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Systematic Review

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Operative efficiency in autologous breast reconstruction: a systematic review

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Abstract

Breast cancer is a leading cause of cancer in women worldwide. With increased public awareness of routine breast cancer screening, the incidence of mastectomy and, therefore, breast reconstruction continues to increase year over year. Value-based healthcare has become a universal priority in medical systems. A systematic review of the literature was performed in March 2024 across four electronic databases (PubMed, Embase, Google Scholar, and MEDLINE) and in accordance with the PRISMA guidelines. Screening was performed at two levels (title/abstract and full text screening) by two independent reviewers. Data items extracted included: year, authors, country, study size, duration, strategy implemented, main aims, area of application, study design and methodology, outcomes, relevant statistical analysis, and follow-up. Eleven articles were identified that met all inclusion criteria. Six were retrospective reviews and five were prospective cohort studies. The efficiency models implemented included Lean Six Sigma, the Four Disciplines of Execution, and process mapping and analysis. Emphasizing efficiency is pivotal in delivering outstanding breast reconstruction services and enhancing the overall patient journey.

Keywords: Autologous breast reconstruction, microsurgery, DIEP, efficiency, process analysis

INTRODUCTION

The predominant method of breast reconstruction both in the United States and globally is prosthetic-based[1,2]. However, recent studies have demonstrated an increasing rate of microsurgical autologous breast reconstruction (MABR) compared to prosthetic breast reconstruction[3,4]. MABR has demonstrated superior long-term aesthetic outcomes, heightened patient satisfaction, and improved psychosocial and sexual well-being compared to prosthetic reconstruction[5-10]. In the irradiated breast, MABR is considered the gold standard[11,12]. It is highly probable that increasing trends of MABR will continue, given the increased awareness among both patients and surgeons regarding implant-related risks, such as breast implant illness (BII) and breast implant-associated lymphoma (BIA-ALCL). Primary obstacles to autologous reconstruction are surgical factors, including prolonged operative times, increased scarring, and extended hospital stays[13,14].

Operative duration is among the primary challenges in MABR, impacting both patients and surgeons. This intricate procedure involves recipient vessel preparation, dissection and harvesting of perforators and pedicles, microsurgical anastomoses, flap placement, and donor site closure. In numerous practices, bilateral MABR can extend beyond 12 h. Literature consistently highlights increased complication rates associated with prolonged operative times across various surgical fields, including MABR[15-18].

The current economic climate in healthcare is marked by declining reimbursements and rising care costs. The benefits of improved efficiency include reduced surgery backlogs, optimized patient safety and outcomes, and cost reduction through decreased operating room time and reduced hospital stays. There is a burgeoning interest in enhancing operative efficiency within breast microsurgery, with several high-volume practices demonstrating the safety and effectiveness of "efficient" microsurgical breast reconstruction in four hours or less[19-23]. This systematic review aims to underscore the processes that can positively impact operating room efficiency, with a focus on implications in MABR.

Value-based healthcare: the "why" of efficiency in microsurgery

Value-based healthcare represents a strategic shift in healthcare delivery, emphasizing the optimization of patient outcomes while containing costs[24-26]. This model redefines the traditional fee-for-service approach by centering on the value provided to patients, focusing on enhancing quality and efficiency in care delivery. In surgery, the value-based framework prioritizes patient results and experiences, striving for favorable outcomes while simultaneously controlling expenditures. This necessitates a thorough understanding of the dynamics between cost, quality, and patient-centered outcomes, streamlining surgical interventions to maximize effectiveness while minimizing avoidable complications or unnecessary procedures. As healthcare systems globally pivot toward value-based care models, the operating theater will remain a heavily scrutinized area both in terms of quality and cost of care.

Caution must be taken when considering the value of healthcare, specifically in surgery. Simply quantifying cost reduction with no consideration for outcomes achieved may lead to false "savings" and potentially limit effective care. Healthcare payment legislation passed in recent years has begun to prioritize outcomes as opposed to fee-for-service models and represents an overall shift toward value-based care[27,28].

