Early detection and prevention of lymphoedema

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Background: Derby Lymphoedema Service

- Three lymphoedema services based in Acute Hospitals at Derby, Nottingham and Mansfield.
- Covering an area of 1.5 million people.
- Referrals accepted for all patients with chronic oedema, lipodystrophy including children and “out of area”.
- Approximately 750 new referrals per year.
Derby Lymphoedema Service

- 3 Palliative Medicine Consultants
- 1 Nurse Professor
- 3 Band 7 Team Leaders
- 9 Band 6 therapists
- 2 Research Nurses
- 2 HCAs
Incidence of cancer related lymphoedema

- Incidence of lymphoedema is unclear due to disparities in the definition of what constitutes lymphoedema.

- This reflects the different measurement techniques and lack of a gold standard.
Identifying lymphoedema

- Lack of agreed diagnostic criteria:
  - 10% difference between limbs,
  - 200ml difference between limbs,
  - 2cm difference circumferential measurements
  - 10% change from baseline
  - ≥5% change from baseline
  - >3% change from baseline, sub-clinical,
  - Patient reported symptoms (swelling, heaviness)
Incidence of lymphoedema: Cancer Related

- Breast cancer related lymphoedema (BCRL) is the most studied.
  - Axillary node clearance (ANC) at 25-28%.
  - 5-8% for sentinel node biopsy (SNB).
- Incidence of gynaecological cancer related lymphoedema dependent on type of cancer and surgery. Ranges between 9 – 70%.
- Urological cancer and lymphoedema is less well studied and the incidence varies according to type and location of tumour. Estimated up to 50% in advanced penile cancer
Varied incidence following groin dissection for malignant melanoma, soft tissue sarcoma and small cell carcinoma.

- Estimated 12 – 51% malignant melanoma
- Up to 69% for SCC vulva

Little literature available for head and neck cancer, studies differ in treatment given, length of follow up and diagnostic criteria.

- Overall between 12 – 54%
- Recent study identified 75% sample had some degree of lymphoedema affecting internal and/or external structures.
Lymphoedema / Chronic Oedema

- Population prevalence of 1.33 per 1,000 for all ages rising to 5.4 per 1,000 >65 years.
- Recognised as an underestimate.
- Local Acute Hospital: 25% current inpatients met the chronic oedema definition (>3/12 history of swelling).
- Primary lymphoedema is rare and estimated to affect 1.15 per 100,000 of the population under 20 years of age.
Other conditions causing chronic oedema

- Chronic venous hypertension: associated with the development of chronic oedema and leg ulcers. Prevalence identified 35% of patients being treated for leg ulcers also had chronic oedema.
- Cellulitis and recurrent skin infections.
- Immobility.
- Obesity.
- Non cancer related surgery / trauma.
## Pattern of referrals (Derby)

<table>
<thead>
<tr>
<th>Category</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer Treatment Related</td>
<td>22.8%</td>
<td>17.9%</td>
<td>19.1%</td>
</tr>
<tr>
<td>• BCRL</td>
<td>13.2%</td>
<td>11.3%</td>
<td>10.4%</td>
</tr>
<tr>
<td>Advanced Cancer</td>
<td>9.5%</td>
<td>9.8%</td>
<td>7.5%</td>
</tr>
<tr>
<td>Primary Lymphoedema</td>
<td>13.5%</td>
<td>9.5%</td>
<td>13.1%</td>
</tr>
<tr>
<td>Secondary lymphoedema – non cancer related</td>
<td>7.2%</td>
<td>10.9%</td>
<td>16.7%</td>
</tr>
<tr>
<td>Lymphovenous oedema</td>
<td>21%</td>
<td>26.7%</td>
<td>33%</td>
</tr>
<tr>
<td>• Immobility</td>
<td>18%</td>
<td>21.1%</td>
<td>24.3%</td>
</tr>
<tr>
<td>• Obesity</td>
<td>2%</td>
<td>5.6%</td>
<td>8.6%</td>
</tr>
<tr>
<td>Venous disease</td>
<td>6.6%</td>
<td>9.1%</td>
<td>4.9%</td>
</tr>
</tbody>
</table>
Derby Lymphoedema Service

- RDH: Approximately 300 new referrals / year
- 10% new referrals BCRL
- Prior to February 2010:
  - No pre-treatment assessment
  - Referral by BCN, Surgeon, Oncologist, GP
  - Diagnosis confirmed by clinical assessment, limb volume measurement
Risk factors pertaining to BCRL

- Surgery with axillary lymph node dissection,
- Radiotherapy,
- Drain, wound or infection complications,
- Cording,
- Seroma formation,
- Taxane chemotherapy,
- Raised BMI, weight change during treatment,
- Skin puncture.
- Predisposition to BCRL
Early detection and prevention

- It has been recognised that there is a relationship between the early detection and treatment of breast cancer related lymphoedema and improved outcomes.
- Baseline or pre-treatment assessment enables increased accuracy in diagnosing this condition.
Baseline assessment.

