducted to assess the treatment outcomes of iZMC fractures at a multi-specialty hospital in Punjab, India. Data relevant to the demographic profile of the patients such as age and gender, cause of injury, other associated injuries (noncranio-facial), and surgical treatment provided was collected. Only those patients with iZMC fractures without any other facial bone injury were included in this study. Patients who presented with displaced iZMC fractures causing aesthetic or functional problems that needed surgical intervention underwent standard preoperative investigations. All patients were given peri-operative antimicrobial prophylaxis, adjunct analgesics and supportive medication with restricted soft diet for 2 weeks post-treatment. Patients not requiring surgical

intervention were also given antimicrobial prophylaxis, analgesics and were restricted to a soft diet for a 3-week period. Follow-up period for all patients ranged from 1 month to 3 months. Based on the clinical presentation and treatment modality, the fractures were classified into non-displaced or minimally displaced (low-energy), displaced fractures requiring reduction and fixation (middle-energy), and comminuted fractures involving the buttresses requiring orbital reconstruction (high-energy).[3]

Treatment outcomes were considered successful if there was no obvious facial deformity or asymmetry, no functional limitation and minimal surgical morbidity, such as scar at the site of the incision where made extra-orally. Any alteration in these outcome variables was recorded as either suboptimal treatment outcome or a complication of the procedure.

RESULTS

A total of 25 patients with iZMC fractures were included in the study. The age ranged from 17 years to 56 years, and the sample consisted of 8 females and 17 males. The reporting time after injury varied from 0 day to 6 days and the time to surgical intervention after injury ranged from 1 day to 7 days. Four patients did not require any surgical intervention. Among the patients that required surgical intervention, the following protocols were observed: (1) Reduction of the iZMC fracture segment was performed via buccal sulcus incision (n = 21), (2) reduction of iZMC fracture without bone plate fixation (n = 5), (3) one-point fixation with a bone plate at the zygomatico-maxillary (ZM) buttress (n = 4), (4) two-point fixation with bone plates at the ZM buttress and fronto-zygomatic (FZ) buttress (n = 6), (5) two-point fixation at ZM buttress and infra-orbital margin (IOM) (n = 2) and (6) three-point fixation at ZM buttress, FZ buttress and IOM (n = 4) [Table 1]. The most common cause of injury was road traffic accidents (n = 13). Overall, 17 surgeries were performed under general anesthesia and the remaining under local anesthesia (n = 4). Ten patients were classified as middle-energy group while the remaining were classified into the high-energy (n = 6) and low-energy (n = 6) groups. Surgical access to the FZ buttress and the infra-orbital rim was obtained by standardized lateral eyebrow incision and infra-orbital incision.

The treatment outcome was considered satisfactory in 19 patients that underwent surgical intervention and all patients that did not require surgery. Two patients had complications that required removal of the bone plate from the ZM buttress region. Wound dehiscence was observed on post-operative week 2 in one patient and on post-operative week 3 in another patient. These patients were treated with oral irrigation for local wound care for a total of 5 weeks post-operatively before removal of bone plates, after consolidation of bone healing. Furthermore, 2 other patients developed chronic sinusitis, which was managed by conventional antibiotic protocol, and 3 patients complained of persistent infra-orbital nerve paresthesia until the last follow-up.

Table 1: Distribution of patients by treatment protocol

Treatment protocol (n = 25)	Age	Gender	Cause of injury	Facial side	Type of anesthesia
No surgical intervention (n = 4)	22	Male	IPV*	Left	-
	24	Male	SPORT†	Right	-
	30	Female	RTA‡	Right	-
	42	Male	RTA	Right	-
Surgical reduction only (n = 5)	28	Female	IPV	Left	General
	42	Male	FARM§	Right	Local
	20	Female	RTA	Left	Local
	37	Male	RTA	Left	Local
	33	Female	RTA	Left	General
Reduction+ZMB‖ fixation (n = 5)	56	Male	RTA	Left	General
	27	Male	IPV	Left	Local
	37	Male	FARM	Right	General
	19	Male	RTA	Right	General
	34	Male	IND#	Right	General
Reduction+ZMB+FZB** fixation (n = 5)	31	Female	RTA	Left	General
	26	Female	RTA	Left	General
	17	Male	RTA	Right	General
	19	Male	IPV	Right	General
	19	Female	RTA	Right	General
Reduction+ZMB+IOM†† fixation (n = 2)	48	Male	IND	Left	General
	20	Male	FARM	Right	General
Reduction+ZMB+FZB+ IOM fixation (n = 4)	20	Male	RTA	Left	General
	32	Male	IPV	Left	General
	36	Female	IPV	Left	General
	32	Male	RTA	Left	General

*Inter personal violence, †Sports injury, ‡Road traffic accident, §Farming injury, #Industrial accident, ‖Zygomatico-maxillary buttress, **Fronto-zygomatic buttress, ††Infra-orbtial margin

DISCUSSION

The zygomatic complex is commonly involved in maxillofacial trauma, but iZMC fractures are less common. Fractures of the ZMC most commonly occur due to assault and motor vehicle accidents.[4] The most common cause of iZMC was motor vehicle accidents in our sample. Bogusiak and Arkuszewski[5] found a higher incidence of assaults in their review of ZMC fractures in the Polish population. Ma[6] reported that 20% of patients in their study in China suffered injury due to industrial accidents while in our study only 8% of the sample suffered due to the same reason. The gender distribution of patients in this study is analogous to those reported by many studies, whereby a higher number of males suffered from iZMC fractures than females.[7] Sometimes patients with a facial injury suffer iZMC fractures with minimal displacement of bone and no functional limitation or cosmetic derangement or deformity. Such patients need only longitudinal observation without active surgical intervention. However, displaced fractures require surgical reduction and stabilization.[3,4] In this study, 21 out of 25 patients required surgical intervention. Majority of the patients in this study had middle-energy fractures which are similar to those reported by other authors.[8,9]

Facial edema and peri-orbital swelling may hamper clinical examination and immediate surgical procedure among these patients. Other factors that may delay surgical treatment include: preanesthetic review and investigations,

neurological clearance in patients with possible head injury, or other traumatic injuries of the body.[10] It is acceptable to wait for the peri-orbital edema to resolve since it allows for better palpation and manipulation of the fracture segments intraoperatively.[2] In this study, all these reasons accounted for the delay in surgical treatment after injury ranging from 0 day to 6 days. Various surgical approaches for reduction of iZMC fractures and nonrigid methods of fixation have been proposed even with the advent of mini-plate osteosynthesis.[11] However, recent reviews state that each case must be individualized because fixation requirements differ greatly from one fracture to another.[2]

A detailed review of iZMC fractures was performed by Ellis and Kittidumkerng.[8] They proposed an algorithm to assess the need for fixation of reduced iZMC fractures and concluded that each case must be individualized for type of surgical fixation. As per the suggested algorithm, reduction of the fractured segment is followed by assessment of fracture line alignment and stability of the bone under controlled pressure. Further fixation is done after such evaluation. In the management of our patients with iZMC fractures, we also followed a similar protocol and primarily used exposure of the ZM buttress in order to reduce and assess reduction of the iZMC segment. This approach has also been successfully used for primary reduction by other authors.[4,12] Palpation of orbital margins was also performed to confirm the reduction. Need for surgical fixation was determined by evaluating the stability of the fracture segments when force was applied judiciously. In patients with clinical and radiographic features suggestive of orbital floor involvement, surgical exploration via infra-orbital incision was performed. In all other patients, infra-orbital reduction was visually confirmed with exploration via the maxillary sulcus incision.

It is recommended to use low profile titanium mini-plates for the management of ZMC fractures as they provide improved cosmesis and less discomfort to the patients.[8,9,13] In this study, low-profile titanium mini-plates were used in seven patients while stainless steel plates were used in 14 patients mainly due to financial constraints of the patients. Different protocols have been proposed for the site of fixation and points of fixation of iZMC fragments. These range from no fixation to one-point fixation,[4] two-point fixation[14] and even three-point fixation.[15] In this study, 7 patients underwent two-point fixation, and 4 patients underwent three-point fixation. Decision of number and points of fixation was done as per Ellis and Kittidumkerng's protocol as mentioned above.[8] Exploration of the orbital rim and floor is also a controversial topic in management of ZMC fractures. Most authors recommend that it should be performed only if necessary.[3] In this study, exploration and repair of the orbital floor was performed in only 6 patients when it was indicated on preoperative evaluation or during surgical exposure of the ZM buttress and reduction of the fracture fragments.

Many authors have noted complications in the management of iZMC fractures and they range from malunion, improper reduction, failure of hardware, aesthetic and functional impairment.[4,14,16] In this study, bone plates were removed in two patients due to dehiscence of the oral wounds. No other significant complications were noted. Two patients complained of persistent infra-orbital nerve paresthesia, which is an accepted side effect of ZMC fractures and their treatment. This side effect may or may not be related to actual surgical manipulation.[17]

Our review of patients with iZMC fractures shows that an individualized approach to need for surgical reduction and type of fixation provides optimum outcomes with minimal complications.

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Original Article | Plastic and Aesthetic Research

Comperative analysis of unilateral cleft lip closure using absorbable and nonabsorbable sutures: a randomised clinical study

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ABSTRACT

Aim: Patients with cleft lip usually undergo multiple procedures that require hospitalization resulting in emotional stress to their family members. Young patients often require sedation or general anesthesia (GA) for suture removal on a sensitive area to prevent disruption of the repair. In this study, we compared absorbable and nonabsorbable sutures for primary cleft lip repair. **Methods:** Patients with cleft lip who presented to Smile Train Unit, Child Hospital and Research Institute, Nagpur, India, were randomly assigned to two groups and underwent surgical repair using either Vicryl Rapid suture (Group 1) or Prolene suture (Group 2). Patients were followed up at 1 month, 6 months, and 1 year. Photographs of the patients were obtained at these visits and rated using a validated 100-mm cosmesis visual analogue scale (VAS) by three people (social worker, surgeon, and patient's mother). A VAS score of 15 mm or greater was considered as clinically important difference. **Results:** A total of 60 patients were enrolled in this study, and they were equally divided into two groups. There was no difference in age, race, sex, wound length, number of sutures, and layered repair rates between the groups. The average age of the patient was 3 months. There was no significant difference in the rates of infection which was 6% in this study, wound dehiscence, and hypertrophic scar formation. No significant difference was found in cosmetic outcome in both the mean VAS score of 90.3 in Group 1 and 91.7 in Group 2. **Conclusion:** Absorbable sutures are a viable alternative to nonabsorbable sutures in the repair of primary cleft lip repair. We prefer absorbable sutures because they do not require removal under GA or sedation.

Key words:

Absorbable sutures, primary cleft lip, visual analogue scale

INTRODUCTION

Cleft lip and cleft palate are the most common craniofacial abnormalities seen worldwide. The prevalence of these anomalies ranges from 1:300–1200 live births for cleft lip and 1:2500 for cleft palate.[1] The history of surgical and aesthetic outcomes of cleft lip repair is fascinating. The earliest attempts at cleft lip repair in China involved creating the raw edges and passing straight needles through each side of the wound.[1] The advent of modern suture materials and improved surgical techniques resulted in acceptable aesthetic outcome.[2] These congenital deformities have a significant psychological and socioeconomic effect on both the patient and their family. It often leads to disruption of psychosocial functioning and decreased quality of life.[3]

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Current surgical repair involves anatomical dissection and geometric rearrangement of muscle, mucosa, and skin flaps to achieve an improved functional and cosmetic result.

The type of suture material used in surgery has been a long-standing debate among surgeons. Many surgeons prefer nonabsorbable suture material as it is easier to

tie, unlikely to break prematurely, and induces minimal inflammatory response. Others feel that these issues are not important and prefer absorbable sutures because they do not have to be removed and thus, decreasing patient's anxiety and discomfort.[4]

This study aims to compare the cosmetic outcomes and complications of primary cleft lip repaired with absorbable sutures versus nonabsorbable sutures. It also aims to identify a feasible surgical technique for Indian patients.

METHODS

This study was conducted at the Smile Train Unit of Department of Cleft and Craniofacial Surgery at Child Hospital and Research Institute in Nagpur, India. The children's parents involved in this article agreed to publish their children's facial pictures and signed the form. Patients with cleft lip who presented here from June 2010 to May 2012 were selected for this study with the following inclusion criteria:

1. Patients with unilateral primary cleft lip
2. Patients with 10 weeks age, 10 gm Hb %, and 10 pounds of weight
3. Patients physically fit to undergo general anesthesia (GA).

A total of 60 patients who met the criteria were included in this study, and they were divided into two groups randomly:

- Group 1: (n = 30) Cleft lip repair was performed using absorbable suture (Vicryl Rapid) [Figure 1].
- Group 2: (n = 30) Cleft lip repair was performed using nonabsorbable suture (Prolene) [Figure 2].

All patients underwent routine blood tests, and informed consent was obtained from parents prior to surgery. The study was approved by the institution's Ethical Committee. All patients underwent standard Millard's rotational advancement technique by the same surgeon to repair the cleft lip. Patients were randomized by providing the surgeon with a sealed envelope that stated the type of suture to be used in the procedure before entering the operation theater.

All patients in Group 2 required GA or sedation for removal of sutures on 7th postoperative day.

Patients in both groups were evaluated for postoperative healing, infection rate, disruption of the wound, wound dehiscence, hypertrophic scar formation, and postoperative esthetic outcome. Patients were followed and evaluated at 1 month, 6 months, and 1 year. Patient's photographs were evaluated by three different people (social worker, surgeon and patient's mother) using a validated 100 mm cosmesis visual analogue scale (VAS). In this study, a VAS score of 15 mm or greater was considered as a clinically significant difference.[5]

Descriptive statistical analysis was used to compare demographics and wound characteristics of the study groups. Differences between the groups were analyzed using variance analysis on rank data. VAS with a clinical difference of 15 mm or less was considered clinically significant.

RESULTS

The average age of the patient was 3 months. There was no significant difference in the rates of infection which was 6% in this study, wound dehiscence, hypertrophic scar formation. There was no significant difference in the rates of infection, wound dehiscence, and hypertrophic scar formation. The postoperative wound infection was treated by oral amoxicillin in both groups [Table 1]. No significant difference was found in cosmetic outcome in both the groups with mean VAS of 90.3 in Group 1 and 91.7 in Group 2 [Tables 2–4].

DISCUSSION

Orofacial clefts are the most common head and neck congenital malformations. Cleft lip and cleft palate have significant psychological and socioeconomic effects on patient and affect their quality of life thus, requiring a multidisciplinary approach for management. The complex interplay between genetics and environmental factors plays a significant role in the formation this anomaly.[1]

The primary goals of surgical repair are to restore normal function for speech development and facial aesthetics.

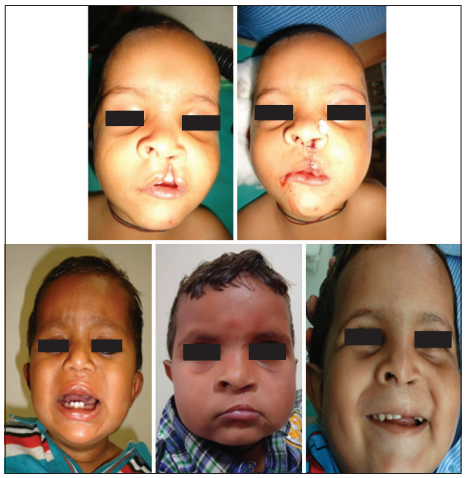

Figure 1: Preoperative and postoperative photo at 1 month, 6 months, and 1 year follow-up for Group 1

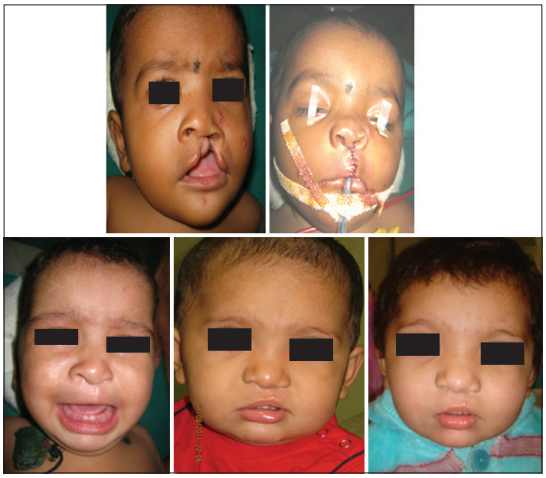

Figure 2: Preoperative and postoperative photo at 1 month, 6 months, and 1 year follow-up for Group 2

Table 1: Complications in both groups

Complications	Number of patients	
	Group 1	Group 2
Infection	2	2
Wound dehiscence and disruption	0	3
Hypertrophic scar	1	1

Table 2: VAS scoring at 1 month

VAS observer	Group 1	Group 2	*P* value
Observer 1 (blinded observer)	87.1–90.6 (mean: 90.3)	88.3–94.0 (mean: 91.7)	<0.05 statistically no significant difference
Observer 2 (surgeon)	89.1–93.6 (mean: 90.3)	88.3–96.0 (mean: 91.7)	<0.05 statistically no significant difference
Observer 3 (patients parent)	78.4–90.1 (mean: 84.2)	86.9–93.4 (mean: 90.1)	<0.05 statistically no significant difference

VAS:Visual analog scale

Table 3: VAS scoring at 6 months

VAS observer	Group 1	Group 2	*P* value
Observer 1 (blinded observer)	88.1–94.6 (mean: 90.3)	89.3–95.0 (mean: 91.7)	<0.05 statistically no significant difference
Observer 2 (surgeon)	88.1–94.6 (mean: 90.3)	89.3–95.0 (mean: 91.7)	<0.05 statistically no significant difference
Observer 3 (patient's parent)	76.4–92.1 (mean: 84.2)	86.9–95.4 (mean: 90.1)	<0.05 statistically no significant difference

VAS:Visual analog scale

Table 4: VAS scoring at 1 year

VAS observer	Group 1	Group 2	*P* value
Observer 1 (blinded observer)	88.1–94.6 (mean: 93.3)	89.3–95.0 (mean: 92.7)	<0.05 statistically no significant difference
Observer 2 (surgeon)	88.1–94.6 (mean: 92.3)	89.3–95.0 (mean: 93.7)	<0.05 statistically no significant difference
Observer 3 (patients parent)	76.4–92.1 (mean: 90.2)	86.9–95.4 (mean: 93.1)	<0.05 statistically no significant difference

VAS:Visual analog scale

Different techniques are employed based on surgeon's expertise and patient's anatomical variations. These patients undergo multiple surgical interventions at a very young age which poses a great challenge for the surgeons.

An understanding of both the physical properties of the material and the resulting tissue response to the material is important for choosing the suture material for the procedure. Sutures that are absorbable may initiate a prominent tissue response and result in suboptimal outcomes including a persistent scar, tenderness, and suture extrusion.[6]

To the best of our knowledge, there are very few studies reported in the literature that studied the cosmetic outcomes and complications after cleft lip using absorbable and nonabsorbable suture materials. Luck *et al.* compared the long-term cosmetic outcomes of absorbable versus nonabsorbable sutures for facial lacerations in children and concluded that fast-absorbing catgut suture is a viable alternative to nonabsorbable suture in the repair of facial lacerations in children.[7,8] Holger *et al.*[9] and Karounis *et al.*[10] compared the use of absorbable and nonabsorbable suture in traumatic pediatric lacerations and found no significant difference in the cosmetic outcome and complication rate.

Al-Abdullah *et al.*[11] performed a systematic review of randomized controlled trials that compared the cosmetic outcomes and complications of traumatic lacerations and found no statistically significant difference between absorbable and nonabsorbable sutures in short-term or long-term cosmetic score, scar hypertrophy, infection rate, wound dehiscence, and wound redness/swelling. This meta-analysis suggests a lack of large, methodologically sound study evaluating the effectiveness of absorbable versus nonabsorbable sutures.

Shinohara *et al.*[12] used monofilament nylon as nonabsorbable material and polyglyconate, polydioxanone as absorbable suture material and found no significant difference in the cosmetic appearance of the scars. These studies support the view that absorbable sutures are preferable to nonabsorbable sutures for primary cleft lip repair.[12,13] In addition, Collin *et al.*[14] published the disadvantages of using nonabsorbable sutures in cleft lip repair. These include a need for additional dressing, and return to the hospital for removal of the sutures under sedation or GA. All of these contribute to distress in the child and potential disruption of the repair.[14]

This study shows no significant difference between absorbable and nonabsorbable suture groups considering the cosmetic outcome in primary cleft lip repair. It has been shown that the VAS is a useful way to document subjective analysis of cosmetic outcome in this study.[5] As patients' assessment of aesthetic outcome is subjective, the use of VAS in this study was appropriate.

A motivational factor to use an absorbable suture for cleft lip patients in this study was to avoid exposure to anesthesia for suture removal after 7 days. Furthermore, this study shows no clinically significant differences in cosmetic appearance between absorbable and nonabsorbable sutures at 1 month, 6 months, and 1 year. The results of this study are consistent with previously published reports.

This study demonstrates that there are no long-term differences in cosmetic outcome and complication rates between absorbable and nonabsorbable sutures in patients with primary unilateral cleft lip. All the patients enrolled in this study were operated by one surgeon using absorbable and nonabsorbable sutures and showed equal results. We recommend the use of absorbable suture for the closure of primary cleft lip as this technique saves one additional exposure of the child for the GA for suture removal.

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Original Article Plastic and Aesthetic Research

Perceived aesthetic impact of malocclusion in 16–24 year-old adults in the rural areas of India

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ABSTRACT

Aim: The purpose of this study was to assess the self-perception of patients toward their dental appearance using the aesthetic component (AC) of index of orthodontic treatment need (IOTN) index and whether age and gender had any influence on it. **Methods:** A cross-sectional study was carried out to assess the perceived esthetic impact of malocclusion in 16–24 year-old subjects selected from the rural population of Faridabad, Haryana, India. The sample was divided into two groups, older adolescents and younger adults, and the AC of the IOTN index was applied. **Results:** The results showed that most subjects scored themselves as having an attractive dentition with no need for orthodontic treatment (60.91%). Gender-wise differences were not found to be statistically significant in relation to the perceived needs ($P = 0.095$), whereas age-wise differences were found to be statistically significant in relation to the perceived needs ($P < 0.001$). **Conclusion:** While the age seemed to have an impact on the perceived esthetic impact of malocclusion, the gender did not seemingly influence this self-perception.

Key words:

Esthetic component, index of orthodontic treatment need, self-perception

INTRODUCTION

Human self-esteem is influenced by acceptable physical appearance, including the condition of the teeth. Further, well-aligned teeth and a pleasing smile reflect positively at all social levels, while irregular or protruding teeth reflect negatively. The major desire for orthodontic treatment is usually related to aesthetics, and to look attractive for self-esteem. Altered dentofacial esthetics and malocclusion less frequently compromise oral function but can influence a person's self-esteem, emotional development, and social integration worldwide.[1-3]

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Although dissatisfaction with dental appearance is broadly related to occlusal irregularities,[4,5] there are differences in the recognition and evaluation of the dental features.[6,7] Studies revealed that people seem aware of their malocclusion trait, but they do not perceive a need for treatment to the same extent as a dentist or an orthodontics.[8,9]

Facial features may be viewed differently in different races and what is considered as pleasing in one race might not be so in another race.[10] The perception of beauty not only is an individual preference, but also might have cultural and ethnic biases.[11-13] Cultural, social and psychological factors and personal perceptions influence what an individual might consider to be physically attractive. It has been seen that physical attractiveness plays a major role in social interaction and influences the impression of an individual's social skill.[14,15]

It has also been suggested that age, gender, and socio-economic background are factors playing a role in the self-perception of dental appearance.[16,17] Dentofacial esthetics is an important motivational factor to seek orthodontic treatment, therefore, an improvement in appearance should be an essential treatment goal.

Personal esthetic perceptions of the dentofacial complex and the associated psychosocial need are directly reflected in perceived need for orthodontic care. Treatment is, therefore, often influenced more by demand rather than by need.[18] In the past, orthodontic treatment need was evaluated from a strictly professional viewpoint (normative need), but several studies have stated that self-perceived dental appearance is also important in the decision to seek orthodontic treatment.[19-21]

Although dissatisfaction with dental appearance is broadly related to the severity of the occlusal irregularities, there are differences in the recognition and evaluation of the dental features.[14,22] For this reason, professional opinions regarding evaluation of facial esthetics may not coincide with the perceptions and expectations of patients.[23,24]

The aims of present study were to:

- Assess self-perceived dental appearance among rural Indian population using aesthetic component (AC) of the index of orthodontic treatment need (IOTN) index
- Determine if gender and age influence patient self-perception.

METHODS

Ethical considerations

The study protocol was approved by Institutional Ethical review committee of Sudha Rustagi College of Dental Sciences and Research, Faridabad. Voluntary consent was obtained from each participant before the study.

Study population

A cross-sectional study was carried out to assess the perceived aesthetic impact of malocclusion in 16–24 year-old subjects selected from the rural population of Faridabad, Haryana, India. A pilot study was conducted to assess the methodology and to estimate the sample size. A sample size of 990 was calculated to be satisfactory. Older adolescents and younger adults were selected since they are at an age when facial aesthetics including those of teeth are of importance. A stratified two-stage cluster sampling technique with villages as the primary sampling unit was utilized. All subjects between 16 and 24 years old, willing to participate and to give their consent, were selected. Subjects with presence of mixed dentition, any structural abnormality in the teeth concerned and those undergoing or with a history of any orthodontic treatment were excluded. The study was conducted from July to November 2013.

The perceived orthodontic treatment need was assessed using the AC of IOTN.[25]

All readings were recorded on a specially prepared form.

Calibration of examiner

A single calibrated examiner performed all measurements. The intra-examiner test was performed in the measurement of the IOTN-AC. Reliable results were seen with $\kappa = 0.82$.

INDEX OF ORTHODONTIC TREATMENT NEED–AESTHETIC COMPONENT[26]

Each subject was shown 10 colored photographs depicted in the AC of IOTN [Figure 1] and was asked to choose the one with the closest resemblance to their actual smile. This was done on memory recall basis, and the subjects were not allowed to check their smile in the mirror. The score of the chosen photograph was used to determine the perceived need for orthodontic treatment. A definite need of treatment was represented by photos 8–10, while borderline and no need for orthodontic treatment were represented by photos by photos 5–7 and 1–4, respectively.

Statistical analysis

The data was analyzed using the SPSS software (version 11.5) (SPSS Inc., Chicago, IL, USA). Bivariate analyses using the Chi-square test (χ^2) at 5% significance level were performed to test the influence of age and gender on perceived orthodontic treatment needs.

RESULTS

Table 1 shows the age-wise and gender-wise distribution of study population. A total of 528 males (53.33%) and 462 females (46.67%) were selected. Of these, 210 males (49.65%) and 213 females (50.45%) were in the age group of 16–18 years, whereas 318 males (56.08%) and 249 females (43.92%) were in the age group of 18 years old and above.

Table 2 represents the distribution of the individual scores according to the IOTN-AC index. Maximum number

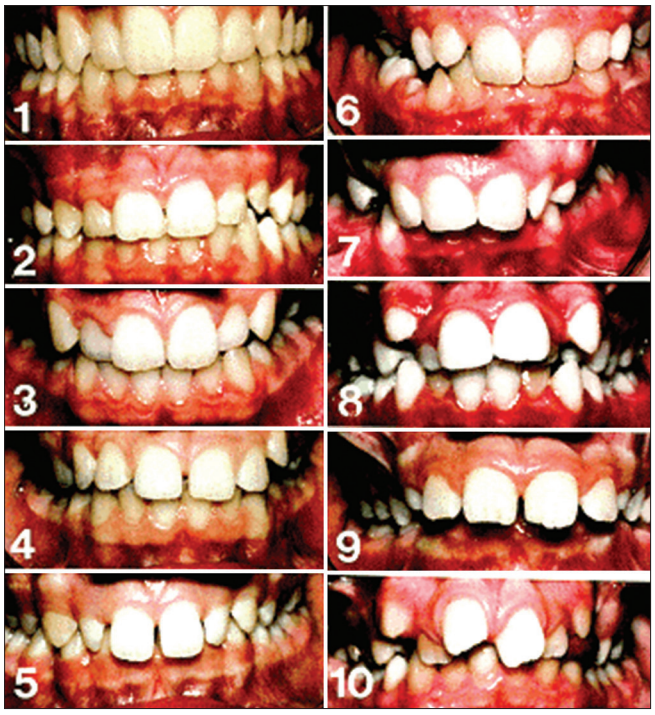

Figure 1: Photographs depicted in the esthetic component of the index of orthodontic treatment need (IOTN)

of subjects (n = 165) reported a score of 3, followed by score 1 (n = 156). Score 10 was reported by least subjects (n = 24).

When the IOTN-AC scores are divided into three categories based on the need for orthodontic treatment, maximum subjects were found to report scores of 1–4 (60.9%), followed by scores 5–7 (27%) and scores 8–10 (12.1%).

Table 3 represents the gender-wise differences according to the IOTN-AC scores. The differences were not found to be statistically significant in relation to the perceived needs (P = 0.095).

Table 4 summarizes the perceived orthodontic need IOTN-AC scores according to age groups. The age wise differences were found to be statistically significant in relation to the perceived needs (P < 0.001). Significantly greater proportion of the older adolescents (60%) showed perceived orthodontic treatment.

DISCUSSION

The sample analyzed composed of older adolescents and younger adults ranging in age between 16 and 24 years old. People of this age range tend to be more socially aware and conscious about their appearance than a comparatively younger school going population. Further, young people tend to show less physiological wear, wasting diseases, and periodontal diseases in their teeth which if present might affect the accuracy of the method.

In this study, it appeared that the gender of the patients did not influence the perception of their own dentition. The female and male subjects of both age groups had a tendency to score their dental appearance more favorably and allocate themselves toward the more attractive end of the scale.

When self-perceived orthodontic treatment need was evaluated by means of the AC of IOTN, only 12.12% of the subjects self-scored as presenting a definite need for orthodontic treatment. Consistent to some other studies, no statistically significant differences were observed in perceived orthodontic needs according to gender.[15,18] However, these findings were not consistent to those of other studies.[24,27-30] This is probably because subjects were from a rural area and had a general lack of awareness of the presence of malocclusion. The race, level of expectations (probably affected by their culture), and socioeconomic status of each population might also contribute to this.

Statistically significant differences were found for perceived needs according to age. Significantly greater part of the older adolescents (60%) self-scored as presenting a definite orthodontic treatment need compared to younger adults. Similar findings were observed in a study conducted by Alhaija *et al.*[30] where significant differences were found when age groups were compared for the perceived need for treatment. However, this is in contradiction with some other studies[16,24,28,29] where significant differences were not seen. Adolescence is the time when concern over appearance and facial attractiveness is developing, which translates to an increased awareness of body image. Teenagers, in particular have been found to attach great importance to an attractive dental appearance. The differences between studies may result from ethnic variation and the age range of the adolescents in this present study. Ethnicity does have an effect on self-perceived need due to differences in acceptable facial appearances and what is deemed as acceptable occlusion by different ethnic groups. It would thus be useful to validate the IOTN in different ethnic groups.

Table 1: Age-wise and gender wise distribution of study population

	Male		Female		Total	
	n	%	*n*	%	*n*	%
16-18 years	210	49.65	213	50.45	423	100
>18 years	318	56.08	249	43.82	567	100
Total	528	53.33	462	46.67	990	100

Table 2: Distribution of the IOTN-AC scores in the study population

IOTN score	*n*	Percentage
1	156	15.8
2	150	15.2
3	165	16.7
4	132	13.3
5	120	12.1
6	93	9.4
7	54	5.5
8	60	6.1
9	36	3.6
10	24	2.4
Total	990	100.0

IOTN: Index of orthodontic treatment need, AC: Aesthetic component

Table 3: Gender wise distribution of the IOTN-AC scores

Gender	Male		Female		Total	
	n	%	*n*	%	*n*	%
Score 1–4	315	52.24	288	47.76	603	100
Score 5–7	156	58.42	111	41.58	267	100
Score 8–10	57	47.50	63	52.50	120	100
Total	528	53.33	462	46.67	990	100

P = 0.095. IOTN: Index of orthodontic treatment need, AC: Aesthetic component

Table 4: Age-wise distribution of the IOTN-AC scores

Age	16–18 years		>18 years		Total	
	n	%	*n*	%	*n*	%
Score 1–4	234	38.81	389	61.19	603	100
Score 5–7	117	43.82	150	56.18	267	100
Score 8–10	72	60	48	40	120	100
Total	423	42.73	567	57.27	990	100

P < 0.001. IOTN: Index of orthodontic treatment need, AC: Aesthetic component

Disease does not always negatively affect subjective perceptions of well-being, and even when it does, its impact depends on expectations, preferences, material, social and psychological resources and more importantly, socially and culturally derived values.[9] What is considered aesthetically pleasing in one culture will often not match that which is thought of as aesthetically pleasing in another. Thus, the lack of perceived need in the population evaluated might be because this rural population probably does not have the same notions of beauty as their British peers, where the index was developed. The level of education may also be a factor influencing perceived treatment need and demand.[18]

It is possible that subjects replied defensively and subconsciously trying to allocate themselves to the attractive side in order to avoid treatment. Alternatively since each picture shows the dentition only from the front, it is possible that the patients could not differentiate between some features of malocclusion as increased overjet and deep bite and subsequently they could not score. It might be that patients could not estimate the malocclusion and subsequently could not classify the teeth in any of these grades. Further, it is likely that the IOTN is not sensitive enough to account for all types of malocclusion as Class III, open bite, cross bite and scissors bite.[29]

Epidemiological analysis of the prevalence of various oral health problems has evidenced an enormous lack of data related to malocclusion. This is due to the accumulated treatment needs of the problems of caries and periodontal disease, an issue that is strongly correlated to the current healthcare model as well as to the inequality in access to healthcare services. Thus, those responsible for planning orthodontic treatment in both the public and private sector should concern themselves with the desires of the community as well as with the large body of evidence that supports the importance of facial characteristics in the lives of individuals.