Microsurgical autologous breast reconstruction (MABR) is a relatively standardized surgical procedure where one can measure results versus costs. Regarding the "inputs" and "outputs" of the system, the outputs of MABR are flap survival, time to discharge, overall aesthetic results, and patient-reported outcome measures, whereas costs are operative time, the human cost of staff/surgical team (perioperative nursing, scrub technicians, anesthesia), cost of medications (anesthesia, ERAS pathways), flap monitoring devices, *etc*. This allows tracking both the input and output of the entire process. The overall goal of a value-based system should be to reduce inputs while maintaining or increasing the outputs[23].

Models of efficiency in the operating room

Efficiency models within operating rooms primarily focus on optimizing workflow, enhancing patient care, and maximizing resource utilization. Several models have been proposed and implemented to improve operational efficiency in surgical settings. These efficiency models aim to streamline operations, enhance quality, reduce costs, and ultimately improve patient outcomes in surgical settings.

Four disciplines of execution

The 4 Disciplines of Execution (4DX) model is a performance management strategy developed by Sean Covey, Chris McChesney, and Jim Huling, designed to assist organizations in achieving their wildly important goals (WIGs) amidst the whirlwind of daily operations[29]. This model is structured around four key disciplines. First, it emphasizes the identification of clear and compelling WIGs, defining specific outcomes that require exceptional focus. Second, it advocates the establishment of lead measures, quantifiable predictors of goal achievement, allowing teams to proactively influence results. Third, it underscores creating a scoreboard, enabling teams to visually track progress and engage in a consistent feedback loop. Finally, the model establishes a cadence of accountability through regular team meetings where members commit to actions, review progress, and hold each other accountable for results. The 4DX model acts as a systematic approach to drive focus, engagement, and accountability within organizations, enhancing their ability to accomplish their most critical objectives in the face of competing priorities. The 4DX model has been implemented in MABR. Easton *et al.* demonstrated a significant reduction in operative time, from 828 min pre-intervention to 619 min post-intervention for a bilateral DIEP breast reconstruction[30]. Length of stay was decreased, and no increase in complications was identified.

Lean and six sigma

Taiichi Ohno first described the Lean methodology in his role at Toyota. He described the “seven wastes”, later expanded to eight: waiting/idle time, inventory, defects, transportation, motion, overproduction, over-processing, and untapped potential. By reducing these wastes, the goal of streamlined production, improved quality, and increased efficiency can be achieved. The Lean methodology has been adapted to healthcare, including the MABR system[31-33]. Its principles, including value stream mapping and continuous improvement, have been applied to identify and rectify inefficiencies in operating room processes.

Lean methodology aims to eliminate waste within processes, while the Six Sigma methodology is aimed at reducing variability in processes and eliminating defects. Lean focuses on speed and efficiency, whereas Six Sigma emphasizes quality and precision by reducing variability. The core idea of Six Sigma is to use data analysis to pinpoint problems and variability, and then use specific techniques to systematically remove these. This is accomplished through the DMAIC (Define, Measure, Analyze, Improve, Control) cycle for existing processes, or the DMADV (Define, Measure, Analyze, Design, Verify) for creating new product or process designs.

Over the last twenty years, the two concepts have been combined into a hybrid improvement process called “Lean Six Sigma”. By combining the elimination of waste and defects within a given system, Lean Six Sigma seeks to streamline surgical processes, improve quality, and minimize variation in outcomes. This model employs data-driven decision making, process mapping, and statistical tools to measure, analyze, and improve the efficiency of surgical procedures, ultimately leading to reduced costs, shorter cycle times, improved patient satisfaction, and superior clinical outcomes in the operating room. This framework has also been adopted in MABR by multiple groups. In 2016, Hultman *et al.* reported their results of pre-, intra-, and post-intervention in a group of patients undergoing DIEP flap breast reconstruction, demonstrating a significant reduction in operative times (714 to 607 min) and length of stay (6.3 to 5.2 days)[33]. In 2021, Stein *et al*. published their experience with value stream mapping, finding that only 47% of instruments within a given surgical tray were being used[31]. By reducing the number of instruments needing to be processed and sterilized in each case, they propose an overall decrease in waste and subsequent increase in efficiency.

