Post-traumatic lymphedema: review of the literature and surgical treatment options

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Abstract

Post-traumatic lymphedema (PTL) is a complex, debilitating, and potentially common disease which has received limited attention to date. The available literature is reviewed to identify injury patterns and critical lymphatic areas associated with the disease. A deeper understanding of these critical anatomic regions allows the reconstructive surgeon to potentially identify PTL patients earlier in order to apply surgical and nonsurgical interventions in the acute phase, improving lymphatic physiology and, ultimately, patient outcomes. Current diagnostic and treatment approaches are discussed in detail, with a focus on lymphatic microsurgical techniques developed and applied to PTL within the last decade.

Keywords: Post-traumatic lymphedema, traumatic lymphedema, secondary lymphedema, lymphatic reconstruction, lymphatic restoration

INTRODUCTION

The advent of improved lymphatic imaging and supermicrosurgical techniques has rapidly expanded treatment options for lymphedema in the last decade. Improvements in treatment have been accompanied by renewed interest in the physiology, etiology, and prevention of lymphedema. Amid a resurgence of lymphedema research, post-traumatic lymphedema (PTL) remains a poorly understood and
underdiagnosed disease.

Lymphedema results from a malformation, insult, injury, or obstruction of the lymphatic system and can be classified as primary or secondary. The most common cause of secondary lymphedema in developed countries is lymphadenectomy and radiation for cancer treatment, at approximately 1 in 1000\(^2\). Primary lymphedema caused by a malformation or repair defect of the lymphatic system is rare, with an estimated prevalence of 1 in 100,000\[^3\]. The population frequency of PTL has not been studied but uses persistent limb swelling after trauma as a proxy, and the incidence may be as high as 20\%\[^4,5\].

While iatrogenic lymphedema has been well-characterized and studied, the available descriptions of PTL consist mainly of case reports and case series, as well as more recent articles discussing specific approaches to diagnosing and treating PTL with a focus on restoration of lymphatic function. This review synthesizes the available data in an attempt to help further advance the understanding and management of patients with PTL, and ultimately improve their quality of life and outcomes.

**LYMPHATIC RESPONSE TO TRAUMATIC INJURY**

Injuries to bone and soft tissues are usually followed by edema, which develops immediately after soft tissue injury or fracture\[^6\]. Unlike edema from chronic venous obstruction, post-traumatic edema presents with pain at the site of injury, erythema, and increased skin temperature. These clinical findings are indicative of a protracted inflammatory reaction characterized by immune cell infiltration and activation of an inflammatory cascade\[^6,7\].

A prospective study of 21 patients with post-traumatic lower extremity edema demonstrated dilated lymphatics with the decreased lymphatic flow on lymphoscintigraphy\[^6\]. Minor trauma, however, seldom leads to chronic lymphedema. Post-traumatic edema and acute PTL are part of the normal physiologic wound healing process, occurring up to three months following trauma and is a consequence of the inflammatory response\[^6\]. The lymphatic system undergoes repair during this period through lymphangiogenesis. Transient direct pressure on initial and terminal lymphatics in an experimental setting temporarily damages lymphatics, but lymphatic function is eventually restored\[^9\]. Occasionally, as wound healing progresses, scar tissue may develop and restrict the continuous flow of the lymphatic vessels, leading to lymphatic dysfunction\[^10\]. In these instances, lymphedema can persist past the physiologic three months and become pathologic.

In chronic cases, upstream lymphatics begin progressing through three histopathological stages as a consequence of the downstream injury\[^11\]. In stage 1, lymphatic channels dilate and interstitial protein deposition incites inflammation. In stage 2, inflammation stimulates contraction and luminal narrowing due to smooth muscle cell and collagen deposition. Stage 3 is marked by sclerosis and vessel obliteration.