In summary, further studies are required to improve our understanding of self-perceived need for orthodontic treatment, especially in developing countries where different factors than those reported in North American and European countries could be influencing the demand and delivery of orthodontic care. It may even be necessary to use more than one index in an epidemiological study to gather all the required information.

The conclusions derived from this study are of considerable importance for Indian policy makers in their work with planning and implementing public oral health strategies for the rural population of this age group.

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Original Article | Plastic and Aesthetic Research

Hyaluronic acid in calves defects correction

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ABSTRACT

Aim: Since the advent of fillers, new techniques are continuously developed for different uses. In this study, we evaluated the use of hyaluronic acid for calf augmentation. **Methods:** A total of 42 patients were enrolled in this study. All of them underwent augmentation procedure in our centers under local anesthesia, the operations were completed within 1 h with a prompt correction of the defects. **Results:** Thirty-nine patients were satisfied with the treatment (93%), while three had complications, local infection, and lumps, that were resolved quickly (7%). **Conclusion:** Macrofillers can be injected into the calf to correct any defects. The advantages include short duration of treatment; the procedure performed under local anesthesia and limited side-effects that resolve promptly. This study suggests the use of biocompatible macrofillers for the augmentation of not only calves, but also for augmentation of breast and buttocks.

Key words:
Acid, augmentation, calves, hyaluronic, remodeling

INTRODUCTION

The use of fillers to improve cosmesis started in 1899 when silicone was used to improve the esthetic outcome of orchiectomy. Since then, numerous implants and filler substances have been used to reshape body defects. Permanent liquids and gels composed of silicone, paraffin, polyalkylimide, and polyacrylamide hydrogel have been used as fillers.[1,2] However, the incidence of chronic inflammatory reaction, palpable nodule formation, granuloma formation, and migration decreased the use of these materials.[1,3-5] This led to the advent of new materials that are biocompatible and nonpermanent. In 2009, a new formulation of stabilized hyaluronic acid (HA)-based gel (NASHA-based gel; Q-Med AB, Uppsala, Sweden), was generated for restoring volume and contouring body surfaces.[3,6] Since body augmentation requires a large volume of filler this formulation has increased viscosity (i.e. the thicker gel) providing high resistance to deformation. HA gel augments body tissue simply by occupying space.

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Calf augmentation with HA is often performed in patients who describe their calves as excessively tight (in extreme cases they may be described as "stork legs"). These patients often have insufficient muscular mass, fat atrophy, illness such as clubfoot, spastic paralysis, spina bifida, or poliomyelitis.

METHODS

Duration of procedures ranged from 30 min to 60 min.

Materials used include:

- 20–120 mL of HA Blade number 15
- Sharp scissors
- Hudson forceps
- Small Kleimer
- 2.5 × 150 mm, 12G, filling cannula
- 3 × 10 mL syringes
- 1 × 100 mL bottle of physiologic solution

Anesthetic solution was prepared by mixing 6.4 mL of physiologic solution and 3.6 mL of mepivacaine (20 mg/mL) with adrenaline (1/100,000).

A total of 42 cases of calf augmentations were performed at our office operating rooms under local anesthesia. The study was approved by review board of University of Turin.

A photograph of the calf was taken before the treatment. After the first passage, it is necessary a pretreatment evaluation with the design on the skin of the interested area and this is an important passage because it's where anesthesia has got to be performed before the intervention. Later, 2.5 mL of preprepared local anesthesia mixture is injected into the subcutaneous space maintaining 2 cm apart between the injection points.

An 11 blade is used to make a small skin incision for insertion of cannula. Scissors are used to create a tunnel through the incision. Then, the cannula is inserted into the tunnel, and ultrasound guidance is used to navigate dissection through the subcutaneous space to reach the treatment area. The HA is delivered to the subcutaneous space through the cannula in a retrograde technique. Another tunnel is created through the same incision by changing the angle of the cannula [Figure 1]. This procedure is repeated until HA is uniformly filled in the desired location. A total amount of 30 mL of HA is delivered to each calf. Then, massage is performed and in the skin incision was closed with up with Vicryl 5–0 sutures [Figure 2]. Repeated treatments should be needed.

After the treatments, the patient had been asked to judge the results using a subjective evaluation scale in which they were asked to choose their grade of satisfaction between: very satisfied, satisfied, moderately satisfied, and unsatisfied.

Anatomical pearls

The great saphenous vein or the long saphenous vein is a large superficial vein that runs along medial side of leg and thigh. The small saphenous vein is also a large vein that runs subcutaneously along posterior leg. Accidental injury to saphenous veins leads to noticeable hematomas and blood infarction of the implant with possible infection.

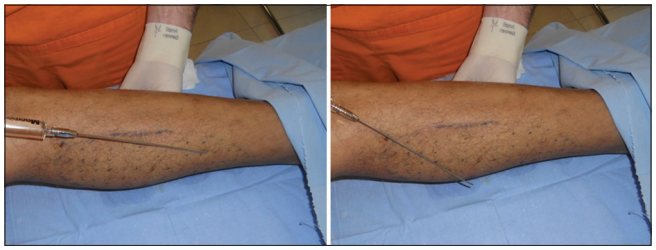

Figure 1: The 15 cm long cannula is used to inject hyaluronic acid subcutaneously into the calf

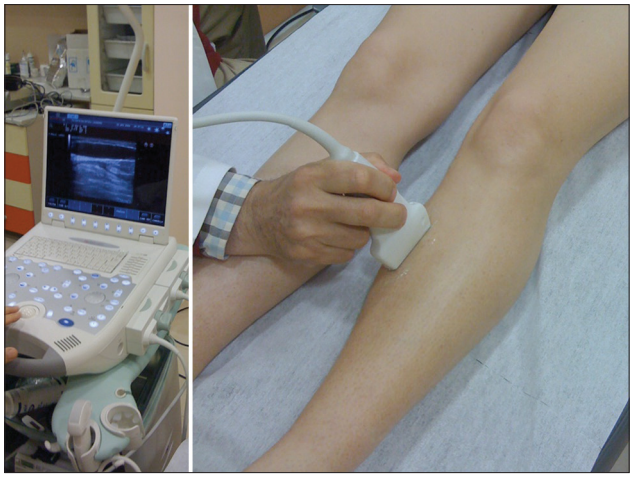

Figure 3: Ultrasound examination of tissues and vessels

Technical pearls [Figures 3–5]

It is important to identify the saphenous vein using visual, tactile, and echographic examination to design the course of saphenous vein prior to injection.

In the subcutaneous space, the cannula should be directed superficial to superficial muscularis fascia of gastrocnemius in order to have a better management of the distribution of the filler and to avoid the rapid reabsorption of the material. The point and area of injection must be decided according to the defect that has got to be corrected.

Complications

Hyaluronic acid does not have tissue specificity and has minimal risk for allergic reactions when injected. However, the degree of complications increases when large volumes are injected. The complications are divided as early or late:

- Early complications are resolved in days to weeks after injection and include overcorrection, local infection, skin necrosis, herpes reactivation, discoloration, and

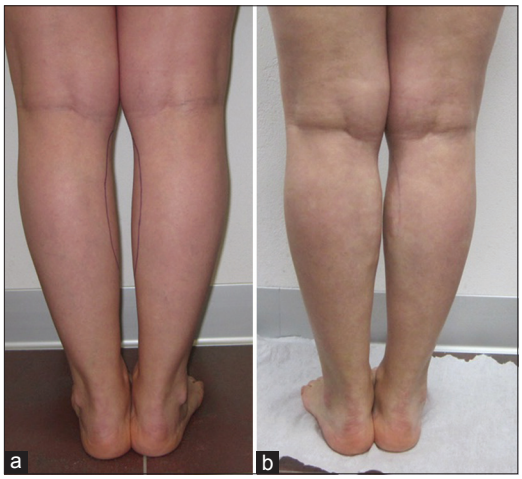

Figure 2: (a) Before, (b) after treatment

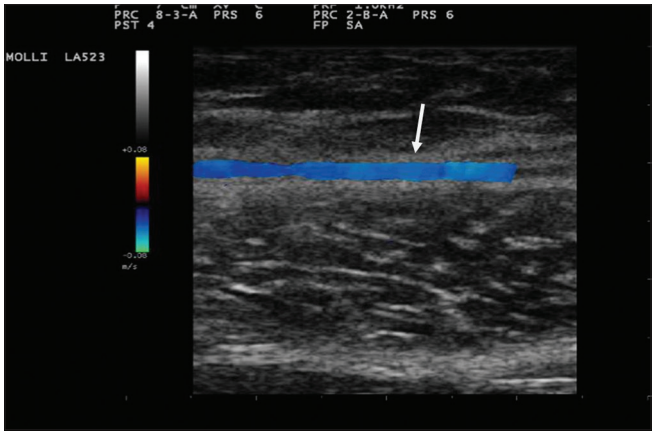

Figure 4: Ultrasound picture of the vein

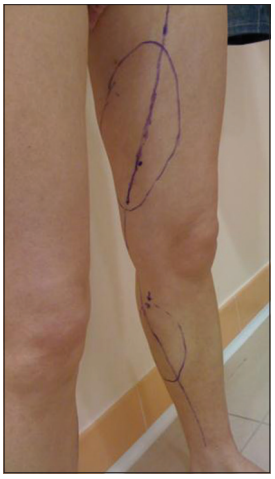

Figure 5: Outline of saphenous vein anatomy

persistent local symptoms (erythema, edema, induration, pruritus, and hyperpigmentation)
- Late complications include: infection, filler migration, delayed hypersensitivity reaction, foreign-body granuloma, and scarring.[7-10]

A case report in 2012 showed cellulitis of calf 5 days after injection of 150 mL of HA subcutaneously. This patient was treated with empiric antibiotic therapy (amoxicillin and clavulanic acid 1 g twice a day) with improvement of symptoms within 72 h.[11] This case shows that a serious complication can be resolved easily.

In this study, complications were seen in three cases. One patient developed local infection that resolved with oral antibiotics (amoxicillin and clavulanic acid).

Furthermore, we had two cases of lumps treated injecting hyaluronidase locally with consequent total reabsorption of the filler and correction of the defects.

Contraindications

Avoid injection of fillers in areas with poor perfusion or in areas of infection or inflammation.

Do not use macrofillers in areas that were previously treated with liquid silicone or other permanent fillers because it could lead to inflammation or infection of the implants.

It is contraindicated to use filler if patient has hypersensitivity to any components of the filler.

DISCUSSION

In patients who consider their calves as excessively tight, calf augmentation can be attained using HA fillers.

Overall, this study shows that patients have satisfactory results with this procedure. About 52% of patients were very satisfied, 24% of patients were satisfied, 10% of patients were moderately satisfied, and 14% were unsatisfied.

Furthermore, we have to underline that 8 patients (19%) had no need to repeat the treatment, 34 patients (81%) repeated the treatment once, and 23 patients (54.7%) repeated the treatment 2 times or more.

Fortunately only three complications occurred: one local infection resolved administering antibiotic and two lumps treated injecting hyaluronidase. In our study, we had no serious side effects unlike what happened to Chaput *et al.* that described a severe case of cellulitis.[11]

Our experience conducted over 42 cases suggests that the use of macrofillers, if compared with major surgery like the insertion of the silicon prosthesis, offers a better balance between efficacy and safety for good aesthetic results, because this technique is less invasive and also because of the low rate of side effects. These are the reasons why this technique should be taken in consideration especially in the case of remodeling and/or small augmentation of calves.

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Original Article | Plastic and Aesthetic Research

Efficacy of autologous platelet-rich plasma in the treatment of chronic nonhealing leg ulcers

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ABSTRACT

Aim: The aim was to evaluate the efficacy of platelet-rich plasma (PRP) in the treatment of chronic nonhealing ulcers. **Methods:** A nonrandomized, uncontrolled study was performed on 24 patients with 33 nonhealing ulcers of various etiologies. All patients were treated with PRP at weekly intervals for a maximum of 6 treatments. At the end of the 6-week period, reduction in size of the ulcers (area and volume) was assessed. **Results:** The mean age of the patients was 42.5 years (standard deviation [SD] 12.48). Of 33 ulcers, there were 19 venous ulcers, 7 traumatic ulcers, 2 ulcers secondary to pyoderma gangrenosum, 2 diabetic ulcers, 2 trophic ulcers, and 1 vasculitic ulcer. The mean duration of healing of the ulcers was 5.6 weeks (SD 3.23). The mean percentage of reduction in area and volume of the ulcers was 91.7% (SD 18.4%) and 95% (SD 14%), respectively. About 100% resolution in the area was seen in 25 (76%) of the ulcers and 100% reduction in volume was seen in 24 (73%) of the ulcers at the end of the 6th treatment. **Conclusion:** Conventional therapies do not provide satisfactory healing for chronic nonhealing ulcers as they are not able to provide the necessary growth factors (GFs) (platelet-derived GF, epidermal GF, vascular endothelial GF, *etc.*) which are essential for the healing process. PRP is a safe, affordable, biocompatible, and simple office-based procedure for the treatment of nonhealing ulcers.

Key words:

Leg ulcers, platelet-derived growth factor, platelet rich plasma

INTRODUCTION

Chronic nonhealing leg ulcer is defined as the "loss of skin and subcutaneous tissue on the leg or foot, which takes more than 6 weeks to heal". Chronic ulceration of the lower leg, including the foot, is a frequent condition, causing pain, social discomfort, and generating considerable costs.[1] The prevalence of leg ulcers is well documented to be vary between 0.18% and 1%.[2] The three major causes of lower extremity ulcers are venous, arterial, and neuropathic.

Chronic nonhealing ulcers lack the necessary growth factors (GFs) and hence do not heal well. Conventional recombinant GF products, including becaplermin (recombinant platelet-derived GF) have been approved by the Food and Drug Administration for the treatment of chronic wounds. However, the medication is in a liquid form, and, therefore, easily dissipates following wound application. In addition, it is expensive and is unaffordable in developing countries such as India.[3]

Platelet-rich plasma (PRP) enhances wound healing through promotion of the healing process by the presence

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of which are important in modulating mesenchymal cell recruitment, proliferation, and extracellular matrix synthesis during the healing process.[4] Autologous PRP is a safe, easy, and cost-effective method with good results in the management of chronic nonhealing ulcers. PRP has been a breakthrough in the stimulation and acceleration of bone and soft tissue healing. It represents a relatively new biotechnology that is part of the growing interest in tissue engineering and cellular therapy today.

METHODS

The aim of this study was to evaluate the efficacy of PRP in the management of chronic leg ulcers. This was a nonrandomized, uncontrolled study conducted from January 2011 to September 2012 at a tertiary hospital in Bengaluru. Ethical clearance was obtained before beginning of the study from Ethical Clearance Committee. A total of 24 patients with 33 nonhealing ulcers of various etiologies were included in this study. Inclusion criteria were ulcers of more than 6 weeks duration. Patients with a bleeding disorder, uncontrolled sugar levels and ulcers with active infection and saphenofemoral junction incompetency were excluded. Detailed history including the name, age, sex, address, contact number, occupation, and history of medication was noted. Patients were thoroughly examined and ulcer size (length, breadth, and width) was measured by the "clock-face" method described by Sussman using a cotton tip applicator and ruler.

Under aseptic precautions, 20 mL of venous blood was drawn and added to a test tube containing acid citrate dextrose in a ratio of 9:1 (blood: acid citrate dextrose). It was centrifuged at 5000 rpm for 15 min to separate the red blood cells from platelet and plasma.[5] The lower part of the plasma was then collected and centrifuged again at 2000 rpm for 5 min. The bottom layer of about 1.5 mL was harvested, and 10% calcium chloride was added to activate PRP (0.3 mL for 1 mL of PRP).[6] Activated PRP was applied onto the wound after proper surgical debridement and was dressed in a nonabsorbent dressing. After activating PRP with calcium chloride, it should be applied immediately onto the wound as 70% of GFs are released within ten minutes and 90% within one hour. Hence, we should activate PRP just before use, rather than in advance, to avoid losing GFs. Because PRP can synthesize additional amounts of GF for about 8 days until depletion, PRP application was repeated weekly. After 1 week, the dressing was removed with normal saline and assessed for improvement. The procedure was repeated once weekly for 6 weeks. Wound area was calculated using the formula for an ellipse: length × width × 0.7854 (an ellipse is closer to a wound shape than a square or rectangle that would be described by simple length × width). The use of an ellipse for calculating wound measurement has been used in randomized controlled trials in wound healing literature.[7] Volume was calculated using the formula (length × width × 0.7854) × depth.

The treatment outcome was defined as a percentage improvement in area and volume of the ulcer.

RESULTS

Twenty-four patients with 33 nonhealing ulcers of various etiologies were treated with PRP at weekly intervals for a maximum of 6 treatments. The mean age of the patients was 42.5 years (standard deviation [SD] 12.48) [Table 1]. Of 33 ulcers, there were 19 (57.75%) venous ulcers, 7 (21.2%) traumatic ulcers, 2 (6%) pyoderma gangrenosum ulcers, 2 (6%) diabetic ulcers, 2 (6%) trophic ulcers, and 1 (3%) vasculitic ulcer [Figure 1]. The duration of the ulcers ranged from 2 months to 1 year with a mean of 4.75 months [Table 2]. The mean duration of healing of the ulcers was 5.6 weeks (SD 3.23). The baseline mean area and volume of the ulcer was 10.93 cm^2 (SD 7.791) and 5.1 cm^3 (SD 4.3). The final mean area and volume of the ulcer at the end of 6 weeks were 1.3 cm^2 (SD 2.72) and 0.4 cm^3 (SD 1.27). The declining trend in the reduction of sum of the area and volume of the ulcers is shown [Figures 2 and 3]. The mean percentage of improvement in area and volume of the ulcers was 91.7% (SD 18.4%) and 95% (SD 14%), respectively [Tables 3 and 4]. The confidence interval is been shown in Table 5. *P* value was set at less than 0.05 and hence the results were found to be significant. About 100% improvement in the area was seen in 25 (76%) of the ulcers and 100% improvement in volume was seen in 24 (73%) of the ulcers at the end of the 6th treatment [Figures 4 and 5]. There were no side effects noted. The before and after PRP therapy photographs are shown [Figures 6–11]. We also noted that there was a

Table 1: Age distribution

Age group (years)	Number of patients	Percentage
<20	0	0
21–30	7	29
31–40	3	12.5
41–50	5	21
51–60	9	37.5
>60	0	0
Total	24	100

Table 2: Duration of the ulcer

Duration of the ulcer (months)	Number of ulcers	Percentage
<3	6	18
3–6	21	64
6–9	3	9
9–12	3	9
Total	33	100

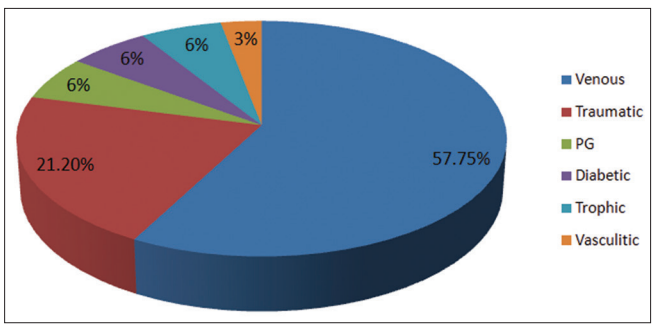

Figure 1: Various causes of ulcer. PG: pyoderma gangrenosum

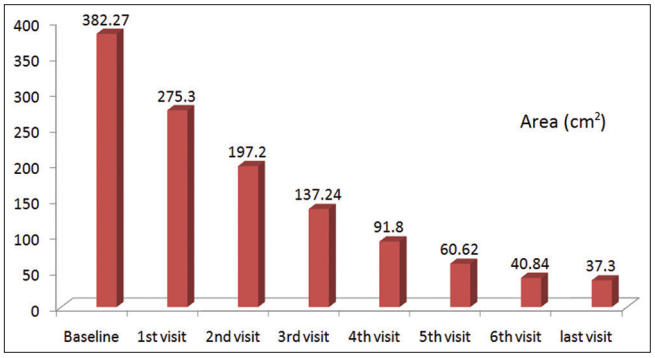

Figure 2: The sum of the mean area of the ulcers from baseline to last visit

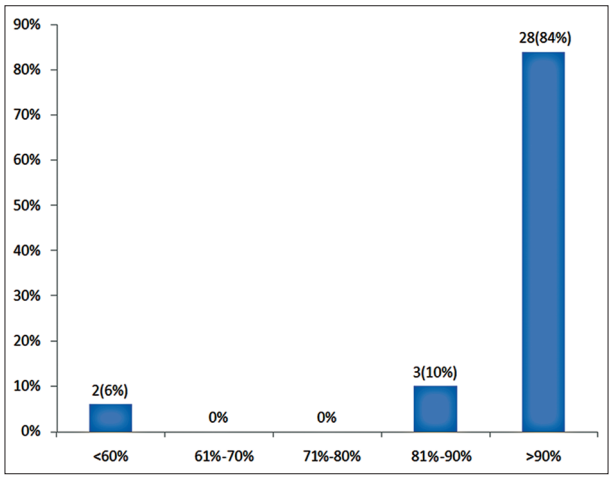

Figure 4: Percentage improvement in area of the ulcers

Table 3: Improvement of area of the ulcer in percentage at the end of 6th sitting

Percentage improvement in area at the end of 6th sitting	Number of ulcers	Percentage
<60	3	10
61–70	0	0
71–80	4	12
81–90	0	0
91–100	26	78

Table 4: Improvement of volume in percentage at the end of 6th sitting

Percentage improvement in volume at the end of 6th sitting	Number of ulcers	Percentage
<60	2	6
61–70	0	0
71–80	0	0
81–90	3	10
91–100	28	84

reduction in pain and discharge within 1 week due to the anti-inflammatory property of PRP, which contains leukocytes. There were no side effects reported.

DISCUSSION

Chronic wounds come with cost and morbidity for patients and society. These wounds are found in all types

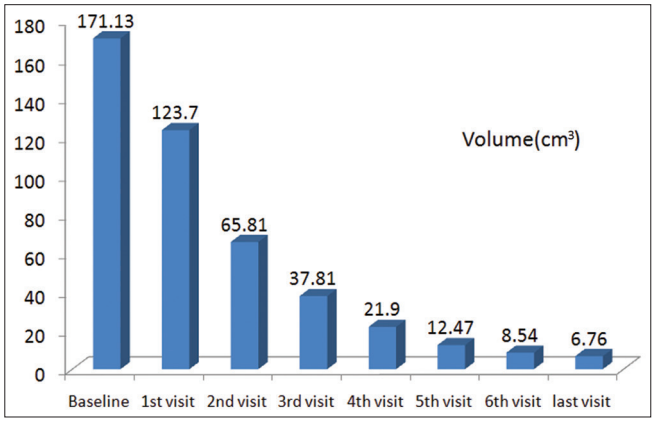

Figure 3: The sum of the mean volume of ulcers from baseline to last visit

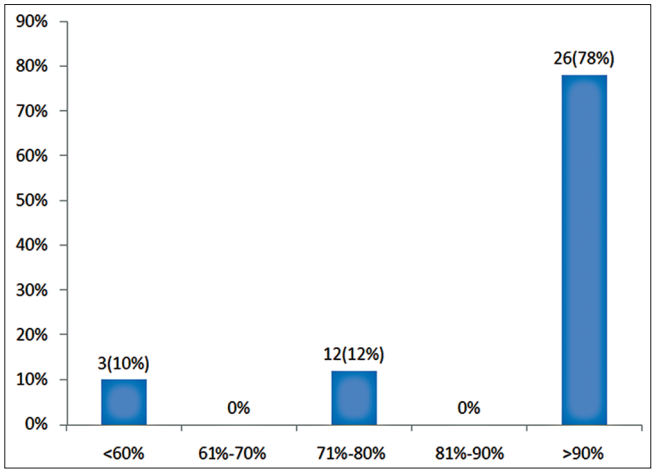

Figure 5: Percentage improvement in volume of the ulcers

of healthcare settings and are a challenge for healthcare providers. Chronic nonhealing ulcers are often difficult to treat. Conventional therapies such as dressings, surgical debridement, and even skin grafting cannot provide satisfactory healing since these treatments are not able to provide the necessary GFs to modulate the healing process.[8]

In 1986, Knighton *et al*.[9] showed that the accelerated epithelialization of granulation tissue leading to complete repair of chronic nonhealing ulcers is attainable by the use of autologous platelet factors. This was the first clinical demonstration that locally acting factors derived from autologous blood promote healing of chronic cutaneous ulcers. In this study, the time to 100% healing after initiation of platelet-derived wound-healing factors (PDWHF) was 7.5 ± 6.5 weeks. There was a direct correlation between the initiation of PDWHF therapy and 100% healing. The age of the patients and the location of the ulcers had no statistically significant effect on PDWHF-stimulated wound repair.

Platelet-rich plasma enhances wound healing by promoting the healing process secondary to its GFs. These include platelet-derived GF ($\alpha\alpha$, $\beta\beta$, and $\alpha\beta$), fibroblast GF, vascular endothelial GF, epidermal GF, insulin-like GF, and transforming GF. These GFs stimulate

Table 5: CI and *P* value which suggests that results were significant

	Baseline	1st visit	2nd visit	3rd visit	4th visit	5th visit	6th visit	Final visit
Area	10.98	8.42	6.24	4.57	3.06	2.02	1.36	1.13
P value		0.1706	0.0125	0.0004	<0.0001	<0.0001	<0.0001	<0.0001
CI		−1.11–6.14	1.05–8.33	2.95–9.76	4.71–11.03	5.88–11.94	6.59–12.55	6.93–12.76
Volume	5.19	3.53	2.19	1.26	0.73	0.42	0.23	0.39
P value		0.1160	0.0020	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
CI		−0.42–3.74	1.14–4.84	2.23–5.62	2.83–6.08	3.18–6.36	3.38–6.54	3.21–6.38

CI: Confidence interval

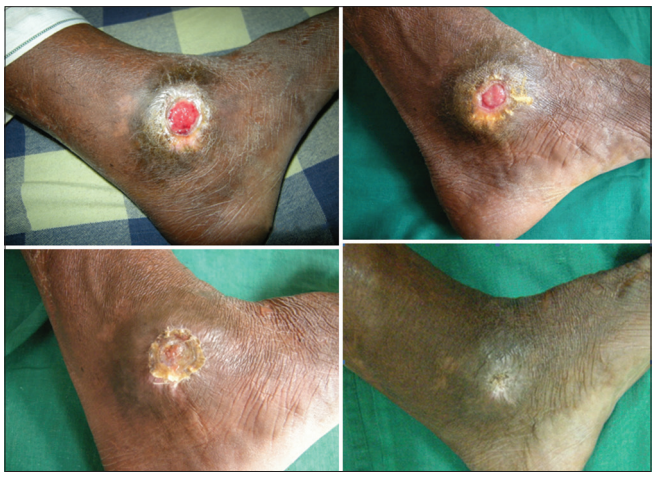

Figure 6: 24 bit (true color) traumatic ulcer of 2 months duration healed after two sittings of platelet rich plasma

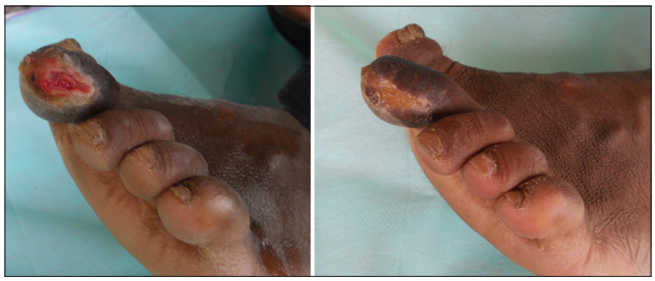

Figure 8: 24 bit (true color) trophic ulcer of 3 months duration healed within 2 weeks

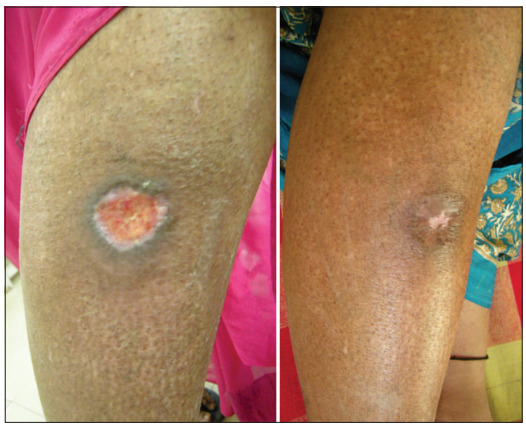

Figure 10: 24 bit (true color) traumatic ulcer healed after one sitting of platelet rich plasma

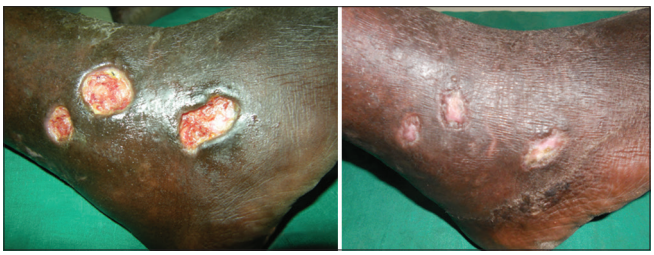

Figure 7: 24 bit (true color) venous ulcer of 6 months duration healed after three sittings of platelet rich plasma

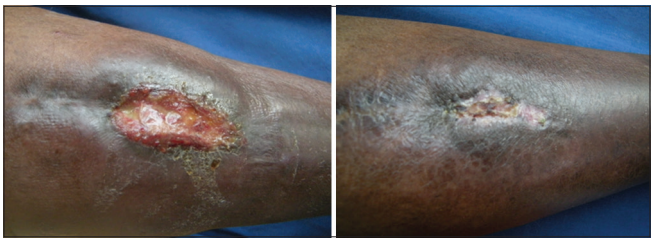

Figure 9: 24 bit (true color) traumatic ulcer of 4 months duration healed after three sittings of platelet rich plasma

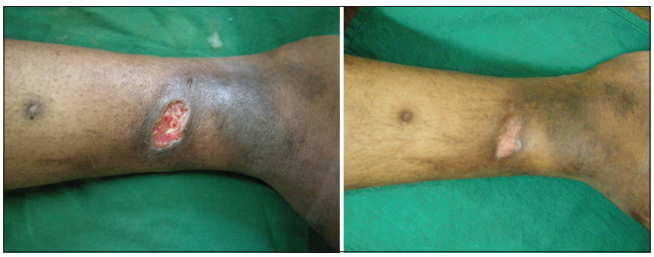

Figure 11: 24 bit (true color) venous ulcer of 7 months duration healed after six sittings of platelet rich plasma

mesenchymal cell recruitment, proliferation, extracellular matrix degeneration, and cell differentiation for tissue regeneration. These factors are released from α granules in response to platelet activation by inducers of platelet aggregation.[10]

The anti-inflammatory factors in PRP also play a role in wound healing because of the presence of leukocytes, which are at high levels in PRP.[8]

In addition to the GFs, platelets release numerous other substances (e.g. fibronectin, vitronectin, and sphingosine 1-phosphate) that are important in wound healing. An advantage of PRP over the use of single recombinant human GF delivery is the release of multiple GFs and differentiation of factors upon platelet activation.[11]

There is no standard method of preparation of PRP in literature. According to Marx, to truly concentrate platelets from autologous blood, the device must use

a double centrifugation technique.[12] Regardless of the rate of centrifugation or the time of centrifugation, a single spin cannot adequately concentrate platelets, because the red blood cells will interfere with their fine separation.[4]

A study conducted by Frykberg *et al*.[13] on 49 patients with 65 nonhealing ulcers showed that 63 of 65 ulcers responded with a reduction in area, volume and undermining of the ulcers in a mean duration of 2.8 weeks with 3.2 treatments.

Steenvoorde *et al*.[14] conducted a study on 12 patients with 13 wounds, showing that 7 of 13 wounds required more than 1 application, with a mean number of 2.2 applications and a mean treatment period of 4.2 weeks.

Kakudo *et al*.[15] treated five cases of intractable skin ulcer with autologous PRP, among which three ulcers healed completely within 4 weeks and epithelization of wound occurred within 6.6 weeks on average.

In our study, 24 patients with 33 ulcers were treated with PRP and the mean duration of healing of the ulcers was 5.6 weeks (SD 3.23). We also noticed a decrease in pain.

Chronic wounds are a frequent problem in developing countries. Because these wounds lack the necessary GFs for healing, they are often difficult to heal and are frequently complicated by superinfection. PRP contains various GFs that are necessary in wound healing. In addition, the high concentration of leukocytes present in PRP is also helpful in preventing infections.[16]

Currently, there is a paucity of critical scientific data regarding the beneficial effects of PRP in clinical procedures. In the current study, PRP was found to be useful in treating chronic leg ulcers. However, further controlled, randomized prospective clinical trials are necessary to definitively demonstrate its efficacy. There is also a need for the development of a standard protocol for the preparation of PRP, as literature currently there is no standardization of the procedure.