Time-driven activity-based costing

Time-Driven Activity-Based Costing (TDABC) is an innovative methodology designed to provide more accurate cost assessments by focusing on the actual activities involved in providing a service and the time required to perform these activities. Unlike traditional costing methods, which often allocate overhead costs somewhat arbitrarily, TDABC assigns costs based on the efficient time required to perform each activity and the cost per unit time of the resources used. This approach involves determining the cost of supplying resources for each business process and then multiplying this by the time taken to carry out the process. A key advantage of TDABC is its simplicity and flexibility, which make it easier to implement and update compared to traditional activity-based costing systems, especially in dynamic environments like healthcare[34].

TDABC has been applied to and analyzed within the context of MABR. Mericli *et al.* developed a decision-analytic model to compare ERAS *vs*. standard of care recovery pathways following MABR[35]. The authors included 5 relevant studies and a total of 986 MABR patients: 596 in the standard-of-care arm, and 390 in the ERAS arm. The mean length of stay was 1.5 days shorter in the ERAS cohort. The cost of the ERAS pathway was found to represent a cost-savings of $735.04 per case and 1 additional day of quality-adjusted life.

Process mapping and analysis

The Process Mapping and Analysis model is a structured approach used in surgical settings to systematically diagram, assess, and optimize the sequence of activities within operative procedures. This model involves creating visual representations of the entire surgical process, from preoperative preparation to postoperative care, identifying steps, resources, and potential bottlenecks. By employing process mapping and analysis, surgical teams can effectively identify and rectify operational inefficiencies, leading to smoother procedures, minimized errors, and ultimately, improved patient outcomes. Sharma *et al.* outlined the "100 steps of a DIEP flap" using a Process Mapping technique[36]. The authors reviewed over 5,000 cases, subdivided the procedure into 100 steps over 9 subcategories, and analyzed two cohorts: the Process Mapping group and the non-Process Mapping group. They demonstrated an overall reduction in operative time from 219.2 min (non-Process Mapping group) to 163.1 min (Process Mapping group), though significant differences between the groups were reported.

Our own institution has significant experience with process mapping to improve efficiency for MABR[37]. In the seminal study covering a 10-month period (June 2018–April 2019), 147 bilateral DIEP breast reconstructions were performed. The procedure was divided into eight critical maneuvers, and the time of each of these steps was cataloged. Total operative time was reduced by 73 min, with significant differences identified to correlate with the experience level of the surgeons [Figure 1].

METHODS

A systematic review of the literature was performed in March 2024 across four electronic databases (PubMed, Embase, Google Scholar, and MEDLINE) and in accordance with the PRISMA guidelines. The search strategy included selecting studies with patients undergoing autologous breast reconstruction, and abstracts were reviewed to identify relevant literature. Searches were conducted with the following phrase:

