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Review

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Vascularized omental tissue transfer for the treatment of lymphedema: a review

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Abstract

Lymphedema is a debilitating disorder caused by impaired drainage of the lymphatic system. In the Western world, lymphedema most often arises secondary to the treatment of malignancy. Patients with lymphedema experience progressive swelling, pain, numbness, and tingling, and decreased quality of life. Those with persistent symptoms may be subject to chronic cellulitis. The advent of microsurgery has enabled clinicians to transplant donor lymph nodes and their blood supply from a healthy site to the affected area in a procedure known as vascularized lymph node transplant (VLNT). One donor region is the omentum. Vascularized omental lymph node transfer (VOLT) has been shown to decrease limb volume, circumference, and subjective symptoms of lymphedema. The immunologic properties of the omentum make it a particularly useful lymph node donor site for patients with lymphedema-related cellulitis. The omentum may be harvested laparoscopically, with robotic assistance, or through a small laparotomy incision. In this review, we describe the relevant anatomy and history of VOLT as well as operative techniques. The risks, benefits, and relevant outcome studies will be reviewed. Recent applications of robotic surgery to VOLT will be addressed.

Keywords: Lymphedema, VOLT, VLNT, laparoscopy, laparotomy, gastroepiploic vessels, cellulitis

INTRODUCTION

Lymphedema is a progressive condition, caused by the failure of the lymphatic drainage system, resulting in the excessive retention of lymphatic fluid in the interstitial compartment. The estimated prevalence of lymphedema varies widely based on etiology, gender, and age of onset. The etiology of lymphedema can be divided into primary or secondary lymphedema. Primary lymphedema is rare, and 30% of patients have a genetic mutation-most commonly a mutation of the vascular endothelial growth factor signaling pathway[1]. The prevalence is 1 in 100,000 individuals and most often presents during childhood, affecting the lower extremities, but sparing the arms and genitalia. 1 Secondary lymphedema accounts for 99% of reported cases, and worldwide the most common cause is filariasis[1].

Most cases of lymphedema amenable to surgical management are caused by an insult to the lymphatic system which may be infectious, traumatic, or as a result of malignancy or its treatment[2]. The most common etiology is breast cancer- related lymphedema (BCRL) secondary to lymphatic dissection during extirpative surgery. Axillary lymph node dissection impairs lymphatic drainage and is the biggest risk factor for developing BCRL. Radiation therapy increases the risk of developing BCRL since radiation induces fibrosis of lymph nodes and damage to lymphatics in the dermis[3]. A systematic review of 72 studies found that the pooled incidence of upper extremity lymphedema among breast cancer survivors is 17%[4]. A meta-analysis of non-breast malignancies found an overall lymphedema incidence of 16%, with an incidence of 20% in the lower extremity and an incidence of 5% in the upper extremity[5]. Regardless of cancer type, lymphadenectomy is the strongest predictor of lymphedema[5].

Congestion of lymphatic fluid causes chronic inflammation, leading to fibrosis and further damage to the lymphatic vessels. Persistent lymphatic stasis decreases oxygen tension, causing inflammation and reactive tissue fibrosis, cellular proliferation, and fat deposition. Clinically, patients experience progressive swelling, pain, numbness, and tingling[1,2,6-8]. Eventually, patients develop hypertrophy, acanthosis, and hyperkeratosis that results in skin breakdown[1,2,7]. In rare cases, lymphedema progresses to elephantiasis nostras verrucose in which the skin over the affected area has warty, hyperkeratotic, “mossy” or “cobblestoned” appearance and is prone to ulcers and fissures. A feared consequence of lymphedema is the development of cellulitis, lymphangitis, and lymphatic malignancies[3]. Lymphedema is associated with a decreased quality of life, embarrassment due to cosmesis of the affected limb, and financial burden. Patients report a decreased ability to perform activities of daily living and maintain employment[9,10].

