DAY OF SCIENCE AND INNOVATION ABSTRACTS

Imaging the Lymphatic Response to Manual Lymphatic Drainage and Pneumatic Compression Devices

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Objective: Manual lymphatic drainage (MLD), as a component of complete decongestive therapy, has formed the basis of the initial treatment for lymphedema (LED), and pneumatic compression (PC) has been used in the maintenance phase (at-home treatment). The physiologic mechanism, however, of methods to promote lymph drainage for both MLD and PC has not been rigorously established. Recent developments in near-infrared fluorescence lymphatic imaging (NIRFLI) have enabled the visualization of the lymphatic response to these therapies nearly in real time and provide opportunities to assess the physiologic impact of these manual interventions. Herein we summarize the results of seven studies, published and unpublished, assessing the acute and longitudinal impact of MLD or PC therapy in patients with phlebolymphedema or standard arm, leg, or head and neck LED.

Methods: After informed consent and under Food and Drug Administration-approved investigational new drugs for off-label administration of indocyanine green (ICG) as an imaging agent for NIRFLI, we visualized lymphatic anatomy and contractile pumping activity in study participants. Patients received intradermal injections of ICG distal to the area of vascular interest, typically in the hands and feet. Imaging was performed by illuminating the skin with near-infrared light and collecting the fluorescent light emanating from the ICG-laden lymph. Whereas imaging times varied between each study, imaging was conducted immediately before and after treatment and, when possible, during treatment. In one study, NIRFLI was also performed before and after 2 weeks of PC therapy in patients with head and neck LED. Images were assessed for changes in lymphatic uptake and contractile pumping.

Results: Overall 69 patients, 51 affected and 18 control, undergoing MLD or PC therapy were imaged. The first study of 10 LED and 12 control patients showed a 23% and 28% increase in lymph velocity and a 9% and 23% reduction in propulsion period in symptomatic and control limbs, respectively, in response to MLD. Other NIRFLI studies demonstrated enhanced lymphatic uptake after PC therapy in control patients and patients diagnosed with phlebolymphedema or standard LED. One study, using a clear PC device, demonstrated the ability to image the statistically significant improvement in lymphatic contractile propulsion during and after PC therapy. A recent unpublished study of 10 patients with head and neck LED demonstrated enhanced lymphatic uptake in all patients and a reduction of abnormal lymphatic anatomy in 75% of patients after 2 weeks of daily at-home PC therapy.

Conclusions: NIRFLI enables the assessment of manual lymphatic interventions, demonstrating enhanced lymphatic uptake and improved lymphatic contractile pumping in response to MLD and PC therapy in patients with LED.

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The Proportion and Causes of Lymphedema in a Large Administrative Insurance Database

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Objective: Lymphedema (LED) has been called the forgotten vascular disease, given such limited knowledge about the prevalence of LED and in particular its associated comorbidities and causes. Such information on the proportion of patients with LED and its causes may assist in diagnostic decisions and health care planning.

Methods: To determine the proportion of patients with LED and the possible causes of LED, deidentified Health Insurance Portability and Accountability Act-compliant commercial administrative claims from the Blue Health Intelligence (BHI) research database (165 million Blue Cross Blue Shield members) were queried. To identify the proportion affected with LED and the comorbidities (potential causes) associated with LED, we analyzed a BHI study sample of 26,902 patients with LED who had been enrolled with continuous medical benefits for 12 months before and after the index date for the complete years 2012 through 2016. It was the purpose of this study to analyze the BHI data set to determine the proportion of LED that occurs in a "real-world" setting and to identify the specific causes of LED.

Results: Overall, 84,579,269 patients were available for initial analysis, from which 81,366 patients (0.10%) were identified with LED. From the total population (42,229,536) within the BHI data set for women, 74,807 (0.18%) women were identified with LED; from the total population of men in the BHI data set (42,349, 733), a lower number of men, 28,358 (0.07%), had LED. Based on an assessment of 26,902 eligible patients (determined by continuous enrollment criteria), breast cancer, which occurred in nearly 9000 patients (32.1%), was the most common comorbidity associated with LED. The category of venous disease as a whole accounted for 10.4% of patients with LED. Within that category, venous ulcer compromised the majority of the venous disease group (9.6%). The combined entity of pelvic cancers in women (uterine, ovarian, and cervical cancer) accounted for 3.3% of all causes of LED. Finally, melanoma was observed in 2.1% of patients with LED. Prostate cancer was a less frequent cause of LED, which was observed in 188 patients (0.7%). The sequelae of treating sex-specific cancer (breast and pelvic) in women accounted for >35% of patients with LED.

Conclusions: To our knowledge, this is the largest study to date providing the real-world proportion of patients with LED and detailing the causes of LED. Our findings confirm the major role of cancer, particularly breast cancer, as an important cause of LED. Furthermore, this study highlights the role of advanced venous disease as a cause of LED.

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Contemporary Lymphedema Management Among Insured U.S. Patients: Correlation of Disease Etiology With Treatment Choices

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Objective: Lymphedema (LED) therapy aims to reduce edema and to improve function, comfort, and skin hygiene. These nonsurgical treatments can be categorized into conservative (CONS)—complex physical therapy with manual lymphatic drainage (MLD), massage, garments, and bandaging; and intermittent pneumatic compression with simple nonprogrammable pneumatic compression devices (SPCDs) or advanced programmable pneumatic compression devices (APCDs). We sought to define how frequently patients with a diagnosis of LED are provided LED-specific therapy and to determine what diagnoses are most commonly associated with advanced targeted LED therapies.