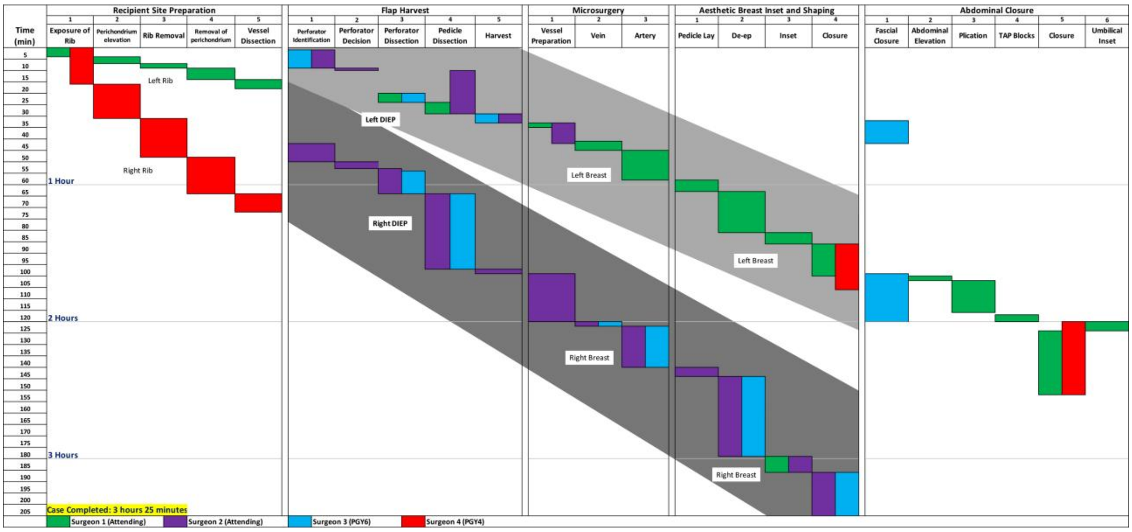

Figure 1. Mapping diagram of a delayed bilateral DIEP flap breast reconstruction in a 58-year-old patient with a BMI of 25.6. The first DIEP flap had one intermediate perforator and the second DIEP flap had three lateral perforators. There were no revisions. The procedure was completed in 3 h and 25 min. De-ep: De-epithelialization; TAP: transversus abdominus plane; DIEP: deep inferior epigastric perforator flap.

(breast AND reconstruction) AND (microsurgery OR free flap OR autologous) AND (efficiency OR process analysis OR lean OR six sigma OR four discipline). Data items extracted included: year, authors, country, study size, duration, strategy implemented, main aims, area of application, study design and methodology, outcomes, relevant statistical analysis, and follow-up.

Screening was performed at two levels (title/abstract and full text screening) by two independent reviewers (T. S. and N. H.). The initial criteria for full text screening included articles describing the implementation of efficiency models in microvascular breast reconstruction. Studies were excluded if they were not available in the English language, animal or cadaveric studies, studies published before the year 2004, publications formatted as a letter, editorial, or conference abstract, those that did not list a process or depicted the process as a map, or did not have a novel process-mapping for the selected center(s). Due to the lack of randomized control trials and a diverse range of study aims and outcomes, meta-analysis was not applicable.

RESULTS

A total of 256 records were identified through the literature search [Figure 2]. After removing duplicates and screening titles/abstracts, 29 full-text publications were reviewed. Eleven articles met all inclusion criteria [Table 1]. Six were retrospective reviews and five were prospective cohort studies. Six articles centered around the standardization of operative technique without a predefined "model of efficiency", whereas five articles highlighted a specific implementation protocol of an efficiency model. Of these five, one used a Lean Six Sigma model, one used a 4DX model, and three used a process mapping and analysis model.

DISCUSSION

Microvascular breast reconstruction represents a sophisticated, multi-stage procedure necessitating the collaboration of a sizable surgical team. The degree of complexity inherent in the process, as well as the involvement of numerous personnel, underscores the potential benefits of employing process analysis for

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Table 1. Systematic review of MABR and efficiency models

Author, year	Country, length	Flap type	Number of flaps	Study design	Intervention	Co-surgery?	Outcomes measured
Elliott *et al.*, 2007[19]	United States, 3 years	ms-fTRAM	111 (91 uni, 10 bi)	Retrospective	Standardization of operative sequence	N/A	Operative time, complications
Lee *et al.*, 2008[38]	United States, 3 years	DIEP	225 (pre-intervention: 50 uni, 50 bi post-intervention: 25 uni, 25 bi)	Prospective	Intraoperative pathway - "relational coordination teamwork"	N/A	Operative time, complications, OR/hospital costs, OR staff satisfaction surveys
Canizares *et al.*, 2015[21]	United States, 6 months	DIEP	104 (32 uni, 36 bi)	Retrospective	Standardization of operative sequence	N/A	Operative time
Marsh *et al.*, 2016[20]	United Kingdom, 12 months	DIEP	163 flaps (laterality not defined)	Retrospective	Standardization of operative sequence	Yes	Operative time
Hultman *et al.*, 2016[33]	United States, 5 years	"perforator flap breast reconstruction"	168 (undefined)	Prospective	Six-sigma interventions	N/A	Operative time, LOS, complications, unplanned return to OR, physician/hospital revenue, and revenue per minute of OR time
Shama *et al.*, 2019	UK (duration not stated)	DIEP	20 (unilateral)	Prospective cohort	Process mapping, standardization of operative sequence	No	Operative time (each step)
Haddock & Teotia, 2020[37]	United States, 10 months	DIEP	147 (unilateral)	Prospective	Process mapping, standardization of operative sequence	Yes	Operative time, complications
Haddock & Teotia, 2021[57]	United States, 8 months	DIEP	100 (bilateral)	Prospective	Process mapping, standardization of operative sequence	Yes	Operative time, complications
Easton *et al.*, 2023[30]	United States, 5 years	DIEP, TRAM, PAP, TUG	32 (bilateral)	Retrospective	Preoperative (clinic, IV access, markings, blocks) & intraoperative (surgical teams, standardized instruments, *etc.*)	Yes	Operative time, LOS, complications
Haddock *et al.*, 2023[47]	United States, 18 months	DIEP	375 (bilateral)	Retrospective	Process mapping	Yes	Operative time, complications
Todd *et al.*, 2023[39]	Canada (15 years)	DIEP	1056 flaps (416 uni, 320 bi)	Retrospective	Standardization of operative sequence, surgeon experience	Yes	# of cases, operative time, intraoperative variables, LOS, readmission rate