The clinical progression of lymphedema is described by the International Society of Lymphology staging system\[^12\]. In stage 0, despite a normal clinical exam, there is asymptomatic lymphatic damage which can be detected on lymphoscintigraphy or impedance spectroscopy. Stage 1 is clinically visible, but reversible since excess volume comprises lymphatic fluid accumulation secondary to downstream obstruction. This manifests as pitting edema responsive to elevation and compression. In stage II, irreversible changes are noted as interstitial protein deposition, and a macrophage-induced inflammatory state causes tissue fibrosis and fat deposition. Clinically, swelling is not fully reversible and becomes non-pitting. Patients can experience limb heaviness and discomfort. Stage III denotes a markedly enlarged limb with hardened, fibrotic tissue, which can become unusually tender to touch. Patients with persistent PTL in particular often
suffer from chronic sequelae such as hyperpigmentation, hyperkeratosis, delayed wound and bone healing, and frequent bouts of cellulitis[4-7].

METHODS
MEDLINE searches were performed (1948 to October 2021) using the terms “PTL”, “traumatic” (and) “lymphedema”, “lymphedema” (and) “trauma”, (and) “lymphedema” (and) “injury”. These searches revealed 41, 106, 854 and 839 results, respectively. After excluding articles in non-English languages, duplicates, and articles unavailable electronically, 963 studies were available. The abstracts were fully reviewed using the inclusion criterion of lymphedema as a consequence of injury or trauma. All 30 resulting studies were included. Relevant bibliographies of the included studies were subsequently reviewed and included as secondary sources as well.

In this review, we first discuss available case reports and case series, with commonalities and unique scenarios highlighted to reflect the breadth of the literature. We then review studies focused on the diagnosis and treatment of PTL, particularly those geared toward lymphatic restoration.

INJURY PATTERNS
Musculoskeletal injuries
Musculoskeletal injuries are the most commonly reported traumatic insult leading to PTL. Acute edema to some degree is expected with musculoskeletal trauma. However, persistent swelling after mechanical insult diagnosed as lymphedema has been reported following a wide variety of insults and in a variety of anatomic regions[3,13-15].

Unsurprisingly, extensive injuries such as limb amputation with replantation have been reported to cause secondary lymphedema[16]. In the available literature, however, there are no reports of attempts at immediate or delayed lymphatic reconstruction in the setting of replantation. In striking contrast, minor musculoskeletal injuries, with contusion as the only clinical sign, can also lead to the development of secondary lymphedema[17-19].

The majority of reports of PTL involve fractures as inciting events. Secondary lymphedema has been reported in fractures treated both operatively and non-operatively. Two case reports discuss the development of lymphedema after distal radius fracture, specifically after Colles fracture. In one, the fracture was treated non-operatively, and ipsilateral hand lymphedema developed immediately after cast removal with persistence despite conservative measures[14]. Interestingly, given the lack of operative intervention, the author deemed the lymphedema self-induced and secondary to “psychogenic causes”. In the second report, the patient’s fracture was treated operatively with open reduction and internal fixation. Persistent ipsilateral swelling was noted immediately after cast removal, and at two months postoperatively, the patient was diagnosed with lymphedema due to progressive limb asymmetry and non-pitting edema[3].

Fractures can cause secondary lymphedema in other anatomic regions as well. Many studies describe fractures of the lower extremities as inciting injuries, including tibial, fibular, and pilon fractures[13,20,21]. There are reports of facial and eyelid lymphedema associated with facial fractures[15,22]. Some of these patients were examined via lymphoscintigraphy along with patients with facial lymphedema, non-traumatic etiologies to delineate facial lymphatic flow patterns[22]. This study identified four main lymphatic pathways of the face, which could be evaluated with a single technetium injection at the level of the forehead, between the eyebrows.
Burns

Burns are another significant etiology of PTL\[^8,23\]. Lymphatic channels exist in a complex network abundant in the reticular dermis and underlying fat\[^8\]. This superficial location makes lymphatics particularly susceptible to any trauma to the skin, including deep burn injuries. A 2004 study by Hettrick et al.\[^8\] included a review of the literature, along with both retrospective and prospective studies regarding lymphedema following burns. This study found a 1% prevalence and noted that fascial excision and circumferential extremity involvement as risk factors for the development of lymphedema after burn injury. It further noted that although burn scar was difficult to distinguish from the fibrosclerotic and color changes associated with lymphedema, other typical clinical diagnostic signs of lymphedema were found to be useful in the burn population.