Methods: To determine the frequency of the various treatments of LED and their relationship to the cause of the LED, we queried claims for the years 2012 to 2016 from a deidentified Health Insurance Portability and Accountability Act-compliant commercial administrative insurance database with 165,000,000 members. We identified patients with an LED diagnosis code who had at least one inpatient or two outpatient claims filed with Blue Cross Blue Shield and who were enrolled in Blue Cross Blue Shield with continuous medical benefits for at least 12 months before and after the index date. Identified patients were then analyzed as to associated comorbidities and the treatments coded in these claims. Treatments were grouped as no treatment, CONS, SPCD, and APCD.

Results: We identified 81,366 patients with a diagnosis of LED, of whom 26,902 had sufficient continuous medical benefits to meet inclusion criteria; 5291 (19.7%) patients with a diagnosis of LED received no LED-specific treatment. CONS therapies alone were used in 17,387 (64.6%) of LED patients. Within this CONS group, 73% used MLD as a component of care. SPCD was the only pneumatic compression code entered for 680 (2.5%) patients, whereas the more advanced APCD codes were used in 3544 (13.2%) LED patients. Within each of these treatment groups, the Table

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Table. Distribution of diagnoses according to therapy chosen

	CONS treatment, %		Pneumatic compression, %	
	No MLD	MLD	SPCD	APCD
Cancer	40.8	74.7	16.5	44.3
Venous disease	25.4	11.0	42.8	30.0
Other diagnosis	33.9	14.3	40.7	25.8
	100	100	100	100

APCD, Advanced pneumatic compression device; *CONS,* conservative; *MLD,* manual lymphatic drainage; *SPCD,* simple pneumatic compression device.

displays the two most common categories of comorbidities (cancer vs venous diseases) coded in LED patients receiving treatment. The Table represents findings from the study.

Conclusions: Many LED patients receive no disease-specific treatment of LED. In general, CONS treatment, which incorporates MLD, and pneumatic compression therapy, which incorporates APCDs, are considered more aggressive than approaches limited to no MLD or SPCDs. These data demonstrate that cancer patients treated for LED are more likely than venous patients to receive the more aggressive MLD and APCDs. These data raise the question as to whether there are disease-specific differences in severity of symptoms or response to therapy that justify what appears to be a less aggressive treatment approach in venous compared with cancer patients or whether treatment decisions are driven by the patient's or physician's preference, insurance constraints, or other factors.

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Limb Salvage for "Hopeless" Lymphedema: Reviving the Charles Procedure

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Objective: The Charles procedure offers radical excision of lymphedematous tissue followed by skin grafting. This procedure is rarely offered because of the potential for complications, but it may provide excellent outcomes in improving quality of life. We describe our experience with a modified technique and a multidisciplinary team approach in treating patients with advanced lymphedema.

Methods: Seven patients with severe lower extremity lymphedema were treated with radical surgical excision. Patients' demographics, operative details, and postoperative follow-up course were recorded. The operation entailed radical excision of the skin and lymphedematous tissues in a modified Charles procedure. The dissection was taken to the level of the fascia from the dorsal forefoot or ankle and continued to the knee or thigh, with wound vacuum-assisted closure for initial dressings. Split-thickness skin grafting was performed 5 to 7 days postoperatively. All patients were managed with a predefined postoperative care protocol.

Results: Seven patients were referred to the clinic for evaluation of massive lower extremity lymphedema. There were four men and three women, with age range of 36 to 64 years. All patients had history of >2 years of lifestyle-limiting swelling and recurrent bouts of cellulitis requiring hospitalization and intravenous antibiotic treatment. Six patients had chronic wounds of the affected legs due to skin breakdown, and three had significant disability in ambulation. Comorbid conditions included obesity (in five patients), hypertension (in four patients), chronic obstructive pulmonary disease or asthma (in three patients), depression (in three patients), and diabetes (in one patient). In the three patients with bilateral disease, intervention targeted the more severely affected limb. One patient in our series had disease confined only to the thigh. Postoperative complications included wound infection, requiring débridement or antibiotics, in four patients; readmission for débridement in one patient; and reintubation postoperatively in one patient. Length of stay was an average of 27 days (range, 14-55 days).Patients were observed for an average of 15 months (range, 3 month-3 years). All patients reported an improvement in quality of life postoperatively and had complete wound healing by final follow-up, without recurrence.

Conclusions: Although it is an underused procedure, the Charles procedure presents a viable means of limb salvage for severe lymphedema. We present a multidisciplinary approach with excellent patient outcomes in a series of six patients.

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Multidisciplinary Approach to Management of Severe Lymphedema with One-Stage Radical Excision and Split-Thickness Skin Grafting

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Objective: Patients with severe lymphedema often experience recurrent cellulitis, ulcerative lesions, and deleterious effects on quality of life. Cumulative damage to extremities may result in limb deformity, creating functional limitations with emotional and psychosocial distress. Physiologic or reductive surgical treatments are reserved for failure of conservative management. The reductive approach aims to remove lymphedematous tissue acquired from prolonged lymphatic stasis. One such reductive approach is the Charles procedure, direct excision followed by skin graft application to the defect. We present two cases of severe lymphedema treated with one-stage direct excision by the modified Charles procedure.

Fig 1. Preoperative image.