PATHWAYS EXPANDED ARTICLE AND REFERENCES: Spring 2015

Treatment Options

Surgical Treatment Options for Lymphedema

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This article aims to present an overview of current trends in the treatment for lymphedema and increase the reader's awareness of the realistic outcomes that can be expected from each procedure. Breast cancer has undoubtedly delivered lymphedema awareness to the forefront of cancer related complications and will remain an important focus. It is however time to broaden our perspective and include a discussion of lymphedema in other populations.

Lymphedema represents a progressive and debilitating condition associated with dysfunction of the lymphatic system. In the developed world Lymphedema commonly occurs after lymph node dissection and/or radiotherapy to nodal basins for the diagnosis or treatment of breast cancer, malignant melanoma, or gynecologic cancers. Less commonly, lymphedema occurs as a result of congenital causes (1-4). Regardless of the initiating event, its onset is often a distressing experience and reported as having a negative impact on the quality of life (5-7).

The epidemiology of cancer-related lymphedema is changing, increased attention is focused on the modification of anticancer therapies in an effort to minimize lymphatic compromise and reduced lymphedema incidence in early-stage cancers. As a consequence, patients with high-risk cancer (eg, large tumors and several positive lymph nodes) constitute an increasing proportion of lymphedema patients because of their need to receive more comprehensive treatments. Sentinel lymph node biopsy is an example of a surgical procedure developed to preserve lymphatic function as much as possible while still providing adequate diagnosis and staging. Concurrent with the development of less invasive treatments, the field of lymphedema management has evolved rapidly over the past decade. Despite this lymphedema is reported to occur in up to 49 % of breast, 20 % of gynecologic, 16 % of melanoma and 10 % of genitourinary cancers. Even among patients who undergo isolated axillary sentinel lymph node biopsy, up to 7 % have measurable arm differences, and up to 10 % have subjective symptoms of lymphedema (8-15).

Acquired lymphedema results from the abnormal accumulation of protein rich fluid in the affected limb due to interruption of the normal lymph return to the circulation. In the early stage, the swelling is due to excess pooling of lymphatic fluid and is characterized clinically by a pitting edema, which is soft to palpate. This is the fluid phase of the disease process and the edema is potentially still reversible at this stage, but if neglected or inadequately treated, the chronic build up of inflammatory cells is believed to subsequently produce scarring and gradual fatty tissue deposition. Further tissue fibrosis, blistering and skin breakdown acts as a vicious cycle which ultimately leads to worsening of the condition and paves the way for the onset of a more chronic and less reversible stage characterized by a non-pitting solid lymphedema (16-17). The time frame for this transition from fluid to solid can vary considerably between patients.

Much of the challenge in managing lymphedema is the inconsistency in the diagnostic standards. If it is impossible to reach a consensus on diagnosis, then it is also impossible to agree on standardized treatment protocols. Therefore Timely diagnosis remains a barrier to optimal lymphedema treatment for many patients. This can be a complicated undertaking aggravated by lymphedema's frequently insidious onset. While some patients develop dramatic swelling soon after the initial insult, more commonly this swelling is transient without any permanent consequences. Many can be free of any lymphedema for many years before they experience the first symptoms.

Risk of developing lymphedema

Patients who undergo lymph node removal or irradiation are at some risk of developing lymphedema. This risk increases directly as treatments become more aggressive and anatomically disruptive (18-19). Each patients 'at risk'' territory depends on the area drained by the lymph nodes involved in the treatment. For example breast cancer patients are solely at risk in the axillary region on their affected side. This includes the arm, breast, and upper truncal quadrant. On the other hand patients treated for gynecological cancers potentially have a much more extensive territory at risk because their pelvic lymph nodes as well as deeper seated nodes around the aorta which are responsible for draining both legs, lower truncal quadrants and genitalia may have been resected and irradiated. Therefore treatment of gynecological cancers potentially places the entire lower half of the body at risk for developing lymphedema. Obesity is another important factor to consider as it has been proven to increases the risk of lymphedema progression and rendering it more resistant to conventional therapies (20-21). Recurrent soft tissue infections, which tend to occur in the affected limb can harm the lymphatic system, which further compromises the lymph drainage and ultimately lead to worsening of the lymphedema. On the other hand, medical conditions, including diabetes, hypertension, heart failure, and autoimmune conditions, have not been implicated in lymphedema despite considerable scrutiny. Studies have shown that activities requiring repetitive use of the arm also do not appear to increase lymphedema risk in breast cancer patients (22-23). In fact advice against exercise or other repetitive activities have potentially adverse consequences for patients' quality of life as well as general well being. Similar studies have yet to be conducted with patients who have developed or are at risk of lower-extremity lymphedema.