VASCULARIZED OMENTAL LYMPH NODE TRANSFER

VLNT

The International Society of Lymphology has developed a staging system based on clinical exam and volume differences between the affected and unaffected extremity[11]. For patients with advanced lymphedema, (ISL stages II-III), VLNT is a physiologic procedure that has been shown to decrease limb volume and improve symptoms of lymphedema[12,13]. During this procedure, healthy lymph nodes, along with their vascular supply, are transferred to the affected area. The newly transplanted lymph nodes act as a sponge to absorb lymphatic fluid and direct it into the vascular system[14]. Furthermore, these lymph nodes secrete growth factors that stimulate the generation of new lymphatic vessels at the site of disease. Vascularized lymph node transfer typically utilizes groin, thoracic, submental and supraclavicular nodes. However, concerns about iatrogenic donor site lymphedema at donor sites remain. VOLT has come into favor due to negligible donor site lymphedema and the immunologic properties of the omentum-such as the abundance of lymph nodes and milky spots-which makes it particularly favorable for patients with lymphedema associated with cellulitis or recurrent infections[15-18]. Thus, the purpose of this report is to describe the utility of the VOLT for the treatment of lymphedema, its relevant anatomy, and harvest techniques.

Relevant anatomy

The greater omentum is derived from the peritoneal layers covering the anterior and posterior stomach[19]. The right omentum continues to the lower portion of the superior duodenum. The left omentum continues laterally to enclose the short gastric branches of the splenic artery. The omentum can extend inferiorly as an apron toward the pelvis to cover the small intestine before turning on itself and extending superiorly to envelop the transverse colon. The greater omentum is perfused by the left and right gastroepiploic arteries. The superior aspect of the omentum contains these vessels and the accompanying veins as they pass inferior and parallel to the greater curvature of the stomach.

Operative technique

Open omental harvest

The procedure is performed through a short midline epigastric incision, 6-8 cm in length[14]. The omentum is identified. The right portion of the omentum is separated off the transverse mesocolon without disruption to its blood supply to prevent bowel ischemia. Dissection is continued to the greater curvature of the stomach, where the branches to the greater curvature are ligated, while preserving a safe distance from the gastroepiploic pedicle. Dissection proceeds parallel to the greater curvature of the stomach toward the right and left extent of the gastroepiploic vessels. When the flap has been mobilized, the gastroepiploic vessels are clipped and divided[15]. Most often, the right gastroepiploic is used as the primary pedicle. It is usually possible to palpate lymph nodes near the proximal pedicle which may be included but caution is required to avoid the pancreas[14]. Kenworthy *et al*. advocate for the use of ICG angiography to assess perfusion of the flap as there are frequently regions of relative ischemia within the omentum[14]. Once the flap is harvested, the gastroepiploic vessels are anastomosed to the already-isolated and prepared recipient vessels. To avoid venous hypertension after microanastomosis of the primary artery and vein, a distal venous anastomosis second recipient vein should be considered[15].

A unique advantage of the VOLT is that the consistent caliber of the gastroepiploic vessels, running longitunally through the flap, enableing division of the omentum into multiple flaps. Thus far, omentum is the only donor site that is capable of flap transfer to multiple recipient sites, or a dual-level transfer[14]. In the upper extremity, arterial recipient vessels include the radial recurrent artery or end to side on the distal radial artery, and venous recipient vessels include deep vena comitans or the cephalic vein[14].

Laparoscopic omental harvest

The laparoscopic omental harvest begins with a 10-mm infraumbilical port and insufflation. 5-mm ports are placed lateral to the right rectus abdominis, above and below the level of the umbilicus. Any adhesions noted on visualization of the omentum should be taken down at this stage. The stomach is retracted anteriorly and the short gastric vessels supplying the greater curvature of the stomach are individually clipped and divided, maintaining the line of dissection parallel to the greater curvature of the stomach, to preserve the length of the gastroepiploic vessels. As before, the right or left gastroepiploic vessels can be preserved for eventual anastomosis. The omentum is then separated from both the stomach and the transverse colon, as described before. After extending one of the port incisions to 4-cm, the omentum can be removed from the abdominal cavity and used as a free flap[19-24] [Figure 1].

