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**An overview of the  
treatment of primary  
and secondary  
lymphatic diseases:  
the effort of the ESL to  
put some order**

**43th ESL Congress  
European Society of  
Lymphology**

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ESL

Panel of experts' considerations and  
practical recommendations on  
lymphedema and related disorders

43rd European Congress of Lymphology  
26 – 27 May 2017

# Panel of Experts

## Surgeons

Baumeister Rüdiger (Germany)  
Boccardo Francesco (Italy)  
Brorson Hakan (Sweden)  
Campisi Corradino (Italy)  
Olszewski Waldemar (Poland)  
Papendieck Cristobal (Argentina)  
Pissas Alexandre (France)  
Wald Martin (Czech Rep.)

## Internists

Eliska Oldrich (Czech Rep.)  
Földi Etelka (Germany)

## Physical Education

Leduc Albert (Belgium)

## Angiologists

Cestari Marina (Italy)  
Dimakakos Evangelos (Greece)  
Hamade Amer (France)  
Michelini Sandro (Italy)

## Physical Medicine and Rehabilitation

Forner-Cordero Isabel (Spain)

## Radiation Oncology, Nuclear Medicine and Lymphatic Imaging

Bourgeois Pierre (Belgium)

## Physiotherapists

Belgrado Jean Paul (Belgium)  
Johansson Karin (Sweden)  
Leduc Olivier (Belgium)  
Moneta Gianni (Italy)

# Group Goals

- Early diagnosis
- Threshold for definition of excess volume
- Need of surveillance
- Patient education/self care
- Complications
- Risk factors
- Role of genetics
- Prevention (primary, secondary and tertiary)
- Treatment (conservative, surgical; early and late stages)

# Recommendations

## 1) Early diagnosis

- **Subjective symptoms and physical examination:** swelling, pain, aching, numbness, stiffness, cording.
- **Objective assessments:** circumferential **tape measurements** are acceptable as a minimum standard (threshold of 2 cm, being measure every 4th cm); **limb volumes** can be calculated using the formula of a truncated cone, by water displacement or Archimede's principle; **bioelectrical spectroscopy, tissue dielectric constants and infrared perometry** can detect subclinical lymphedema (limit the risk of false negative or false positive results of circumferential tape measures); **lymphoscintigraphy; indocyanine green (ICG) lymphography; ultrasonography** for skin thickness.
- **MRI, CT, SPECT and SPECT CT lymphoscintigraphy** have been used to define and detect the structural changes such as the honeycomb distribution of fluid and to visualize dilated lymphatic structures. However, their primarily role is in the assessment of late stages for surgical interventions and chylous disorders.

# Recommendations

## 2) Threshold for definition of edema

- Lymphedema Relative Volume (LRV)
  - $\geq 5\%$  -  $< 10\%$  minimal ly.
  - $\geq 10\%$  -  $< 20\%$  mild ly.
  - $\geq 20\%$

Compared to the contralateral limb and better if compared to pre-op measurements

# Recommendations

## 3) Need of surveillance

- Lymphedema negatively impacts overall **quality of life** and represents a financial burden for patients, caregivers, and society
- An **early stage diagnosis** offers the best opportunity for **early intervention** and **early cure**
- Many guidelines do not recommend one particular technique as the gold standard screening option
- The diagnosis of lymphedema is improved with a **combination of assessments**

# Recommendations

## 4) Patient education/self care

- As concerns secondary lymphedemas, clinicians must raise awareness recognizing the **lifetime risk of lymphedema**, especially in the 2 years after surgery. They should inform patients of **early signs and symptoms** of aching, feelings of heaviness, tightness, fullness or stiffness that often precede visible swelling.
- Clinicians should **educate patients** on critical risk reducing strategies that are practical and evidence based (do's and don'ts)
- Clinicians should encourage at risk and affected lymphedema patients to exercise. Resistance and aerobic exercise is safe. **Working with a trained professional to learn to exercise safely is helpful** for affected individuals.



# Recommendations

## 5) Complications

- **Lymphedema progresses** from an early stage with soft tissue, reversible edema, no infections to a debilitating condition with tissue hardness, numbness, skin lesions, recurrent erysipelas due to gradual deposition of fat and fibrotic tissue
- **Role of inflammation** in the generation and maintenance of lymphedema
- In lymphedema, there is remarkable upregulation of the gene expression related to acute inflammation, immune response, complement activation, wound healing, fibrosis, and oxidative stress response
- Potential implications for pharmacological approaches to lymphedema. In the experimental setting, targeted inflammatory inhibition is responsible for substantial structural and functional improvement

# Recommendations

## 6) Role of genetics

- Primary lymphedema is an autosomal dominant disorder with incomplete penetrance
- It can happen that the genetic mutation is of hereditary-familial type
- Primary lymphedema can be sporadic
- In syndromic cases, lymphedema is one aspect of the more complex clinical setting
- It is useful to study genetic mutations in order to better understand the incidence, penetrance and prevalence of the disease.