improved intraoperative efficiency. The term "efficiency" in the realm of healthcare often carries an unintended connotation, insinuating a trade-off between the quality of patient care and cost/resource reduction. However, this perception is misguided; an emphasis on efficiency entails an organized approach that minimizes waste and cultivates an environment dedicated to achieving optimal outcomes across all facets.

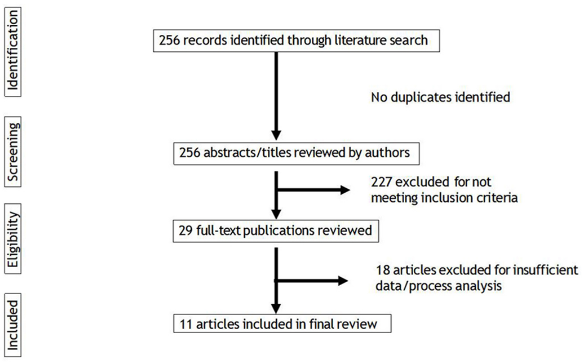

Figure 2. Attrition chart of the systematic review performed.

Modifiable factors to improve efficiency in MABR

Preoperative

Patient selection is a critical component of any surgical intervention. Primary considerations for autologous breast reconstruction include a thorough history and physical exam and extensive counseling on a patient's options. Prior surgical intervention such as abdominoplasty is an absolute contraindication for DIEP flap breast reconstruction, necessitating alternative autologous flaps versus implant-based reconstruction. Severe obesity, uncontrolled diabetes, cardiovascular disease, and coagulopathy are relative contraindications and considered on a case-by-case basis. Preoperative CT angiogram has been repeatedly shown to reduce operative time in MABR and has become the standard of care in the senior authors' practice[38,39]. Other authors have demonstrated similar results with MRI and thermography[40-42]. Preoperative imaging provides several advantages regarding increased efficiency, including detailed anatomic assessment and vascular mapping of the perforators, which reduces the time to perforator identification. Preoperative imaging has also been shown to reduce operative risks and overall blood loss and enhance patient outcomes through increased surgical success rates.

Perioperative

As with any surgical procedure, the expertise and familiarity of the surgical team are invaluable. It is essential that the surgical staff, anesthesia providers, and postoperative nursing care team are well-versed in all stages of microsurgical patient care[43,44]. Additionally, multiple studies have demonstrated decreased OR time, improved patient outcomes, shorter hospital stays, and higher success rates with a co-surgeon[45,46]. In the authors' experience, overall morale is increased and surgeon fatigue is decreased with a co-surgeon model. A review of our practice from 2011–2016 demonstrated an overall reduction in operative time by 193 min when comparing co-surgeon model to solo surgeon and showed reduced length of stay and decreased wound occurrences[47]. A 2022 retrospective review of 150 patients examined the cost of the co-surgeon model in MABR, including the potential opportunity costs, and demonstrated that the co-surgeon model significantly reduced both the operation duration by up to 132 min and costs by approximately $1,389. Additionally, the presence of a co-surgeon was linked to fewer breast-site complications and a trend toward reduced overall major complications. The co-surgeon model remains net-positive from a cost standpoint if the co-surgeon is present for 320 min or less, depending on the level of the co-surgeon (assistant *vs.* associate *vs*. full professor)[48].