HISTORY OF THE OMENTUM FLAP

Although the free vascularized omental flap has come into favor for treatment of lymphedema, it was first described as a pedicled flap[25]. In 1966, Goldsmith, De Los Santos, and Beattie first described the use of omental tissue for the treatment of lower extremity lymphedema[26]. One end of the gastroepiploic pedicle

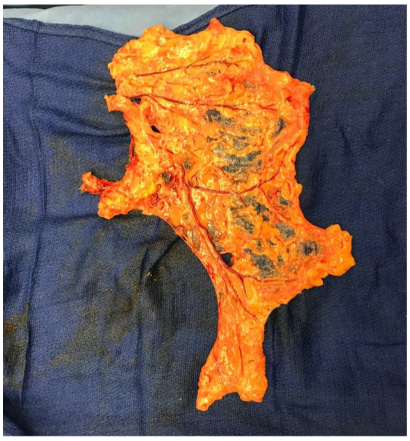

Figure 1. VOLNT Intraoperative photograph. VOLNT: vascularized omental lymph node transfer.

was kept intact and the omentum was unfurled and delivered extra-peritoneally into the proximal lower extremity[26]. The pedicled omental flap was not widely adopted due to severe complications such as iatrogenic hernia[25], and it was not until the widespread use of microsurgery that the utility of this flap was revisited. Chosen due to its rich vascular network and minimal donor site morbidity, the omentum was the first successful clinical free flap when it was used to cover a full thickness scalp defect by McLean and Buncke in 1972[27]. In 2006, Nakajima *et al*. reported the first transposition of free omental tissue to the axilla to treat a patient with BCRL[28]. The patient did experience improved function of the upper extremity leading to better quality of life, but she did suffer a hernia[28].

Due to the intra-abdominal complications associated with a laparotomy, other investigators began to concurrently experiment with laparoscopic harvest of the omentum. Saltz first described the laparoscopic-assisted harvest of the omental flap in a canine model in 1993, where initial identification of the omentum was performed laparoscopically, and then an 8 cm laparotomy was made and the omentum exernalized for pedicle dissection[29]. Improving upon this technique, Kamei *et al*. developed a technique whereby the entire procedure was conducted laparoscopically[22]. The omentum, supplied by the right gastroepiploic vessels, was removed through an extension of the infraumbilical port incision. This technique yielded an inconspicuous surgical scar and decreased postoperative pain[22].

BENEFITS OF TH VASCULARIZED OMENTUM FLAP

In recent years there has been increased interest in the use of the greater omentum as a lymphatic tissue donor site for the treatment of lymphedema. A systematic review by Forte *et al*. found that patients who underwent VOLT for the treatment of lymphedema had decreased circumference and volume of the affected extremity as well as decreased rates of cellulitis[30]. The advantages of using the omentum for lymph node transfer stem from the abundance of lymph nodes found in the omental tissue and its immunogenic and angiogenic properties[15,16,31]. Furthermore, omental lymph nodes produce vascular endothelial growth factor (VEGF) C which promotes lymphangiogenesis[16,31].

This flap is particularly advantageous for patients with lymphedema associated with cellulitis due to its immunogenic properties[15,16,31]. The omentum contains lymphoreticular bodies known as “milky spots” also referred to as omentum-associated lymphoid tissue (OALT), in addition to true lymph nodes[16]. Lymphatics of the omentum begin at the milky spots, where they initiate absorption from the peritoneal space, and drain into the lymphatic collecting system along the right gastroepiploic vessel and subsequently to the efferent lymphatic vessels[15,16]. In their series of 42 patients, Nguyen *et al*. found that the incidence of cellulitis decreased from 74% preoperatively to 5% after omental transfer[16]. As a result, they have modified their clinical algorithm such that patients with a history of recurrent infections receive the vascularized omentum flap[17].

Another benefit is that the omental lymphatic flap can be both a VLNT and lymphovenous anastomosis as it brings both gastric lymph nodes and a lymphatic efferent vessel to the affected site[16]. The efferent lymphatic vessel runs alongside the gastroepiploic vessels, and can be directly anastomosed to a recipient venule for a better anatomic and physiologic reconstruction[16].

Di Taranto *et al*., have begun to use laparoscopic free omental tissue containing gastroepiploic lymph nodes to treat patients with lower extremity ulcers secondary to severe lymphedema[31]. The free omental lymphatic flap brings highly vascularized tissue to cover the defect with the added benefit of bringing in plenty of lymph nodes to improve the lymphatic networks of the affected limb. In their 10 patients, they report no further episodes of infection with a significant decrease in the frequency of cellulitis, decreased circumference, improved quality of life, and complete healing of the wound following surgery[31]. Furthermore, all patients had improved lymphatic drainage on lymphoscintigraphy and new lymphatic vessels could be detected at the site of the flap, demonstrating the lymphangiogenic properties of the omentum flap[31].