Conservative measures to treat lymphedema

Nonsurgical treatment options for lymphedema include an initial course of complex decongestive therapy (CDT) administered by a lymphedema physical therapist. This is achieved by the application of external compression including manual lymph drainage, compression bandaging or garments, therapeutic exercises, intermittent or sequential pneumatic devices and skin care. The objective of these approaches is to 'milk' the interstitial fluid and lymph through the lymphatic system to decongest the affected limb. However, the maintenance therapy and the ongoing use of compression garments required afterward must be continued indefinitely in order to remain effective (22-23). In some cases and despite optimum conservative measures there is worsening of the lymphedema after a period of stability maintained by such measures. Therefore the development of additional methods to treat lymphedema is essential.

Surgical treatments of lymphedema

Surgical procedures to treat lymphedema have existed for over a century. More recently and due to advancements in medical technologies, sophisticated microsurgical procedures have been introduced and in themselves are neither new nor experimental and have been applied broadly for more than 20 years. They should however be reserved for patients who have failed intensive combined medical therapy or in cases where the initial positive effects of conservative measures are no longer capable of maintenance and there is progressive worsening of the lymphedema. Better results are generally obtained if operative intervention is applied in earlier stages of the disease. Imaging technologies have made it possible to visualize lymphatic vessels in real time and perform accurate mapping of their course. Thereby making it possible to routinely perform ever more complex procedures.

Debulking Procedures

The Charles procedure was the first reported debulking procedure described in 1912. This operation involves extensive removal of skin and soft tissue down to the muscles, followed by skin grafting over the excised area. Since then variations of this procedure have been reported with better results in terms of function and incidence of infection (24). However, these remain very disfiguring, they are performed less frequently today and are only offered for extreme cases of lymphedema elephantiasis, where massive skin thickening, swelling and repeated life threatening infections may justify such radical surgery.

Suction Assisted Lipectomy

This intervention can address the solid phase of the lymphedema disease process by removing large volumes of excess fatty tissue deposits that can be aspirated from the lymphedema-affected limb after it is clearly demonstrated with radiologic imaging that the excess lymph fluid has been maximally reduced with conventional decongestive therapies and the cause for persistent increase in the volume of the affected limb is the excess fibrous-fatty tissue as compared to the normal limb. When performed correctly this technique has been shown to reduce large amounts of volume excess effectively in a limited number of patients with mild to moderate lymphedema (25). More significantly, the incidence of dangerous cellulitis can be reduced by up to 75 % as a result (26-27). Despite these improvements it is important to emphasize that this operation does not address the underlying pathophysiological case of lymphedema nor does it restore any lymphatic continuity. Therefore a successful outcome cannot be achieved without commitment to a life-long integrated regimen of complex decongestive therapy and custom fitted compression garments to prevent renewed buildup of excess lymphatic fluid (28-30). This technique differs significantly from conventional cosmetic liposuction and should not be attempted by surgeons not trained in the procedure. Disruption of lymphatic's and increased swelling due to over aggressive or incorrect suctioning are risks if performed by an inexperienced surgeon. Also the compression garments and lymphedema therapist decongestive protocol differ significantly than in cosmetic liposuction and are crucial to the procedure's success.

Lymphatic-venous Anastomosis

This procedure involves connecting lymphatic vessels to small adjacent veins allowing excess lymph fluid to bypass areas of obstructed lymph flow and drain directly into the venous system. Initially described in the 1970s, early attempts were met with limited success due to the formation of clots at the anastomosis site between the veins and lymph vessels (31). However with refinements in the method and introduction of better quality microscopes and ever-smaller sutures in addition to "Super microsurgical techniques" lymphatic-venous

anastomosis can be performed with significant improvement in limb girth, ranging between 42% to 83% in selected patients (32), as well as significant reduction in the frequency of infections. Even with the aforementioned advancements, this surgery remains technically challenging requiring a high level of expertise because lymphatic vessels are tiny and thin walled, ranging from 0.1 to 0.6 mm in diameter, making then tricky to handle. Also the identification of functional lymphatic vessels within the scarred lymphedema-affected extremity and a competent venous system are crucial points to the success of this operation. Better reduction of lymphedema is more likely to result when more numbers of lymphatic-venous anastomosis are performed. Most literature seems to recommend the continued use of complex decongestive therapy and compression garments following this procedure, but to a lesser extent and depending on response to therapy some patients may be able to discontinue conservative treatments. However there is a lack of clear consensus in this regard. Lymph-venous anastomosis are mostly used for secondary lymphedema, but can be also applied to congenital lymphedema where functional lymphatic vessels are present. Despite being successful in the short term, many studies have shown that these vessels can eventually become occluded over time, reversing the initial positive effects (33-37).