- Natural limb differences exist, with the dominant limb often exceeding the non-dominant in size.

- It has been recognised that 20% patients can have limb volume difference of >5%.

- Pre-operative or baseline assessment is recommended as best practice.
Bioimpedance
Perometry
Research Study: BEA

Multi-frequency Bioimpedance in the Early Detection of Lymphoedema after Axillary Surgery

- The purpose of this multi-centre study is to test whether there is concordance between bioimpedance and perometer arm measurements.
- In particular, whether bioimpedance identifies patients who are developing lymphoedema at an earlier stage, before arm volume measurement by perometry shows significant increases in arm volume.
- 7 centres are aiming to recruit 1100 patients in total.
- Follow up is to 5 years post ANC.
- Lymphoedema is defined as a 10% increase in the treated limb from baseline measurement.
Research Study: PLACE

- Prevention of Lymphoedema after Axillary Clearance by early External Compression.

- The primary aim of this trial is to test the efficacy of external graduated compression garments in preventing the onset of lymphoedema 18 months after axillary node clearance for node positive breast cancer in women who develop an arm volume increase of 4-8.9% within the first nine months post surgery.

- Participants are randomised into the control “standard care” or treatment group (daily wear of a compression sleeve for 1 year).

- Both groups are followed up to 5 years post ANC.
Aims of Audit

- Early identification and treatment of patients with BCRL
- Highlight risk factors pertaining to the development of lymphoedema
  - Surgery type / recurrent operations,
  - Adjuvant / neo-adjuvant treatments
  - Post operative complications
- Develop assessment/follow up algorithm.
Measurements undertaken

- Perometry, bioimpedance spectroscopy, symptoms.
- Symptoms: LBCQ swelling, heaviness and numbness in “at risk” limb since last visit.
- Measurements taken at baseline (pre-treatment) and post operatively if willing to be followed up: 1, 3, 6, 12, 18, 24, 36, 48, 60 months.
Results to date

- Between February 2010 – June 2011 470 patients have had pre-treatment arm measurements.

- 0 patients have declined pre-treatment assessment.

- 14 (2.9%) declined follow up assessment.
92.3% of the sample were right hand dominant.

55.5% had surgery on side of their dominant arm.

60% of patients have been reassessed post-operatively.

On average, 2 reassessments have been undertaken.
## Initial Surgery

<table>
<thead>
<tr>
<th>Surgery</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>MXT &amp; SNB</td>
<td>148</td>
<td>31.5</td>
</tr>
<tr>
<td>MXT &amp; ANC</td>
<td>65</td>
<td>13.8</td>
</tr>
<tr>
<td>WLE &amp; SNB</td>
<td>217</td>
<td>46.2</td>
</tr>
<tr>
<td>WLE &amp; ANC</td>
<td>12</td>
<td>2.6</td>
</tr>
<tr>
<td>WLE / MXT</td>
<td>19</td>
<td>4.0</td>
</tr>
<tr>
<td>WLE &amp; ANS</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>ANC</td>
<td>8</td>
<td>1.7</td>
</tr>
</tbody>
</table>
Second Surgery

- 110 (23.4%) patients had a second surgical procedure.
- Overall 96.8% patients had axillary surgery.
- 30.2% patients had an ANC

<table>
<thead>
<tr>
<th>Surgery</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>MXT &amp; ANC</td>
<td>9</td>
<td>8.2</td>
</tr>
<tr>
<td>WLE &amp; ANC</td>
<td>1</td>
<td>0.9</td>
</tr>
<tr>
<td>WLE / MXT</td>
<td>14</td>
<td>12.7</td>
</tr>
<tr>
<td>Re-excision</td>
<td>34</td>
<td>31.9</td>
</tr>
<tr>
<td>ANC</td>
<td>48</td>
<td>43.6</td>
</tr>
<tr>
<td>SNB</td>
<td>4</td>
<td>3.6</td>
</tr>
</tbody>
</table>
### Change over time