Of importance, lymph nodes in the omentum are not crucial to drainage of the donor site, thus avoiding the risk of inducing iatrogenic lymphedema at the donor site[14-16,26]. While, the submental and supraclavicular lymph node flaps are also less likely to cause donor site lymphedema, unsightly scars and potential damage to the marginal mandibular nerve are of concern[26]. Thus, the omentum flap is useful for patients who have previously underwent an unsuccessful lymph node transfer, or who have limited donor sites due to prior surgery or radiation[14,26,31]. Following omental flap transfer, studies have reported an upper extremity circumference reduction from 9%-22.2% and a reduction in lower extremity circumference from 50%-75% with a 2%-29% differential improvement in volumetric measurements[31].

As mentioned, due to its large surface area and longitudinal pedicle, the omentum provides enough lymphatic tissue to be split into two flaps to allow dual level lymph node transfer, to both proximal and distal extremity sites[14,32] [Figure 2A and B]. This can be particularly advantageous if there are two sites or an entire extremity affected, or if scar release and dead space management are necessary at the lymphadenectomy site but there is a separate area with the most edema. Often, the most affected portion of the limb will be the distal aspect, even if the lymphadenectomy was proximal[14,17].

There are several disadvantages of VOLT that must be addressed. The first group of disadvantages stem from invasion of the abdominal cavity. Intra-abdominal complications include adhesions, bowel obstruction, incisional hernia, postoperative abdominal pain, and pancreatitis-a rare complication associated with VOLT[14,16,26,29,31]. Harvesting the flap off the left gastroepiploics may cause injury to the spleen due to vessels that are difficult to identify, but this complication may be avoided by harvesting the right-side omentum[33,34]. The second group of complications arise due to the anatomy of the gastroepiploic vessels. These vessels are thinner than those associated with other vascularized lymph node transfer harvest sites making them more prone to kinking[31]. Furthermore, Kenworthy *et al*. have noted significant venous hypertension after conventional anastomosis of the primary artery and vein when using the VOLT flap[14]. Thus, they routinely perform a second anastomosis of the distal gastroepiploic vein to a second recipient vein[14]. Finally, it should be noted that VOLT may be contraindicated in patients with a history of multiple

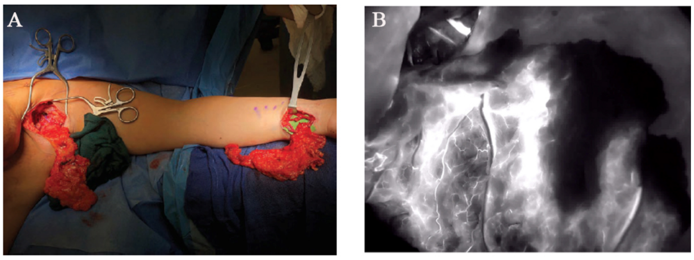

Figure 2. (A) Vascularized omentum lymphatic transplant intraoperative photograph; (B) ICG fluorescence. ICG: intraoperative indocyanine green.

abdominal operations or intra-abdominal infections.

Laparoscopic versus open approach: the debate continues

Thirty years from the first report of a laparoscopic omental harvest, the debate surrounding whether to use an open or laparoscopic approach continues. Kamei *et al*. were first to report the advantages of the laparoscopic approach: a smaller scar burden, less pain, and early recovery[22]. However, due to the difficulty of identifying the left gastroepiploic artery and risk of injury to the spleen, they recommend an open laparotomy when the full volume of the omentum is required[22].