Lymphatic-to-Lymphatic Bypass

First described in 1986 by Baumeister, the method here relies on harvesting healthy donor lymph vessels, usually taken from the inner thigh, and transferring them to bridge the scarred or irradiated region in the lymphedema-affected limb. They are then sutured to patent lymph channels on either side of the scarred area, thus allowing lymph to flow more easily through areas previously obstructed due to lymphatic destruction and scarring. Improvement in the lymphedema and effective drainage of lymphatic fluid is clearly demonstrated early after surgery. Even though most patients experience some alleviation of their symptoms, this appears to be inconsistent, making it difficult to predict the outcome for each patient. A successful result is more likely in the arms than legs and directly proportional to the number of vessels transferred. Similar technical expertise is required for the handling of lymphatic vessels. Despite careful selection and collection of lymphatic vessels to minimize risk of complications at the donor site there is a small but theoretical risk of inducing lymphedema in a previously healthy leg (38).

Vascularized Lymph Node transfer

First described over 20 years ago as a promising alternative for the management of lymphedema. It involves microsurgical transplantation of soft tissue containing lymph nodes to restore lymphatic drainage (39). These can be harvested from donor sites such as the groin, chest wall, or neck along with their nourishing blood vessels and transferred to the lymphedema-affected arm or leg, where these vessels are connected to local vessels to reestablish blood circulation that is crucial to the survival of the transferred nodes. There are several possible recipient sites for lymph nodes in the affected limb. For example, in the upper extremity, the axilla can be the most arduous recipient site for nodes because of scarring and irradiation changes to the tissues. The elbow and wrist on the other hand tend to be healthier recipient sites. The same is true for the lower limb where the groin tends to be the most scarred region. Therefore the best symptomatic improvement is seen when the nodes are transplanted to the more dependent sites where fluid tends to pool, such as the wrist or ankle (40-41). However these regions tend to yield the least pleasing cosmetic results because the transplanted lymph node flap is more obvious even though it appears to be more effective at clearing lymph fluid. The cosmesis here can be improved over time with debulking procedures, despite this many surgeons avoid

transplanting nodes to these sites and opt for more inconspicuous locations.

These transferred lymph nodes appear to act like suction pumps facilitating lymph clearance and restoring local immune response. Thereby reducing the likelihood of infections. Clinically, the lymphedematous limb becomes softer, less heavy, with improved range of movement and skin wrinkling may start to appear in some cases within one week after surgery. The reported mean reduction rate in lymphedema following this procedure is between 40- 50% (40-41). This improvement appears to be sustainable over time because the transferred lymph nodes continue to work at shunting lymph from an expanding area of the surrounding tissues to the venous system. This intervention has been successfully used in both congenital as well as primary lymphedema. If it produces adequate outcome there is the hope that patients will no longer require conservative measures or at least to a much lesser degree. But there have not yet been any published studies with clear evidence in this regard.

The main disadvantage of the lymph node transplant procedure is the potential risk for donor site lymphedema. However more accurate mapping of the lymph node drainage region before surgery helps to further reduce the chance of developing complications at the donor site (42).

If simultaneous breast reconstruction is performed, the lymph nodes can be transferred together in a single operation. There is not one gold standard procedure that can be used for all patients but rather the combined use of, lymph node transfer, lymph-venous anastomosis, and suction assisted lipectomy together with appropriate conservative decongestive therapy into an integrated treatment system tailored to the individual needs of the patient in order to deliver a more successful treatment strategy. For example, some advocate the use of lymph-venous anastomosis as an initial step if functional lymphatic vessels are identified on imaging. This is because it is a relatively easier procedure to perform and carries

fewer risks. If this helps to alleviate the symptoms to an acceptable degree then no further intervention is required. However if this is not the case additional lymph node transfer can be performed at a later time to provide more optimal improvement of lymphedema symptoms. In cases where there is success to clear away the lymph fluid from the limb by a reconstructive method, but there remains a discrepancy between the size of the affected limb as compared to the normal, then suction assisted lipectomy can be performed to remove the solid component of lymphedema. With this combination the aim is to render the lymphedema-affected extremity as normal as possible. This selective application of the appropriate method to treat the fluid or solid phases of lymphedema greatly improves overall outcomes. Despite this fact, it remains important to perform reconstructive procedures while the patients are still in the fluid phase of their condition, before the collection of excess solids occurs. A delay in treatment may allow solids to accumulate and the condition to invariably worsen with time.

While Lymphedema continues to pose a distressing consequence of cancer diagnosis and treatment. There has been over the past number of years increasing enthusiasm in the medical community to research this previously neglected field and discover reliable treatment options. This has led to the evolution of reproducible therapies that have the potential to changed the long term outlook for many suffering with this condition. Such treatments are only offered in very few centers around the world at the current time, there is every hope that it will become more widespread in the near future.

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