<table>
<thead>
<tr>
<th></th>
<th>B/Line</th>
<th>Month 1</th>
<th>Month 3</th>
<th>Month 6</th>
<th>Month 12</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n</strong></td>
<td>470</td>
<td>151</td>
<td>152</td>
<td>149</td>
<td>96</td>
</tr>
<tr>
<td><strong>Median L-Dex (IQR)</strong></td>
<td>0.10 (-3.1, 3.3)</td>
<td>1.15 (-2.4, 4.4)</td>
<td>0.85 (-3.8, 4.5)</td>
<td>1.1 (-2.48, 5.2)</td>
<td>1.9 (-2.2, 6.4)</td>
</tr>
<tr>
<td><strong>L-Dex &gt;10</strong></td>
<td>2%</td>
<td>7.4%</td>
<td>8.8%</td>
<td>8.4%</td>
<td>15.9%</td>
</tr>
<tr>
<td><strong>Delta 10 change</strong></td>
<td>N/A</td>
<td>10.8%</td>
<td>6.8%</td>
<td>4.7%</td>
<td>12.5%</td>
</tr>
<tr>
<td><strong>LVM % change Median (IQR)</strong></td>
<td>N/A</td>
<td>0.92 (-1.69, 2.7)</td>
<td>0.87 (-1.7, 2.3)</td>
<td>0.81 (-1.88, 3.6)</td>
<td>1.19 (-3.15, 5.59)</td>
</tr>
<tr>
<td><strong>&gt;4% LVM</strong></td>
<td>N/A</td>
<td>15.8%</td>
<td>15.1%</td>
<td>20.1%</td>
<td>34.5%</td>
</tr>
<tr>
<td><strong>&gt;10% LVM</strong></td>
<td>N/A</td>
<td>2.1%</td>
<td>1.3%</td>
<td>1.3%</td>
<td>5.4%</td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td>6.4%</td>
<td>30.8%</td>
<td>23.3%</td>
<td>19.4%</td>
<td>22.6%</td>
</tr>
<tr>
<td><strong>No. treated</strong></td>
<td>Nil</td>
<td>2 (1.3%) (3 PLACE)</td>
<td>5 (3.3%) (1 PLACE)</td>
<td>4 (2.7%) (2 PLACE)</td>
<td>14 (14.6%)</td>
</tr>
</tbody>
</table>
Clinical Assessment

- All patients who with signs or symptoms of arm or breast/chest wall oedema were assessed with a doctor.

- Not all patients had a significant change in limb volume or L-Dex but had symptoms or clinical signs of lymphoedema.
Treated patients:

- Between February 2010 June 2012 – 33 patients who have undergone pre and post operative assessments have been treated for lymphoedema.

This includes:

- 3 patients with breast/ chest wall oedema only.
- 1 patient with lymphoedema of the contralateral limb secondary to cellulitis from cannulisation during chemotherapy.

- 4 patients contacted the team and were assessed but no clinical or measurable signs of lymphoedema identified.
Treated patients n=32

- 90.6%, 29 patients had WLE/MXT & ANC (13 patients had WLE/MXT & SNB first).
- 9.4%, 3 patients had WLE/MXT & SNB only.
- More patients requiring a second procedure had BCRL but this demonstrated only a trend to significance ($X^2$, $p=0.66$).
- 59.4% patients had surgery on their dominant side. This was not significant when compared to those without lymphoedema ($p=0.681$).
BCRL: Adjuvant therapy

- 97% received adjuvant treatment.
  - Radiotherapy 84%
  - Chemotherapy 81%
    - 11% neo-adjuvant
    - 73% Taxane regime
  - Hormones 66%

- 81% received a combination of treatments.
Signs & symptoms at treatment (Arm n=29)
Treatment (arm oedema only)

- All patients were initially fitted with a 20-25mmHg sleeve (with mitt, glove if required).
- If a patient was diagnosed with BCRL without a limb volume change >10% they initially wore the sleeve daily for a month.
- If symptoms / assessment improved they wore PRN. 6 patients now wear a sleeve PRN. 3 tried this but the oedema increased and now wear daily.
- Some compliance / concordance issues have been recorded.
Audit Conclusions

- Pre and post treatment assessments are acceptable to patients.

- A combination of arm measurements and symptom assessment alongside clinical assessment identifies lymphoedema.

- Some patients are diagnosed with lymphoedema without a significant change in limb volume change or L-Dex.
Future / current research:

- There are groups that are looking into / have started to use this prospective model of lymphoedema monitoring in other patient groups – groin dissection.

- This model can be applied when there is a control limb or objective measurement to compare future measurements against.
The cost:patient benefit for prospective monitoring has been established for BCRL.

Genetic testing and identification of genes associated with primary lymphoedema and BCRL is being undertaken.

Development of measurement techniques to assess areas of oedema that cannot be assessed with current techniques.

Identification of the prevalence of chronic oedema in specific patient groups and the impact of this oedema.