In 2015, Nguyen and Suami described the laparoscopic free omental lymphatic flap harvest with anastomosis to the forearm. Both patients in their series reported significant improvement in swelling, fatigue, heaviness, tightness, stiffness, sleep loss, aching. Neither patient experienced further episodes of cellulitis postoperatively[15]. Using a laparoscopic approach, they were able to reduce the risk of donor site complications without sacrificing the benefits of free omental lymphatic flap transfer. Volume differentials improved and lymphoscintigraphy demonstrated improved tracer uptake without subjecting patients to postoperative GI symptoms or hernia formation. Thus, they concluded that a minimally invasive approach to free omental transfer circumvents complications that may arise due to the celiotomy or use of a pedicled flap. Subsequently, they conducted the largest prospective cohort study of patients undergoing laparoscopic free omental lymphatic flap transfer. They collected long-term outcomes on 42 patients with a mean follow-up of 14 months. 83% of patients reported subjective improvements in swelling, fatigue, heaviness, tightness, stiffness, sleep loss, aching, and sleep quality at final follow-up[16]. There was a mean volumetric improvement of 22% in the affected extremity in their patient cohort, but four patients had postoperative volume increases. They noted a 42.9% circumferential decrease in the upper extremity above the elbow and 36.4% circumferential decrease below the elbow[16]. Their complication rate was 16% which included one episode of pancreatitis, one patient requiring nasogastric tube replacement due to pedicle dissection close to the body of the stomach, and one flap loss[16].

Chu *et al*. reviewed several series of cases of laparoscopic harvest of the omental flap and reported no major complications related to the donor site, with only transient abdominal pain that quickly resolved[24]. However, due to the risk of complications with minimally invasive techniques, several groups argue that successful laparoscopic free omental lymphatic flap elevation is dependent on the surgeon having both minimally invasive and microsurgical expertise[15,16]. Alternatively, a two-team approach that involves both a general surgeon to harvest the omentum and plastic surgeon to prepare the recipient vessels may increase patient safety[14,24]. In the case of injury to the pancreas or massive bleeding during laparoscopic harvest, a general surgeon will be able to quickly convert the procedure to an open method.

In contrast, Kenworthy *et al*. advocate for an open approach through a limited incision as it allows for use of microsurgical instruments and finer control[14]. In their series of 38 patients, they had an overall complication rate of 15.8%. Donor site complications included one patient developing transient pancreatitis and two patients developing ileus. Among 54 flaps, they only report one flap loss.[14] Importantly, preoperatively patient-reported cellulitis was present in 44.7% of patients and this number decreased to 13.2% postoperatively[14].

Most recently, several groups have adapted the surgical robot for harvest of the free omental flap as poor visualization and inability for fine dissection have been a concern during laparoscopic harvest. Multiple types of robotic-assisted intra-abdominal procedures have shown decreased hospital stay, operative blood loss, and postoperative complications. Ciudad *et al*. first reported robotic-assisted harvest of the right gastroepiploic lymph node flap for the treatment of lymphedema in 2016[35]. Using a two-surgeon approach, a general surgeon performed the flap harvest with guidance from a plastic surgeon. A single 12-mm supraumbilical port was placed for optical trocar and camera placement, followed by 8-mm ports 8 cm lateral and 5 cm below the supraumbilical port on the right and lower left abdomen. 5-mm assistance port was also inserted into the epigastrium. Dissection begins by identifying the omentum and its attachment to the greater curvature of stomach and transverse colon. As in laparoscopic harvest, the omentum is separated from the transverse colon. The vertical gastric branches are then ligated while making sure to maintain an optimal flap width of 5 cm, and to maintain dissection parallel to the greater curvature of stomach. This dissection moves toward the right, toward the pedicle at the right gastroepiploic artery and vein. After the craniocaudal dissection is complete, the left gastroepiploic vessels are ligated. In the final step of the operation, the right gastroepiploic pedicle artery and vein are separated, ligated, and divided[35]. Noted advantages of robotic-assisted as compared to the laparoscopic harvest include: superior visualization of the anatomy in space, which improves precision of the dissection, lowering the risk of vascular pedicle injury.[36] Robot-assisted harvest eliminates tremor and provides for motion scaling[35]. For patients, the robot-assisted harvested offers better cosmetic outcomes compared to an open technique[17,35]. Improved instrument articulation in the robotic system is another advantage[17]. The superior visualization and instrumentation are thought to better preserve the quality of the omental tissue for transfer[17,35].