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Original Article Plastic and Aesthetic Research

The keystone-design perforator-based flap for leg defects: a synthesis of philosophies

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ABSTRACT

Aim: The classical keystone-design flap, although elegantly employed for various trunk defects, has limited movement on the leg. This study aims to modify the keystone–design flaps for leg defects. **Methods:** A keystone-design flap, in which perforators are identified and dissected, is described specifically for elliptical defects overlying the tibia. **Results:** It retains the unique advantages of both the perforator island flap concept as well as the keystone-design philosophy. **Conclusion:** The technique as well as the possibilities of raising such flaps over various areas of the leg is outlined.

Key words:

Flap, keystone, leg defect, lower extremity reconstruction, perforator island flap

INTRODUCTION

Leg defects can be intriguing to treat. Paucity of local tissue has necessitated free flaps especially in the lower third. Reconstructive options have increased with the arrival of perforator-based flaps. These island flaps are versatile in design. Chiefly, the types of movement described are V-Y advancement and propeller. The perforator anatomy of the leg is well elucidated.

The keystone-design flaps were introduced by Behan.[1] Four types are described. In the classical technique, very limited elevation of the flap from its bed is performed. Perforators from the bed of the flap are presumed, but never identified. Keystone flaps have come up as the chief local option for reconstruction of various defects over the trunk.[2] However, difficulties have been encountered in using this flap for lower extremity reconstruction.[2]

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A modification is proposed, which combines the philosophies of perforator-based flaps and the keystone-design, to maximize flap advancement.

METHODS

From April 2012 to March 2013, a total of five patients underwent the keystone perforator-based flap. All of them had defects with limited soft tissue remained over the leg, exposing the tibia. All flaps survived without complications. Two of these are illustrated below.

Surgical planning and technique

Perforators over the leg are Doppler marked preoperatively. This is essential for flap planning, especially over the area adjacent to the defect. A keystone-design flap is marked on the skin adjacent to the defect. The flap is located on the medial calf for a defect on the upper leg, and on the lateral aspect for a defect on the lower leg [Figure 1]. Factors involved in flap planning are dermatomal territory, laxity of local skin, and distribution of Dopplered perforators. The outer curvilinear part of the keystone-design is incised first to the subfascial level. This incision also doubles as the exploratory incision for finding perforators. In contrast to Behan's concept, subfascial dissection is performed, and all perforating vessels identified. One or more dominant perforators are preserved. The rest of

the incisions are completed, and the flap islanded. The inner curvilinear edge of the keystone flap is advanced medially for coverage of the defect. An advancement of 3 cm can be obtained; further advancement would require skeletonization of the perforators. The defect is narrowed by closing either ends in a V-Y fashion. This redistributes tension on the inset also. Interrupted simple sutures are placed. We do not require elaborate suturing (in the HEMMING pattern) as is done in the classical keystone-design.[2] Primary closure of the secondary defect can be achieved especially in the upper leg. In the case of the lower leg, closure requires a skin graft. Two clinical examples are illustrated.

RESULTS

The patient with squamous cell carcinoma

A 50-year-old woman underwent wide local excision of squamous cell carcinoma over the pretibial region of her left leg [Figure 2]. A 20 cm × 9 cm keystone-design perforator-based flap was marked over the medial calf after identifying three perforators with Doppler. These were found to arise from the medial sural artery on exploration. The flap was islanded on these perforators and advanced medially to cover the tibia. Part of the primary defect medial to the exposed bone was skin-grafted. The secondary defect was closed primarily. Healing was uneventful, and the patient is asymptomatic, two years after the surgery.

The patient with Grade IIIb fracture

A 21-year-old male presented with Grade IIIb fracture of both bones of the right leg. The tibia was exposed over the middle third-lower third junction [Figure 3]. A 16 cm × 7 cm keystone-design perforator-based flap was designed over the lateral lower leg. The flap was islanded after identifying and skeletonizing two perforators of the anterior tibial artery. The flap was advanced medially over the site of fracture. The secondary defect was covered with a skin graft. Further, the patient underwent intramedullary nailing of the tibia, successfully.

DISCUSSION

The keystone perforator-based flap is best suited for a defect in the shape of a vertical ellipse with its long axis parallel to the tibia. Such is the ingenuity of the keystone-design that the reorientation of local tissue is akin to performing three V-Y flaps.[3] Advantages are: (1) Replacement of like with like, (2) absence of dog ear, (3) preservation of multiple perforators ensuring flap survival, (4) usage of the best flap design for local tissue recruitment, and (5) potential for primary closure of even the secondary defect (albeit only in the upper half of the leg).

Neither the keystone concept nor the perforator concept is new. In the classical keystone concept[1] and some of its modifications,[4] perforators nourishing

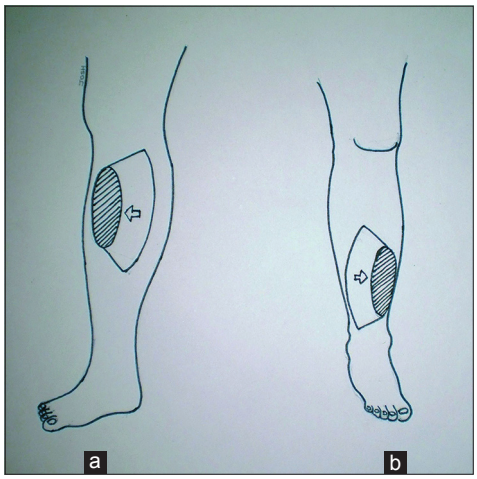

Figure 1: (a) When the defect is on the upper leg, the flap is designed on the medial calf region, and is advanced medially. (b) when the defect is on the lower leg, the flap is designed on the lateral side, and is advanced medially

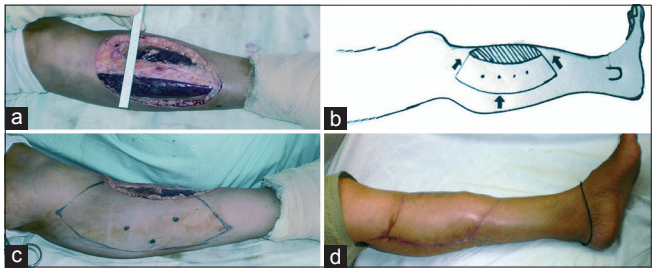

Figure 2: (a) The defect in the leg after excision of a malignant tumor. Upper and middle third of the tibia is exposed. (b) line diagram of keystone flap adjacent to the defect. (c) the keystone flap outline with perforators marked by Doppler. (d) postoperative view

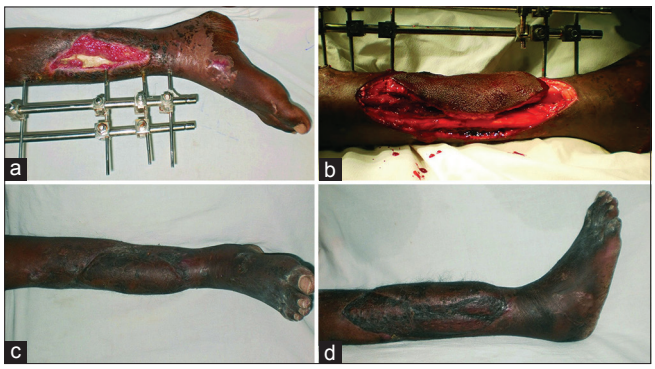

Figure 3: (a) Posttraumatic defect in the lower leg with exposed and fractured tibia, (b) flap elevated from the lateral aspect of the lower leg. (c) two months postoperative view. The external fixator has been removed. (d) well settled skin graft on the lateral aspect of the lower leg

the flap are assumed to be present. The advancement obtained by skin incision and limited elevation has been questioned.[5] In the classical perforator concept, the emphasis is on dissecting perforators and not on design of the skin island. In the leg, where there is relatively no lax skin, these two concepts can be amalgamated with success.

In the present series, perforators were Doppler marked preoperatively. These were then identified and dissected, aiding in the advancement of the flap. Such a method maximizes the advantage of flap design

without compromising on flap vascularity. In short, the key message of this small case series is to emphasize perforator identification, visualization, and preservation, while elevating keystone flaps on the leg.

We find a parallel to the discovery of this idea, in the evolution of the propeller perforator concept. The propeller flap was originally described for coverage of elbow or axillary defects. The flap had a central adiposofascial pedicle, which contained perforators. The existence of these perforators was presumed, and they were never actively sought for or identified. However on the lower extremity, most propeller flaps are nowadays elevated on a single perforator, painstakingly skeletonized and twisted up to 180°.

In the present series, care was taken to include only limited defects of the lower extremity, which required a local flap to advance up to 3 cm. Some important limitations have to be mentioned. Free tissue transfer is the primary choice especially for larger, posttraumatic defects. A split thickness graft close to the site of the flap may not be ideal for patients undergoing cancer excision, as they require radiotherapy. It is difficult to elevate the skin-grafted tissue for future operations too.

A keystone-design perforator-based flap is based on a synthesis of well-established concepts. It provides a solution for performing a local flap in a difficult region such as the leg, where lax and mobile skin is at a premium.

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Commentary

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John *et al.*[1] describe five cases in which a keystone flap was performed for reconstruction of lower extremity defects. In an attempt to address the difficulty of reconstruction of these defects, that is, limited skin laxity, thick deep fascia, and limited availability of perforating vessels, the authors propose identifying the perforating vessels to facilitate flap movement. Vessel locations were detected preoperatively with a Doppler probe. Subfascial dissection of the flap was performed in order to identify the perforators. However, further skeletonization of the vessels was not performed.

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Of the five cases in this series, two are detailed in the article and describe elliptical defects of 20 cm × 9 cm and 16 cm × 7 cm. Only limited defects that required a local flap advancement of up to three centimeters were included, as the authors contend that this is the maximal possible advancement of the flap without skeletonization.

Behan was the first to describe the keystone flap concept in 2003.[2] He described four subtypes of flaps: (1) type one – the classical flap in which very little elevation from the flap bed is performed; (2) type two – allows additional flap advancement by performing a dissection of the lateral deep fascia margin; (3) type three – the use of two keystone flaps in order to repair larger defects; and (4) type four – where subfascial undermining of up to 50% of the flap is required to allow flap movement. All four types of fasciocutaneous flaps do not require identification of the perforators prior to elevation of the flap. Emphasis is made on performing a blunt dissection in order to preserve as many vessels as possible. In this paper, keystone flaps were used to reconstruct trunk and limb defects.

Reconstruction of lower limb defects with the keystone design island flap was subsequently reported by several authors. Khouri *et al.*[3] reported a case series of 28 large defects of the trunk and extremities. Lack of local tissue laxity was significant enough to make the patients candidates for microvascular reconstruction. Preoperative identification of the perforators by a Doppler probe was performed in the smaller reconstructions. According to the authors, this was deemed unnecessary in larger defects because of the frequency of such vessels throughout the body and the assumption that adequate perforators would

be present in a larger flap design. During the procedure, care was taken to ensure the incision was carried down to muscular or deep fascia in order to enhance mobility. A deeper incision was not necessary. Although the series had high-complication rate when all minor wound healing issues were considered, the success rate was reported to be 97%, with only one patient requiring reconstruction by an alternate method.[3]

Additional reports of the use of the keystone flap for lower limb reconstruction demonstrate that this flap can be closed under relative tension,[4,5] since muscular perforator arteries, which exit the surface of the muscle to enter the subcutaneous tissue from directly beneath the flap, there is minimal risk of ischemic necrosis.

Moncrieff *et al.*[6] published the largest series of flap reconstructions for melanoma of the leg, describing the keystone flap as "the end of the skin graft." The study included 176 patients with primary melanomas of the lower limb. In some of the cases in this series, a modified technique was used, in which dermis was incised full thickness, but not deeper, on the lateral border, and the subcutis was released with gentle blunt spreading dissection. The average diameter of the excised specimen was 2.6 cm. The reconstruction comprised 106 standard, 65 modified, and 5 double-opposing type keystone flaps performed from the proximal leg to the dorsum of the foot. The modified technique of the keystone flap, with decreased tissue dissection, was associated with a significant decrease in major complication rate.[6]

Minimizing tissue dissection helps to minimize complications in this type of procedure. For larger defects, more extensive dissection may be warranted to facilitate tissue movement, as described by Behan as keystone flaps type 3 or 4. Preoperative identification of the perforating vessels may contribute to a more accurate flap design. However it has not been demonstrated that it is essential in order to perform a deeper dissection. The selection of limited defects in this work does not allow the authors to conclude that identification of perforator vessels allows better mobilization of the flap. However, we feel that it does facilitate safe elevation of a flap with the knowledge that a perforator is present within the flap design. Having said that, by dissecting out one or two main perforators, many other smaller vessels are transected. While it is likely that the majority of the flap will survive, there is a potential for marginal necrosis from ischemic or congestive insults, as a result, of this "over-dissection". As this plagues other types of flaps (such as propeller flaps and free flaps), a case by case assessment should be made, as always.

A minor point to consider is the length of operative time required for the keystone flap procedure. The OR time in keystone flaps, as described in the literature, was less than two hours.[3,7] This length of time is significantly shorter than most microsurgical procedures, and it is one of the advantages of the keystone-design flap technique. Although not stated, it follows that the identification and skeletonization of perforators would prolong OR time (as well as increase the rate of complications).

In conclusion, the keystone island flap is a useful technique to close both small and large defects of the lower extremities. The advantage of preoperative identification of perforators may allow further flexibility in the utilization of the flap. We encourage the authors to continue to share their experience with this technique, in order to substantiate its role in lower limb defect reconstruction, and expand the variety of defects it can be implemented for.

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Allogeneic epidermal substitutes in the treatment of chronic diabetic leg and foot ulcers

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ABSTRACT

Aim: Diabetic foot ulcers are the most common cause of nontraumatic lower extremity amputations in the industrialized world. Tissue-engineering products offer a lower extremity salvage strategy when healing does not proceed according to the standard of care. New allogeneic sheets are available for the management of diabetic leg and foot ulcers. **Methods:** The endpoints of this case series study regard preliminary outcomes of the application of allogeneic keratinocytes composed of benzyl ester of hyaluronic acid to 16 diabetic foot and leg ulcers in 11 patients with type 2 diabetes mellitus. **Results:** Between 21 and 70 days after cellular therapy, 6 out of 16 lesions were completely healed, reducing the wound dimension by 70% and improving the wound bed score by 52%. **Conclusion:** The clinical results of the new allogeneic sheets indicate that allogeneic keratinocytes may represent an effective and safe therapy for diabetic foot and leg ulcers in the multidisciplinary approach to this diabetes-related complication.

Key words:

Allogeneic keratinocytes, diabetic ulcer, epidermal substitutes, hyaluronic acid

INTRODUCTION

The burden of diabetes-related complications is an inevitable consequence of the rise in the prevalence of diabetes mellitus worldwide. The lifetime probability of diabetics to develop a diabetic chronic ulcer is estimated at 10%–25%.[1] The risk for patients, in particular with type 2 diabetes, of undergoing a lower extremity amputation is 23-fold higher than that of a nondiabetic.[2] Diabetic chronic ulcers definitively represent a significant cause of morbidity, hospitalization, and a huge financial cost.

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Risk factors for diabetic chronic ulcers include vascular anomalies, peripheral neuropathy, imbalanced foot mechanical forces, impaired joint mobility, high body mass, foot instability, and history of previous ulceration or amputation. The standard of care for these wounds, as defined by the International Working Group on the Diabetic Foot, requires multidisciplinary management including control of systemic glucose, extremity vascularization, off-loading, debridement of necrotic tissue, control of local infection, and patient compliance.[3,4]

In this holistic approach, for lesions where the healing process is unsatisfactory, and no other underlying cause exists, there is an increasing need for more effective therapies that will stimulate healing of diabetic chronic ulcers. Tissue-engineered products, especially skin substitutes, both cellular and acellular, are emerging as new local therapy for the treatment of nonhealing diabetic chronic ulcers.[5]

This case-series study was performed to determine wound reduction and healing following use of a new cultured allogeneic keratinocyte sheet in the management of chronic ulcers in diabetic patients. Cultured allogeneic keratinocytes on a hyaluronic acid scaffold have recently been demonstrated to be effective in the treatment of chronic ulcers, but specific studies on a diabetic group have not yet been described.[6] We reviewed 16 chronic ulcers in diabetic patients treated with these novel epidermal substitutes, and discussed the potential benefits, scientific evidence, and safety in the management of this complication. The review board of University of Milan approved this study.

METHODS

From donor cadavers (brain-dead), without infectious microorganisms (hepatitis B virus, hepatitis C virus, human immunodeficiency virus, human T-lymphotropic virus, cytomegalovirus, and negative to the treponema pallidum hemagglutination test), autoimmune, genetic, or infective skin pathologies, a 2 cm × 2 cm biopsy is performed from a sample of glabrous skin. The transfer of the biopsy is performed with a temperature of 4°C, in a sterile container with gentamicin and amphotericin B, to Niguarda Ca' Granda Hospital, the Regional Tissue Bank of Lombardia, Italy. The Skin Bank qualifies, collects, processes, validates, cryopreserves, and distributes skin taken from donor subjects. The biopsy is then sterilized and placed in Dulbecco's modified Eagle's medium (DMEM) containing Dispase II (bacterial enzyme) for 18 h at 4°C or 37°C for about 4 h, in order to split the epidermis from the dermis. The biopsy is then treated with Trypsin-Ethylenediaminetetraacetic acid (EDTA) in DMEM to isolate keratinocytes. The isolated cells can be cultivated in a specific culture medium.

HYAFF11 (Fidia Advanced Biopolymer S.r.l., Abano Terme, Italy) is the biomaterial, composed of hyaluronic acid totally esterified with benzyl ester. Due to its chemical properties, HYAFF11 releases benzyl alcohol and hyaluronic acid to the wound microenvironment because of hydrolysis of the ester bonds caused by the water in the wound exudate. The scaffold is a porous structure, composed of macropores and micropores, constituting the geometrical mesh of the matrix. Macropores (diameter of 0.5 mm) allow cellular distribution on the scaffold and the drainage of exudate when the sheet is put on the wound bed. Micropores (diameter of 40 μm, 6250 poers/cm^2) allow neovascularization of the construct after the application, and cellular migration from the superior to the inferior face of the sheet, that is, the face in contact with a wound bed.[7] HYAFF11 forms a two-dimensional matrix, 20-mm thick, for epidermal substitutes, and a three-dimensional scaffold for dermal constructs.

Skin substitute preparation is divided into two phases: the first phase consists of the primary culture of allogeneic cells in a specific culture medium, and the second consists of the seeding of cells on a hyaluronic acid scaffold for cell expansion with adhesion. The sheets are then ready for application. Keratinocytes are cultivated through Rheinwald and Green's described method.[8] Cells are incubated with a specific medium at 37°C for 20–30 min to inactivate Trypsin-EDTA, and then centrifugated and suspended in a medium without epidermal growth factor (EGF). The cellular pellet is located on a feeder layer of mouse-derived fibroblasts (3t3) inactivated by irradiation, and incubated at 37°C with 5% CO_2. The feeder layer secretes proteins of extracellular matrix and growth factors, promoting adhesion, and proliferation of keratinocytes. Irradiation of 3t3 serves blocks the replication of these cells. EGF is added to the culture medium 72 h following seeding on the feeder layers. The medium is changed every 2 days until semi-confluence is achieved. The sheets can be used fresh, within 21 days of production, or can be cryopreserved in dimethyl sulfoxide and stored at −80°C, thus guaranteeing viability for 2 years.

Patient anamnestic data and outcomes were reviewed through a case series study of 11 patients with well-controlled diabetes type 2, with 16 legs and ankle chronic ulcers, unresponsive to previous conventional therapies (i.e. repeated use of advanced modern dressing for many cycles with a mean duration of 18 months), treated with the new skin substitutes from 2011.

All patients followed the same surgical protocol: chronic wounds incurable with other reconstructive options, such as wound dressings, acellular skin substitutes, and split-thickness autografts, underwent the application of the novel allogeneic skin substitutes in the operating room by the same surgical team. Before the application of sheets, all the wounds were debrided surgically to achieve wound bed preparation, and accurate hemostasis was performed. The skin substitutes were applied once directly to the wound bed without sutures.

Patients were observed weekly for a follow-up period of at least 40–70 days. The follow-up was performed by the physician team at the outpatient wound healing clinic of the Wound Care Unit (Monza, Italy). The wound dressing was the same for the postoperative period and for every control visits: a multicomponent bandage with nonadherent gauze, and polyurethane foam with silver (Biatain Ag, Coloplast) to prevent bacterial superinfection.

At the entry of the study, anamnestic data collected included age, sex, smoking status, and the presence of hypertension, end-stage renal disease, vascular diseases, autoimmune disorders, neurologic or cardiologic problems, or burns. Every chronic wound was classified at the entry of the study for dimension, location, the presence of local infection (absent, mild, moderate, severe), and wound characteristics such as wound bed, perilesional skin disorders, borders, and exudate, to calculate the wound bed score (WBS), as defined by Falanga *et al.*[9] Diagnosis of infection was based on culture obtained with a sterile rongeur. The results of this culture guided the appropriate use of systemic antibiotics. Multiple ulcers were considered different chronic wounds.

At the end of follow-up dimensional reduction, the WBS and presence of the adverse reaction were recorded.

The primary endpoint of the study was to determine the variation in ulcer dimension versus t0. Secondary endpoints included the evaluation of variation in the wound bed and exudate to determine the WBS, the percentage of wound reduction, and the percentage and time to healing.

Abstracted data were stored using an Excel Office database (Microsoft Corporation, Washington, USA) containing fields for clinical data entry. The statistical analysis was performed considering the patient as a unit of analysis initially (for anamnestic data), and then the single-chronic wound (for clinical results). The mean reduction of the skin lesion during follow-up was verified with the Wilcoxon Signed-Rank Test. The variation of WBS versus t0 was analyzed with the Friedman test. The level of statistical significance was fixed to 5% ($P < 0.05$) to reject the null hypothesis.

RESULTS

Between January of 2011 and December of 2013, 11 patients with diabetes type 2 with 16 wounds underwent an application of allogeneic epidermal substitutes on a hyaluronic acid scaffold. Table 1 describes the demographics of all patients. Four out of 11 (36%) patients were females, and the mean age of all patients was 75 ± 8.2 years. Among comorbidities, hypertension (7, 63%) and cardiopathy (3, 27%) were the most frequent.

As described by Table 2, 8 out of 16 (50%) chronic ulcers were located on the ankle or foot, and the other 50% were located on the lower third of the leg. Five (32%) ulcers showed a mild to moderate local infection at the entry of the study; only 1 severe infection was present. The mean preoperative wound size for all diabetic chronic ulcers was 14.37 ± 9.29 cm^2, and the mean preoperative WBS was 9.6 ± 3.5. During the follow-up period, no wound advanced to require amputation of the foot or lower limb, and only one ulcer developed a local severe infection under the application of the sheet, enlarging the wound dimensions. No other adverse reactions were recorded.

Six out of 16 (38%) chronic ulcers healed in a mean time of 42 ± 16 days. The application of the new skin substitutes reduced the mean percentage of the wound dimension by 70% ($P = 0.0007$). The WBS demonstrated an improvement of 52% ($P < 0.0001$) at the end of the follow-up period from the score recorded at the entry of the study.

Case example: ankle diabetic ulcers in a 66-year-old patient treated with allogeneic keratinocyte [Figures 1–5].

DISCUSSION

The chronic wound microenvironment is biologically distinct from the acute wound milieu: venous and diabetic chronic ulcers are hypothesized to be trapped in the inflammatory and proliferative phases of normal healing, respectively. Poor wound healing may be a consequence of abnormal insulin signaling and hyperglycemia, affecting skin proliferation and differentiation.[10] Skin biopsies performed in nondiabetic and diabetic subjects from the edges of chronic wounds have revealed increased expression of transforming growth factor (TGF) beta 3 and low expression of TGF-beta 1, resulting in nonhealing.[11] Abnormal expression of insulin-like growth factor type 1 in diabetic skin may also contribute to delayed wound healing.[12]

The damaged biological background of diabetic wounds explains the necessity to modulate therapeutically the unbalanced levels of growth factors, signaling molecules, and extracellular matrix proteins.[13] How these novel skin substitutes work is still not completely understood. Initially, especially with skin substitutes as cultured epidermis and living bilayered skin construct, some degree of permanent engraftment was thought to assist in healing. As shown by DNA and Y chromosome probes, allogeneic constructs are not the same as autografts: a true take of allogeneic sheets has not been demonstrated.[14] The allogeneic skin constructs usually do not stay on the wound for more than a few weeks, and their function is not to replace tissues or cells, but instead to stimulate tissue repair as pharmacologic agents, secreting healing factors in chronic wound microenvironment. The key role of allogeneic constructs seems to be the secretion of

Table 1: Anamnestic data, length of previous treatments and HbA1c levels

Patient	Age (years)	Sex	Comorbidity	Length of previous treatments (months)	HbA1c (mg/dL) at t0	HbA1c (mg/dL) at end
1	75	Male	Hypertension	14	6.3	6.5
2	73	Male	None	22	6.6	6.4
3	69	Female	hypertension	15	6.2	6.3
4	65	Male	None	17	5.9	6.2
5	70	Male	Hypertension, cardiomyopathy	24	6.7	6.1
6	68	Female	Hypertension, autoimmune diseases	19	6.5	6.2
7	83	Male	Hypertension, cardiomyopathy, end-stage renal disease	24	6.6	6.5
8	90	Female	Hypertension	13	5.8	6.0
9	81	Male	Hypertension, cardiomyopathy	18	5.7	5.9
10	66	Female	Vascular disease	28	6.4	6.1
11	82	Female	Autoimmune disease	32	6.0	5.7

HbA1c: glycated hemoglobin

Table 2: Clinical result

Patient	Ulcer	Location	Wagner ulcer classification	Infection* *t0*	Infection end	Dimension *t0*	Dimension end	WBS *t0*	WBS end	Percentage wound reduction	Time healing (days)
1	#1	Leg	1	Absent	Absent	12.6	0	6	16	100	40
2	#2	Leg	1	Mild (*S. epidermidis*)	Sev (*P. aeruginosa*)	33.82	34.09	7	16	−1	-
3	#3	Ankle	2	Absent	Absent	11.31	0.8	10	16	93	-
	#4	Leg	1	Absent	Absent	28.91	15.01	9	16	48	
	#5	Leg	1	Absent	Absent	6.03	2.44	9	16	60	
4	#6	Ankle	2	Mild (*S. aureus*)	Absent	21.32	19.27	8	10	10	-
	#7	Ankle	1	Absent	Absent	22.68	1.78	7	16	92	
5	#8	Ankle	1	Severe (*E. coli*)	Mild (*E. coli*)	15.68	8.41	3	5	46	-
6	#9	Leg	1	Absent	Absent	3	0	12	16	100	21
7	#10	Ankle	1	Moderate (*P. aeruginosa*)	Absent	19.65	1.35	9	12	93	-
	#11	Leg	1	Moderate (*S. epidermidis*)	Absent	22.7	6.93	8	15	69	
8	#12	Ankle	1	Mild (*P. aeruginosa*)	Absent	8.55	2.28	16	16	73	
9	#13	Leg	1	Absent	Absent	4.85	0	14	16	100	40
10	#14	Ankle	1	Absent	Absent	11.78	0	9	16	100	70
	#15	Ankle	1	Absent	Absent	3.08	0	16	16	100	40
11	#16	Leg	1	Absent	Absent	4.07	0	11	16	100	45
Mean						14.37	5.77	9.62	14.62	70	42.66
Ds						9.29	9.52	3.51	3.09	32	15.75
Maximum						33.82	34.09	16	16	100	70
Minimum						3	0	3	5	−1	21
P value						0.0007		<0.0001			

*Local infection was considered divided into four progressive grades (absent/mild/moderate/severe) based on the results of cultural swabs.
S. epidermidis: Staphylococcus epidermidis, S. aureus: Staphylococcus aureus, E. coli: Escherichia coli, P. aeruginosa: Pseudomonas aeruginosa, WBS: wound bed score

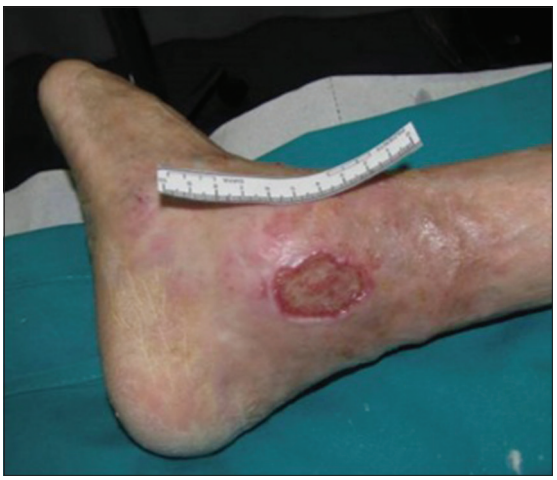

Figure 1: Diabetic ulcer of the ankle of 3 cm × 4 cm

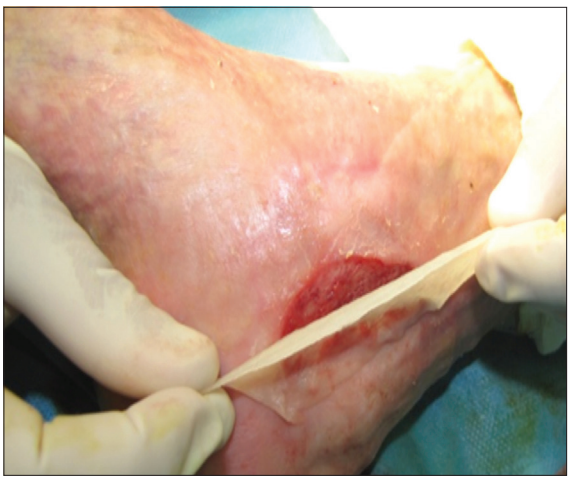

Figure 2: Intraoperative application of the allogeneic sheet on the wound

growth factors and extracellular matrix proteins, and to attract differentiated or stem cells in the wound milieu.[15]

This clinical case-series study based on the utilization of new cultured allogeneic keratinocyte sheets showed promising results, including safety and tolerability of the allogeneic product, good wound healing rate, a great reduction in wound size in a relatively short period, and preparation of the wound bed for alternative reconstructive treatments (i.e. split-thickness autograft). The application of allogeneic keratinocytes on a hyaluronic acid scaffold may allow improvement of diabetic leg and foot lesions not amenable to other therapies or surgical indications, thereby allowing the closure of nonhealing chronic ulcers, and thus reducing morbidity, cost, and length of hospitalization. Allogeneic skin substitutes do not require prolonged operating time or skin biopsy, and are easily applied by the surgeon in contrast to flaps or autograft. In the multidisciplinary approach to diabetic chronic wounds, allogeneic skin substitutes on a hyaluronic acid scaffold may represent a valid alternative when other possibilities have been exhausted. Keratinocyte sheets were also applied when mild to moderate local infection was present, resulting

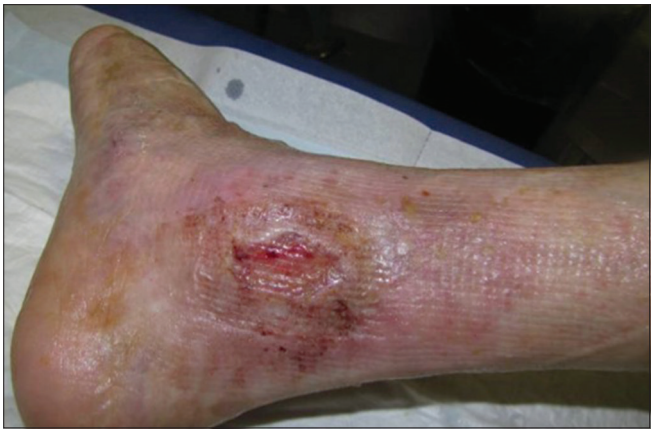

Figure 3: At t1 (9 days postoperative), 50% reduction of dimensions and improvement of wound bed

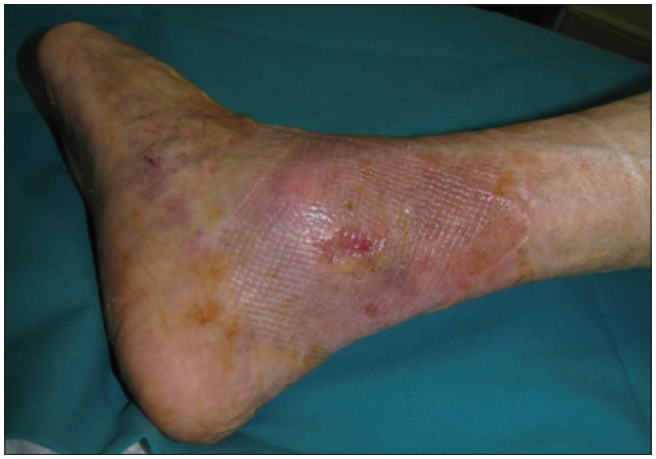

Figure 4: At t2 (23 days postoperative), further reduction of the ulcer

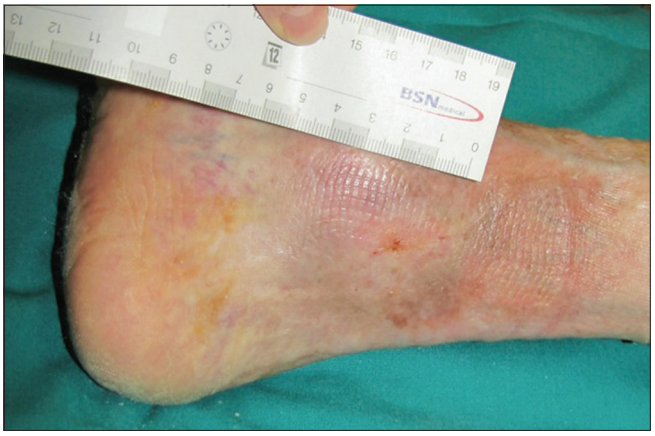

Figure 5: At t3 (45 days postoperative), complete healing of the ulcer

in interesting clinical outcomes. Cultured keratinocytes were, in fact, resistant to bacterial colonization in excised burns and chronic ulcers.[16] In such settings and considering the cost of this new product, allogeneic keratinocytes on a hyaluronic acid scaffold could be considered a second-line treatment in case of prior treatment failure.