Regarding efficiency and process mapping, our institution has implemented a protocol for process mapping for all MABR cases [Figure 1]. Process mapping is a model of deliberate practice that has vastly improved operative time and outcomes for patients in our practice. A typical bilateral DIEP flap breast reconstruction is divided into quantifiable steps: recipient site preparation, DIEP flap dissection and harvest, microsurgery, aesthetic breast inset and shaping, and abdominal closure. Video instruction on recipient site preparation was published and used to instruct the junior members of the team[49]. With the implementation of this deliberate practice, our institution has reduced operative time for bilateral DIEP flap breast reconstruction to an average of less than 4 h.

Our practice adheres to the principle of each site being its own independent operation. With that in mind, the operative field is prepared with each site (left and right breast, left and right abdomen) having its own electrocautery machine, including Bovie electrocautery and bipolar forceps. Other time-saving measures include the use of a venous coupler for all venous anastomoses, umbilectomy and placement of progressive tension sutures for the abdominal donor site, and placement of a single abdominal drain. Of note, the near-universal umbilectomy is a result of critical evaluation of postoperative results. We noticed a relatively high number of umbilical wound complications. By eliminating the umbilicus, we reduced wound complications but subsequently noted an increased frequency of seroma formation. Hence, the addition of progressive tension sutures has reduced complication rates to at or below those reported in the literature. Additionally, this allows better control of muscle plication, scar placement, and ultimately, neoumbilicus placement.

Perfusion evaluation is commonly employed through a variety of methods and is supported in the literature[50-52]. Most commonly, and perhaps the gold standard, is direct visualization of bleeding dermis upon de-epithelialization of the flap during inset. Since the borders of the flap are almost always buried (and therefore de-epithelialized), a healthy bleeding dermis confirms perfusion of all aspects of the flap. In cases where there is questionable perfusion or concern for anastomotic complications, fluorescent angiography with indocyanine green (ICG) dye is used. A retrospective review of 500 flaps at our institution showed that employing ICG for evaluation of flap perfusion decreased rates of postoperative fat necrosis and reduced resection volumes compared to controls[53].

Postoperative

As stated earlier, the primary goal of value-based healthcare is improving patient outcomes while decreasing “inputs” to the system, usually by decreasing costs. Regarding MABR, several institutions have reported safe outcomes for postoperative day 1 (POD1) discharge after bilateral DIEP flap breast reconstruction[54-56]. Reducing operative time has significant downstream effects, including reducing anesthesia time, initiating the recovery process sooner, and advancing through recovery stages more quickly. In a theoretical 10-hour case, the recovery process would not begin until 7:00 p.m., and many patients are not allowed a regular diet until the next morning when they are outside of the 24-hour postoperative window. When reducing operative times to 4 h or less, the recovery process obviously begins much sooner, making a POD1 discharge feasible.

Enhanced Recovery After Surgery (ERAS) pathways have been popularized across all surgical fields, including MABR. The primary goal of these protocols is to facilitate patient recovery, reduce narcotic use, and promote earlier discharge from the hospital. It is typically initiated preoperatively and continued until discharge for maximal effect[57]. Preoperative factors include the administration of celecoxib and acetaminophen, as well as allowing patients to drink 12 ounces of an electrolyte-rich carbohydrate beverage. Intraoperative application of liposomal bupivacaine in regional field blocks provides enhanced analgesia. Intravenous steroids and ondansetron, as well as a scopolamine patch, may be useful for reducing postoperative nausea. Postoperatively, patients are encouraged to ambulate early, potentially on the same day of surgery [Table 2].

Table 2. Preferred enhanced recovery after surgery (ERAS) protocol at the senior author's institution