Frey *et al*. describe a series of five robotic-assisted omental flap harvests using the Intuitive robot[34]. Four patients underwent standard robotic flap harvest with 5 ports and one patient underwent single-port harvest. All patients underwent dual-level transfers, and the flap was split based on nodal distribution and / or watershed regions identified with near-infrared fluorescent angiography[34]. The authors noted improved visualization and depth perception compared to laparoscopy[34]. Robotic equipment offers fluorescent optics which can be used to visualize the vascular and lymph node patterns as well[34]. Felmerer *et al*. recently compared the complication profile of multi-port robot-assisted omental VLNT to supraclavicular vascularized lymph node transfer[36]. In their series, three patients experienced the sensation of abdominal tension but no other donor site morbidities. In the supraclavicular VLNT group, 12 patients experienced donor site complications and one patient required reoperation[36]. Thus, they conclude that robot-assisted omental VLNT is superior due to low donor site morbidity[36].

As healthcare systems aim to decrease costs, the cost effectiveness of laparotomy, laparoscopy, and robotic use should be considered. In the case of robot-assisted omentum harvest, there is an increased cost of robotic interventions that must be considered along with benefits[35]. Recently, Simianu *et al*. compared the cost-effectiveness of open, laparoscopy, and robotic colectomy. They found that open colectomy cost more and achieved lower QOL than robotic and laparoscopic approaches[37]. From both the societal perspective and healthcare sector perspective the robotic colectomy cost more than laparoscopic and yields minimal

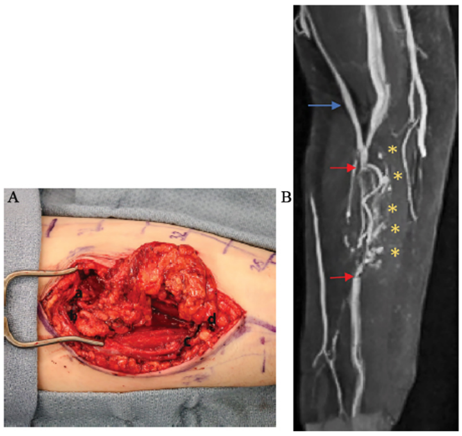

Figure 3. (A) Intraoperative image illustrating the insetting of a flow-through omental flap[39]; (B) Postoperative MRA imaging of an operative extremity after flow-through omental flap inset. The blue arrow reflects the location of the cephalic vein. The red arrows correspond to the arterial anastomoses. *denotes lymph nodes[39].

differences in QOL. Thus, the laparoscopic approach was considered more frequently cost-effective across a wide range of willingness to pay thresholds[37]. However, robotics can surpass laparoscopy in cost-effectiveness if per-case instrument costs decrease, robotic operating room time decreases, increased QOL, and decreased hernia rates[37]. They conclude, that with increased use of robotic technology in colon surgery, the burden to prove its benefits over laparoscopy remain[37]. Similarly, El Hachem *et al*. compared clinical outcomes and costs associated with robotic single-site surgery compared with those of conventional laparoscopy (CL) in gynecology[38]. They found that compared to CL, robotic surgery had comparable clinical outcomes, but higher operative times, higher disposable equipment cost per case and higher total hospital charges[38].

CONCLUSION

Vascularized omental lymph node transplant is a suitable physiologic treatment option for individuals with ISL stage II or III lymphedema and may be especially beneficial for patients with lymphedema-related cellulitis. Vascularized free omental tissue may be harvested laparoscopically or via a laparotomy, but care should be taken to minimize intra-abdominal complications and incisional hernia. Recent advances in robotic surgery make this an attractive harvest method due to superior visualization of the omentum and more precise dissection which minimizes disruption to lymphatic tissue as compared to laparoscopy. However, further investigation on novel minimally invasive approaches for VOLT and novel uses for the flap are necessary [Figure 3A and B].

DECLARATIONS

Authors' contributions

Design, conception, drafting of the manuscript, manuscript preparation: Skladman R
Manuscript preparation: Moritz WR
Manuscript preparation: Tenenbaum EJ
Design, conception, editing of the manuscript, manuscript preparation: Christensen JM
Design, conception, administrative supportconception, administrative support: Sacks JM

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All authors declared that there are no conflicts of interest.

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Not applicable.

Consent for publication
Not applicable.

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