Fortunately, we had no cases of immunologic response to these allogeneic products in our case series. Had this occurred, the application of a topical immunologic suppressant like 5-fluorouracil ointment would have been recommended.

In the literature, other studies have reported clinical outcomes for cellular skin substitutes on various other scaffolds in the treatment of chronic leg and foot diabetic ulcers.[17-20] The differences among these studies in results, methods, products, cost-effectiveness ratio, and follow-up period are highlighted in Table 3. However, comparison of the effectiveness is difficult to perform given the extreme variation in protocols (e.g., skin substitutes were used multiple times on the same ulcer in some studies, or the end of the study was not fixed until 100% wound healing was achieved).[21-23] However, some clinical features have emerged from these studies regarding the use of cellular skin substitutes in the management of chronic diabetic ulcers. The role of allogeneic keratinocytes appears to be central in the cellular therapy of diabetic wounds, although good results have been reported with the use of autologous cells.[24,25] Unlike allogeneic substitutes, autologous sheets are not available for use immediately, a skin biopsy is required, and longer times are necessary for cell processing, with the ever-present risk of ischemia or osteomyelitis. Cellular skin substitutes are formed by two elements: cells and scaffold. In the "dynamic reciprocity" model, the extracellular matrix emerges as capable of influencing wound healing, acting on the others two characters, cells and signal factors.[26] Thus, the scaffold and cells are both fundamental in the clinical outcome of skin substitutes. Hyaluronic acid is a central molecule in human skin, and its functions are diverse. Hyaluronan influences hydration of the extracellular matrix, due to its hydroscopic characteristics, and contributes to the physical and mechanical properties of the dermis. Hyaluronic acid interacts with a number of receptors, resulting in the activation of signaling cascades that influence cell migration, proliferation, and gene expression. Further, fetal-like regenerative wound healing is characterized by a large amount of hyaluronic acid deposition. From these observations, a membrane composed of completely esterified hyaluronic acid was developed, and was shown to support growth of keratinocytes *in vitro* and biocompatibility *in vivo*.[27] Prior studies on cellular therapy for diabetic wounds have emphasized repeated debridement, control of bacterial growth, careful moisture balance to prevent maceration, blood pressure control, management of blood glucose, and perfusion of the extremity. Wound bed preparation remains central for cellular skin substitutes application and efficacy.

The present case series study on skin substitutes based on hyaluronic acid scaffold for the therapy of chronic diabetic leg and foot ulcers allows investigation of the clinical results, in order to find evidence for treatment perspectives, and stimulate biochemical research in the field of regenerative medicine. Comprehensive studies will be necessary to evaluate the cost-effectiveness of these

Table 3: Cellular skin substitutes for diabetic chronic ulcers (costs at the time of writing should be treated as a guide and have been converted into € currency where necessary; the name of the scaffold is present if the product has no commercial name)

Study	Cells	Scaffold	Product	Sheet	Cost €	Follow-up (weeks)	*n* cases	Outcome %	Time healing (days)
Vamos *et al.*[2]	Neonatal allogeneic keratinocytes	Collagen seeded with neonatal allogeneic fibroblasts	Apligraf	7.5 cm diameter disc	763.26	12	82	51.5 healing	84
Veves *et al.*[18]	Neonatal allogeneic keratinocytes	Collagen seeded with neonatal allogeneic fibroblasts	Apligraf	7.5 cm diameter disc	763.26	12	112	56 healing	65
Harvima *et al.*[19]	Allogeneic keratinocytes	Nylon	Tegapore	Not commercially available	Not commercially available	11	18	100 wound reduction	64
Bayram *et al.*[20]	Allogeneic keratinocytes	Polyethylene and silica	Cytoline 1	Not commercially available	Not commercially available	4	20	92 wound reduction	30
Sams *et al.*[21]	Neonatal allogeneic keratinocytes	Collagen seeded with neonatal allogeneic fibroblasts	Apligraf	7.5 cm diameter disc	763.26	24	9	56 healing	84
Marston *et al.*[22]	Neonatal allogeneic fibroblasts	Polyglycolic acid (Dexon™) or polyglactin-910 (Vicryil™)	Dermagraft	5 cm × 7.5 cm	326.52	12	130	30 healing	84
Caravaggi *et al.*[23]	Autologous fibroblasts	Benzyl ester of hyaluronic acid	Hyalograft-3D	8 cm × 8 cm	1200.00	11	43	65.3 healing	57
You *et al.*[24]	Allogeneic keratinocytes	-	Kaloderm	Available sizes: 9-16. 25 and 56 cm^2	Not yet licensed	12	27	100 wound reduction	35
Lobmann *et al.*[25]	Autologous keratinocytes	Benzyl ester of hyaluronic acid	Laserskin	10 cm × 10 cm	1200.00	12	14	78 healing	41
Vaienti *et al.*[7]	Allogeneic keratinocytes	Benzyl ester of hyaluronic acid	HYAFF11	10 cm × 10 cm	1000.00	11	16	70 wound reduction	42

therapies before they become acceptable for general use. The goal is to achieve the cellular therapy that "suits" the specific chronic wound microenvironment in diabetic wounds in the future. However, large, randomized, and controlled clinical trials are required to confirm and validate the clinical results of these novel skin substitutes.

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Case Report Plastic and Aesthetic Research

Supermicrosurgical reconstruction of knee defect using superior medial genicular perforator as a recipient vessel

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ABSTRACT

A 24-year-old male presented after being involved in a motorcycle accident and was found to have soft tissue defects of the knee with exposure of patella. Due to the severe injury from the popliteal fossa to the posterior aspects of the lower leg, repair with a free flap from anterolateral thigh perforator was planned instead of local calf muscle flap. Preoperative angiography was performed, and it showed that superior medial genicular perforator was patent compared with unreliable filling of the superior lateral genicular perforator. The soft tissue defect was repaired using the superior medial genicular perforator as the recipient vessel. This was performed by creating perforator to perforator anastomosis (supermicrosurgery). The flap survived successfully, and the patient was able to ambulate in a few weeks without serious complications. This case indicates that superior medial genicular perforator can be used as the recipient vessel for covering the soft tissue defects of the knee caused by blunt injury.

Key words:

Soft tissue defect of the knee, superior medial genicular perforator, supermicrosurgery

INTRODUCTION

Soft tissue defect of the knee remains challenging and problematic to reconstructive surgeons. Prerequisite for the reconstruction of this region include the flexibility, durability and thickness of the skin paddle to sustain the motion of the knee joint. Numerous surgical trials have been performed using musculocutaneous flaps, fasciocutaneous flaps, perforator flaps, and free flaps to repair these defects with varying degrees of success.[1-3]

Local flaps created from the calf muscle are preferred primary surgical option. However, local flap may not be an option when there is injury to the donor site endangering the vascularity. Although the free flaps are less affected in terms of the donor site selection, selection of the recipient vessel in the vicinity of knee defect remains problematic.

Since perforator to perforator anastomosis (supermicrosurgery) emerged, this technique has been vastly used for reconstructive surgeries without regard to the recipient vessel. We report a case using the superior medial genicular perforator as the recipient vessel and supermicrosurgery techniques to cover the soft tissue defect of the knee.

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CASE REPORT

A 24-year-old male was injured in a motorcycle accident. Patient had a knee injury with soft tissue defect measuring 12 cm × 7 cm and exposure of the patella was noted [Figure 1]. Physical examination revealed severe contusion of the posterior calf. Because of these findings, repair using local gastrocnemius

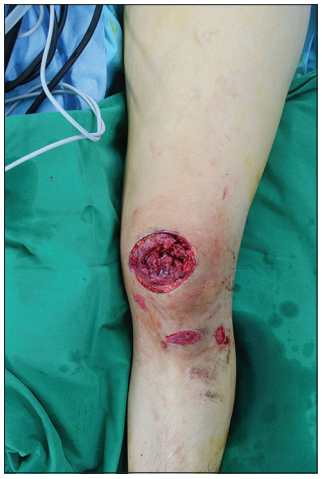

Figure 1: Preoperative finding shows soft tissue defect of the left knee measuring 12 cm × 7 cm with patella exposure

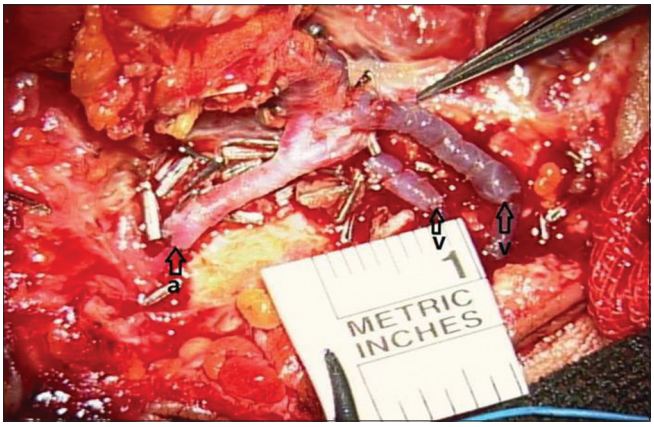

Figure 3: Supermicrosurgical anastomosis of one artery (0.6 mm) and two veins (0.4 mm, 0.7 mm) with 10-0 and 11-0 nylon was made in an end-to-end fashion (a: artery, v: vein)

musculocutaneous flap was excluded to avoid unreliable vascularity of the donor site. Instead, a free flap reconstruction using a vessel in the vicinity of the knee as the recipient was planned.

Conventional angiography instead of computed tomographic angiography was performed to predict the direction of vascular flow around the traumatized knee. It showed abrupt cutoff with retrograde filling of the superior lateral genicular perforator compared with intact superior medial genicular perforator [Figure 2]. Using the intraoperative hand-held Doppler, perforator of superior medial genicular artery was targeted and identified. Elevation of anterolateral thigh perforator free flap with 3 cm pedicle length was performed and the superior medial genicular perforator was identified under a microscope. Perforator to perforator anastomoses of one artery (0.6 mm, descending branch of lateral circumflex femoral artery with superior medial genicular artery) and two veins (0.4 mm and 0.7 mm, venae comitantes) with 10-0 and 11-0 nylon were made in an end-to-end fashion [Figure 3]. Donor site was closed with meshed allogeneic dermal matrix, followed by split thickness skin graft (0.3048 mm).

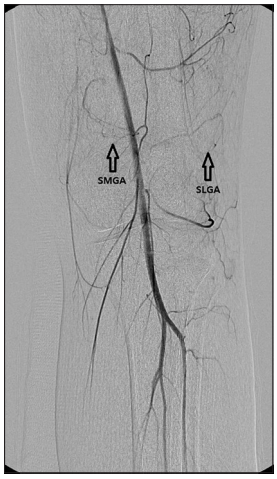

Figure 2: Conventional angiography shows the abrupt cutoff with retrograde filling of the superior lateral genicular perforator compared with intact superior medial genicular perforator (SMGA: superior medial genicular artery, SLGA: superior lateral genicular artery)

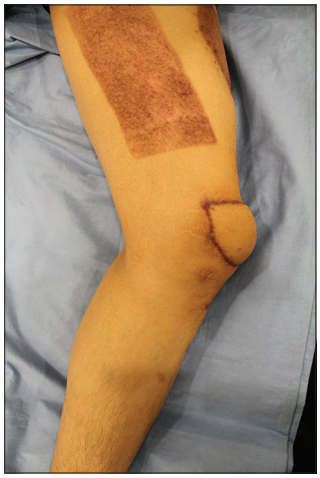

Figure 4: Acceptable functional and aesthetic appearance was obtained at postoperative month 11

The flap survived successfully, and the patient had functional ambulation within 15 days after surgery without any complications. Full flexion of the knee joint was achieved by postoperative week 4. Patient was also able to squat without any discomfort. The patient was satisfied with the contour of the flap at postoperative month 11 [Figure 4].

DISCUSSION

Reconstruction of soft tissue defects surrounding the knee has been well-known for its difficulty and strenuous nature of the process. Damage to the soft tissue around the knee can be caused by trauma, cancer resection, and the exposure of prosthesis.

Several musculocutaneous flaps including gastrocnemius, sartorius, vastus medialis, and vastus lateralis flaps have been applied successfully to cover the soft tissue defect of the knee. Other fasciocutaneous flaps, island flaps and perforator flaps based on the sural artery, superior lateral genicular artery, and the reverse flow of

descending branch of lateral femoral circumflex artery have also been used.[4-6] However, bulky contour of the flap, functional impairment of the donor site, and discomfort on ambulation due to the scar extended from the donor site to the knee may be encountered with these flaps.

To avoid these drawbacks, several free flaps have been introduced.[7-9] However, free flaps using the source vessels may threaten the vascularity around the traumatized knee joint. The evolution of microsurgical techniques has allowed surgeons to anastomose vessels between perforators that are smaller than 0.8 mm in caliber. These techniques are termed as supermicrosurgery. Hong and Koshima used this refined technique on 25 soft tissue defects over knee joint and minimized donor site morbidity.[9] However, their promising results are extremely dependent on the expertise of the surgeon. They preferred free style reconstruction without identifying the recipient vessels, while they could easily find the recipient vessels in the plane between the fascia and muscle.

In this report, we demonstrate the use of conventional angiography to identify superior medial genicular perforator vessel as the recipient in this patient. To the best of our knowledge, this is the first case of supermicrosurgical reconstruction using superior medial genicular perforator as a recipient vessel. Although this procedure is technically demanding, the use of conventional angiography to identify the recipient vessels made it less tasking. Compared to conventional local flap modalities, this technique creates less scarring, providing better contour of the knee and decreased discomfort on ambulation. The patient could flex the knee joint fully and perform exercises such as squats without any discomfort in four weeks.

Further investigation with larger cases should be performed for validation. Nevertheless, this case implies the use of supermicrosurgical techniques and superior medial genicular perforator as an alternative to repair soft tissue defect surrounding the knee when the conservative local flap technique may not be reliable.

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Original Article | Plastic and Aesthetic Research

Anatomic variability of the vascularized composite osteomyocutaneous flap from the medial femoral condyle: an anatomical study

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ABSTRACT

Aim: The anatomical study and clinical application for the vascularized corticoperiosteal flap from the medial femoral condyle have been performed and described previously. Although prior studies have described the composite osteomyocutaneous flap from the medial femoral condyle, a detailed analysis of the vascularity of this region has not yet been fully evaluated. **Methods:** This anatomical study described the variability of the arteries from the medial femoral condyle in 40 cadaveric specimens. **Results:** The descending genicular artery (DGA) was found in 33 of 40 cases (82.5%). The superomedial genicular artery (SGA) was present in 10 cases (25%). All 33 cases (100%) of the DGA had articular branches to the periosteum of the medial femoral condyle. Muscular branches and saphenous branches of the DGA were present in 25 cases (62.5%) and 26 cases (70.3%), respectively. **Conclusion:** The current study demonstrates that the size and length of the vessels to the medial femoral condyle are sufficient for a vascularized bone flap. A careful preoperative vascular assessment is essential prior to use of the vascularized composite osteomyocutaneous flap from the medial femoral condyle, because of the considerable anatomical variations in different branches of the DGA.

Key words:

Descending genicular artery, medial femoral condyle, osteomyocutaneous flap, superomedial genicular artery

INTRODUCTION

The vascularized bone graft is the gold standard for reconstruction of bony defects, especially in case of chronic nonunion.[1] An anatomical studies and clinical applications for the use of a vascularized corticoperiosteal flap from the medial femoral condyle have been performed and described previously.[2,3] In 1991, Sakai and Doi and Sakai[4,5] initially reported the use of a thin, free vascularized corticoperiosteal graft for the treatment of persistent nonunion without significant bony defects in the upper limb. It has been demonstrated that the articular branch of the descending genicular artery (DGA) or the superomedial genicular artery (SGA) perfuses the medial femoral condyle. There are also two branches from the DGA which supply the muscle and skin at the level of the medial femoral condyle; the saphenous branch (SB) supplies the skin at the medial knee and proximal third of the leg, and the muscular branch (MB) normally runs into the vastusmedialis muscle.[4-7] This may allow the use of the DGA and its branches to form a composite

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osteomyocutaneous flap from the medial femoral condyle in the reconstruction of bony defects associated with avascular contracture of the soft tissue.

Although prior studies have described the composite osteomyocutaneous flap, the detail blood vessels in this region have not yet been fully elucidated. The aim of this study was to evaluate the anatomical variability of the vessels and their branches in the medial femoral condyle. Board of Hue Central Hospital approved the study.

METHODS

Ten fresh and 10 formalin preserved adult cadavers were dissected in our study, consisting of 11 males and 9 females. Forty cadaveric specimens were harvested from both thighs. The osteomyocutaneous medial femoral condylar flap was elevated using the medial approach initially described by Sakai and Doi.[4,5,8] Cadavers were placed into the supine position and a 15 cm longitudinal incision was made medially along the posterior border of the vastusmedialis at the level of the distal femur, extending from the adductor hiatus proximally to the medial collateral ligament distally.[9-12] The fascia of the vastusmedialis was then incised, and the muscle was retracted superiorly while the adductor magnustendon was retracted inferiorly. The DGA was exposed on the floor of the muscle compartment proximally and on the surface of the medial femoral condyle distally. The SGA, a medial branch of the popliteal artery, was also studied. The anatomy of the DGA and SGA with their branches and their areas of distribution were dissected, measured, and documented. For the DGA, the length, location of origin, diameter, branches and terminations in the skin as well as in the periosteum overlying the medial femoral condylar region were determined. A dominant artery between the DGA and SGA was defined as a main artery supply to the medial femoral condyle.[7,13] The position of the artery was measured as the distance from the origin to the knee joint. The length of the artery was defined as the distance from its origin to the area of termination. The outer diameter (d) of the artery was calculated through the perimeter (P) of the peripheral arteries by the following formula: $d = P/3.14$.

The perimeter was calculated by flattening the artery at its origin and using a digital caliper (Anyi Instrument Co. Ltd, China) to measure its flat section, and then doubled. In the fresh cadavers, we also performed a dye injection at the origin of the articular and SBs of the DGA. This allowed visualization of the areas of the corticocancellous medial femoral condylar segment and skin paddle.[14,15] All measurements were recorded in millimeters, with an accuracy of 0.02 mm.

RESULTS

The anatomical structures differed on the two sides of the thigh in the cadavers. The DGA origin from the superficial femoral artery (SFA) was found in 33 of 40 cases (82.5%). The DGA was absent in 7 cases. In 3 other cases, the DGA appeared together with the SGA. The SGA was present in 10 cases (25%). The DGA was dominant over the SGA in 33 of 40 cases (82.5%). In the remaining 7 cases (17.5%), the SGA was the major blood supply to the medial femoral condyle.

The DGA usually divided into branches; there were 11 (33.3%) cases of 2 branches, 21 cases (63.7%) of 3 branches and 1 (3%) case of 4 branches. The branches were the articular branches (AB), the SBs, and the MBs. The mean position of the DGA was 119.1 mm above the knee joint with a range of 96.2–148.8 mm (standard deviation [SD] 23.6 mm). The mean outer diameter of the DGA was 2.16 mm (range, 0.94–3.84 mm; SD 0.69 mm). From its origin to the onset of branching, there was a mean length of 11.7 mm (range, 0–40.33 mm; SD 8.61 mm) [Figure 1].

All 33 cases (100%) of the DGA sent AB to the periosteum of the medial femoral condyle. The AB further divided into smaller branches to the periosteum, with 1 branch in 19 cases, 2 branches in 13 cases, and 3 branches in 1 case. The mean location of its origin was 100.7 mm above the knee joint with a range from 70.3 to 129.4 mm (SD 13.4 mm). Its average length from the origin to the bone was 56.4 mm (range, 23.8–80.5 mm; SD 14.4 mm). The mean outer diameter was 1.5 mm (SD 0.4 mm). The mean area of the periosteum of the medial femoral condyle that the AB perfused was 37.8 mm × 25.7 mm [Figure 2].

In 39 (97.5%) cases the MB supplied blood to the distal aspect of the vastusmedialis muscle, and in 1 case the MB entered the gracilis muscle. In 25 cases (62.5%) the MB was a branch from the DGA, in 14 cases (36%) it came from the SFA, and in 1 case it branched off the AB. The mean length of the MB was 16.8 mm (SD 6.5 mm). The mean outer diameter was 1.6 mm (SD 0.9 mm).

In 37 specimens (92.5%) the SB supplied the skin at the medial part of the knee and the proximal leg. In 3 specimens from the fresh cadavers, the SB ran to the gracilis muscle instead of toward the skin. The SB came off the DGA in 26 (70.3%) cases and the SFA in 11 (29.7%) cases. The mean location of the origin of the SB was 103 mm (SD 18.5 mm). Its mean outer diameter was 1.3 mm (SD 0.4 mm). Ten SB had 1 branch, and 27 SB had 2 branches to the skin at the medial part of the knee and the proximal part of the leg. In 13 specimens from the fresh cadavers, methylene blue was injected. A cutaneous angiosome distribution of the SB was noted on the medial aspect of the knee and proximal leg. The average perfusion area at the level of the skin was 244 mm × 115 mm [Figure 3].

The superomedial genicular artery (SGA) existed in 10 (25%) specimens, and it was dominant over the DGA in 7 cases (17.5%). The mean outer diameter was 1.33 mm (SD 0.4 mm). The mean location of its origin was 88.5 mm (SD 17.8 mm) above knee joint. The mean length of the SGA to the periosteum was 37.5 mm (SD 16.9 mm).

DISCUSSION

Either the DGA or SGA perfuse the medial femoral condyle. The current study evaluated the anatomical structures and variations of the DGA and SGA as well as their branches in adult cadavers. One half of cadavers were studied in fresh condition to facilitate the evaluation of the perfusion area of skin and bone.

Prior studies have shown that the outer diameter of the artery from fresh frozen cadavers was maintained. While the diameter of arteries from cadavers preserved in formalin retracts and loses its shape, the perimeter of the artery is maintained.[7] We calculated the outer diameter of the artery through its perimeter according to the following formula: $P = 2R \times 3.14 = d \times 3.14$ (R: radius = $d/2$). This measurement allowed us to determine the outer diameter in noninflated arteries.

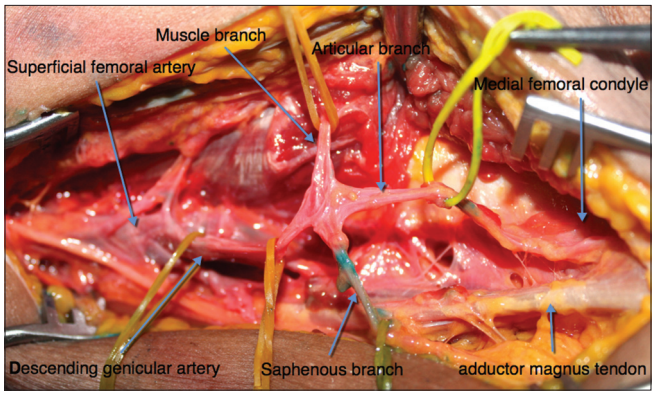

Figure 1: The vascular distribution of the descending genicular artery and its branches at the left femur in the fresh cadaver

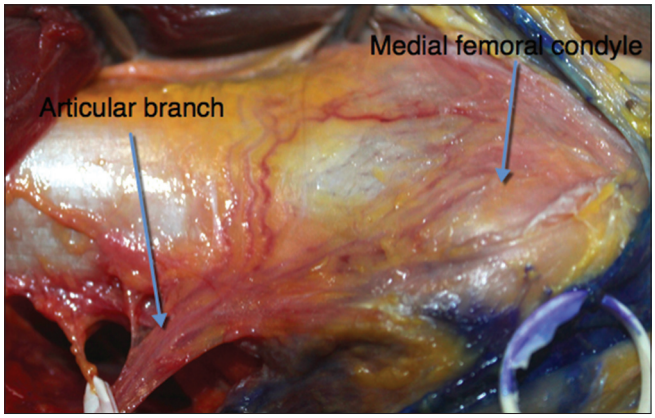

Figure 2: Anatomy of the articular branch from the descending genicular artery for blood supply to the medial femoral condyle

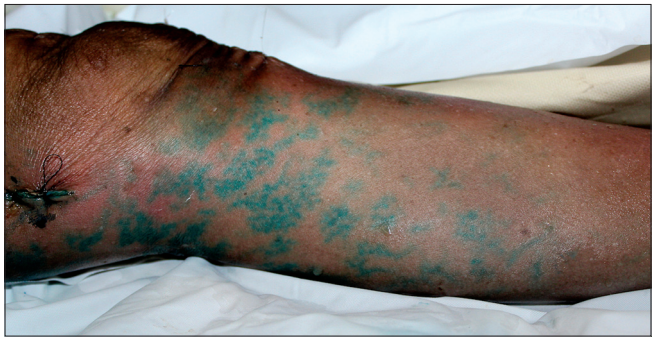

Figure 3: Cutaneous angiosome distribution of the saphenous branch at the medial side of the knee and proximal leg after injected methylene blue in fresh cadavers

Our study detected the DGA in 82.5% and the SGA in 25% of the 40 specimens. Yamamoto *et al.*[7] found the DGA in 89% and the SGA in 100% of the 19 specimens. Rahmanian-Schwarz *et al.*[1] harvested the DGA in 100% of the 21 specimens and Iorio *et al.*[16] also discovered the DGA in 100% of the 12 specimens. The difference between the studies is secondary to the number of specimens.

In the current study, the dominant vessels supplying the medial femoral condyle were the DGA in 82.5% of cases and the SGA in the DGA and 17.5% of cases. Van Dijck *et al.*[6] showed that in 70% of cases the DGA was dominant, while in 21% of cases the SGA was the dominant vessel. In 9% of cases the DGA and SGA supplied the medial femoral condyle equally. A comparison between the measurements of the DGA in the current study and other studies is made in Table 1.

Similar to previous studies, the current study demonstrated that the DGA generally divides into 3 branches (63.7% of cases) or 2 branches (33.3% of cases). In addition, the AB of the DGA or the SGA always nourishes the periosteum of the medial femoral condyle. These arteries have adequate diameter and length to supply the medial femoral condylar flap. In the absence of the DGA, the SGA has sufficient size, but the vascular pedicle is shorter, and SGA is used only for a pure bone flap.[8] The results of previous studies of Jones *et al.*[10] Yamamoto *et al.*[7], Van Dijck *et al.*[6] and De Smet[13] also made similar conclusions about the viability of this bone flap using the DGA or the SGA for treatment of small bony defects, especially in the treatment of nonunion fractures that require a good blood supply for bone grafting. In the specific study of Jones *et al.*[11], vascular pedicles of the vascularized medial femoral condylar flap for the treatment of scaphoid nonunion were the DGA in 10 cases and the SGA in 2 cases.[11]

In many cases of chronic nonunion, the soft tissue usually has a fibrous scar, infectious environment and avascular contracture. Extensive debridement of infected and devitalized tissue and bone back to bleeding tissue is required. Vascularized bone graft associated with a well-vascularized muscle or skin paddle is necessary in

Table 1: The comparison between current and prior studies on anatomy of the DGA

Studies	The mean outer diameter of DGA (mm)	The mean length from the origin to its branching (mm)	The mean location above the knee joint (mm)
Present study	2.16 ± 0.69	11.7 ± 8.61	119.1 ± 23.6
Van Dijck *et al.*[6]	2.43 ± 0.88	89 ± 21.8	137 ± 18.8
Rahmanian-Schwarz *et al.*[1]	2.9 (1.5–4.5)	25 (5–40)	147 (120–70)

DGA: Descending genicular artery

these cases. In the case of small bony defects (< 6 cm), the vascularized composite osteomyocutaneous flap from medial femoral condyle can fill the dead space of bone and soft tissue. It also minimizes the risk of deep tissue infection. By increasing the vascularity and the blood supply of the composite flap, limb salvage can be obtained with a single surgical procedure. Vascularized bone grafting can be combined with muscle tissue and a skin island, and thus can be used to solve complex problems in cases with bone and soft tissue defects.

The current study showed 100% of AB, 62.5% of MB, and 70.3% of SB branches come from the DGA. It allows the use of the medial femoral condylar bone flap, and this can be combined with muscle or skin in some cases. However, preoperative vascular assessment of this flap with an angiogram is very important due to the anatomical variation of the DGA as well as its muscular and SBs. This result differs from previous reports which studied fewer specimens; Iorio *et al.*[16] identified the SB in 11 of 12 specimens (92%). Rahmanian-Schwarz *et al.*[1] studied 21 specimens, and in 91.5%, the DGA split into three branches: AB, MB, and SB. Yamamoto *et al.*[7] showed that the SB was detected in 79% of their 19 specimens, branching off a common trunk with AB. Van Dijck *et al.*[6] found that the SB was present in 14 (41%) of the 27 cases.

The current study demonstrates that the size and length of the vessels supplying the medial femoral condyle are sufficient for a vascularized bone flap. This graft is very helpful in the treatment of chronic nonunion and small bone gap reconstruction. Although many studies have reported the viability of the vascularized composite osteomyocutaneous flap from the medial femoral condyle, a careful preoperative vascular assessment is essential secondary to the considerable anatomical variations in the different branches of the DGA. Further clinical studies will be required to clearly define the success of this composite osteomyocutaneous flap.

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Original Article | Plastic and Aesthetic Research

Superiorly based perforator plus flap for inguinal defects

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ABSTRACT

Aim: Inguinal block dissections for metastasis to inguinal lymph nodes and occasionally trauma are always associated with soft tissue loss over the groin region. A clinical study was undertaken to demonstrate the ability to utilize a superiorly-based perforator flap with reliable vascularity and less donor site morbidity to cover defects in the inguinal region. **Methods:** A prospective study was performed on 7 patients with inguinal soft tissue defects managed in our institution from January 2013 to September 2013. During the study period, a "superiorly-based perforator plus flap" was used for soft tissue coverage over the femoral vessels in the inguinal region. Hyperbaric oxygen therapy was administered postoperatively. The postoperative period, hospital course, and follow-up after radiotherapy was documented in patients with inguinal block dissection. **Results:** Seven patients presented with soft tissue defects in the inguinal region. Five of the defects were secondary to prior surgery, and 2 were secondary to trauma. A superiorly-based perforator plus flap was performed in all patients. The defect sizes ranged from 9 cm × 4 cm to 17 cm × 8 cm. The flap dimensions ranged from 12 cm × 5 cm to 20 cm × 10 cm. No secondary procedures were necessary following surgery. Postoperatively, there was no evidence of partial or total flap loss. No flap revisions were required, and no complications were experienced at either the donor or recipient site following radiotherapy. Patients were followed-up for 10-18 months. **Conclusion:** Inguinal defects require stable soft tissue coverage to withstand radiotherapy following inguinal block dissection surgery, and are susceptible to wound complications. The superiorly-based perforator plus flap technique is simple, requires little operative time, and is a reliable flap for coverage of the femoral vessels and inguinal region with improved tolerance to postoperative radiotherapy.

Key words:

Hyperbaric oxygen therapy, inguinal lymph nodes, soft tissue defect, superiorly-based perforator plus flap

INTRODUCTION

Inguinal block dissections are commonly performed for skin malignancies of the lower limb and genital regions. Wound complications including skin necrosis, infection, lymphorrhea, and lymphedema are not uncommon following inguinal block dissections. Occasionally, trauma may also result in a soft tissue defect in these regions. Morbidity can be reduced by providing a bulky, vascularized flap to the inguinal soft tissue defect, which provides coverage to the femoral vessels, obliterates the dead space, and promotes healing. Reconstructive options currently available for soft tissue defects in the inguinal region include the tensor fascia lata (TFL) flap, the anterolateral thigh flap, and the rectus abdominis flap. We present a "superiorly-based perforator plus flap" which provides stable soft tissue coverage over the femoral vessels, reduces the risk of wound dehiscence and lymphatic drainage problems, improves tolerance to radiotherapy, and decreases the incidence of donor site morbidity when compared to other flaps.

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METHODS

The study was conducted and approved at the Jubilee Institute for Surgery of Hand, Aesthetics and Microsurgery, Jubilee Mission Hospital, Thrissur, India. The patients were enrolled in the Plastic Surgery Department of the Jubilee Mission Hospital. A soft tissue reconstruction with a superiorly-based perforator plus flap was planned and executed after assessment of the inguinal defect. Seven patients with inguinal soft tissue defects were operated on from January 2013 to September 2013. The postoperative period following reconstructive surgery, the hospital course, and follow-up after radiotherapy was noted in patients who had undergone inguinal block dissection.

Anatomy

The femoral artery gives off the profunda femoris artery branch, which arises 2–5 cm below the inguinal ligament and further divides into the medial and lateral circumflex femoral arteries. The lateral circumflex femoral artery further divides into the ascending, transverse and descending branches. The ascending lateral circumflex femoral artery travels in a superolateral direction from medial to lateral. These branches provide many musculocutaneous and septocutaneous perforators which supply the skin over the lateral aspect of the thigh. The vascularity of the skin, subcutaneous tissue and TFL flap is based on the excellent longitudinal network of vessels overlying the iliotibial tract formed by anastomoses between branches of the transverse branch of the lateral circumflex femoral and individual branches of the profunda perforators, which emerge along the lateral intermuscular septum [Figure 1].