Abdominal lymphedema

Abdominal lymphedema after trauma is a rare but reported complication after both penetrating and blunt trauma, and manifests as chylous ascites or chyloretroperitoneum\[^24\]. These injuries are typically not isolated since the forces required to disrupt the cisterna chyli or the thoracic duct in the chest, abdomen, or neck will typically also injure other structures such as the liver, duodenum, kidney, and pancreas. Lymphangiography is the imaging modality of choice\[^24\]. One patient with penetrating zone II neck injury developed transient interruption of lymphatic flow and chyloretroperitoneum after ligation of the thoracic duct at the level of drainage into the internal jugular vein. This self-resolved five days later once collateral lymphatic flow was compensated\[^25\]. Of note, aside from initial stabilization maneuvers such as ligation of the injured thoracic duct, all reported cases of abdominal lymphedema were treated conservatively with paracentesis, total parenteral nutrition, medications (octreotide, somatostatin), and a low-fat diet with medium-chain triglyceride supplementation.

Critical lymphatic areas

Critical lymphatic areas have been identified in the upper and lower extremities. In these regions, the increased density of lymphatic vessels creates susceptibility to lymphatic disturbances in the event of trauma\[^4\]. These critical lymphatic areas include the anteromedial leg, medial aspect of the arm and thigh, and medial aspect of the elbow and knee. Several case reports support this in their description of lymphedema following high energy, but very focal trauma.

Three case reports discuss focal injuries to the anteromedial leg, which resulted in lymphocele, lymphorrhea, or intractable ulcers\[^17-19\]. Two case reports involve PTL secondary to isolated penile trauma. In one case, secondary to paintball injury, severe penoscrotal lymphedema was diagnosed by magnetic resonance and required several debulking and resurfacing procedures of the penis\[^26\]. More recently, a case of chronic post-traumatic penile lymphedema was successfully treated with lymphovenous anastomosis\[^27\]. Another report documents isolated blunt trauma to a patient’s medial leg region due to striking the steering wheel in an accident. This resulted in ipsilateral lymphedema diagnosed via indocyanine green (ICG) lymphography\[^28\]. Finally, one case report regarding a susceptible upper extremity region involved a patient with repeated self-injury to the medial arm. Although incised wounds rarely cause peripheral lymphedema, disruption of multiple collecting lymphatic vessels with repeated injury in a lymphatically dense region was enough to cause lymphedema of the limb, diagnosed by lymphoscintigraphy\[^29\].

**DIAGNOSTIC AND TREATMENT APPROACH**

**Diagnosis of PTL**

Diagnosis of PTL is possible with any modality normally used to diagnose lymphedema, including MR lymphangiography, lymphoscintigraphy, and ICG. Indocyanine green, however, has several significant advantages in PTL. Unno originally described the method in 2007 as an alternative to lymphoscintigraphy,
which is less costly, more expeditious, and can provide real-time information[30]. In 2015 Ito et al.[28] described for the first time the use of ICG lymphography specifically in the diagnosis of PTL.

While lymphoscintigraphy can image deep lymphatics and nodes beyond the depth of ICG (1 to 2 cm), it has lower sensitivity for superficial lymphatics, which may be focally injured in PTL. The lymphatic vessels are visualized in real time to characterize patency, pattern, and function. A linear pattern is typically observed in limbs with preserved lymphatic function as it represents intact, linear lymphatic collectors. Lymphatic dysfunction is indicated by dermal backflow patterns, including reticular, splash, stardust, and diffuse patterns[31,32]. Although lymphoscintigraphy has traditionally been considered the gold standard for the general diagnosis of lymphedema, ICG lymphography has been the primary diagnostic modality in all PTL studies since its advent, and may represent a new standard.

**Early conservative treatment and prevention**

Early conservative treatment and prevention of lymphedema must be emphasized before discussing surgical treatments. Acute lymphatic dysfunction is a normal physiologic reaction after trauma, to a certain extent; continued lymphatic dysfunction leads to progressive pathology. It is therefore imperative to support lymphatic return and lymphangiogenesis in this early phase to encourage a return to homeostasis as quickly and completely as possible.

