Pneumatic Compression for Lymphedema: Continued Benefits

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DISCLOSURES

- Tactile Medical: Consultant and Principal Investigator for sponsored VA multicenter trial.

Lymphedema

Interstitial accumulation of protein-enriched fluid

- Affects over 90 million worldwide
- Chronic disfiguring disease secondary to excessive fluid and protein accumulation in the interstitium as a result of lymphatic system stasis or obstruction

Lymphedema

- Primary lymphedema:
  - congenital malformation
  - lymphedema praecox
  - lymphedema tarda
- Secondary lymphedema:
  - Surgery
  - Lymphatic trauma
  - Obesity
  - Radiation therapy
  - Chronic Venous Insufficiency

Signs/symptoms

- Edema
  - Expansion of the interstitial space
  - Swelling extends to the toes: Stemmer’s sign
  - Swelling is initially soft with “pitting edema”
  - Induration and Fibrosis
- Pain
  - Rare
  - Aching/heaviness of the limb

Cellulitis
VENOUS INSUFFICIENCY AND LYMPHEDEMA
C0, C1, C2 - Lymphatic involvement in early clinical stages of chronic venous disease

CEAP Stage
C0 – No clinical signs
C1 – Telangiectasies or reticular veins
C2 – Varicose veins

Lymphatic stage & involvement
Lymphedema Stage 0: Latent, no clinical signs.
Lymphatic system is already impacted as early as C0. The lymphatic system is operating at increased capacity to manage the venous filtrate – becoming engorged with some dermal backflow seen.

Healthy Lymphatic Flow


VENOUS INSUFFICIENCY AND LYMPHEDEMA
Traditional treatment approach
MAINTENANCE NOT CURE

• Mainstays of treatment for lymphedema:
  • Skin hygiene
  • Diet and Exercise
  • Pressure and trauma avoidance
  • Manual lymphatic drainage
  • Compression wraps and elevation
  • Pneumatic Compression
  • (Surgery?)

Pneumatic compression
• Concept dates back to the early 1800s with the first single chamber device introduced in 1934
• Flexitouch® pneumatic compression is unique:
  • 32 curved chambers
  • Self inflate and deflate sequentially, mimicking a functional drainage system
  • Treatment sessions are approximately 45 mins

Pneumatic Compression Device Treatment of Lower Extremity Lymphedema Elicits Improved Limb Volume and Patient-reported Outcomes

- 196 total limbs
- The cohort was characterized by more female patients (68%)
- Individuals with secondary lymphedema accounted for nearly 80% of the study population
- The follow-up clinical assessment: 60+/- 27 days (range 17-242; median 55.5)

Table 1. Baseline demographic and clinical characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>N (%)</th>
<th>Mean ± SD</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Female</td>
<td>131 (66%)</td>
<td>71.2 ± 21.4</td>
</tr>
<tr>
<td>Age</td>
<td>Median</td>
<td>65 (IQR)</td>
<td>40-100</td>
</tr>
<tr>
<td>Type of lymphedema</td>
<td>Primary</td>
<td>25 (13%)</td>
<td>65.8 ± 18.2</td>
</tr>
<tr>
<td></td>
<td>Secondary</td>
<td>171 (91%)</td>
<td>71.4 ± 21.0</td>
</tr>
<tr>
<td>Prevalence</td>
<td>Median</td>
<td>24 (IQR)</td>
<td>9-72</td>
</tr>
<tr>
<td>Disease duration</td>
<td>Median</td>
<td>62 (IQR)</td>
<td>37-112</td>
</tr>
<tr>
<td>Post-trauma</td>
<td>Median</td>
<td>24 (IQR)</td>
<td>9-72</td>
</tr>
<tr>
<td>Pneumatic PDX</td>
<td>Median</td>
<td>24 (IQR)</td>
<td>9-72</td>
</tr>
</tbody>
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S.C. Make, L.H. Whiten, T.E. Taylor

Division of Vascular and Endovascular Surgery
Rutgers New Jersey Medical School
Conclusions from this study:

- 90% of APCD-treated patients experienced a significant reduction in limb volume
- 35% had a limb volume reduction >10%
- Mean limb volume reduction was 1,150 mL or 8% (p < .0001)
- Greater baseline limb volume and BMI were strong predictors of LV reduction (p < .0001)

METHODS

- Primary endpoints include both generic Quality of Life (QoL) assessment (SF-36) and disease-specific (LYMQOL) at 12, 24, and 52 weeks follow-up.
- Secondary endpoints compare changes in limb circumference and skin assessment (lymphedema stage) at each follow-up interval visit.
- Complications: cellulitis episodes, number of clinic visits and hospital admissions associated with cellulitis were recorded.
General Demographics/Type of Lymphedema for All Subjects with 52 week follow-up (n=74)