Surgical technique

Surgery was performed under general or regional anesthesia with the patient in the supine position. The soft tissue defect following block dissection or debridement was measured, and the flap was planned. A hand-held Doppler was used to identify the location of the perforators at the base of the flap. A superiorly-based flap was planned from the anterolateral aspect of the thigh, with the base of the flap at the lateral end of the inguinal defect, at the level of the greater trochanter of femur. The anterior border of the flap starts at the lateral border of the soft tissue defect. The flap is elevated from distal to proximal in the plane superficial to the TFL, preserving the perforators to the flap from the lateral side. The pivot point lies over the lateral aspect of the base of the flap. The posterior border is planned according to the size of the defect. The medial flap, overlying the soft tissue of the anterior thigh, was elevated superficial to the deep fascia of the thigh. A blunt, careful dissection is performed at the base of the flap to identify as many perforators as possible in these regions. The size of the perforators is assessed intra-operatively. Because most of the perforators travel from medial to lateral, medial and lateral perforators with minimal dissection could be included within the flap, avoiding kinking of the vessels. With adequate medial perforators, some lateral perforators could easily be sacrificed without compromising flap viability. Care is taken to include some branches of the lateral cutaneous nerve of the thigh to the flap. Anterior branches of the lateral cutaneous nerve lying over the fascia should be carefully preserved for this reason. The medial and lateral flaps are transposed in such way to provide coverage to the inguinal defect and easy closure of the donor defect. Flap inset is then completed. Hyperbaric oxygen therapy was administered in the postoperative period for six sessions.

RESULTS

Five patients presented with malignant tumors involving the inguinal lymph node and 2 patients presented with defects following trauma. Their ages ranged from 8 to 59 years with a mean of 41.7 years. Among 7 patients, 5 were males, and 2 were females. In all cases, a superiorly-based perforator plus flap was performed. The size of the defect ranged from 9 cm × 4 cm to 17 cm × 8 cm. Flap with

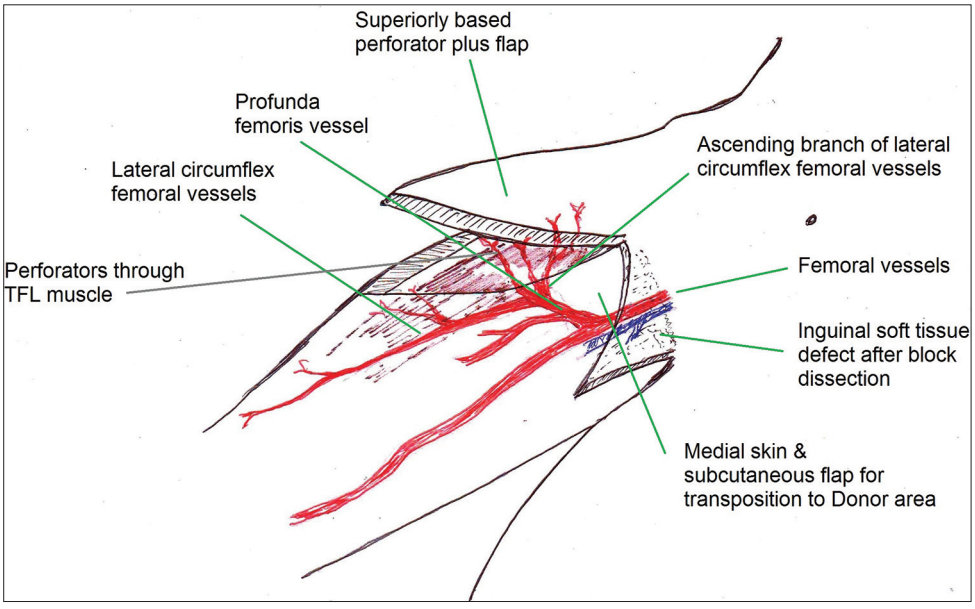

Figure 1: Anatomical description of the superiorly-based perforator plus flap

dimension ranging from 12 cm × 5 cm to 20 cm × 10 cm were created. There was no need for any secondary procedures following surgery. Drains were removed between 4 and 7 days and sutures were removed on the 14th–17th postoperative day. Postoperatively, there was no evidence of either partial or total flap loss. No flaps required revision, and no fat necrosis was noted. There were no flap complications or donor site morbidity following radiotherapy [Table 1]. Patients were followed for 10–18 months after surgery. During this period, there was no recurrence of the tumor in the case of patients who had undergone inguinal block dissection.

Patient with squamous cell carcinoma of the left leg

A 58-year-old male patient presented with squamous cell carcinoma of the left leg. Multiple inguinal lymph node were involved and were adherent to each other and to the overlying skin. Wide excision of the primary lesion and ilio-inguinal block dissection with resection of the involved inguinal skin and soft tissues was performed [Figure 2a]. A plan was made for reconstruction of the [Figure 2b] soft tissue defect over the exposed femoral vessels in the inguinal defect. The superiorly-based perforator plus flap was performed [Figure 2c and d], allowing coverage of the defect and primary closure of the donor site defect. Postoperatively, six sessions of hyperbaric oxygen therapy were administered. The flap healed well [Figure 2e and f]. Regular follow-up was performed. The flap tolerated radiotherapy well.

Table 1: The patients treated using superiorly based perforator plus flaps for inguinal soft tissue defect

Age in years/sex	Diagnosis	Flap dimensions length × width at base (cm × cm)
59/male	Squamous cell carcinoma of left leg with multiple inguinal LN	20 × 10
8/female	Soft tissue defect due to trauma with defect of 9 cm × 4 cm right groin region	12 × 5
42/male	Squamous cell carcinoma of left foot with multiple inguinal LN	18 × 9
48/male	Squamous cell carcinoma right foot with fungating inguinal LN	18 × 10
52/male	Carcinoma penis with right side inguinal LN	16 × 8
56/female	Carcinoma ovary with ilio inguinal LN	19 × 9
27/male	Soft tissue defect due to trauma with defect of 14 cm × 6 cm right groin region	15 × 6

LN: Lymph nodes

Patient with fungating right-sided inguinal lymph nodes

A 48-year-old male patient presented with fungating inguinal lymph nodes on the right side. He had previously undergone surgery for squamous cell carcinoma of the right foot and received radiotherapy to the right inguinal region. A palliative inguinal block dissection was performed [Figure 3a]. The inguinal defect was covered with a superiorly-based perforator plus flap [Figure 3b and c]. Postoperatively, six sessions of hyperbaric oxygen therapy were administered. The flap healed well.

Patient with soft tissue defect over the inguinal region

An 8-year-old female child was involved in a road traffic accident, resulting in a soft tissue defect over the inguinal region [Figure 4a and b]. The patient was stabilized, and debridement was performed [Figure 4c]. The resulting soft tissue defect was covered with a superiorly-based perforator plus flap [Figure 4d and e]. Postoperatively, six sessions of hyperbaric oxygen therapy were administered, and the flap healed well [Figure 4f and g].

DISCUSSION

Lymph node involvement is an important prognostic marker in primary skin appendage tumors, melanomas

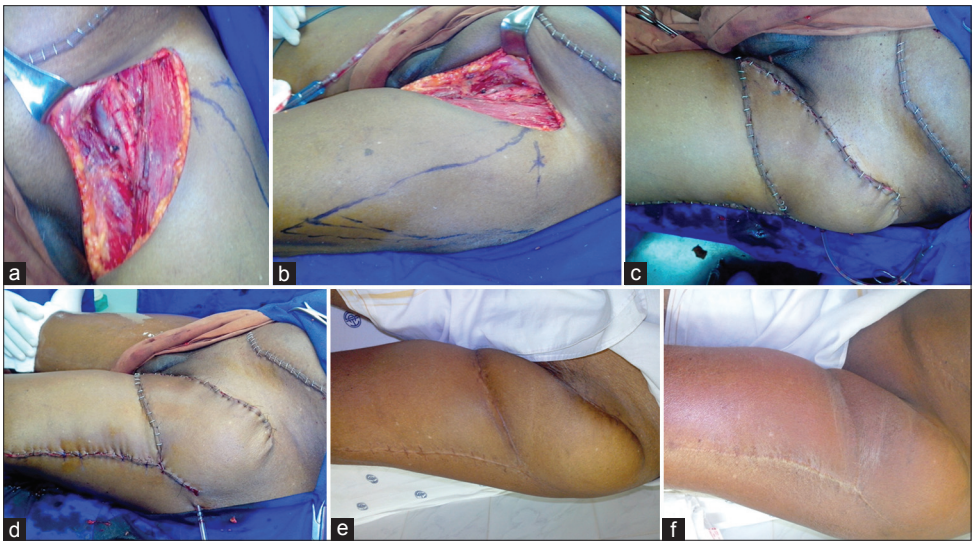

Figure 2: The patient with squamous cell carcinoma of the left leg. (a) Soft tissue defect inguinal region following dissection; (b) planning of superiorly-based perforator plus flap; (c) immediate postoperative view of the superiorly-based perforator plus flap lateral view; (d) immediate postoperative lateral view to show primary closure of donor defect; (e) late postoperative picture after 1 month; (f) late postoperative picture after radiotherapy

of the genital and anorectal region, and in tumors involving the lower extremities.[1] The clinical presentation of locally advanced primary and nodal disease is not uncommon in India. Surgery may be curative or palliative in such presentations, which requires radical surgery for the primary tumor and *en bloc* inguinal or ilio-inguinal lymphadenectomy. Inguinal node dissection has been always associated with a high incidence of wound complications. The surgical oncologist has moved from radical dissection to sentinel lymph node dissection to reduce the morbidity due to surgery. Still the role of radical inguinal lymphadenectomy cannot be avoided in certain situations. Potential complications following inguinal block dissection are infection (6–20%), lymphorrhea (6–40%), lymphedema (8–69%) and skin flap necrosis (27–85%).[2] Removal of the adipofascial layer in a groin dissection damages the subdermal plexus, potentially leading to skin flap necrosis. To reduce complications-related to wound healing, various primary reconstructive procedures such as muscle transposition and myocutaneous flaps are used for groin reconstruction. Many of these patients require adjuvant radiotherapy following surgery. Hence, these patients require stable skin coverage over the operated site for the prevention of tissue edema, fibrosis and complications due to wound healing. Primary reconstruction of the groin should, therefore, always be considered for patients undergoing ilio-inguinal node dissection.

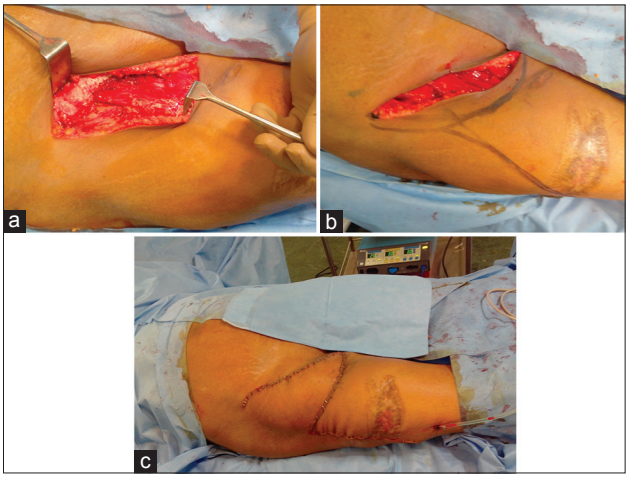

Figure 3: The patient with fungating right sided inguinal lymph nodes. (a) Soft tissue defect inguinal region following dissection; (b) planning of superiorly-based perforator plus flap; (c) immediate postoperative view of the superiorly-based perforator plus flap

Trauma to the inguinal region with soft tissue defects is not uncommon. A high index of suspicion for injuries to the femoral vessels is needed in such cases. With soft tissue defects over the inguinal region, there is always a need for stable soft tissue coverage over the femoral vessels.

Aims of primary reconstruction of the soft tissue defects over the groin region are protection of the femoral vessels, provision of well-vascularized tissue from a distant area, coverage of the dead space in the femoral triangle, a decrease in seroma formation, wound closure without tension, initiation of radiotherapy as early as possible, and a decrease in the length of the hospital stay.[3]

Reconstructive options available for coverage of inguinal defects include the random pattern flap, the tensorfascia lata flap, the perforator propeller-type TFL flap, the modified TFL flap, the gracilis and sartorius flaps, the anterolateral thigh flap, the omental flap, the rectus femoris flap and the rectus abdominis flap. Skin grafting is not sufficient for stable coverage over exposed bones, nerves and vessels. Free tissue transfer requires enhanced microsurgical expertise and may overburden patients in critical condition with progressive malignant disease. In such situations, sufficient soft tissue coverage can be achieved by simple and reliable techniques with minimal donor site morbidity.

The TFL flap was first described in 1934 by Wangensteen[4] and was popularized by Nahai *et al.*[5] for the reconstruction of pressure ulcer defects and for complications following block dissections. Disadvantages of the TFL flap include proximal bulkiness with a thin distal flap, a depressed donor region with an unsightly appearance of the grafted area, and potential loss of stability of the knee due to the sacrifice of fascia lata.

The modified TFL flap includes the muscle with a hatchet shaped incision, which provides adequate mobility of the flap and reduces the dog ear deformity, ensuring closure of the donor area without the need for a skin graft or local flap. Variations in the incision for the flap may not significantly contribute to the reduction of the donor site deformity when the muscle is included in the flap.

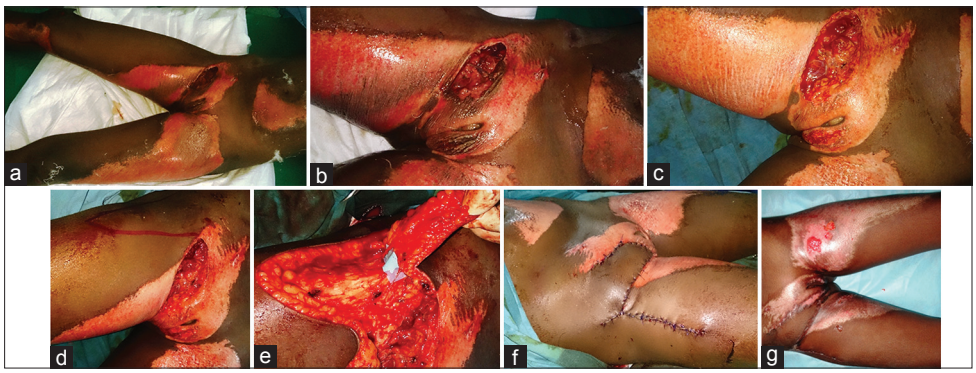

Figure 4: The patient with soft tissue defect over the inguinal region. (a) Soft tissue defect right inguinal region following trauma; (b) closer view of contaminated soft tissue defect groin region; (c) soft tissue defect following debridement; (d) planning of superiorly-based perforator plus flap; (e) identification and preserving the perforators entering the flap; (f) immediate postoperative view of the superiorly-based perforator plus flap; (g) late postoperative picture

However, in our method, the flap is based on perforators without including the muscle. The requirement for mobilization of the local flap ensures tension-free closure of both the donor and recipient sites.

The perforator TFL flap was first described by Deiler *et al.*[6] as a free tissue transfer for the reconstruction of Achilles tendon defects. Kimura *et al.*[7,8] further refined the microdissection technique and described the emergence of septocutaneous perforators between the gluteus medius and TFL muscles. Vegas and Martin-Hervas[9] described the distribution of the branches to the skin from the perforator between the TFL muscle and the gluteus medius and minimus muscles. As a propeller flap, the perforator flap could well be utilized to cover a defect over the inguinal region. The need for microsurgical expertise, the utilization of intramuscular dissection time, the possibility of venous congestion, and the division or noninclusion of the cutaneous nerve within the flap are the disadvantages experienced, while performing this procedure. The superiorly-based perforator plus flap relies on multiple perforators, without sacrifice of the neural component and has a decreased risk of venous congestion when compared to perforator propeller flaps.

Other flaps utilized in the reconstruction of the soft tissue defect over the inguinal region include the anterolateral thigh and vertical rectus abdominis muscle flaps. All these flaps are reliable and provide good soft tissue coverage but at the expense of the sacrifice of a functioning muscle.

After the advent of the angiosomal concept and perforator flaps, skin and subcutaneous tissue-only flaps could be elevated in these regions by preserving the perforators through the area of the TFL. The vascular anatomy of the TFL flap was further studied in detail by Hubmer *et al.*[10] The author described the blood supply of the TFL as the ascending branch of the lateral circumflex femoral artery with multiple direct septocutaneous and indirect musculocutaneous perforators. Clinically, an additional ultrasound color Doppler is necessary to ensure the perforator point of the flap, because there is always some vessel variation in this region (4–23%). A perforator flap avoiding the TFL muscle will provide all the advantages of the TFL flap, minimizing the donor site morbidity and other difficulties arising from the bulkiness of the flap.

The literature has demonstrated that hyperbaric oxygen therapy enhances oxygen delivery to peripheral tissues affected by vascular disruption, cytogenic and vasogenic edema, and cellular hypoxia. Tissue edema significantly affects the perforator flaps, wherein the flaps may experience venous congestion. In our institution, we include hyperbaric oxygen therapy in our treatment protocol to reduce postoperative complications related to postsurgical inflammatory events.

In the present study, a superiorly-based perforator plus flap was used to provide stable soft tissue coverage over the femoral vessels, reducing the risk of wound dehiscence and lymphatic drainage problems with minimal donor site morbidity when compared to other flaps. The flap is designed as a random pattern flap based on the subdermal plexus, taking advantage of the rich blood supply; perforators can be added to enhance the viability of the flap. Hence, the flap could be designed with a length: width ratio in the range of 3:1. The technique is simple, with lower operating time (approximately 50–60 min), and appears to be a reliable flap for coverage of the femoral vessels and inguinal region with good tolerance to radiotherapy. As a single-stage procedure, the superiorly-based perforator plus flap meets the criteria formulated by Gupta *et al.*,[3] with a reliable blood supply[11,12] and a perforator arterial supply away from the field of resection or radiation. However, assessment of the aesthetic and functional outcomes of the superiorly-based perforator plus flap when compared to other flaps requires additional investigation.

Locally advanced genital malignancies, as well as advanced stage cutaneous melanomas of the lower extremity, are common in Asian populations. Radical surgery for the primary and *en bloc* inguinal or ilio-inguinal lymphadenectomy is often required in such situations. Posttraumatic soft tissue defects in the inguinal region are not uncommon. To reduce the complications related to wound healing in the groin region and to withstand postoperative radiotherapy, there is a need for a simple, reliable flap in such patients. The superiorly-based perforator plus flap can be successfully used to reconstruct the inguinal region with reliable coverage of the inguinal vessels and early initiation of radiotherapy.

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Original Article | Plastic and Aesthetic Research

Autologous bone graft harvested during implant site preparation: histological study

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ABSTRACT

Aim: The bone particles harvested during osteotomy could be used as autogenous bone graft materials to correct a bony defect prior to implant placement. **Methods:** A simple surgical procedure was described in which autogenous bone was harvested from the drills during the preparation of implant sites. Eleven samples were obtained from bone drilling during fixture installation in 11 patients (5 men and 6 women) with an average age of 57 years. These samples were subjected to histological preparation, in order to evaluate for the presence of viable osteoblasts. **Results:** Histological evaluation of the samples suggested that the viability of the bone tissue was maintained. **Conclusion:** The results show that this method of harvesting autogenous bone may be useful in situations where small amounts of bone are required.

Key words:

Bone graft, bone harvesting, oral implantology

INTRODUCTION

In our clinical practice, a bone graft is often necessary to correct a bony defect prior to implant placement. Autologous bone is considered to be the "gold standard" for bone grafting,[1-3] as it does not produce adverse reactions and has optimal biocompatible remodeling patterns and osteoinductive capabilities.[4-6] Grafting particulate bone is considered to be a better option than *en bloc* harvesting due to the former's capacity to adapt to the site of engraftment; it enables a larger quantity of harvested material to be grafted, with advantages in terms of long-term cell survival, although the latter is influenced both by the harvesting technique and the dimensions of the particles.[7]

The aim of this study was to assess the presence of viable osteoblasts in bone tissue harvested with drills during implant site preparation.

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METHODS

Clinical procedure and patient selection

A total of 11 patients (5 men and 6 women, aged between 35 and 75 years, with an average age of 57 years), in good general health condition, were included in this study. Patient selection criteria for this study were established so as to include patients with loss of one or more dental elements and with moderate alveolar atrophy diagnosed in preoperative X-ray examinations, including panoramic radiography. An Ethical Committee evaluated and accepted the guidelines of the study. All patients gave their informed consent to participate in the study.

Surgical procedure

All surgeries were performed under sterile conditions. Chlorhexidine 0.2% was used to rinse the oral cavity for 2 min prior to surgery. Local anesthesia consists of 1:200,000 mepivacaine-epinephrine was infiltrated into the mandibular/maxillary surgical site. An implant of adequate length was selected by radiographic examination, and a full thickness flap was designed. Implants were

then placed following a modified drilling sequence to undersize the osteotomy and increase the insertion torque. The implant system's drills were of kind implant fixture with parallel shape. Drills set a low speed were used in succession, harvesting autogenous bone from the drills for later bone defect grafting. A precision initial drill allowed accurate positioning of the osteotomy within the palatal alveolar wall. Once the direction of drilling was established, the site was enlarged with a 2 mm pilot drill. Subsequent twist drills were used to widen the osteotomy following the manufacturer's instructions. The final drill however, was only utilized to a depth of approximately two-thirds of the implant length.

Implant site was prepared using a surgical motor (Implantmed, W and H GmbH, Burmoos, Austria) at a speed of 350 rpm and a torque setting of 45 Ncm. A particulate bone graft was harvested from the drills, while the implant site was prepared without irrigation with saline solution [Figures 1 and 2].

Finally, internal implants with a laser microgrooved coronal design (Biohorizons, Birmingham, Ala) were placed. Implant placement was performed using a surgical motor (Implantmed, W and H GmbH, Burmoos, Austria) at a speed of 15 rpm and a torque setting of 45 Ncm. In all cases, a ratchet wrench was used to fully seat the implants as the torque required exceeded the 45 Ncm set on the motor. The harvested material was used to fill the bony defects. At that time, a small sample of the harvested material was also sent for histological analysis.

Following surgery, patients were instructed not to brush or irritate the surgical sites for 10 days, to irrigate their mouth with chlorhexidine 0.2% 3 times a day for 1 week, and to maintain a soft diet for about 6 weeks. Analgesics (ibuprofen, 400 mg) and antibiotics (amoxicillin, 1,000 mg, 3 times daily) were prescribed to be taken for 1 week. Ten days after implant insertion, the sutures were removed.

Histological analysis

The samples harvested for histology at the time of implant installation were fixed for 24 h in a neutral formaldehyde solution of 10% Leica ASP 300S® (Leica Biosystems Richmond, Inc. IL 60071) Tissue Processor. Subsequently, they were decalcified in a vial containing 10% ethylenediaminetetraacetic acid (EDTA) for 4 weeks. The EDTA solution was changed every week in order to remove the calcium from the bone fragments through chelation. After decalcification, the samples were embedded in paraffin, sliced with a microtome (Leica RM2125RT Microtome®, Leica) and stained with hematoxylin and eosin in Leica Autostainer ST5020® (Leica), after which they were ready for microscopic analysis.

RESULTS

Histological evaluation of the samples with an optical microscope showed that, even in a particulate state, the bone structure was well-preserved [Figures 3 and 4], containing a large number of osteocytes within the

Figure 1: Particulate bone graft is harvested from the drill

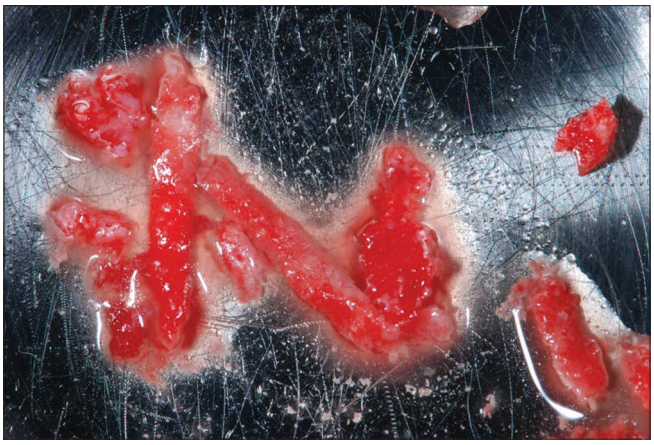

Figure 2: A harvested particulate autologous bone graft

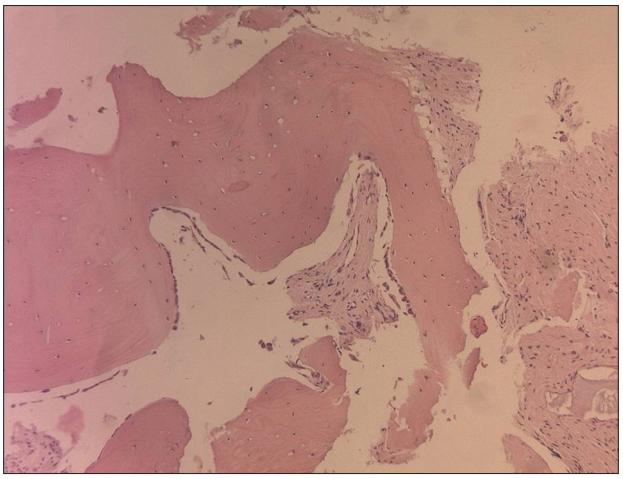

Figure 3: Panoramic view. Histological appearance of the bone harvested from the drills (HE, ×10)

calcified matrix and a large number of osteoblasts, expressing viable cells, and suggesting that the viability of the bone tissue was maintained and able to begin ostogenesis. A large number of osteocytes and osteoblasts were contained in all samples.

DISCUSSION

Bone particles harvested during implant site preparation consist of a mixture of cortical bone and cancellous bone,

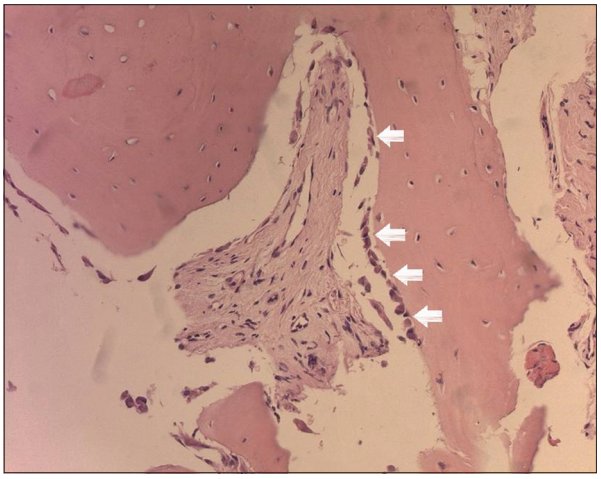

Figure 4: The picture shows continuous osteoblasts line (arrows) on mature bone (HE, ×20)

and have histologically well-preserved structures with a large number of osteocytes in a calcified matrix.[8] In an animal study, Coradazzi *et al.*[9] found that harvested bone resorbed more rapidly and showed higher osteoinductive potential than particulate bone in the early healing stages.

Particle size and available bone volume are important factors for graft material. In general, small particles are preferred secondary to more rapid resorption, greater surface area, and enhanced ostogenesis,[10-12] but particles that are too small lack the space for the migration and proliferation of cells, vessels, and bone. A pore size of at least 100 μ is necessary. Zaner and Yukna[12] recommended that an appropriate particle size would be 300–500 μ.

Grafting particulate bone is considered a better option than *en bloc* harvesting because of the former's capacity to adapt to the site of engraftment; it enables a larger quantity of harvested material to be grafted, with advantages in terms of long-term cell survival, although the latter aspect is influenced both by the harvesting technique and the dimensions of the particles.[7]

The drill was set at low speed as this has been shown to preserve viable osteocytes.[13,14] For these reasons, an investigation was made on the methods of obtaining autogenous bone tissue by means of drills, and the possibility for preservation of cells with bone induction capacity was evaluated.

The use of bone harvested should be considered to be an extremely conservative technique, since it eliminates the need to obtain autogenous bone material from a second surgical site, which can be complex.[15]

There are no studies to date which have histologically evaluated the bone harvested during implant site preparation. From the results obtained it is concluded that the harvesting method described is capable of preserving cells with bone induction capacity, secondary to a large number of osteoblasts and the expression of viable cells. This suggests that the viability of the bone tissue is maintained and can begin osteogenesis. Another positive factor is the utilization of autogenous bone tissue of membranous and not of endocondral origin, a material known to be more efficient because it has lower reabsorption levels.[16]

The surgical technique described for the procurement of particulate intraoral autogenous bone material is simple, efficient and safe. The possibility of harvesting bone graft while the implant site is being prepared allows the procurement of the particulate bone without the disadvantages of donor site morbidity.

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Original Article Plastic and Aesthetic Research

The influence of national guidelines on soft tissue sarcoma patient outcome: a single center experience

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ABSTRACT

Aim: The aim was to study the impact of nationwide clinical practice guidelines for soft tissue sarcomas (STS), introduced in 1994 and again in 2005 in North Savo, Finland. **Methods:** We retrospectively reviewed all the patients whose sarcoma was treated by a multidisciplinary team between the years 2000 and 2009 with mean follow-up time of 68 months. The patients were divided into 2 groups according to years: Group A (2000–2005, 72 patients) and Group B (2006–2009, 64 patients). Primary outcomes were local recurrence, metastases, and overall survival. **Results:** Fifty-five percent were men with an average age of 59 years. The most common sarcomas were pleomorphic sarcoma (37%) and liposarcoma (26%). Although there were significantly less amputations in Group B (A: 15%, B: 3%), there were more metastases (A: 10%, B: 23%) with an overall lower overall survival rate (A: 70%, B: 58%) than in Group A. Conversely, Group A had a higher 1st year survival rate (A: 100%, B: 87%). We found that upper limb sarcomas were more likely to be diagnosed with incisional biopsies, but there was no correlation between incisional biopsy and recurrence, metastases or survival. **Conclusion:** Due to nonadherence of the 2005 national treatment recommendations, there has been no improvement either in management or survival. The importance of educating guidelines to doctors referring patients to specialized units cannot be overemphasized to affect successful management in the treatment of STS.

Key words:

Clinical guidelines, follow-up, incisional biopsy, soft tissue sarcoma

INTRODUCTION

Soft tissue sarcomas (STSs) are a rare group of heterogeneous malignant tumors derived from mesenchymal cell lines.[1] They represent approximately 1% of all malignancies.[2-4] STS can occur at any age, but the peak of incidence is in the late adult life. Introduction of multidisciplinary teams and referral of patients to specialized care units with diagnostic radiology, histopathology, surgical expertise and neoadjuvant and adjuvant therapy has improved the management of STS.[1]

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The Hospital District of North Savo is comprised of 7 hospital areas and 855,000 (year 2000) and 843,000 (year 2009) inhabitants. The multidisciplinary STS group of Kuopio University Hospital was established in 1994. The group meets on a weekly basis to discuss the best approach for each patient with STS utilizing a multidisciplinary team.

In this study, we analyzed all patients whose sarcoma was evaluated by this multidisciplinary team over a 10 years period: 2000–2009. At the beginning of the study, the algorithm for examination and treatment in primary health care for STS was not what it is today. To increase awareness regarding tumor diagnostics, accurate biopsy methodology and imagining, the current clinical practice guidelines were introduced to the primary care units and tertiary centers by lectures and bulletins. Guidelines

included tumor characteristics necessitating referral to specialized units. These were a fast-growing mass, diameter wider than 5 cm, location close to the deep fascia, development of pain in a previously painless lump and a newly formed tumor in the same location as benign tumor noted previously.

In order to measure the impact of the multidisciplinary groups and clinical guidelines, we divided the time period into 2 parts and compared the results of treatment. The first period, Group A, comprised the early part of the study (2000–2005) when the knowledge was still poor. The last 4 years after introduction of guidelines (2006–2009) comprised the second period as Group B.

The aim of this study was to determine, if there were any differences in the outcome of STS in Hospital District of North Savo, when diagnostic methods, the treatment results, local recurrences, metastases, and overall survival were analyzed between the 2 periods.

METHODS

All the material was retrospectively collected from the files of multidisciplinary sarcoma group meetings. Accordingly the patients' medical reports were reviewed for medical data. The patient demographics were collected [Table 1]. The interval between the symptoms and the histological sample collection was measured, and information about tumor characteristics (the type of the sarcoma, tumor size, location, grade, sample collection method, metastasis, and recurrence) were clarified [Table 1]. In addition, we studied if there were any previous condition, which required surgical intervention in the sarcoma site. Furthermore, the patients' previous oncological treatments before the sarcoma diagnosis were examined [Table 1]. Desmoid tumors were excluded from the study.

Samples were studied by an experienced pathologist, (Professor Ylermi Soini), and classified according to the guidelines of the World Health Organization: classification of soft tissue and bone tumors using routine H and E staining and immunohistochemistry including vimentin, desmin, S-100, protein CD34, sytokeratin PAN (AE1/AE3), Ki67 (all from Roche Biotechnology) and desmin (Dako, Glostrup, Denmark) and stained with an automatic immunostainer (Ventana and Dako).

Statistical analyses were done with Statistical Package for the Social Sciences SPSS® Base version 18 (SPSS, Inc., Chicago, Illinois, USA).

The study was approved by the Ethical Committee of Kuopio University Hospital, and all patients gave their written informed consent for participation in the study 15/2009.