# Recommendations

## 7) Risk factors for secondary lymphedemas

- Extensive surgery
- Radiation therapy
- Specific systemic therapies especially taxane-based regimens
- Body mass index / Morbid obesity
- Inactivity
- Injuries to derivative lymphatic pathways

# Recommendations

## 8) Prevention (primary, secondary and tertiary)

- **Primary:** meaning to minimize injury of the lymphatic system by cancer treatment is now possible only with reverse mapping and LYMPHA technique.
- **Secondary:** to support the lymphatic system after cancer treatment to avoid development of lymphedema, manual lymph drainage, slight compression, pumping exercises and self-massage are often suggested but have not been sufficiently evaluated.
- **Tertiary:** to diagnose arm lymphedema at an early stage and start conservative treatment with compression therapy when the lymphedema still is mild and thereby prevent development of severe lymphedema. Early microsurgery in case of poor response to conservative treatment.

# Recommendations

## 9) Treatment (conservative, surgical; early and late stages)

- **Combined Physical Therapy (CPT)** is the gold standard for the conservative management of lymphedema. However, for early stages both meta-analysis and Cochrane has proven compression to be the best first treatment followed by MLD only if compression does not work.
- CPT is a **4 part** physiotherapy program consisting of: 1) Manual Lymphatic Drainage; 2) Gradient compression bandaging; 3) Therapeutic exercises; 4) Skin care.
- All patients with symptoms or measured changes should be referred for evaluation with a lymphedema physical therapist, formally educated, and provided **graduated intervention** according to the staging.

# Recommendations

## 10) Treatment (conservative, surgical; early and late stages)

- **Microsurgical approaches** are physiologic procedures that aim to reconnect or reconstruct the lymphatics and have shown to be effective in multiple studies to reduce excess lymphatic fluid in early stage lymphedema
- **Proximal multiple LVA technique** creates multiple lymphatic-venous anastomoses at the proximal site of the affected extremity using the lymphatic collectors just below the site of lymphatic flow obstruction. The lymphatic-venous pressure gradient and competent venous valve promote lymph flow through the anastomoses.
- As concerns preoperative diagnostics, superficial and deep **lymphoscintigraphy** is the main diagnostic tool that supplies a precise functional assessment of both supra and subfascial lymphatic pathways allowing the surgeon to plan a proper and physiologic procedure to treat the lymphatic obstruction.

# Recommendations

## 11) Treatment (conservative, surgical; early and late stages)

- Indocyanine green fluorescence can demonstrate only subdermal lymphatic vessels not providing a complete investigation of either superficial or deep lymphatic pathways, which is indispensable for a surgeon to have a proper assessment of lymphatic circulation.
- Another LVA technique uses small, distal, subdermal lymphatico-venular anastomoses however, the pressure from the venous circulation may impede lymph flow through the anastomoses in these cases.
- Excess volume reduction is variable with these techniques and it depends on the stage of the disease. Microsurgical reconstructive procedures are more effective for early lymphedema because functional lymphatics are still present, and there is minimal fibroadipose deposition.

# Recommendations

## 12) Treatment (conservative, surgical; early and late stages)

- The understanding of the indications for **vascularized lymph node transfer (VLNT)** and its mechanism of action are still evolving
- Major concerns relating to VLNT include **donor site morbidity** and patient selection.
- **VLNT can increase VEGF-C concentration locally** which has been associated with lymphatic regeneration in normal tissue but also theoretically lends increased metastatic potential in tumors. The clinical impact of these theoretical advantages and disadvantages remains unknown



# Recommendations

## 13) Treatment (conservative, surgical; early and late stages)

- **Debulking techniques** include minimally invasive approaches, such as **liposuction**, that is performed to remove accumulated fat and fibrotic tissue in late stages
- Liposuction effectively removes nearly **100% excess volume** from affected limbs but does not address the underlying pathophysiology or etiology of lymphedema
- Therefore, patients must **maintain continuous postoperative compression and follow up with a lymphedema therapist**
- Recent proposed technique by a lymph vessel sparing procedure (so-called **Fibro-Lipo-Lymph-Aspiration with Lymph Vessel Sparing Procedure- FLLA-LVSP** - by green indocyanine fluorescent microlymphography).

# Recommendations

## 14) Treatment (conservative, surgical; early and late stages)

- Patients should be assessed by a **multidisciplinary team** that has an understanding of lymphedema and after care where **surgery is considered part of a multimodality treatment plan**. Baseline and follow up assessments should be made including **functional lymphatic assessments**.