<table>
<thead>
<tr>
<th>Age (Years)</th>
<th>N</th>
<th>74</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>67.0 ± 11.4</td>
<td></td>
</tr>
<tr>
<td>Min, Max</td>
<td>39.3, 98.6</td>
<td></td>
</tr>
<tr>
<td>Median [IQK]</td>
<td>69.9 [51.4, 79.5]</td>
<td></td>
</tr>
</tbody>
</table>

Gender
- Female: 4 (5.5%)
- Male: 70 (94.5%)

Body Mass Index (kg/m²)
- N: 74
- Mean ± SD: 22.8 ± 5.9
- Min, Max: 16.1, 30.2
- Median [IQK]: 20.0 [18.4, 21.7]

Body Mass Index Group (kg/m²)
- N: 74
- <18: 24 (32.4%)
- 18 - <25: 24 (32.4%)
- ≥25: 26 (35.2%)

Limb Girth
- Baseline
- 12 Week
- 24 Week
- 52 Week

Quality of Life: SF-36

- Physical Component
- Mental Component

The SF-36 questionnaire showed a trend towards QoL improvement in all areas at 52 weeks (Physical component 39.9 vs 41.7 (p=0.1); Mental component 49.3 vs 51.3 (p=0.2)).

Quality of Life: LYMQOL-LEG

LYMQOL-LEG scores showed significant continued improvement at each time point.

Cellulitis occurring in 52 week period pre and post-APCD (Flexitouch); n=74

Pre-Flexi
- 18

Post-Flexi
- 7

P=0.0019

P=NS
Comparison of Cellulitis Incidence and Event Counts

<table>
<thead>
<tr>
<th>Cellulitis</th>
<th>One Year Prior to Enrollment</th>
<th>One Year Post Enrollment</th>
<th>p Value (Paired)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% (n)</td>
<td>16/24 (74)</td>
<td>7/24 (74)</td>
<td>0.018</td>
</tr>
<tr>
<td>Cellulitis Event Count Per Patient</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>2.6 ± 2.6</td>
<td>2.6 ± 2.6</td>
<td></td>
</tr>
</tbody>
</table>

Comparison of Medical Encounters in patients with a Medical History of Cellulitis

<table>
<thead>
<tr>
<th>Any Clinic Visits</th>
<th>One Year Prior to Study Entry</th>
<th>One Year Post Study Entry</th>
<th>p Value (Paired)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% (n)</td>
<td>12/20 (60)</td>
<td>8/20 (40)</td>
<td>0.0026</td>
</tr>
<tr>
<td>Any Hospital Admissions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% (n)</td>
<td>1/20 (5)</td>
<td>0/20 (0)</td>
<td></td>
</tr>
</tbody>
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Study Design:

- Analyzed health insurer administrative database of 34 million individuals
- Identified patients with lymphedema who received the Flexitouch System (total n = 718)
- Examined health outcomes and costs for cancer-related (n = 374) and non-cancer-related (n = 344) lymphedema patients

Follow-Up Ends

Baseline Begins

First receipt of a PCD (Index Date)

12 months continuous insurance eligibility

Jan 2007

Nov 2013

First receipt of a PCD (Index Date)

Follow-Up Begins

Follow-Up Ends

Table 1: Adjusted lymphedema-related encounter rates in a medical history and after the PCD receipt

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Baseline Follow-Up</th>
<th>Follow-Up</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphedema diagnosis</td>
<td>Cancer-Related</td>
<td>Non-Cancer-Related</td>
<td>Cancer-Related</td>
</tr>
<tr>
<td>Lymphedema diagnosis</td>
<td>321 (20)</td>
<td>226 (20)</td>
<td>0.018</td>
</tr>
<tr>
<td>Lymphedema diagnosis</td>
<td>285 (25)</td>
<td>209 (25)</td>
<td>0.056</td>
</tr>
<tr>
<td>Lymphedema diagnosis</td>
<td>123 (16)</td>
<td>88 (16)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Lymphedema diagnosis</td>
<td>69 (9)</td>
<td>44 (9)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Lymphedema diagnosis</td>
<td>11 (1.5)</td>
<td>6 (1.5)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Lymphedema diagnosis</td>
<td>10 (1.5)</td>
<td>5 (1.5)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Lymphedema diagnosis</td>
<td>8 (1.1)</td>
<td>4 (1.1)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Lymphedema diagnosis</td>
<td>5 (0.7)</td>
<td>3 (0.7)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Lymphedema diagnosis</td>
<td>3 (0.4)</td>
<td>2 (0.4)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Lymphedema diagnosis</td>
<td>2 (0.3)</td>
<td>1 (0.3)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Lymphedema diagnosis</td>
<td>1 (0.2)</td>
<td>1 (0.2)</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>


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Conclusions:

- Pneumatic compression works

- 90% of patients show significant reduction in limb volume
  - Greater baseline limb volume and BMI may serve as predictors of LV reduction

- Continued linear improvement in QoL at least up to one year beyond the initial clinical benefit of decreased limb girth

- A significant decrease in episodes of cellulitis as well as fewer associated clinic and hospital visits
  - may explain the noted improvement in QoL for the patient
  - can represent significant cost savings to the health care system