RESULTS

One hundred and thirty-five patients with STS were treated in Kuopio University Hospital between 2000 and 2009 [Table 1]. Seventy-four (55%) of them were men and 61 (45%) women. Average age for the all patients was 59 years (64 mean [13–89]). Only 2 of the patients were under 18 years. The mean follow-up time was 68 months (range: 12–149).

Annual incidence of STS in Group A was 1.39/100, 000 (inhabitants) and 1.89/100,000 in Group B.

Soft tissue sarcoma histology

When the total time period (2000–2009) was analyzed, the most common sarcomas in descending order were found to be pleomorphic sarcoma (37%), liposarcoma (26%), fibrosarcoma (10.4%) and leiomyosarcoma (9.6%) [Table 2]. Pleomorphic sarcoma

Table 1: Patient demographics

Characteristics	Total (%)	Group A (%)	Group B (%)
Gender			
Male	74 (55)	39 (55)	35 (55)
Female	61 (45)	32 (45)	29 (45)
Total	135	71	64
Age			
Median	64	64	65
Operation	118 (87)	63 (90)	55 (84)
Oncological treatment			
Chemotherapy	15 (11)	10 (14)	5 (8)
Radiotherapy	63 (47)	31 (44)	32 (50)
Recurrence	22 (16)	10 (14)	12 (19)
Metastases	22 (16)	7 (10)	15 (23)
Survival			
Deaths	48 (36)	21 (30)	27 (42)

Description of patients, treatment and survival characteristics of the 135 patients with soft tissue sarcoma treated in Kuopio University Hospital years 2000–2006 (Group A) and 2006–2009 (Group B)

Table 2: Tumor characteristics

Characteristics	Total (%)	Group A (%)	Group B (%)
Histology			
Pleomorphic sarcoma	50 (37)	25 (35)	25 (39)
Liposarcoma	35 (26)	20 (15)	15 (23)
Fibrosarcoma	15 (11)	8 (11)	7 (11)
Leiomyosarcoma	13 (10)	8 (11)	5 (8)
Angiosarcoma	3 (2)	0 (0)	3 (5)
Chondrosarcoma	4 (3)	2 (3)	2 (3)
Synovialsarcoma	4 (3)	2 (3)	2 (3)
Other[a]	11 (8)	6 (9)	5 (8)
Site			
Lower limb	78 (58)	46 (65)	32 (50)
Trunk	31 (23)	14 (20)	17 (27)
Upper limb	22 (16)	10 (14)	12 (19)
Head and neck	3 (2)	1 (1)	2 (3)
Sampling method			
CNB[b]	89 (66)	47 (66)	42 (66)
Excisional	24 (18)	11 (16)	13 (20)
FNB[c]	5 (4)	2 (3)	3 (5)
Incisional	14 (10)	9 (13)	5 (8)

Description of histology, site and sampling method characteristics of the 135 patients with soft tissue sarcoma treated in Kuopio University Hospital years 2000–2006 (Group A) and 2006–2009 (Group B).
[a]Malignant schwannoma, [b]Core needle biopsy, [c]Fine needle biopsy

was equally common in both genders (38%), as so was leiomyosarcoma (men 9.5%, women 9.8%). Fibrosarcoma was found to be more than twice as common in men (14.9%) than women (6.6%). Liposarcomas, fibrosarcomas, synovial sarcomas and chondrosarcomas occurred usually in young adults and in middle-aged people. Among elderly patients' liposarcomas and pleomorphic sarcomas were the most common tumors. The incidence of leiomyosarcomas was same in all age groups studied.

Tumor location

In this study, 78 patients (58%) had a tumor in their lower limb and 20 tumors were diagnosed below the knee [Table 2]. Thirty-one patients (23%) had a tumor in the trunk, 22 (16%) in the upper limb and 3 (2%) in the head or neck region. In Group A, 46 patients (65%) had sarcoma in the lower limb, 14 (20%) in the trunk, 10 (14%) in the upper limb and 1 (1%) in the head and neck region.

In the latter Group B, 32 patients (50%) had sarcoma in the lower limb, 17 (27%) in the trunk, 12 (19%) in the upper limb and 2 (3%) in the head and neck.

Sampling method

In this study, 89 tumors (66%) were diagnosed with core needle biopsy (CNB), 5 (4%) with a fine-needle biopsy, while 24 tumors (18%) were excised for the histology and 14 (10%) were analyzed by incisional biopsy (excision with positive margins). In Group A, 47 were (66%) diagnosed with CNB, 11 (16%) with excisional resection, 2 (3%) with fine-needle aspiration biopsy (FNAB) and 9 (13%) with incisional biopsy. In the Group, B 42 were (66%) diagnosed with CNB, 13 (20%) with excisional resection, 3 (5%) with FNAB and 5 (8%) with incisional resection. The number of tumors that were diagnosed by incisional biopsy was found to be high if the tumor was located in the upper limb ($P = 0.002$). These incisional biopsies were performed in tertiary centers or in local hospitals without consulting specialists. However, there were no statistical difference between the sampling methods used when occurrence of metastases, local recurrence or death were analyzed.

Treatment

The most common surgical treatment was wide local excision (56 patients, 42%). Total myectomy was done for 49 patients (36%) and amputation for 13 patients (10%). Seventeen patients (13%) were treated conservatively. When comparing the groups, there were no differences between operation methods except for the amputation rate. Limb amputation were done to 11 patients in Group A, whereas only 2 in Group B. In this study, 63 patients (47%) received radiotherapy and 15 patient's chemotherapy (11%). There were no differences in adjuvant therapy between the 2 groups.

Survival

In Group A, 10 patients (14%) got a recurrence tumor during the follow-up period and in Group B 12 patients (19%) [Table 3]. All the recurrences occurred within 2.5 years (range: 1–27 months) after the primary operation. Twenty-two of all patients (16%) got a recurrence during 2 years' follow-up.

Table 3: Primary outcomes

Outcome	Group A (%)	Group B (%)
Recurrence	10 (14)	12 (19)
Metastases	7 (10)	15 (23)
Survival	50 (70)	37 (58)

In Group A, 8 out of 10 recurrences were high-grade tumors (7 pleomorphic sarcoma, 1 leiomyosarcoma). Two tumors were low-grade sarcomas (liposarcomas). Six of the 10 patients died with recurrences during the follow-up time of 5 years.

In Group B, 12 tumors recurred, from which 5 were pleomorphic sarcomas, 3 liposarcomas, 2 fibrosarcomas, and 2 angiosarcomas. Ten of these 12 tumors were high-grade tumors. One was a low-grade liposarcoma, which was diagnosed by incisional biopsy. Four patients were diagnosed with an excisional biopsy, and 3 were operated intralesionally for diagnosis. Four patients got lung metastases and 8 died during the follow-up time. There were no significant differences in local recurrence between the 2 groups.

A total of 22 patients (16%) had metastases, of which the most common sites were lung, bone and lymph nodes [Table 3]. Two skin metastases were found in patients with pleomorphic sarcoma, 5 patients had lymph nodes metastases (chondrosarcoma, liposarcoma, pleomorphic sarcoma and fibrosarcoma), and 4 patients had bone metastases (pleomorphic sarcoma, liposarcoma and malignant schwannoma).

During the follow-up time, 7 patients (10%) in Group A got metastases, whereas in the Group B incidence of metastases was higher (15 patients, 23%) ($P = 0.033$).

A total of 48 patients (36%) died during the follow-up time. Seventeen patients were treated conservatively without surgical intervention. These patients were either unsuitable for operation because of their co-morbidity, or they declined the surgery. Among all the patients who underwent surgery, mortality rate was 23% (31 patients).

In Group A, 21 patients (30%) died during the follow-up period whereas 27 patients (42%) died in the Group B. All deaths occurred within 22 months after the diagnosis (range: 1 month–6 years with a median period of 12.5 months). There were no statistical significance differences in overall survival between the groups for the follow-up period but there was a difference in the survival for the 1st year [Figure 1]. The 1st year survival was 100% in the Group A and 87% in the Group B.

DISCUSSION

The present study shows that increasing the general awareness about STS management among general practitioners did not improve either the results or the survival. But it may have improved the referral rate

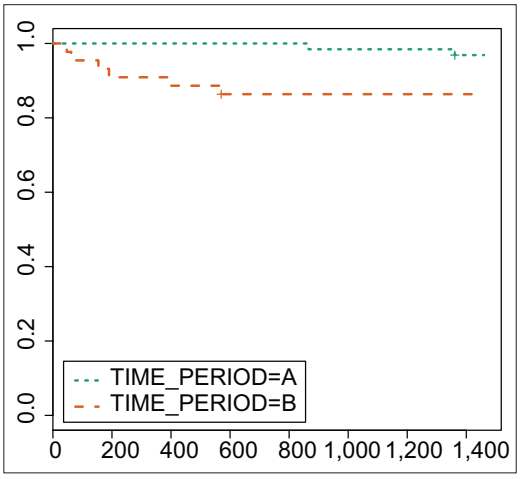

Figure 1: Soft-tissue sarcoma specific survival between the time periods; Group A (green) and Group B (red)

after the knowledge about tumor diagnostics improved. In the latter years of the study, the number of sarcoma patients increased. In the year 2001 there were 8 patients diagnosed with STS, in 2008; 19 patients and in 2009; 15 patients. This likely resulted from improved knowledge of these tumors by primary care practitioners and improved referral patterns to specialized units.

When comparing our single institution's STS results with a nationwide population based study in Finland, no statistically significant differences in surgical treatment, local recurrence, metastasis or survival were noted.[5] STS local recurrence in our series was 22% and as opposed to 30% in earlier studies.[1]

In this study, Group B had more metastases [Figure 1] a lower survival rate as well as a shorter survival time. We also noted that the 1st year survival was better in Group A. Because this was a retrospective study, we were not able to analyze the effect histologic grading on cervical. Between the years, 2000 and 2009 sarcomas were primarily divided into 3 histologic grades: grade I presenting the low-grade tumors and Grade II and III the high-grade tumors. This histological grading system is proposed by the French Federation of Cancer Centers and is the most commonly used system for assigning tumor grading.[6,7] Although there were only minimal differences in grading between the groups, it is notable that Grade III tumors were equally prevalent in the 2 groups studied: (A: 43%, B: 45%).

Despite the grading, we found that tumors in the Group B to be more likely to have metastases with a lower overall survival rate. After consideration of all parameters studied, we found that there were more trunk sarcomas in the Group B. Many studies have shown that sarcomas located in the trunk (chest wall, internal trunk and retroperitoneum) have a worse prognosis and a higher rate for local recurrence.[1,8,9] This is mainly due to the difficulty of gaining adequate resection margins and lack of thick barriers such as the muscle fascia's.

Interestingly, a remarkable number of upper limb tumors were diagnosed by an incisional biopsy. This was done in either tertiary centers or local hospitals with appropriate consulting. Presumably, the delay between detecting the lump and getting treatment was short because upper limb tumors are easily found by the patients themselves, and even small tumors are visible in this area. However, this study showed that even though the tumors were biopsied incisionally, this did not result in cancer spreading or poor survival. The patients whose tumors were incisionally biopsied had the same outcomes with those whose tumors were diagnosed according to the national practice guidelines. According to the literature, the risk of residual tumor tissue is 24–60% after an unplanned surgery[10,11] and therefore confirms the fact that unplanned surgery increases the risk of local recurrence.[12,13] But still many patients are operated in tertiary centers without accurate imagining and biopsy.[14,15]

There were many patients who had had a previous benign tumor in the same location. In addition to the previous tumor diagnosis and treatment, the newly formed tumor should always be examined as an independent disease, according to the recommendations. Furthermore, we found that in some cases histological evaluation was never made and thus the diagnosis was delayed.

National guidelines are still not being followed correctly. Sarcomas are being incisionally biopsied without appropriate imagining. A failure to implement guidelines is primarily due to the rarity of this malignancy. Only a few doctors come to face STS during their practice and therefore the guidelines are not easy to remember. To increase the awareness of tumor diagnostics, the national guidelines should be effectively and repeatedly processed in tertiary centers. Written recommendations in the Internet are not enough. Guidelines have to be introduced by personal education, lectures, and program with easy availability to all doctors who take part in referring patients to specialized units.

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Original Article | Plastic and Aesthetic Research

Differential fat harvesting

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ABSTRACT

Aim: Volume replacement with fillers is regularly performed with the use of diverse volumetric materials to correct different structures around the face, depending on the volume enhancement required and the thickness of the soft tissue envelope. Differential fat harvesting and posterior grafting is performed to place the correct fat parcel size for each target area, expanding the potential applications of fat. **Methods:** Sixty patients consecutively recruited on a first come basis undergone a facial fat grafting procedure, in private practice setting between March 2012 and October 2013. Fat grafting quantity and quality was predicted for each case. Differential harvesting was performed, with 2 fat parcels size. Processing was performed through washing. Fat infiltration was carried out through small cannulas or needles depending on the treated area. Outcomes were analysed both by the physicians and the patients at 7 days, 1 month, 3 months and 6 months through a perceived satisfaction questionnaire. Parameters considered were downtime or discomfort, skin benefits, volume restoration, reabsorption rate estimated and overall improvement. **Results:** Full facial differential fat grafting procedure lasted an average of 1.5–2.5 h. Average downtime was 3–4 days. Follow-up was performed to a minimum of 6 months. Both patient and physician overall satisfaction rates were mostly excellent. Adverse events like lumps or irregularities were not encountered. **Conclusion:** Differential fat harvesting and posterior grafting is a valid alternative, to expand the repertoire of fat use, allow a more homogeneous effect, reduce the potential complications, speed up the process, improve graft survival, and to enhance overall aesthetic outcome.

Key words:

Adipose stem cells, differential harvesting/grafting, facial fat grafting, mesofat, sharp needle intradermic fat grafting

INTRODUCTION

Volume replacement with fillers is regularly performed with the use of diverse volumetric materials to correct different areas around the face, depending on the volume enhancement required and the thickness of the soft tissue envelope that allows concealing the product.

Fat grafting, according to Coleman,[1] has been traditionally done with tissue harvested with 2 mm port cannulas which only allows a gross correction of volume.

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The former technique presents several limitations and complications especially in the lower eyelid region.[2] In this area, the gross fat parcels cannot be hidden by a thin soft tissue envelope without risking overcorrection or lumps.

Micro fat grafting has been proposed as an option to bypass the former problems, and to extend the application of lipostructure to the superficial layers of the skin.[3] However, this is time consuming and inefficient in volume restoration. Moreover, harvesting through small hole cannulas can affect the integrity of adipocytes.[4,5]

Fat processing is another key factor in fat grafting, which allow us to get rid of all the toxic and inflammatory agents that may affect graft retention. Centrifuging, washing and decanting have been proposed as valid alternatives. Nevertheless, recent data suggest that strong centrifugation can damage adipose graft integrity and decanting is not able to get rid of the oil vacuoles present within the graft. Washing, therefore, remains as the single most important phase in fat processing.[6] The same authors have proposed

a soft centrifugation (400 g/L min [1,000 rpm/L min]) as an alternative following washing of the graft.

Both traditional fat grafting and micro fat grafting have pros and cons. Differential fat harvesting is performed in an attempt to obtain the correct fat parcel size for each target area, expanding the potential uses of fat, and allowing for superior homogeneity and aesthetics.

METHODS

Sixty consecutively recruited patients underwent facial fat grafting, between March 2012 and October 2013 in private practice setting. The procedure was explained in detail and informed consents and ethical statements were signed for each case.

A Torres facial fat grafting record was used to predict the quantity and quality of the fat to be used in each case [Figure 1].

Facial fat consumption was estimated taking into consideration:

1. Fat to be placed in critical areas (periorbital, temples, lips, nasal)
2. Fat for needle placement prediction (sharp needle intradermic fat [SNIF] grafting or mesofat technique)[7,8]
3. Fat for adipose stem cell (ASC) enhancement estimation
4. Fat for volume enhancement in the rest of the face.

Super wet infiltration of the donor site was performed with a low dose of lidocaine solution (maximum 20 mL lidocaine 2% in 500 mL saline), trying to infiltrate an equal volume of liquid compared to the volume of fat to be removed.[9]

Following the record, the differential harvesting concept was applied, where fat was extracted in two different manners.

Thin fat parcels (i–iii) were extracted manually with a six port (0.8 mm each) Tulip Tonnard harvesting 2 mm width × 15 cm length cannula (Tulip medical, San Diego, CA) coupled to a 20 mL syringe.

Thick fat parcels (iv) are automatically extracted with a Shippert four port (5 mm × 2 mm each) harvesting 3 mm width × 15 cm length cannula (Shippert medical, Denver, CO) connected to a biplane luerlok handle attached to a 250 mL Filtron Unit (Shippert Medical, Denver, CO) linked to an surgical aspirator.

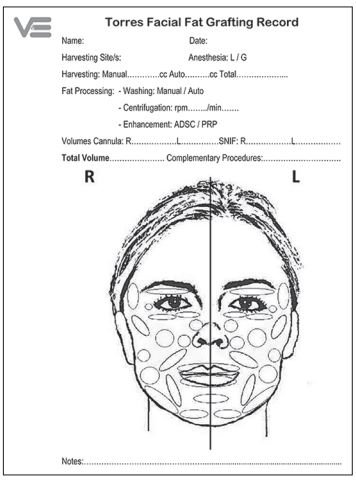

Figure 1: Torres fat grafting module. It helps to estimate pre operatory fat volumes and type of fat needed for each case, that will command the differential harvesting and posterior grafting

Fat processing was performed through washing in a closed manner with the aid of Filtron device for the thick fat and manually in an open system for the thin fat extracted.

Facial regional blocks were performed with mepivacaine prior to infiltration phase.

Thin fat parcel infiltration was carried out through 0.9 mm × 5 cm Tulip injector cannula (Tulip medical, San Diego, CA) in critical areas (temples, periorbital, lips, and nasal) or with needles; 23 G × 30 mm in SNIF or 27 G × 4 mm in Mesofat technique. Needle was placed in superficial wrinkles and lines, to enhance corrections at an intradermal plane for deep folds, and in cases of strong photo and chrono aging (Mesofat).

When available ASCs filter Mystem (Bimedica SRL, BG, Italy) was used in combination with fine parcel fat to obtain ASC enhanced serum to be mixed with fat prior to infiltration.

Thick fat parcels were infiltrated using a 1.2 mm × 7 cm Tulip cannula in all the other parts of the face. This placement was favoured whenever the primary goal was volumetric enhancement and when soft tissue envelope was thick.

The amount and type of fat injected in each area is summarized in Table 1.

Parameters analysed were downtime and discomfort, skin benefits, volumetric enhancement, reabsorption rate, and overall improvement, all of which were recorded using a patient satisfaction questionnaire [Table 2], applied at 7 days, 1 month, 3 months and 6 months. Satisfaction scores were considered as excellent (15–20 points), good (10–14 points), minor (5–9 points) and poor (< 5 points). Statistical analysis was performed in Excel 2013.

Table 1: Amount and type of fat injected per area

Area	Type of fat	Amount of fat injected (mL)
Eyebrow	Thin fat	1*
Temples		2*
Lower palpebral medial		1*
Lower palpebral lateral		1*
Lateral canthus		0.3*
Lips		3
SNIF (glabella, lips and NLF)		2
Zygoma	Thick fat	2–3*
Malar		2*
Buccal		3*
NLF		1*
Canine fossa		1*
Labiomental fold		1.5*
Mental crease		1*
Total per side		21.8
Total for full face approach		43.6

*Per side. SNIF: Sharp needle intradermic fat, NLF: Nasolabial fold

RESULTS

The study included, 48 women (age range: 37–58 years, mean: 49 years) and 12 men (age range: 32–34 years, mean: 33 years).

Full facial differential fat grafting procedure last between 1.5 and 2.5 h, and was performed under local anaesthesia and minor sedation in the majority.

Average volume harvested manually was 21 mL (mean: 21 mL; median: 21.5 mL; standard error: 0.61 mL; range: 18 mL) (of fine parcels fat) and automatically 35 mL (mean: 35.02 mL; median: 35 mL; standard error: 0.635 mL; range: 25 mL) (of thick parcels fat). Average fat infiltrated was 45 mL (mean: 45.14 mL; median: 45 mL; standard error: 0.995 mL; range: 35 mL).

Harvesting sites were: abdominal (50%), outer thighs (20%), back (10%), triceps (10%), inner thighs, and knee (10%).

ASC filter was used only in six cases, which did not allow us to statistically analyse the data.

Table 2: Patient satisfaction questionnaire, for satisfaction assessment at 7 days, 1 month, 3 months and 6 months

Parameter evaluated	Score
Downtime or discomfort	
No downtime or discomfort	4
Very slight discomfort (downtime 24 h)	3
Average discomfort (downtime 2–5 days)	2
Moderate to severe discomfort (downtime 5–10 days)	1
Severe discomfort (downtime > 10 days)	0
Skin benefits	
Excellent (improves in tone, elasticity and texture)	4
Moderate improvement	3
Slight improvement	2
None	1
Worsening of skin quality (acne lesions, scars, *etc*.,)	0
Volume restoration outcome	
Very satisfied	4
Moderately satisfied	3
Slightly satisfied	2
Not satisfied	1
Dissatisfied (important over or under corrections)	0
Reabsorption rate estimated (%)	
0–20	4
20–30	3
30–50	2
50–70	1
> 70	0
Overall evaluation	
Very satisfied	4
Moderately satisfied	3
Slightly satisfied	2
Not satisfied	1
Dissatisfied (important overcorrections or under corrections)	0
Total possible score for fat grafting procedure	20

Satisfaction was defined as: excellent (20–15 points), good (14–10 points), minor (9–5 points), and scarse (< 5 points)

Average downtime was 3–5 days, with minimum to moderate inflammation.

Follow-up was performed for a minimum of 6 months (range: 6–12 months) [Figures 2–4].

Satisfaction questionnaires showed high test scores at 5 days (mean: 16.42, standard error: 0.26, median: 16, mode: 15, and standard deviation: 1.93). Slight descent trend in the test scores were seen at 6 months (median: 16, standard error: 0.29, median: 16, mode: 16, and standard deviation: 2.1). Global patient test scores and trend lines are shown in Figure 5. Satisfaction scores evaluations were defined as excellent 89% (n = 193), good 8.8% (n = 19), minor 1.85% (n = 4).

Adverse events like lumps or irregularities were not evidenced.

Dissatisfaction was referred by 2 patients for under correction in the buccal region (1 patient) and temporal area (1 patient).

Skin improvements were mild to moderate and were often referred spontaneously by the patients.

Both patient and physician satisfaction rate was excellent in 81.5% (n = 44) of the cases.

DISCUSSION

Traditionally Coleman lipostructure has promoted fat harvesting with 2 mm port cannulas, followed by a strong centrifugation (3,000 rpm for 3 min), removal of the supra and infranadant, and final reinfiltration with the aid of 16 G cannulas.[1] The former has permitted to achieve gross good aesthetic improvements with long lasting results. Nevertheless, extensive discomfort and healing time (15 days), unpredictable reabsorption, need of overcorrections, frequent retouches and lower lid complications[2] have made the technique less attractive for patients and physicians. Therefore, efforts have been made to find a more predictable and forgiving technique.

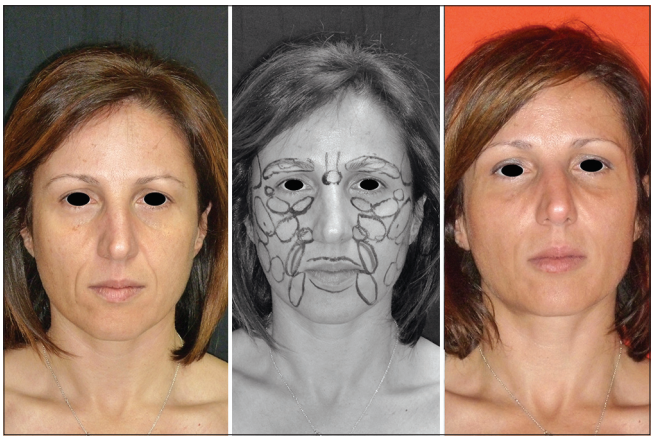

Figure 2: Clinical case 1. Patient before, intra operatory design, and 6 months postoperative

According to Eto *et al.*,[10] micro fat lobules are easy to inject, have a greater three-dimensinal cellular interaction and generate less nodules or bumps incidence. Moreover they have greater versatility of use, being placed using cannulas or needles and in different anatomical planes (subcutaneous or intradermal). Recently, it has been proposed that greater tissue disruption obtained with smaller cannulas has been associated with higher amount of ASC in the lipoaspirate, especially of the superficial layers of fat.[11]

Indications for thin fat parcels harvesting include: the treatment of facial critical areas of delicate skin with thin soft tissue envelope (like periorbital, temporal and perioral regions), the delivery of fat through needles (SNIF or Mesofat techniques),[7,8] main treatment goal to be skin regeneration, and the use of fat for ASC enhancement through filters.

Nevertheless their extraction is much slower than traditional harvesting. Furthermore, reduced diameter or ports from harvesting cannulas generate greater adipose cells stress, cellular breakdown and oil content in the harvested tissue, resulting in less viable adipose cells, with greater necessity of fat processing (washing or centrifugation) [Figure 6].[4,5]

All above, has put micro lipofilling into fashion, increasing its popularity and interest in the medical community. It has also created greater confusion widening the possible range of variables regarding fat grafting. This has been reflected in recent publications that try to obtain a recipe for the correct technique.[12]

The goals of a fat grafting treatment are: volume restoration and skin regeneration. Volume is determined mainly by the adipocytes, and the process known as primary adipocyte integration should be considered a primary goal within the treatment.

Cellular regeneration, is principally explained by the presence of ASC in the lipoaspirate. It is an important event, but it is not the only factor involved.

Cannulas port size affects directly the adipocytes. The larger the aspiration cannula, the greater the viscosity, retention and quality of the graft.[4,5]

On the other hand the smaller the cannula size, the lesser the viscosity, and higher tissue disruption, oil content and amount of ASC within the graft [Figure 7]. A fluid grafts allows needle or fine cannula placement and avoids irregularities in critical areas.

In this context, the concept of differential harvesting is raised.

The term differential fat harvesting stands for fat harvesting through different cannulas (port sizes or

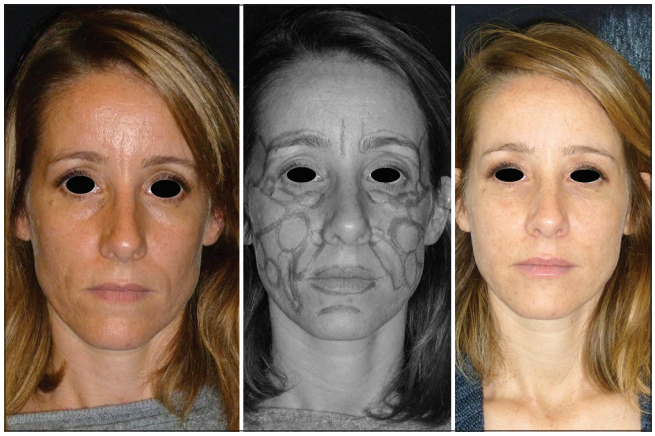

Figure 3: Clinical case 2. Patient before, intra operatory design, and 6 months postoperative

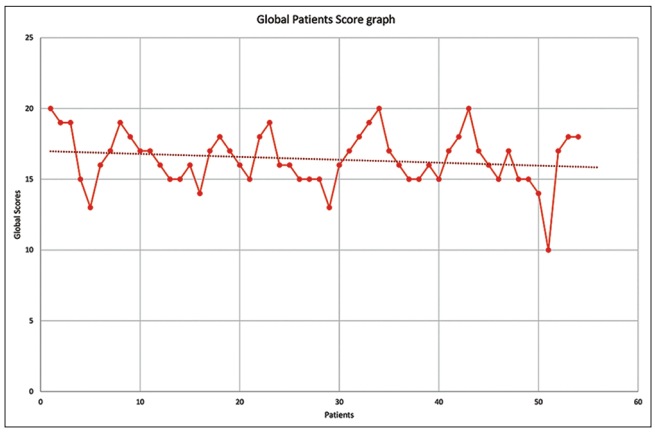

Figure 5: Global patient scores graph on satisfaction questionnaire and trend line

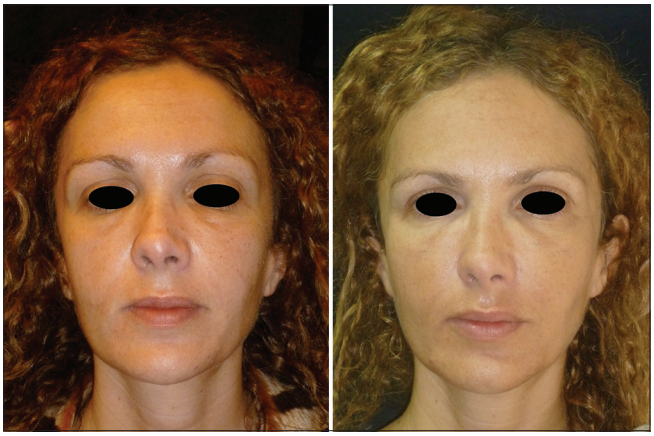

Figure 4: Clinical case 3. Patient before and 12 months postoperative

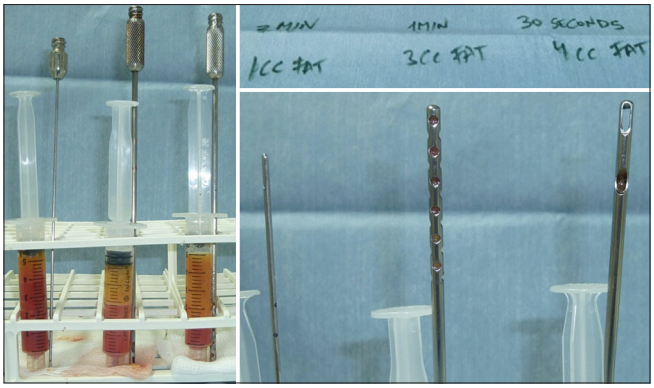

Figure 6: Different cannula port sizes and time needed for harvesting and amount of fat and oil extracted

diameter) based on the placement area, technique to be used, or intended cellular population.

This technique allows to obtain different sizes of fat parcels and to perform a differential fat grafting, to gain as much as possible from each individual treatment goal, volume restoration and skin regeneration, for greater patient and surgeon satisfaction.[11]

The benefits of the differential harvesting are versatility of fat, more precise corrections, and achiving homogeneous results.

It improves fat survival in critical spots and reduces the overall fat oil content resulting in reduced inflammation and downtime for patients.

Furthermore it may reduce the potential complications, and speed up the whole process.

Moreover it allows us to obtain different extraction samples to be processed or enhanced in different ways.

In areas of great muscular mechanical stress, a fact known as an important factor determining early absorption of fillers,[13] it allows multiplane corrections (intradermal, subcutaneous, and supraperiosteal) permitting to obtain a better volumetric survival, because we do not overcorrect on one plane, we expand all of them in a manner that the transplanted cells may establish new circulatory connections and posterior survival.

The other important factor is the dead space created in the infiltrative phase. The bigger the cannulas, the more important the trauma becomes as the dead space to be filled with serum on the scarring tissue will interfere in cell integration. By having different adipose parcel sizes, small cannulas and needles can be used for delivery, reducing the trauma and dead space in the healing phase. The lesser the inflammation the closer the transplanted cells will be to the vessels.

Finally it is well known that whatever the ASC does relies mainly on the cellular niche or immediate micro ambient surrounding.[14] Cellular niche is different in the intradermal, subcutaneous and supra periosteal plane, so we can expect different actions from this cells depending on the plane transplanted.

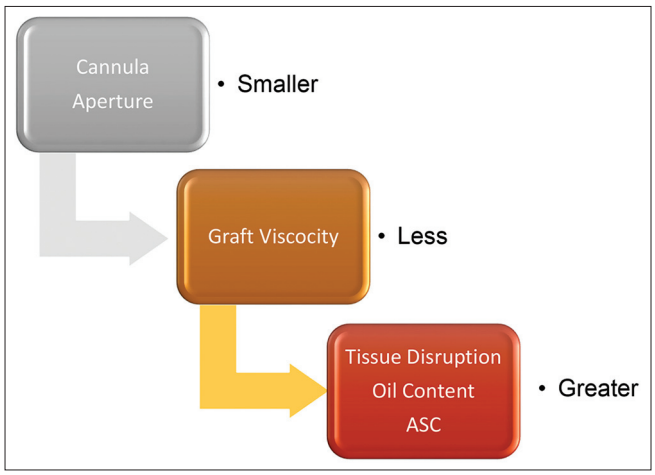

Figure 7: Diagram relation between cannula port – width size and tissue disruption, oil content and adipose stem cell

Differential fat harvesting and posterior differential grafting is a valid alternative, to expand the repertoire of fat use, allow a more homogeneous effect, reduce the potential complications, speed up the process, improve graft survival, and enhance overall aesthetic outcome.

The mastery of this technical modifications, which affect our graft, together with the understanding of recipient site[15-17] and systemic factors, will allow us to get long lasting and reproducible results for the benefit of our patients.

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Case Report Plastic and Aesthetic Research

Craniofacial abnormalities in goldenhar syndrome: a case report with review of the literature

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ABSTRACT

Goldenhar syndrome (oculo-auriculo-vertebral spectrum) is a rare congenital anomaly of unclear etiology and characterized by craniofacial anomalies such as hemifacial microsomia, auricular, ocular and vertebral anomalies. In many cases, this syndrome goes unnoticed due to a lack of knowledge about its features and because of its associated wide range of overlapping anomalies. Herewith, we present a case of Goldenhar syndrome in a 21-year-old male, who presented all the classical signs of this rare condition. This article also summarizes the characteristic features of patients with Goldenhar syndrome.