Initiation of conservative treatment measures early is highly encouraged in patients with orthopedic traumas utilizing methods such as compression therapy and complete decongestive therapy (CDT) (also known as complex physical therapy, or decongestive lymphatic therapy)[7]. CDT consists of a 4-6 week intensive phase aimed at volume reduction, including wrapping with low-stretch bandages, lymphatic massage (manual lymphatic drainage), and limb exercises. If symptoms persist, a maintenance phase is initiated with a fitted compression garment that is worn according to the patient’s needs[33]. These methods have shown positive results in significantly reducing lymphedema and limb volumes in orthopedic trauma patients[7,33].

Although the long-term effects of prophylactic CDT on lymphedema have not been studied, a 2017 study used CDT in acute pilon fracture management to improve orthopedic outcomes[20]. Pilon fractures are typically high-energy injuries which may require a temporary external fixator until the injured soft tissue envelope is ready for definitive fixation. Initiating CDT at the time of presentation decreased the median time to internal fixation by 9 days compared to a group which did not receive CDT, and there was no difference in wound complications. Similarly, another 2017 study in patients with burn injuries found that initiating myofascial-manual lymphatic massages early in their treatment algorithm led to increased wound microcirculation, with decreased rates of hypertrophic scarring and intralesional steroid injections over time[34].

Surgical treatments of PTL fall into two categories: debulking and physiologic.

**Debulking procedures**

Debulking procedures include excision and liposuction. They are non-specific to the mechanism of injury and deal with the late consequences of lymphedema. Excisional procedures involve extrafascial dermolipectomy, typically with local flap closure. Liposuction is less invasive, utilizing cannulas to effectively remove excess fat without skin resection. Debulking procedures carry a high morbidity and require lifelong compression[35]. In the modern era of lymphedema surgery, these procedures are rare, typically reserved for refractory or end-stage disease states with a focus on salvage to improve
symptomatology, rather than restoring lymphatic physiology\[26\]. With regard to PTL treatment specifically, debulking is only mentioned by one study in conjunction with vascularized lymph node transfer (VLNT) as a first stage procedure, to optimize the local environment one month in advance of VLNT\[36\].

**Lymphovenous anastomosis**

Lymphovenous anastomosis (LVA) has been described for a case of intractable ulcer with lymphorrhea in the setting of post-traumatic and obesity-induced lymphedema\[19\]. Lymphovenous anastomosis bypasses obstructed lymphatic channels by connecting patent upstream lymphatics to nearby, low-pressure subdermal veins and shunting fluid directly into the venous system\[37\]. This supermicrosurgical technique demands dedicated instruments for handling 11-0 or 12-0 suture and a surgeon’s tactile sense to detect the intima of the vessels and the lymphatic flow\[38\]. Multiple LVAs are usually required\[35\]. In this case, the patient was treated with 3 LVAs distal to the ulcer site, and experienced resolution of the lymphorrhea and ulceration 2 weeks later without recurrence\[19\]. A single LVA was also described to treat isolated penile lymphedema without recurrence of swelling despite complete removal of compressive garments at 6 months\[27\].

**VLNT**

VLNT, also called autologous lymph node transplantation, is another physiologic method of lymphatic reconstruction. A recipient site is prepared within the lymphedematous area by excision of scar tissue. Recipient vessels are dissected and prepared for anastomosis. A small lymph node-containing free flap is harvested from a donor site while ensuring that the harvest does not cause donor site lymphedema. The lymph node packet is anastomosed to the recipient blood vessels without any direct lymphatic anastomosis\[35\]. The transferred nodes initially act as a “wick” via their afferent lymphatic channels, which partially drain into the efferent vein of each node\[39\]. They also secrete lymphangiogenic growth factors, including VEGF-C, which promote the ingrowth of new lymphatic channels over time\[38\]. The excision of scar tissue likely contributes to successful outcomes by clearing the site of obstruction to lymphatic regeneration\[35\]. VLNT donor sites include the supraclavicular, submental, groin, lateral thoracic, and omental lymph nodes\[40, 41\]. The selection of donor site is dictated primarily by minimizing morbidity\[42\]. Donor site complications specific to VLNT include lymphocele, lymphatic fistula, and lymphedema of donor limb\[43\]. Donor site iatrogenic lymphedema can be reduced using reverse lymphatic mapping\[44\], which uses technetium-99 sulfur colloid and ICG to distinguish between lymph nodes draining the trunk and those draining the extremities.