Phase of care	Intervention
Planning & optimization	Smoking cessation (4^+ wks) Alcohol abstinence (4^+ wks) CBC, BMP, type/screen (if Hgb < 12.5) Referral to endocrine, PCP, cardiology when indicated Preadmission patient education regarding the protocol per anesthesia in our presurgical testing clinic
Preoperative	Antibiotics within 60 min of incision; cefazolin (or clindamycin if B-lactam allergy) Acetaminophen 1 g PO Celecoxib 400 mg PO Scopolamine patch or aprepitant PO at discretion of anesthesia NPO solids after midnight; clear liquids permitted until 2 h prior to surgery 12 oz gatorade or carbohydrate beverage on the morning of surgery
Intraoperative	Induction with: lidocaine, propofol, vecuronium per anesthesia team Dexamethasone 4-8 mg IV Maintenance with desflurane, sevoflurane, or propofol infusion, titrated to BIS 45-55 Lidocaine infusion 1-2 mg/kg/h, stopped 30 min before liposomal bupivacaine administration Ketamine 0.5 mg/kg bolus at induction followed by 0.2 mg/kg/h infusion or hourly bolus Acetaminophen 1 g IV every 8 h following pre-op dose Balanced electrolyte solution aimed at euvolemia, 1-4 mL/kg/h Avoid use of vasopressors Maintenance of neuromuscular blockade with vecuronium infusion Ondansetron 4 mg IV 30 min prior to emergence Reversal of neuromuscular blockade
Postoperative	Flap monitoring every hour Acetaminophen 1,000 mg PO, started POD 0 Encouragement of early ambulation Early feeding: clear liquids and ice chips POD 0 Thromboprophylaxis

BID: Twice daily; BIS: bispectral index; BMP: basic metabolic panel; CBC: complete blood count; Hgb: hemoglobin; IV: intravenous; NPO: nothing by mouth; PCP: primary care provider; PO: by mouth; POD: postoperative day; PRN: pro re nata; mg: milligram; kg: kilogram; h: hour; wks: weeks.

In the specific context of microvascular breast reconstruction, certain variables resist easy standardization. Patient-reported outcome metrics, as exemplified by the BREAST-Q tool, contribute to standardizing the patient's perspective on the reconstruction process. While these metrics encompass aesthetic outcomes, they may not entirely capture the nuanced dimensions of patient satisfaction. The aesthetic component in microvascular breast reconstruction, integral to the patient experience, remains challenging to standardize. Reconstructive surgeons must uphold their commitment to optimal cosmetic results, even within an efficient procedural model. A pertinent example is presented, wherein a patient underwent bilateral DIEP breast reconstruction in 2 h and 5 min, subsequently undergoing a single revision for skin paddle removal, yielding an overall excellent aesthetic outcome [Figure 3].

LIMITATIONS

This systematic review was limited by the heterogeneity of the studies, the relatively low number of studies identified that met inclusion criteria, and the overall lack of randomized controlled trials.

CONCLUSION

In summary, efficiency assumes a crucial role in microsurgical breast reconstruction, presenting an avenue to provide high-quality care while managing costs. Embracing inventive efficiency models and refining surgical protocols empower surgeons to improve patient outcomes, reduce complications, and secure optimal aesthetic results. In a healthcare landscape increasingly oriented toward value-based principles, prioritizing efficiency becomes indispensable for delivering outstanding breast reconstruction services and enhancing the holistic patient experience.

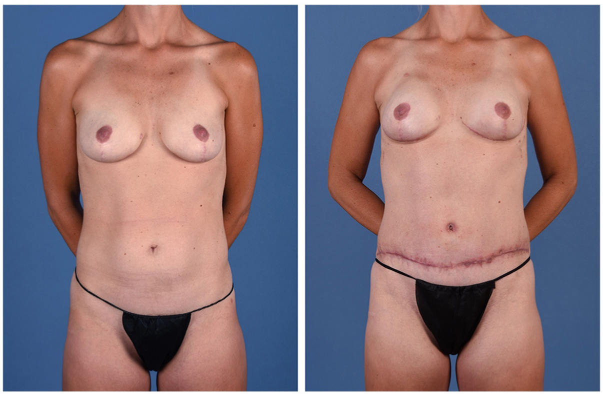

Figure 3. Example before (left) and after (right) photo of a patient undergoing a bilateral DIEP flap reconstruction in 2 h and 2 min. She underwent one revision to excise and bury the skin paddles.

DECLARATIONS

Authors' contributions

Made substantial contributions to the conception and design of the study and performed data analysis and interpretation: Haddock NT, Steele T, Teotia SS

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Due to the systematic review, the information used in this database is publicly available and unrestricted re-use is permitted under open license.

Consent for publication

Not applicable.

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