Key words:

Congenital abnormalities, eye abnormalities, Goldenhar syndrome, oculo-auriculo-vertebral spectrum

INTRODUCTION

Goldenhar syndrome is a rare developmental anomaly involving structures derived from first and second branchial arches of the first pharyngeal pouch, the first branchial cleft, and the primordial stapedial artery of the temporal bone.[1,2] Goldenhar syndrome and its variants, also referred to as Goldenhar anomalad, occupy a central position in the broad spectrum of overlapping anomalies related to the eyes, ears, face and vertebral column.[2]

In many cases, this syndrome goes unnoticed secondary to its associated wide range of overlapping anomalies.[3] This work reports a case of Goldenhar syndrome in a 21-year-old male, who presented all the classical sign of this rare condition. The patient agreed to publish his facial pictures and signed the consent form.

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CASE REPORT

The patient is a 21-year-old male who reported to the Department of Oral Medicine and Radiology, with complaints of an unaesthetic facial and dental appearance. He was the product of his mother's second pregnancy, the first terminated by spontaneous abortion at about 2 months of gestation. Prenatal history revealed that the mother suffered from frequent severe vaginal bleeding during the first trimester of her pregnancy. He was born at full term after a normal delivery with a bilateral complete cleft lip/palate and a congenital epibulbar dermoid of the right eye. His parents were nonconsanguineous, and there was no relevant family history.

At 6 months of age, he underwent surgery for cleft lip repair, and cleft palate closure was performed at 18 months of age. He sustained multiple episodes of epilepsy until the age of 6 years at which time he was diagnosed with hydrocephalus, and a ventriculoperitoneal shunt was placed. At the age 8, he underwent a minor surgical procedure for excision of preauricular tags on the left side of his face.

Physical examination at the age of 21 years was remarkable for developmental and mental disability

with a slow gait. On extra-oral examination, the patient demonstrated gross facial asymmetry, and severe retrusion of the midface and mandible. Well-demarcated postcleft deformities were noted. There was marked deviation of the nasal septum toward the left side of the face, and the patient was noted to be an obligate mouth breather [Figures 1 and 2]. The scar on the left cheek region indicated a previously excised preauricular tag, and soft tissue is deformity involving the left ear was present [Figure 2].

Intraoral examination revealed a V-shaped, constricted maxillary arch and a scar secondary to his repaired cleft palate. A large nasoalveolar fistula was noted in the line of the cleft palate repair, resulting in the hypernasality on pronation. The patient maintained poor oral hygiene with heavy calculus deposition and the generalized gingivitis. Dental examination revealed an anteriorly protruding mandible and loss of teeth 11, 21 and 22 [Figure 3]. The tongue was enlarged with hypertrophied bilateral adenoids.

Ophthalmologic examination revealed a yellowish white sub-conjunctival mass measuring 3 mm × 3 mm, located at the nasal limbus at the 9 O'clock position in the left eye. The mass, which contained dermal elements, was found to encroach upon the cornea by 1.5 mm. These findings are suggestive of a limbal dermoid [Figure 4a]. The lateral canthus of the left eye additionally showed a soft, mobile whitish mass growing in the bulbar area, which was clinically suggestive of a dermolipoma. Examination of the right eye revealed a reddish sub-conjunctival mass around the inferior half of the cornea, almost filling the palpebral fissure from medial canthus to the lateral canthus, suggestive of a bleeding epibulbar dermoid [Figure 4b].

Lateral cephalogram showed a concave skeletal profile and high mandibular angle with clockwise rotation indicating increased vertical growth. The shadow of the ventricular shunt was also evident along the cervical region [Figure 5]. Water's view X-ray revealed left malar hypoplasia [Figure 6]. Maxillary occlusal radiograph demonstrated a cleft alveolus and palate with impaction of teeth 12 and 23.

Based on the classical signs and associated abnormalities we arrived at a clinical diagnosis of Goldenhar syndrome. The patient was informed about the requirement for a multidisciplinary treatment approach due to the wide range of anomalies. Thorough oral prophylaxis reinforced

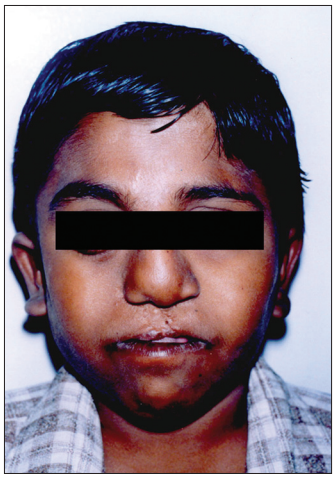

Figure 1: Extroral photograph; frontal view showing facial asymmetry and cleft lip surgery secondary deformity

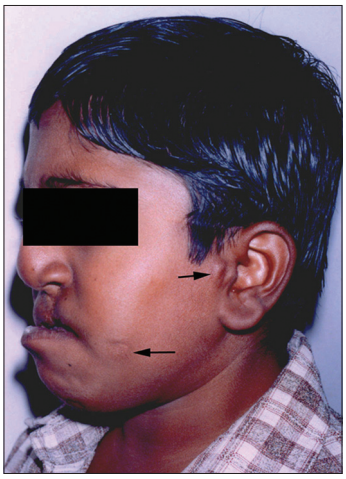

Figure 2: Extra-oral photograph; left lateral view showing preauricular tag and midface retrusion

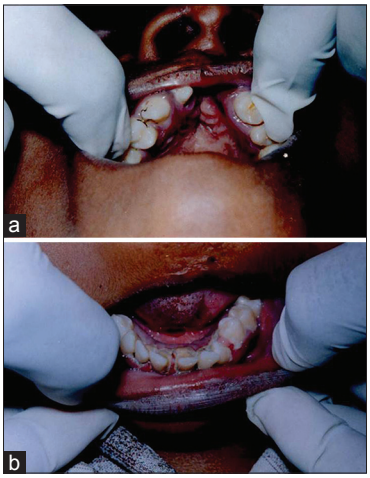

Figure 3: Introral view. (a) Maxillary arch showing constricted maxillary arch and nasoalveolar fistulae; (b) mandibular arch showing protrusive mandibular anteriors and inflamed gingiva

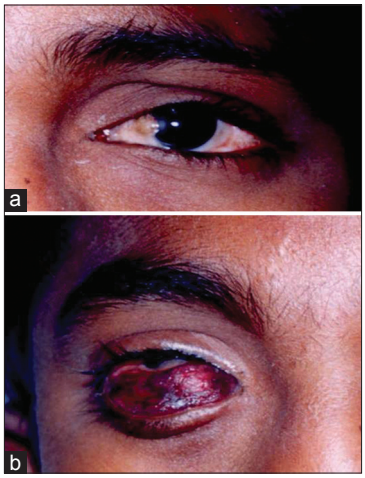

Figure 4: (a) Left eye showing limbal dermoid in the nasal aspect and dermo-lipoma in the temporal aspect; (b) right eye showing extensive epibulbar dermoid

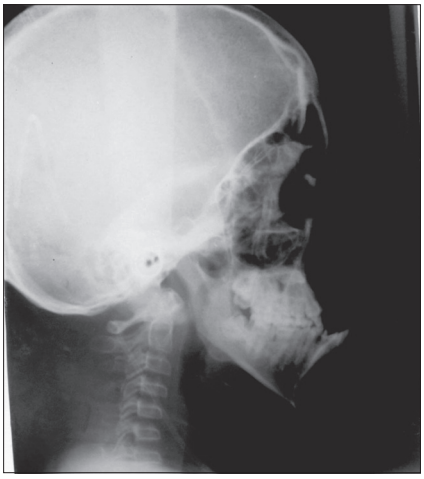

Figure 5: Lateral cephalogram demonstrating a high mandibular angle with a clockwise rotation, midface retrusion and the shadow of ventricular stunt

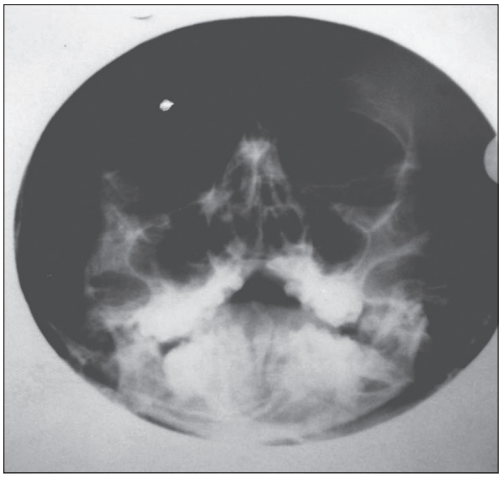

Figure 6: Water's view X-ray revealing malar hypoplasia on the left side of the face

with education should improve the oral hygiene status of the patient. A series of surgical treatments including alveolar bone grafting, Lefort I osteotomy and maxillary advancement, followed by rhinoplasty and pharyngoplasty was suggested. The need for extensive orthodontic intervention, speech therapy and an additional ophthalmic intervention were also emphasized.

DISCUSSION

Goldenhar syndrome is a rare congenital defect characterized by a heterogeneous constellation of malformations classically involving the face, eyes and ears.[4] It was first recorded by the German Physician Carl Ferdinand Von Arltin in 1845, but was not recognized as a syndrome until 1952 when Dr. Maurice Goldenhar described this condition as a disease that presents with a combination of several anomalies including dermal epibulbar tumors, preauricular appendages and mandibular hypoplasia.[3,5-7] In 1963, Gorlin *et al*.[8] named this syndrome oculo-auriculo-vertebral syndrome due to the presence of additional vertebral anomalies. Hence, it was also known as Goldenhar-Gorlin syndrome.[9]

The clinical manifestations of Goldenhar syndrome closely resemble those of hemifacial microsomia and hence Smith[10] used the term facio-auriculo-vertebral anomaly to include both Goldenhar syndrome and hemifacial microsomia. Within the medical literature, the term oculo-auriculo-vertebral spectrum is often used synonymously with Goldenhar syndrome and hemifacial microsomia. However, due to the complexity and varying severity and expression of the oculo-auriculo-vertebral spectrum, some researchers suggest that the hemifacial microsomia and Goldenhar syndrome actually represent different aspects of severity within the oculo-auriculo-vertebral spectrum.[11] According to the medical literature, when malformations primarily involve the jaw, mouth, and ears and in most cases, affect one side of the body, the disorder is often referred to as hemifacial microsomia. If abnormalities of the vertebra and/or the eyes are also present, the disorder is often called Goldenhar syndrome. Our patient presented with malformations involving mouth, jaws, ears and also eyes and therefore we arrived at the diagnosis of Goldenhar syndrome.

Since the description of Goldenhar and Gorlin, the variety and variability of anomalies associated with Goldenhar syndrome have been increasingly appreciated, although few authors have reported diverse ocular, skeletal, cardiac and visceral defects.[7] In the early 1990's, this condition was better understood and it was agreed that, this syndrome may exhibit a wide range of anomalies that includes eye anomalies,[7] disturbance of the central nervous system, cleft lip/cleft palate,[7] facial asymmetry, developmental dental disturbances,[12] skeletal anomalies,[7] mental retardation,[4,11,13] vertebral[14-16] and congenital heart anomalies,[17-20] growth abnormalities,[21] pulmonary abnormalities,[15] and labyrinthine, tracheoesophageal,[15] renal[15,16,22] and genitourinary abnormalities [Table 1].[17,20]

Its estimated prevalence is 1–9/100,000,[13] with an incidence of 1 in 25,000–45,000 births,[28] with a male to female ratio of 3:2.[4] The study of this condition is still controversial because the symptoms and the physical features vary greatly in range and severity from case to case. The characteristic combination of external ear anomalies and ipsilateral facial underdevelopment is the hallmark of this syndrome. In most of the reported cases, such malformations affect one side of the body; nevertheless, in 10–50%[4,16] of affected individuals, both sides of the body were involved with one side, with the right side typically more affected than the left.[4] In our patient, both sides had virtually equal involvement of the anomaly; while he had left hemifacial hypoplasia and a notable epidermoid cyst with preauricular appendages, he also presented with an extensive epidermoid cyst of the right eye and bilateral cleft lip/palate.

The disease is seen sporadically, and its etiology is unclear. Two patho-physiologic mechanisms have been proposed for Goldenhar syndrome, reduced blood flow and focal hemorrhage in the developmental region of the first and second branchial arches occurring around 30–45 days of pregnancy, in the blastogenesis period (Poswillo's

Table 1: Reported clinical findings in oculo-auriculo-vertebral spectrum patients and their frequencies

Clinical features	Frequency (%)
Facial abnormalities[4,20]	76
Unilateral[20,23]	70–85
Bilateral[4,16]	10–50
Facial asymmetry[15,24,25]	65–85
Unilateral facial hypoplasia[3,4,9,11,16]	83
Hypoplasia of mandible/condyle/maxillary/malar bone[7,15,23]	50–64
Cleft lip/palate[4,7,9,15,16,24,25]	5–56
Lateral facial cleft[16]	29–40
Lateral cleft like extension of corner of the mouth[2]	
Macrostomia[7,12,24]	
High arched palate[7,9]	
Gingival hypertrophy[12]	
Delayed tooth development/misaligned/ supernumerary teeth[4,12]	
Enamel and dentin malformations[12]	
Hypoplastic/bifid tongue[4,7,24]	
Agenesis of coronid process/palatine bane[7]	
Deviated nasal septum/choanal atresia[4,9]	
Facial muscle hypoplasia[12]	
Hypoplasia/aplasia of parotid glan[12]	
Congenital salivary fistulae of accessory salivary glands[2]	
Upslanting palpebral fissure/telecanthus	
Ocular abnormalities[16,25]	25–94
Epibulbar/ocular dermoid[14,15,25]	33.3–78
Unilateral[14]	53
Limbal dermoid/lipodermoid[14,15]	47–53
Unilateral	28
Bilateral	19
Coloboma of upper eyelid/iris/choroidea/ retina[14,15,24]	24–60
Bilateral[14]	3
Anopthalmos/micropthalmos[15,16,24,25]	10–53
Strabismus/nystagmus[4,24]	
Duane retraction syndrome[14,24]	
Decreased corneal sensation[4,14,16]	
Cataract and iris abnormalities[4,15,16]	
Neuroparalytic keratitis	
Dacryostenosis[24]	
Proptosis[16]	
Auricular abnormalities[20,23,25,26]	82–100
External ear[20,26]	82–100
Preauricular appendages and pits[19,25,26]	53–90
Bilateral[14]	30
Ear abnormalities	
Microtia[25,26]	50–100
Bilateral[26]	18–50
Anotia[25]	16.60
Atresia of outer ear canal	
Stenosis of outer ear canal	
Middle ear[18,26]	67–75
Incomplete development of the tympanic cavity	
Opacified middle ear	
Agenesis of the middle ear	
Hypoplasic/agenesis of the tympanic cleft	
Hypoplastic/displaced ossicular chain	
Widened or decreased tympanic cavity	

Contd...

Table 1: Contd...

Clinical features	Frequency (%)
Absence of the tympanic tensor muscle	
Inner ear[18,26]	27–36
Hypoplastic inner ear	
Agenesis of the inner ear canal	
Altered cochlear morphology	
Altered semicircular canal	
Absence of the cochlear aqueduct	
Absent/abnormally coursing facial nerve canal	
Duplicated inner ear canal	
Displaced endolymphatic duct	
Conductive and sensorineural hearing deficit[3,15,16,23]	50–100
Temporal bone anomalies[15]	
Poorly pneumatized mastoid antrum	
Lengthened mastoid antrum	
Enlarged cartilaginous portion of the eustachian tube lumen and absence of the cartilaginous lateral lamina of the eustachian tube	
Cranial abnormalities[15,21]	8–85
Cranial asymmetry[15]	85
Microcephaly[15,16]	8–43
Skull defects[15]	47
Holoporencephaly/anencephaly/platybasia[15]	
Hypoplasia of petrous bone/ethmoid bone[15]	
Neurological abnormalities[18,20,27]	12–47
Diffuse cerebral hypoplasia[27]	12
Dilated lateral cerebral ventricles (asymptomatic hydrocephalus)[15,27]	12–42
Corpus callosum dysgenesis[27]	12
Frontal hypodensities[27]	12
Mental retardation[3,15,20]	23–82
Intracranial dermoid/calcifications[15]	30
Encephalocele[15]	13
Facial nerve paralysis[2,3,20,24]	12
Asymmetric lateral ventricles[15]	
Hidrocephalus due to aqueduct of sylvius stenosis[24]	
Corpus callosum lipoma[24]	
Hypoplastic/absence of septum pellucidum[15]	
Hypothalamic hamartoma[24]	
Open myelomeningocele	
Arnold-Chiari malformation	
Frontal lobe dysplasia	
Calcified anterior falx cerebri seizures	
Cardiac abnormalities[2,9,17,18-20,24]	5–58
Conotruncal/outlet defects[2,19,24]	38.5–45
Fallot's tetralogy[15,24]	15–50
Intraventricular communication with pulmonary atresia[24]	8
Transposition of great vessels[2]	
Double inlet of the left ventricle	
Septal defects[2,19,24]	23–32
Interatrial communication ostium secundum	
Interventricular communication	
Atrioventricular septal defect	
Others	
Patent ductus arterious[19]	4
Pulmonary artery stenosis[19]	4
Cor triatriatum[24]	
Dextrocardia	

Contd...

Table 1: Contd...

Clinical features	Frequency (%)
Skeletal abnormalities[20]	23
Vertebral abnormalities[4,14-16,24]	19–69
Hemivertebrae[15,24]	
Hypoplastic/butterfly vertebrae[15,24]	
Absence/fusion of cervical vertebra	
Kyphosis/scoliosis[15]	
Lumbar lordosis/spina bifida occulta[24]	
Rib alterations[24]	
Radial abnormalities[15,24]	13
Short stature[15,16]	13–43
Anomalies of extremities[15,16]	11–33
Hormonal abnormalities[21]	
Growth hormone deficiency[15,21]	
Growth retardation[15]	43
Esophagic/pulmonary abnormalities[9,15,24]	6.70
Pulmonary atresia[9]	
Esophageal/duodenal atresia[24]	
Tracheoesophageal fistula[24]	
Laryngotracheomalacia[24]	
Bronchogenic cyst[24]	
Abdominal abnormalities[20]	12
Pyloric hypertrophic stenosis	
Accessory spleen	
Umbilical hernia[24]	
Urogenital abnormalities[7,16,20]	18–23
Renal anomalies-renal agenesis[7,15,16,22,24]	10–13
Absent hymen	
Renal hypoplasia/hydronephrosis	
Genital alterations/short perineum	
Maldescensus testis/hypospadias	
Anal imperforations	

hypothesis). It is thought that the etiology may also be related to a deficiency in mesodermal formation or a defective interaction between the neural crest and mesoderm.[4] Other evidence has suggested that there are genetic determinants in some cases. A few cases have been reported families with recessive autosomal or dominant, autosomal inheritance.[2] The literature also contains several descriptions of chromosomal anomalies, environmental factors, drug ingestion (cocaine, retinoic acid, thalidomide and temoxifen), and maternal diabetes[2] as factors that may contribute to the development of the disease. Jongbloet in his hypothesis states that among various complications of pregnancy, vaginal bleeding in very early pregnancy is closely related to the early condition of the fertilized egg and predates the formation of the relevant facial and vertebral structures in a 3–5 weeks old embryo. Therefore, this may be a common cause of dysmorphogenesis.[18] In our case, the prenatal history revealed that the mother suffered repeated vaginal bleeding during the first trimester of her pregnancy, and this may be linked with the etiology in the current case.

Dentofacial anomalies may include cleft lip and palate, highly arched palate, hypoplasia of the maxillary and mandibular arches, micrognathia, gingival hypertrophy, supernumerary teeth, enamel and dentin malformations, and delayed tooth development.[4,9,15,16,20] Due to the presence of an underdeveloped lower jaw, the patient may suffer malocclusion and macrostomia. Facial asymmetry and hypoplasia of the mandible are characteristic features of Goldenhar syndrome. The present patient showed marked malar and mandibular hypoplasia with bilateral cleft lip/plate and malalignment of the teeth.

Ophthalmologic anomalies occur in about 50% of cases and commonly involve epibulbar dermoids and lipodermoids followed by micropthalmia and upper palpebral coloboma.[16,20,24,25] Limbal dermoids or lipodermoids are mainly located in the infratemporal region of the eye.[25] Our patient presented with a limbal dermoid on the nasal region and a lipodermoid in the temporal region of the left eye, and an epibulbar dermoid in the right eye. In the right eye, the mass encroached the entire cornea with loss of vision.

Ear abnormalities vary, but as a rule, are required for the diagnosis of Goldenhar syndrome.[7] Microtia and other minor ear malformations such as preauricular appendages and pits, either alone or in combination, are viewed as one of the minimal criteria for diagnosing this syndrome.[18,23,26,27] Our patient had only minor ear abnormalities consisting of two preauricular tags, and this was a unilateral finding. He has not suffered any hearing disturbances or facial nerve dysfunction.

Vertebral anomalies reported in the literature include hypoplasia, and fusion or absence of certain vertebra,[14-16] but no vertebral anomalies were detected in our patient. Despite the reported frequency of cardiovascular alterations ranging from 5% to 58%,[17-20] this patient had no cardiovascular alterations. Similarly, other systemic abnormalities including pulmonary, genitourinary, and/or gastrointestinal were not present in our patient.

Tasse *et al.*[16] reported that anomalies of the eye or orofacial clefts in Goldenhar syndrome patients are predictive of brain malformations. Consistent with this finding, our patient had ocular anomalies, an oral cleft, and also central nervous system alteration, specifically hydrocephalus.

Various classification systems have been introduced in order to clinically categorize the patient with Goldenhar syndrome or oculo-auriculo-vertebral spectrum and to aid in prognosis.[16,25] The recently introduced classification system by Tasse *et al.*[16] is simple and clinically applicable. In categorizing our patient in this classification system, the patient presented with 2 of their 3 minimal diagnostic criteria including unilateral preauricular appendages and hemifacial microsomia, classifying our patient as group 2u. In addition our patient also presented with additional clinical features consisting of an orofacial cleft, dermoids, brain anomaly, delay of motor and speech development and short stature, attaining a score of 10/18, which reflects the severity of the syndrome.

The treatment of this disease varies with age and systemic associations. Although it may be mainly cosmetic in uncomplicated cases, it still demands a multidisciplinary

team approach.[12] There are several methods for surgical correction of facial hypoplasia, such as conventional reconstruction with bone grafts and distraction followed by future orthodontic treatment.[4] Structural anomalies of the eyes and ears are corrected by reconstructive surgery. Furthermore, long-term regular follow-up is required to monitor the growth and development of patients.

De Catte *et al.*[29] reported sonographic detection of Goldenhar syndrome in a foetus at 15 weeks gestation, by observing a maxillary cleft in association with unilateral micropthalmia, indicating of the possibility for early prenatal diagnosis, with the option for pregnancy termination in severe cases. Although these individuals typically have normal life span, the prognosis varies depending on the severity of the systemic associations.

Traditionally, the presence of ear abnormalities, which leads to the search of mandibular hypoplasia and vertebral alterations, is the main clinical feature associated with the diagnosis of Goldenhar syndrome.[25] However, the absence of obvious characteristic features and the general lack of knowledge make the diagnosis difficult and delayed. Hence, this article represents an effort to summarize the characteristic features of patients with Goldenhar syndrome.

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Case Report | Plastic and Aesthetic Research

Isolated sporadic bilateral split hand malformation: a case report and review of the literature

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ABSTRACT

Typical cleft hand is a rare disorder usually inherited in an autosomal-dominant manner. We report a case of bilateral typical cleft hand in a 6-year-old male. There was no positive family history of such presentation, and no systemic manifestations were associated with this entity. Preanesthetic evaluation revealed no systemic or airway challenges and parents were counseled for routine surgical and anesthetic risks. The hands underwent successful surgical reconstruction with no peri-operative complications. To the best of our knowledge, this is the first report of an operated case of an isolated, bilateral, and sporadic typical split hand malformation.

Key words:

Cleft hand, congenital anomalies, split hand malformation, syndactyly

INTRODUCTION

Surgical or medical co-morbidities of anesthetic or airway difficulties in patients with congenital anomalies need special consideration during corrective management, especially in the pediatric population.[1-4] Split hand malformation (SHM), characterized by median cleft in the hand, syndactyly, and/or a variable degree of underdevelopment of phalanges and metacarpals, is a rare entity.[5,6] Associated co-morbidities can include sensori-neural hearing loss which can be challenging to identify when eliciting history during preanesthetic evaluation or during the anesthetic induction as such patients can be difficult to counsel. The literary evidence indicates the occurrence of multiple anomalies with SHM, but a literature search for isolated cleft hand anomaly yielded only two results.[5,6] The reported cases in the literature described only unilateral afflictions. We report a unique case of sporadic, isolated, bilateral SHM with syndactyly in both feet, which was successfully managed surgically and anesthetically with no untoward peri-operative incidents.

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CASE REPORT

A 6-year-old male presented to the Orthopedic Outpatient Department with congenital abnormalities in both the hands and feet. He was the second of three children, born out of a nonconsanguineous marriage, delivered vaginally at full term with uneventful antenatal and perinatal course. Chief complaints of the parents pertained to the cosmetic concerns due to visible deformities. There were no skin lesions and no associated cleft lip/palate observed during a physical examination. The left hand was dominant, and there was no history of sensorineural deafness. On local examination, it was observed that there was complete obliteration of first web space in the right hand with the absence of the middle finger in both the hands. The right foot showed hypoplasia of the second toe with syndactyly between the third and fourth toes. The left foot had syndactyly between the third and fourth digits [Figure 1].

Radiographs were obtained which showed the absence of middle finger phalanges in both the hands. In the right hand, there was a variable absence of the third metacarpal while in the left hand the third metacarpal was almost fully developed. Two small transverse bones were visible on either side of the central ray in the left hand [Figure 2]. No bony deficiency was visible on radiographic examination of the feet. A hypoplastic second digit on the right foot was found to be devoid of the bony skeleton and the "great toe" consisted of first and second rays [Figure 3].

Preanesthetic evaluation did not reveal any systemic involvement, but the patient had a Mallampatti grade II with normal neck movements and body weight of 22 kg. The patient was administered 5 mL syrup promethazine as a part of the premedication. In the operating theater, induction of anesthesia was achieved with oxygen in nitrous oxide, sevoflurane, propofol (2 mg/kg body weight), 50 μg of fentanyl, and 2.5 vecuronium bromide for facilitation of endotracheal intubation using a cuffed endotracheal tube of 5.5 mm internal diameter. The first surgical procedure lasted for 2 h, with extubation and the postoperative course uneventful. Diclofenac sodium was administered for postoperative pain relief. Surgery was performed in a staged manner with an interval of 3 weeks. The right hand underwent operation first: the central hypoplastic ray was excised, drill holes were made in the second and fourth metacarpals, and the 2 were held together using a 22-gauge stainless steel wire [Figure 4].

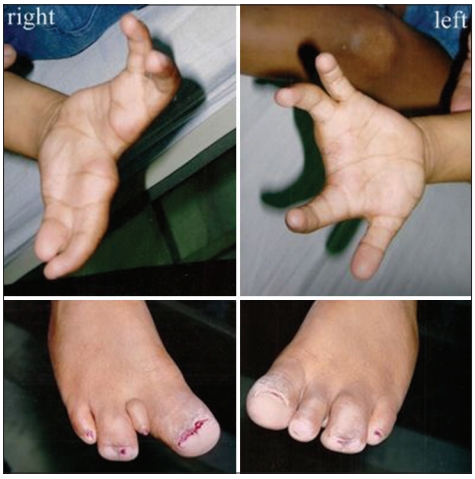

Figure 1: Preoperative clinical photographs of the hand and feet; right hand showing syndactyly between the thumb and index finger; the right foot showing syndactyly between the third and fourth rays and a hypoplastic second toe; the left foot showing syndactyly between the third and fourth toes

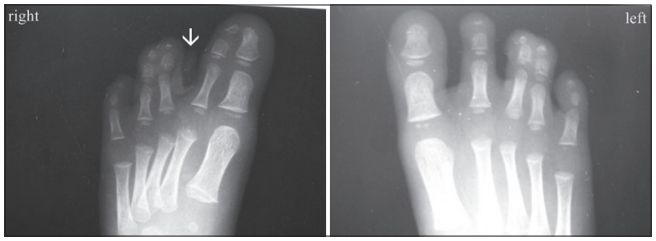

Figure 3: Radiographs of both feet; the hypoplastic toe in the right foot has no bony scaffold

A Z-shaped incision was made for syndactyly release. Adequate thumb abduction was achieved intraoperatively. In the left hand, central ray and transverse bony bridges were excised, and cleft closure was done. The diverging rays were held together employing a soft tissue sling functioning as the transverse metacarpal ligament. Postoperatively mobilization and strengthening exercises were instituted. Active abduction of the thumb on the right hand was especially encouraged. The patient was followed for 3 years, with a good functional and cosmetic outcome [Figure 5].

DISCUSSION

The literature is abundant with case reports where congenital abnormalities have always troubled surgeons and anesthesiologists whenever such patients present for surgical correction. However, in the present case, no such difficulties were encountered.

Split hand foot malformation (SHFM) involving the central rays of the extremities is usually inherited in an autosomal-dominant fashion. Various causative genes have been discovered, variable penetrance of which leads to the difference in severity of the manifestation.[7-9] In the present case, a thorough pedigree analysis revealed a negative family history. Sporadic cases are usually encountered which show atypical cleft hands, which have more severe manifestations and are characterized by variable absence of middle, ring and index fingers.[10]

The cleft divides the hand in two separate radial and ulnar components. Sometimes a transverse bar of bone may be present at the base of the cleft, but multiple fragments were encountered in the present case. Syndactyly (most commonly thumb-index finger, as in the present case) and polydactyly are not uncommon associated findings.

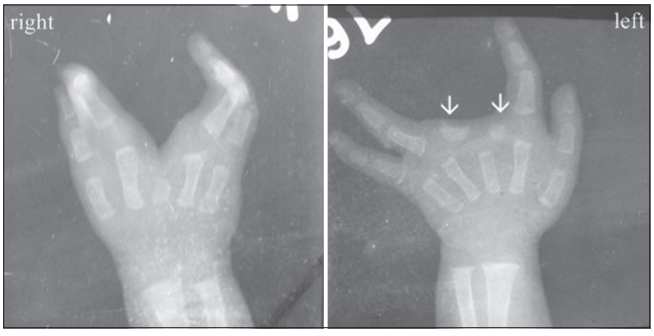

Figure 2: Preoperative radiographs of the hands; note the accessory transverse bony pieces in the cleft in the left hand (marked by arrows)

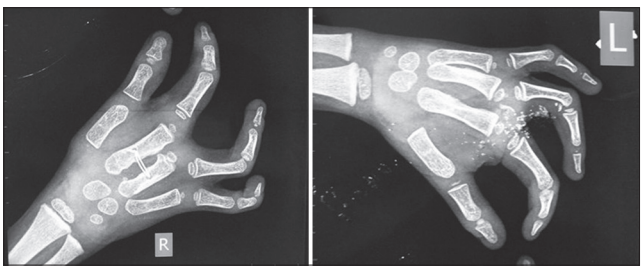

Figure 4: Postoperative radiographs of both hands

Figure 5: Functional and cosmetic outcome 1 year after surgery

Contraction of the first web space and limitation of thumb adduction is the main functional handicap encountered in such cases, based on which Manske and Halikis devised a severity classification.[11]

Numerous clinical associations of SHFM have been documented; cleft lip/palate seems to be a consistent accompanying manifestation. Such manifestations pose airway difficulties which can lead to a potential higher morbidity and mortality. The constellation of findings most commonly reported is ectrodactyly ectodermal dysplasia cleft lip/palate syndrome – ectrodactyly (SHFM), ectodermal dysplasia (coarse dry skin, glandular abnormalities), and cleft lip/palate. In the present case, a thorough search was made for associated systemic anomalies, but fortunately none were observed. Sporadic, isolated, bilateral typical cleft hand as reported above is indeed a rare entity.

Clinical diagnosis of SHFM is quite straightforward. Although there is no evidence in the literature regarding differences in outcome for patients presenting as syndromic cases or in isolation, the associated anomalies should be actively sought and treated accordingly. Radiographic examination of the bilateral hands, feet and skull should be carried out. In our opinion skin, biopsy is not a useful tool even if manifestations of ectodermal dysplasia are absent, as done by some authors.[6] The outcome of skin biopsy findings do not guide decision-making.

Basic treatment goals are cleft closure for cosmetic reasons, syndactyly release, and restoration of the first web space for function. Mild cases are causing little functional impairment can be left untreated. Other issues that need attention in the treatment protocol are the cosmetic appearance of the limb and the overall psychology of the child. The ideal time for scheduling corrective surgery is at 18 months of age. The advantages of early surgery seem to be a correction of the deformity before the development of refined motor skills and the prevention of negative psychological effects on the child. In developing countries, this may be problematic due to the absence of a well-organized referral system. In the present case surgical intervention was undertaken at 6 years of age, albeit with a good outcome.