There are three descriptions of VLNT for the treatment of PTL. One used groin node flaps to treat two patients with PTL of the upper extremity (one burn and one blunt force trauma)\[36\]. Both patients were treated in a staged manner one month following extrafascial dermolipectomy and local advancement flaps, and experienced improvement. The other two studies are case reports using chimeric lateral thoracic nodes with thoracodorsal system flaps in patients with lower extremity PTL. In one case, the flap also included a fasciocutaneous thoracodorsal artery perforator flap\[41\]. The second case incorporated a latissimus and split serratus flap due to the presence of more than one defect\[45\].

**Lymphatic vessel free flap**

Lymphatic vessel free flap (LVFF) is the most recent form of physiologic lymphatic reconstruction applied to PTL\[46\]. The technique of LVFF was first described by Yamamoto et al.\[47\] in 2018. It involves free tissue transfer in which no lymph nodes are harvested. However, lymphatic channels are purposefully included and transplanted with the flap in order to bypass lymphatic blockages and restore lymphatic flow at the recipient site. By designing the flap in regions with high lymphatic channel density, such as the groin, lymphatic channels are reliably included. Supermicrosurgical anastomosis is not required, but the axial ends
of respective donor and recipient lymphatic vessels must be in close proximity to achieve lymphangiogenesis\cite{47}. Lymphatic vessel free flaps may provide the advantage of decreased risk of donor site lymphedema compared to VLNT and carry them skin for soft tissue resurfacing.

The initial report of LVFF in PTL was a case of upper extremity lymphedema secondary to degloving injury, treated with superficial circumflex iliac artery perforator lymphatic vessel (SCIP-LV) flap\cite{46}. There was clinical improvement within two weeks and a 55% reduction of excess limb volume at four months, with ICG uptake into the flap. A follow-up study included 11 patients who received SCIP-LV flaps to prevent \((n = 6)\) or treat \((n = 5)\) PTL\cite{46}. In the PTL treatment group, the mean reduction of excess limb volume was 63\%, and quality of life improved by 51\%. No patients in the prevention group developed PTL.

**SUGGESTED DIAGNOSTIC AND TREATMENT PRACTICES**

Reconstructive surgeons should recognize critical lymphatic areas and keep these regions in mind as susceptible to lymphatic injury when evaluating trauma patients. Even small insults without massive trauma in a critical area should prompt close surveillance, with quick initiation of appropriate workup and treatment as needed.

Workup for PTL should include ICG lymphography. The diagnostic gold standard, lymphoscintigraphy, can be normal in the setting of localized or superficial lymphatic dysfunction, which can be seen in PTL. ICG lymphography provides real-time visualization of the superficial lymphatics, allowing precise diagnosis and optimizing surgical planning.

PTL treatment should be individualized per patient exam and ICG findings. All patients with PTL should be initiated early with conservative measures including compression and CDT. When reconstructing extremity defects, one should take into account critical lymphatic areas and choose options which are least disruptive to lymphatic function. Additionally, immediate reconstructive approaches can be tailored to include a lymphatic component, such as immediate LVA or a flap which contains nodes or lymphatic vessels. For late presentations with non-pitting or mixed presentations, liposuction can be added before, after, or concomitantly with these physiologic procedures\cite{48}.

**CONCLUSION**

Post-traumatic lymphedema is a complex, debilitating, and potentially common disease which has received limited attention to date. Awareness of injury to critical anatomic areas may help the reconstructive surgeon prevent lymphedema in the acute phase via surgical or nonsurgical techniques. Wider awareness of PTL and understanding of appropriate workup may facilitate earlier identification of these patients. Following diagnosis, treatment should be tailored to each patient depending on their needs, with a focus on restoring lymphatic physiology. Prospective and comparative studies are necessary to determine the incidence of PTL, as well as the optimal strategies for prevention and treatment.

**DECLARATIONS**

**Authors’ contributions**

Made substantial contributions to conception and design of the study, drafting and revisions, as well as performed data acquisition, analysis and interpretation: Minasian RA, Brazio PS

Made substantial contributions to data acquisition, analysis, and interpretation, as well as drafting of manuscript: Samaha Y
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