The cleft closure is achieved by excision of excess tissue including the third metacarpal and transverse bone bar if present. To hold the diverging metacarpals together, numerous techniques have been employed, such as heavy chromic catgut sutures or stainless steel wires, the latter done in the present case.[12] For the restoration of the first web space, Snow and Littler advocated syndactyly release and utilization of skin from the palmar side.[13] Barsky *et al.* employed a diamond-shaped flap from the cleft area itself to create a web space.[12] In our case, the first web space was created surgically in the right hand by simple closure with a series of Z-plasties. The child may require rotational osteotomies of the metacarpals, especially the marginal ones, to achieve a useful pincer grasp if not restored adequately.[12] No such procedure was done in this case as the patient and relatives were satisfied with the primary surgery outcome. Surgery for cleft foot is rarely required for hallux valgus correction and still rarer for cosmetic reasons.[14]

Typical and atypical cleft hand deformities occur with varying degrees of severity. Children learn to adapt from an early age and frequently develop remarkable functionality. If surgery is to be done, it should be planned carefully for each patient. The aim of surgery in these cases is mostly cosmetic. Any surgical procedure done should not jeopardize existing functions of the hand.

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Case Report Plastic and Aesthetic Research

Lipoma causing Guyon's canal syndrome: a case report and review

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ABSTRACT

Compression of the ulnar nerve in Guyon's canal leads to Guyon's canal syndrome. Lipoma is a rare cause of such compressions with only 12 cases reported previously. We report a 55-year-old man who presented with swelling in the left hand with decreased sensation in the ring and little fingers. Magnetic resonance imaging revealed high signals in T1-weighted and T2-weighted images with suppression of the short T1 inversion recovery signal, suggestive of lipoma. On exploration a well-encapsulated, dumbbell-shaped, fatty tumor was seen in the hypothenar space and Guyon's canal. The tumor was enucleated in toto. At 6-month follow-up, the patient had fully regained sensation. A review of the literature is presented for similar cases where a lipoma was the cause of Guyon's canal syndrome.

Key words:

Guyon's canal, lipoma, ulnar neuropathy

INTRODUCTION

Guyon's canal, named after Felix Guyon, is a fibro-osseous tunnel within the ulnar side of the wrist.[1] It is bound radially by the hamate, volarly by the volar carpal ligament, dorsally by the transverse carpal ligament, and ulnarly by the pisiform and the flexor carpi ulnaris. The ulnar neurovascular bundle enters the hand through this tunnel. Ulnar nerve compression in this enclosed space leads to Guyon's canal syndrome, first described by Hunt.[2] The common causes are ganglion, repetitive trauma, vascular lesions, tumors, and anomalous muscles.

Lipoma, though termed universal tumor due to its ubiquitous presence, is rare in Guyon's canal. This is probably due to the paucity of adipose tissue in this fibro-osseous tunnel. There are only 12 previously reported cases. We report a case of lipoma in the Guyon's canal causing ulnar neuropathy.

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CASE REPORT

A 55-year-old male presented with swelling in the left hand with a duration of 3.5 years. He complained of numbness in the ring and little fingers. On examination, a diffuse swelling was noted in the hypothenar area extending from the distal palmar crease to the proximal wrist crease [Figure 1]. The swelling was soft but tense.

Sensory examination recorded diminished sensation over the little finger and the ulnar half of the ring finger on their volar surfaces. The patient rated the sensation as three out of ten in the "ten test" ("ten test" is a semi-quantitative assessment in which the patient ranks the quality of sensation in the affected digit compared with that in the normal contralateral digit on a score of 1–10). Sensation on the dorsal aspect was normal. There was no motor weakness, and the adductor pollicis, lumbricals, and interossei had normal function.

Magnetic resonance imaging (MRI) revealed a 6.5 cm × 4 cm × 2.5 cm well-encapsulated swelling in the hypothenar space extending into Guyon's canal. The lesion was hyper-intense on T1-weighted and T2-weighted imaging with suppression of the short T1 inversion recovery signal, suggestive of lipoma [Figure 2].

Surgical exploration under axillary block with tourniquet control revealed a well-encapsulated, dumbbell-shaped

tumor in the hypothenar space and Guyon's canal [Figure 3]. The distal sensory branches of the ulnar nerve were firmly adherent to the tumor and were splayed by it. It appeared as if the branches were embedded in the tumor capsule. There was inadvertent injury to the ulnar digital nerve to the little finger, which was repaired with 8–0 nylon.

Postoperative recovery was uneventful. The histopathological examination showed mature fat cells, suggestive of lipoma. At 6-month follow-up, the patient was doing well with normal sensation on the ring and little fingers.

DISCUSSION

Lipoma in Guyon's canal is rare, with only 13 cases reported, including the present case [Table 1].

Except for the case of an 8 years old,[9] all others were reported in adults, ranging from 36 to 74 years old, with a mean age of 52.2 years. There were 7 males and 6 females. Nine of the 13 cases occurred on the right side. The tumor size varied from 1.5 cm × 1 cm (area) to 6.5 cm × 4 cm × 2.5 cm (volume), with this largest lesion seen in the present case. Six patients had only sensory involvement, 2 had only motor symptoms, and 4 patients had a combined neuropathy. One patient had no neuropathy and was the only pediatric patient in the series. This was attributed to unique anatomical and physiological differences for Guyon's canal and the attending nerves.[9] MRI was taken in 7 cases. It gave accurate diagnosis in 5 patients, while, in 2 cases, the findings were suggestive of ganglion.[6,13] Surgical removal alleviated symptoms in all patients.

Shea and McClain have classified lesions of Guyon's canal into three types: type I – proximal lesions having both sensory and motor involvement (30%), type II – lesions causing weakness of the intrinsic muscles (52%) and type III – distal lesions causing only sensory abnormalities (18%).[14] Recently Wu *et al.* have suggested a classification into five types.[15] Type I is a mixed motor and sensory neuropathy with the lesion at the proximal end of Guyon's canal. Type II is a pure sensory neuropathy, with the lesion involving only the sensory branch. Type III is a pure motor neuropathy, with the lesion proximal to the branch supplying the hypothenar muscles. Type IV spares the hypothenar muscles with the lesion distal to the hypothenar muscle branch. Type V involves only the adductor pollicis and first dorsal interosseous muscles. The present case is type III according to Shea and McClain and type II according to the Wu classification.

Ganglions are the most common causes of Guyon's canal syndrome. Other causes include giant cell tumors, neurilemmomas, repetitive trauma, vascular lesions, anomalous muscles, carpal fractures and rheumatoid arthritis. Lipoma is a rare cause of nerve compression at this site.

The cellular origin of lipoma in Guyon's canal is debatable. Balakrishnan *et al.*[10] reported a case in which the branches of the ulnar nerve were splayed by the tumor; these authors postulated that the lipoma originated from the nerve itself and termed it an "intra neural lipoma". Our case was similar in presentation. The lipoma was present between the superficial and deep branches of the ulnar nerve. The superficial sensory branches were splayed by the tumor and appeared to be embedded in the capsule. Hence, an intraneural origin cannot be ruled out.

The possibility of nerve injury should always be discussed with the patient preoperatively. Extreme caution should

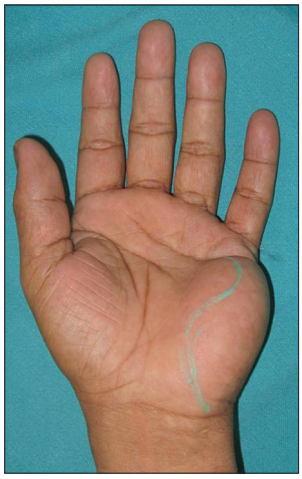

Figure 1: Diffuse swelling in the hypothenar area

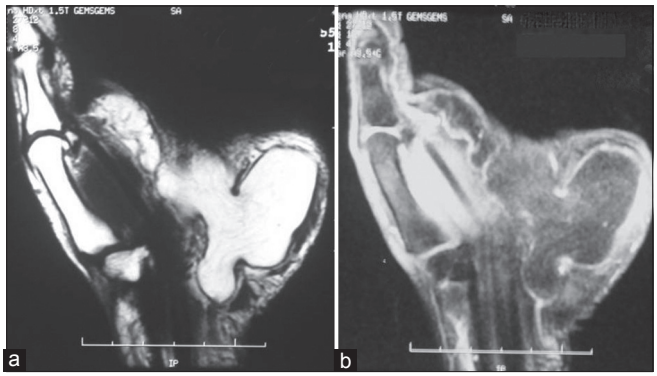

Figure 2: Magnetic resonance imaging finding of hyper-intense lesion in T1 (a) with short T1 inversion recovery suppression (b) in hypothenar space and Guyon's canal

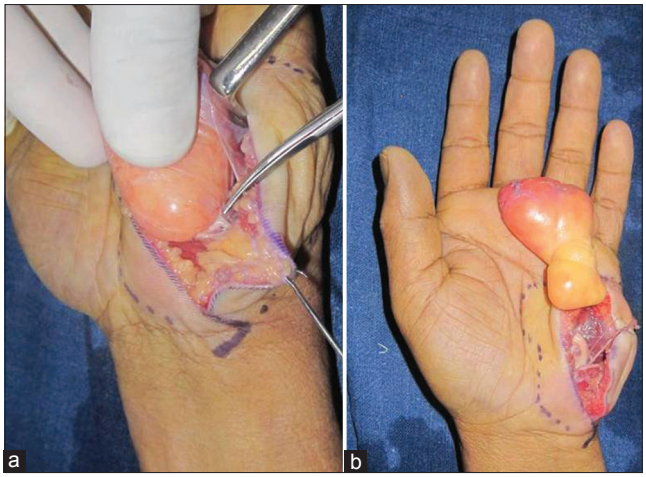

Figure 3: Intra-operative pictures showing (a) dissection and (b) enucleated specimen and underlying ulnar nerve and its branches

Table 1: Details of previously reported cases of Guyon's canal lipoma

Patient profile	Side	Duration	Neuropathy	Size of lipoma (cm)	Main author
54/female	Right	7 years	Motor	NA	Grantham[3]
36/male	Right	3 months	Motor	2.7 × 1.4	McFarland and Hoffer[4]
53/male	Right	2 days	Combined	6.5 × 3.7 × 2	Zahrawi[5]
74/female	Right	3 months	Combined	1.5 × 1	Sakai[6]
61/female	Right	2 years	Sensory	5 × 4 × 2	Galeano *et al.*[7]
49/female	Right	6 years	Sensory	5 × 2	Galeano *et al.*[7]
64/male	Left	NA	Sensory	NA	Bui-Mansfield *et al.*[8]
8/male	Right	3 years	No	3.3 × 5.5 × 4.4	Ulusal *et al.*[9]
42/female	Right	2 years	Sensory	4 × 3	Balakrishnan *et al.*[10]
36/female	Right	6 months	Combined	NA	Rohilla *et al.*[11]
66/male	Left	2 years	Combined	NA	Ozdemir *et al.*[12]
37/male	Left	2 years	Sensory	3 × 2 × 1.5	Paget *et al.*[13]
55/male	Left	3.5 years	Sensory	6.5 × 4 × 2.5	Present case

NA: Not available

be exercised while approaching these tumors as the nerve fibers may be splayed and embedded in the capsule. The capsule should be incised in the area least likely to contain nerve fibers and the tumor carefully enucleated.

It is difficult to predict whether a tumor in our case grew into Guyon's canal from the hypothenar space or grew out of Guyon's canal. As tumors grow in areas of least resistance, it is less likely that the lipoma would have entered the tight compartment.

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Letter to Editor | Plastic and Aesthetic Research

Unburied K-wire induced injuries: taking the edge off

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Sir,

Unburied K-wires left projecting from the fingers after hand surgery can lead to inadvertent injuries if left open, especially in children or disoriented patients, particularly at the time of reversal of anesthesia and in the immediate postoperative period. Different ways have been described to circumvent this. Many surgeons twist the K-wire on itself along with capping of the wire tip, but this requires considerable twisting force on an already inserted K-wire, which can lead to malalignment or even refracture.[1] Furthermore, the bent K-wire acts like a hook, catching onto dressing materials or clothes and subsequently may migrate out.

We present a simple and effective way of preventing such mishaps caused by unburied K-wire ends using silicone blocks. Silicone blocks are routinely used in procedures like dorsal nasal augmentation and interpositional arthroplasty for temporomandibular joint ankylosis.[2] A small cuboid of silicone block is obtained from a solid silicone block or from a left-over silicone block after sculpting for other indications. The block is approximately 0.5 cm × 0.5 cm × 1.5 cm in size and is inserted gently and with constant pressure over the K-wire end.

The silicone block fits snugly over the K-wire and in our experience spontaneous expulsion of the block from the K-wire tip has not occurred [Figure 1]. The chance of the deeper migration is also minimized.

Sterilization of the silicone block is not essential but is desired, especially in the case of left-over blocks. Capping of the K-wire can be done as the last step of hand surgery after dressing. However in procedures where further operative steps are needed following K-wiring, sterilization of the silicone is a must. This can be planned preoperatively. Our theatre nurse routinely makes a sterilized block of silicone available in all hand surgery cases where K-wiring is needed.

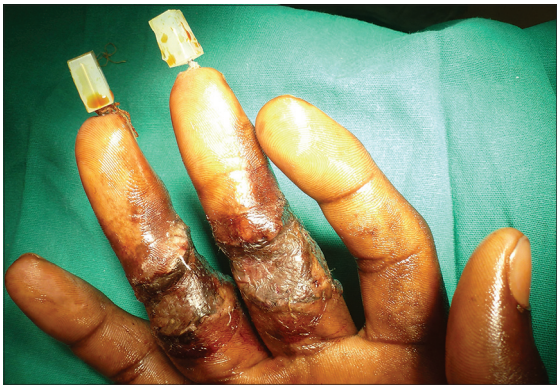

Figure 1: Silicone blocks capped over two unburied K-wires after a case of contracture release

The semi-rigid consistency of the silicone minimizes chances of penetrating injuries to the patient or caretakers. However, patients are counseled regarding proper precautions to prevent inadvertent injuries due to long silicone blocks. Being inert, there is less chance of allergenicity as well. One major advantage is the availability of silicone blocks in most operation theatres.

Silicone block capping is a simple and effective way of preventing injury due to unburied K-wire tip.

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A unique late complication with the use of calcium hydroxylapatite filler in facial lipoatrophy rehabilitation

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Sir,

Radiesse (Merz Aesthetics, Franksville, WI, USA) is an injectable filler material composed of synthetic calcium hydroxylapatite (CaHA) microspheres suspended in an aqueous carrier gel. Cosmetic use of Radiesse in facial rejuvenation is well-known. Treatment sites amenable to calcium hydroxylapatite (CH) injection include the naso-labial folds, marionette lines, perioral lines, prejowl sulcus, zygoma and malar eminence, tear trough depressions, nose, chin, acne scars, and it is also Food and Drug Administration-approved for facial augmentation in HIV patients with facial lipo-atrophy.[1]

Calcium hydroxylapatite filler enjoy an excellent safety record. The adverse events reported are similar to those observed with other short-acting fillers such as hyaluronic acid. There is no evidence of granuloma formation occurring with CaHA.[1] Although, presence of visible skin nodules has been reported, they are related to techniques, especially due to superficial injection of CH or its inappropriate use.

We describe a unique unreported complication, related to CH filler injection in an HIV positive patient. A 37-year-old, HIV positive, Caucasian male patient was referred to our University Hospital for facial lipo-atrophy rehabilitation [Figure 1]. We performed, as per our protocol,[2] the rehabilitation in one session injecting 7.5 mL of CH filler. After 10 days postinjection swelling and hematoma resolved [Figure 2]. Three weeks later, the patient came back to us with a complaint of a soft tissue swelling, involving the areas where the filler was injected [Figure 3]. The swelling was soft, nontender with sudden onset in the morning after waking up from sleep. A bromelina based therapy was prescribed for a week (Ananase, Rottapharm S.p.a., Milano) by us. After 2 weeks the swelling resolved completely with no recurrence in 8 months of follow-up [Figure 4]. To

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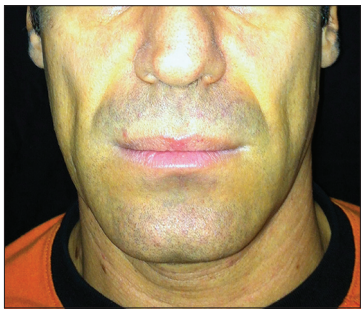

Figure 1: Preoperation photo of the patient

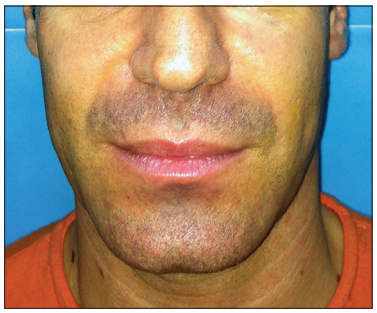

Figure 2: Result at the 10th days after calcium hydroxylapatite injection

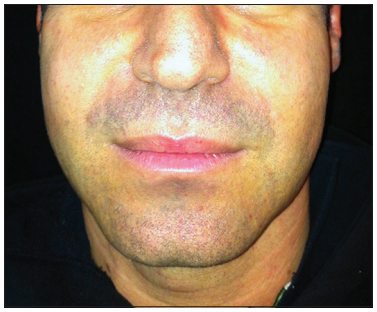

Figure 3: Swelling appeared at the 21st day postinjection

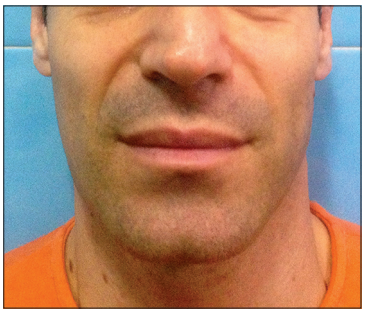

Figure 4: After 2 more weeks the swelling gradually disappeared

the best of our knowledge and after extensive literature search we could not determine the reason for this complication nor has such adverse effect ever reported in the literature.

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1.5 Work Funded by the National Institutes of Health

If an accepted manuscript was funded by National Institutes of Health (NIH), the author may inform editors of the NIH funding number. The editors are able to deposit the paper to the NIH Manuscript Submission System on behalf of the author.

2. Submission Preparation

2.1 Cover Letter

A cover letter is required to be submitted accompanying each manuscript. It should be concise and explain why the study is significant, why it fits the scope of the journal, and why it would be attractive to readers, etc.

Here is a guideline of a cover letter for authors’ consideration:

In the first paragraph: include the title and type (e.g., Original Article, Review, Case Report, *etc*.) of the manuscript, a brief on the background of the study, the question the author sought out to answer and why;

In the second paragraph: concisely explain what was done, the main findings and why they are significant;

In the third paragraph: indicate why the manuscript fits the Aims and Scope of the journal, and why it would be attractive to readers;

In the fourth paragraph: confirm that the manuscript has not been published elsewhere and not under consideration of any other journal. All authors have approved the manuscript and agreed on its submission to the journal. Journal’s specific requirements have been met if any.

If the manuscript is contributed to a special issue, please also mention it in the cover letter.

If the manuscript was presented partly or entirely in a conference, the author should clearly state the background information of the event, including the conference name, time and place in the cover letter.

2.2 Types of Manuscripts

There is no restriction on the length of manuscripts, number of figures, tables and references, provided that the manuscript is concise and comprehensive. The journal publishes Original Article, Review, Meta-analysis, Case Report, Commentary, *etc*. For more details about paper type, please refer to the following table.

Manuscript Type	Definition	Abstract	Keywords	Main Text Structure

Original Article	An Original Article describes detailed results from novel research. All findings are extensively discussed.	Structured abstract including Aim, Methods, Results and Conclusion. No more than 250 words.	3-8 keywords	The main content should include four sections: Introduction, Methods, Results and Discussion.
Review	A Review paper summarizes the literature on previous studies. It usually does not present any new information on a subject.	Unstructured abstract. No more than 250 words.	3-8 keywords	The main text may consist of several sections with unfixed section titles. We suggest that the author include an "Introduction" section at the beginning, several sections with unfixed titles in the middle part, and a "Conclusion" section in the end.
Case Report	A Case Report details symptoms, signs, diagnosis, treatment, and follows up an individual patient. The goal of a Case Report is to make other researchers aware of the possibility that a specific phenomenon might occur.	Unstructured abstract. No more than 150 words.	3-8 keywords	The main text consists of three sections with fixed section titles: Introduction, Case Report, and Discussion.
Meta-Analysis	A Meta-Analysis is a statistical analysis combining the results of multiple scientific studies. It is often an overview of clinical trials.	Structured abstract including Aim, Methods, Results and Conclusion. No more than 250 words.	3-8 keywords	The main content should include four sections: Introduction, Methods, Results and Discussion.
Systematic Review	A Systematic Review collects and critically analyzes multiple research studies, using methods selected before one or more research questions are formulated, and then finding and analyzing related studies and answering those questions in a structured methodology.	Structured abstract including Aim, Methods, Results and Conclusion. No more than 250 words.	3-8 keywords	The main content should include four sections: Introduction, Methods, Results and Discussion.
Technical Note	A Technical Note is a short article giving a brief description of a specific development, technique or procedure, or it may describe a modification of an existing technique, procedure or device applied in research.	Unstructured abstract. No more than 250 words.	3-8 keywords	/
Commentary	A Commentary is to provide comments on a newly published article or an alternative viewpoint on a certain topic.	Unstructured abstract. No more than 250 words.	3-8 keywords	/
Editorial	An Editorial is a short article describing news about the journal or opinions of senior editors or the publisher.	None required	None required	/
Letter to Editor	A Letter to Editor is usually an open post-publication review of a paper from its readers, often critical of some aspect of a published paper. Controversial papers often attract numerous Letters to Editor.	Unstructured abstract (optional). No more than 250 words.	3-8 keywords (optional)	/
Opinion	An Opinion usually presents personal thoughts, beliefs, or feelings on a topic.	Unstructured abstract (optional). No more than 250 words.	3-8 keywords	/
Perspective	A Perspective provides personal points of view on the state-of-the-art of a specific area of knowledge and its future prospects. Links to areas of intense current research focus can also be made. The emphasis should be on a personal assessment rather than a comprehensive, critical review. However, comments should be put into the context of existing literature. Perspectives are usually invited by the Editors.	Unstructured abstract. No more than 150 words.	3-8 keywords	/

2.3 Manuscript Structure

2.3.1 Front Matter

2.3.1.1 Title

The title of the manuscript should be concise, specific and relevant, with no more than 16 words if possible. When gene or

protein names are included, the abbreviated name rather than full name should be used.

2.3.1.2 Authors and Affiliations

Authors' full names should be listed. The initials of middle names can be provided. Institutional addresses and email addresses for all authors should be listed. At least one author should be designated as corresponding author. In addition, corresponding authors are suggested to provide their Open Researcher and Contributor ID upon submission. Please note that any change to authorship is not allowed after manuscript acceptance.

2.3.1.3 Abstract

The abstract should be a single paragraph with word limitation and specific structure requirements (for more details please refer to Types of Manuscripts). It usually describes the main objective(s) of the study, explains how the study was done, including any model organisms used, without methodological detail, and summarizes the most important results and their significance. The abstract must be an objective representation of the study: it is not allowed to contain results which are not presented and substantiated in the manuscript, or exaggerate the main conclusions. Citations should not be included in the abstract.

2.3.1.4 Keywords

Three to eight keywords should be provided, which are specific to the article, yet reasonably common within the subject discipline.

2.3.2 Main Text

Manuscripts of different types are structured with different sections of content. Please refer to Types of Manuscripts to make sure which sections should be included in the manuscripts.

2.3.2.1 Introduction

The introduction should contain background that puts the manuscript into context, allow readers to understand why the study is important, include a brief review of key literature, and conclude with a brief statement of the overall aim of the work and a comment about whether that aim was achieved. Relevant controversies or disagreements in the field should be introduced as well.

2.3.2.2 Methods

Methods should contain sufficient details to allow others to fully replicate the study. New methods and protocols should be described in detail while well-established methods can be briefly described or appropriately cited. Experimental participants selected, the drugs and chemicals used, the statistical methods taken, and the computer software used should be identified precisely. Statistical terms, abbreviations, and all symbols used should be defined clearly. Protocol documents for clinical trials, observational studies, and other non-laboratory investigations may be uploaded as supplementary materials.

2.3.2.3 Results

This section contains the findings of the study. Results of statistical analysis should also be included either as text or as tables or figures if appropriate. Authors should emphasize and summarize only the most important observations. Data on all primary and secondary outcomes identified in the section Methods should also be provided. Extra or supplementary materials and technical details can be placed in supplementary documents.

2.3.2.4 Discussion

This section should discuss the implications of the findings in context of existing research and highlight limitations of the study. Future research directions may also be mentioned.

2.3.2.5 Conclusion

It should state clearly the main conclusions and include the explanation of their relevance or importance to the field.

2.3.3 Back Matter

2.3.3.1 Acknowledgments

Anyone who contributed towards the article but does not meet the criteria for authorship, including those who provided professional writing services or materials, should be acknowledged. Authors should obtain permission to acknowledge from all those mentioned in the Acknowledgments section. This section is not added if the author does not have anyone to acknowledge.

2.3.3.2 Authors' Contributions

Each author is expected to have made substantial contributions to the conception or design of the work, or the acquisition, analysis, or interpretation of data, or the creation of new software used in the work, or have drafted the work or substantively revised it.

Please use Surname and Initial of Forename to refer to an author's contribution. For example: made substantial contributions

to conception and design of the study and performed data analysis and interpretation: Salas H, Castaneda WV; performed data acquisition, as well as provided administrative, technical, and material support: Castillo N, Young V.
If an article is single-authored, please include "The author contributed solely to the article." in this section.

2.3.3.3 Availability of Data and Materials

In order to maintain the integrity, transparency and reproducibility of research records, authors should include this section in their manuscripts, detailing where the data supporting their findings can be found. Data can be deposited into data repositories or published as supplementary information in the journal. Authors who cannot share their data should state that the data will not be shared and explain it. If a manuscript does not involve such issue, please state "Not applicable." in this section.

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All sources of funding for the study reported should be declared. The role of the funding body in the experiment design, collection, analysis and interpretation of data, and writing of the manuscript should be declared. Any relevant grant numbers and the link of funder's website should be provided if any. If the study is not involved with this issue, state "None." in this section.

2.3.3.5 Conflicts of Interest

Authors must declare any potential conflicts of interest that may be perceived as inappropriately influencing the representation or interpretation of reported research results. If there are no conflicts of interest, please state "All authors declared that there are no conflicts of interest." in this section. Some authors may be bound by confidentiality agreements. In such cases, in place of itemized disclosures, we will require authors to state "All authors declare that they are bound by confidentiality agreements that prevent them from disclosing their conflicts of interest in this work.". If authors are unsure whether conflicts of interest exist, please refer to the "Conflicts of Interest" of OAE Editorial Policies for a full explanation.

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Research involving human subjects, human material or human data must be performed in accordance with the Declaration of Helsinki and approved by an appropriate ethics committee. An informed consent to participate in the study should also be obtained from participants, or their parents or legal guardians for children under 16. A statement detailing the name of the ethics committee (including the reference number where appropriate) and the informed consent obtained must appear in the manuscripts reporting such research.
Studies involving animals and cell lines must include a statement on ethical approval. More information is available at Editorial Policies.
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2.3.3.7 Consent for Publication

Manuscripts containing individual details, images or videos, must obtain consent for publication from that person, or in the case of children, their parents or legal guardians. If the person has died, consent for publication must be obtained from the next of kin of the participant. Manuscripts must include a statement that a written informed consent for publication was obtained. Authors do not have to submit such content accompanying the manuscript. However, these documents must be available if requested. If the manuscript does not involve this issue, state "Not applicable." in this section.

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2.3.3.9 References

References should be numbered in order of appearance at the end of manuscripts. In the text, reference numbers should be placed in square brackets and the corresponding references are cited thereafter. Only the first five authors' names are required to be listed in the references, other authors' names should be omitted and replaced with "et al.". Abbreviations of the journals should be provided on the basis of Index Medicus. Information from manuscripts accepted but not published should be cited in the text as "Unpublished material" with written permission from the source.

References should be described as follows, depending on the types of works:

Types	Examples
Journal articles by individual authors	Weaver DL, Ashikaga T, Krag DN, Skelly JM, Anderson SJ, et al. Effect of occult metastases on survival in node-negative breast cancer. N Engl J Med 2011;364:412-21. [PMID: 21247310 DOI: 10.1056/NEJMoa1008108]
Organization as author	Diabetes Prevention Program Research Group. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. Hypertension 2002;40:679-86. [PMID: 12411462]

Both personal authors and organization as author	Vallancien G, Emberton M, Harving N, van Moorselaar RJ; Alf-One Study Group. Sexual dysfunction in 1,274 European men suffering from lower urinary tract symptoms. J Urol 2003;169:2257-61. [PMID: 12771764 DOI: 10.1097/01.ju.0000067940.76090.73]
Journal articles not in English	Zhang X, Xiong H, Ji TY, Zhang YH, Wang Y. Case report of anti-N-methyl-D-aspartate receptor encephalitis in child. J Appl Clin Pediatr 2012;27:1903-7. (in Chinese)
Journal articles ahead of print	Odibo AO. Falling stillbirth and neonatal mortality rates in twin gestation: not a reason for complacency. BJOG 2018; Epub ahead of print [PMID: 30461178 DOI: 10.1111/1471-0528.15541]
Books	Sherlock S, Dooley J. Diseases of the liver and billiary system. 9th ed. Oxford: Blackwell Sci Pub; 1993. pp. 258-96.
Book chapters	Meltzer PS, Kallioniemi A, Trent JM. Chromosome alterations in human solid tumors. In: Vogelstein B, Kinzler KW, editors. The genetic basis of human cancer. New York: McGraw-Hill; 2002. pp. 93-113.
Online resource	FDA News Release. FDA approval brings first gene therapy to the United States. Available from: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm574058.htm. [Last accessed on 30 Oct 2017]
Conference proceedings	Harnden P, Joffe JK, Jones WG, editors. Germ cell tumours V. Proceedings of the 5th Germ Cell Tumour Conference; 2001 Sep 13-15; Leeds, UK. New York: Springer; 2002.
Conference paper	Christensen S, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer; 2002. pp. 182-91.
Unpublished material	Tian D, Araki H, Stahl E, Bergelson J, Kreitman M. Signature of balancing selection in Arabidopsis. Proc Natl Acad Sci U S A. Forthcoming 2002.

For other types of references, please refer to U.S. National Library of Medicine.
The journal also recommends that authors prepare references with a bibliography software package, such as EndNote to avoid typing mistakes and duplicated references.

2.3.3.10 Supplementary Materials

Additional data and information can be uploaded as Supplementary Materials to accompany the manuscripts. The supplementary materials will also be available to the referees as part of the peer-review process. Any file format is acceptable, such as data sheet (word, excel, csv, cdx, fasta, pdf or zip files), presentation (powerpoint, pdf or zip files), image (cdx, eps, jpeg, pdf, png or tiff), table (word, excel, csv or pdf), audio (mp3, wav or wma) or video (avi, divx, flv, mov, mp4, mpeg, mpg or wmv). All information should be clearly presented. Supplementary materials should be cited in the main text in numeric order (e.g., Supplementary Figure 1, Supplementary Figure 2, Supplementary Table 1, Supplementary Table 2, etc.). The style of supplementary figures or tables complies with the same requirements on figures or tables in main text. Videos and audios should be prepared in English, and limited to a size of 500 MB or a duration of 3 minutes.

2.4 Manuscript Format

2.4.1 File Format

Manuscript files can be in DOC and DOCX formats and should not be locked or protected.

2.4.2 Length

There are no restrictions on paper length, number of figures, or number of supporting documents. Authors are encouraged to present and discuss their findings concisely.

2.4.3 Language

Manuscripts must be written in English.

2.4.4 Multimedia Files

The journal supports manuscripts with multimedia files. The requirements are listed as follows:
•Video or audio files are only acceptable in English. The presentation and introduction should be easy to understand. The frames should be clear, and the speech speed should be moderate.
•A brief overview of the video or audio files should be given in the manuscript text.
•The video or audio files should be limited to a duration of 3 min and a size of up to 500 MB.
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2.4.5 Figures

•Figures should be cited in numeric order (e.g., Figure 1, Figure 2) and placed after the paragraph where it is first cited;
•Figures can be submitted in format of tiff, psd, AI or jpeg, with resolution of 300-600 dpi;
•Figure caption is placed under the Figure;

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•Tables should be cited in numeric order and placed after the paragraph where it is first cited;
•The table caption should be placed above the table and labeled sequentially (e.g., Table 1, Table 2);
•Tables should be provided in editable form like DOC or DOCX format (picture is not allowed);
•Abbreviations and symbols used in table should be explained in footnote;
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2.4.7 Abbreviations

Abbreviations should be defined upon first appearance in the abstract, main text, and in figure or table captions and used consistently thereafter. Non-standard abbreviations are not allowed unless they appear at least three times in the text. Commonly-used abbreviations, such as DNA, RNA, ATP, *etc*., can be used directly without definition. Abbreviations in titles and keywords should be avoided, except for the ones which are widely used.

2.4.8 Italics

General italic words like *vs*., *et al., etc*., *in vivo*, *in vitro*; *t* test, *F* test, *U* test; related coefficient as *r*, sample number as *n*, and probability as *P*; names of genes; names of bacteria and biology species in Latin.

2.4.9 Units

SI Units should be used. Imperial, US customary and other units should be converted to SI units whenever possible. There is a space between the number and the unit (i.e., 23 mL). Hour, minute, second should be written as h, min, s.

2.4.10 Numbers

Numbers appearing at the beginning of sentences should be expressed in English. When there are two or more numbers in a paragraph, they should be expressed as Arabic numerals; when there is only one number in a paragraph, number < 10 should be expressed in English and number > 10 should be expressed as Arabic numerals. 12345678 should be written as 12,345,678.

2.4.11 Equations

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