

Lymphedema diagnosis

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Transcapillary fluid balance

controlled by: hydrostatic pressures  
osmotic pressures




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Transcapillary fluid balance

Starling forces


Starling:  $F = CFC((P_c - P_d) - \sigma(COP_{pl} - COP_d)) = L$



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Transcapillary fluid balance

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## Transcapillary fluid balance

$$\text{Starling: } F = \text{CFC}((P_c - P_d) - \sigma(\text{COP}_{pl} - \text{COP}_d)) = L$$



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## Transcapillary fluid balance

$$\text{Starling: } F = \text{CFC}((P_c - P_d) - \sigma(\text{COP}_{pl} - \text{COP}_d)) = L$$



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**Transcapillary fluid balance**

Starling:  $F = CFC((P_c - P_{if}) - \sigma(COP_{pl} - COP_{if})) = L$   
 carefully balanced system  
 change any factor in Starling:

EDEMA

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**Edema**




**Increased filtration**  
 Venous insuff.  
 Heart failure  
 Infections  
 Protein deficiency  
 NaCl retention  
 etc.

**Reduced lymphatic transport**

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**Edema**




**Increased filtration**  
 Venous insuff.  $\searrow$  distal pressures  
 Heart failure  $\swarrow$

Starling:  $F = CFC((P_c - P_{if}) - \sigma(COP_{pl} - COP_{if})) = L$

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**Edema**




**Increased filtration**  
 Venous insuff.  $\searrow$  distal pressures  
 Heart failure  $\swarrow$   
 Infections  $\longleftarrow$  permeability

Starling:  $F = CFC((P_c - P_{if}) - \sigma(COP_{pl} - COP_{if})) = L$

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**Edema**




**Increased filtration**

- Venous insuff. > distal pressures
- Heart failure > distal pressures
- Infections > permeability
- Protein defic. > osmolality
- NaCl retention > osmolality

Starling:  $F = CFC((P_c - P_f) - \sigma(COP_{pl} - COP_f)) = L$

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**Edema**



**Increased filtration**


- Venous insuff. > distal pressures
- Heart failure > distal pressures
- Infections > permeability
- Protein defic. > osmolality
- NaCl retention > osmolality

**Reduced lymphatic transport**

Starling:  $F = CFC((P_c - P_f) - \sigma(COP_{pl} \cdot COP_f)) = L$

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**Edema**



**Increased filtration**

- Venous insuff. > distal pressures
- Heart failure > distal pressures
- Infections > permeability
- Protein defic. > osmolality
- NaCl retention > osmolality

**Reduced lymphatic transport**

«low output failure»  
overall reduction in lymphatic transport

«high output failure»  
overall overload of lymphatic transport

- hepatic cirrhosis (ascites)
- nephrotic syndrome (anasarca)
- chronic venous insufficiency

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**Clinical investigations**

Diagnosis can be evident



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### Clinical investigations

Diagnosis can be challenging

### Clinical history

- time of onset in-born youth adult
- acute/gradual onset
- degree of progression days/weeks/months/years stable
- «morning edema»
- progression during the day temp. standing
- distribution (lokalization) uni/bilat. face generalised
- distal edema (toes, fingers)
- response to elevation

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### Clinical history

- previous edema episodes
- previous infections NB erysipelas
- family history
- cancer treatment
- surgery
- trauma/injuries
- travels/trophics
- medication
- comorbidity

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### Physical examination

extent/localization  
unilateral/bilateral

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### Physical examination

extent/localization  
unilateral/bilateral  
only upper limbs /lower limbs /generalized

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### Physical examination

extent/localization  
unilateral/bilateral  
only upper limbs /lower limbs /generalized  
abdomen/face



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### Physical examination

extent/localization  
unilateral  
only upper limbs /lower limbs /generalized  
abdomen/face  
how distal  
how proximal



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### Physical examination


extent/localization  
pitting



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### Physical examination


- extent/localization
- pitting
- dystrophy
  - hyperkeratosis
  - acanthosis
  - pigmentation
  - fatty deposits
  - warty overgrowths
  - ulcers



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### Physical examination


- extent/localization
- pitting
- dystrophy
- Stemmer sign
  - inability to pinch the skin of the proximal phalanx of the second or third toe
- "Squaring of toes"



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### Physical examination


- extent/localization
- pitting
- dystrophy
- Stemmer sign
- "buffalo hump"
  - puffiness of the forfoot



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### Physical examination


- extent/localization
- pitting
- dystrophy
- Stemmer sign
- "buffalo hump"
- "ski-jump nails"
  - Hypoplastic and concave toenails
  - phenotype of primary lymphedema



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**Physical examination**


- extent/localization
- pitting
- dystrophy
- Stemmer sign
- "buffalo hump"
- "ski-jump nails"
- varicose veins
- venous edema without evident varicose veins



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**Physical examination**


- extent/localization
- pitting
- dystrophy
- Stemmer sign
- "buffalo hump"
- "ski-jump nails"
- varicose veins
- pigmentation
- enlarged extremities/edema, pigmentation, uncharacteristic venous localization
- vascular malformations with lymphedema (e.g. KTS)



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**Physical examination**

- extent/localization
- pitting
- dystrophy
- Stemmer sign
- "buffalo hump"
- "ski-jump nails"
- varicose veins
- pigmentation
- arterial perfusion



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**Physical examination and Clinical history**

Not diagnostic but indicative

Clinical signs tend to be unreliable

J. Jayaraj et al. J Vasc Surg Venous Lymphat Disord 2019

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### Supplementary investigations important:

- Differential diagnosis: venous insufficiency causing edema

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### Supplementary investigations important:

- Differential diagnosis: venous insufficiency causing edema
- Comorbidity: increasing edema      kidney or liver disease
- Comorbidity: affecting treatment      congestive heart failure

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### Supplementary investigations

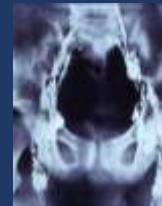
Lymphangiography  
Lymphoscintigraphy  
MR  
CT  
B-mode  
Fluorescent imaging  
Volume estimations/volumetry  
COP measurements  
patent-blue  
others

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### Supplementary investigations

Lymphangiography  
Oil-based contrast

- complications
  - pain
  - thrombophlebitis
  - lymphangitis
  - fever
  - etc.

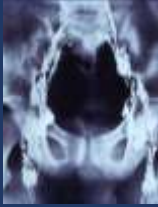


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### Supplementary investigations

Lymphangiography  
Oil-based contrast


- complications
- contrast damage of lymphatics
- lymphedema progression
- complex conditions with chylous reflux or injury/changes to ductus thoracicus



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### Supplementary investigations

- Lymphangiography
- Lymphoscintigraphy
- MR
- CT
- B-mode
- Fluorescent imaging
- Volumestimations/volumetry
- COP measurements
- patent-blue
- others




interdigital injection of radio-tracer  
subsequent gamma camera monitoring.

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### Supplementary investigations

Lymphoscintigraphy  
parameters

- number and size of lymphatic vessels
- number and size of lymph nodes
- collaterals
- dermal lymphatic reflux
- symmetry contralateral limb
- radiotracer transport/transport capacity




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### Supplementary investigations

Lymphoscintigraphy  
parameters

- Qualitative lymphoscintigraphy:*  
lymphatic morphology – number and size of lymphatic channels and lymph nodes
- Quantitative lymphoscintigraphy:*  
lymphatic flow - transport capacity

i.e. estimate of function and quality of lymphatic channels



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### Supplementary investigations

Lymphoscintigraphy parameters


	Sensitivity	Specificity
Qualitative lymphoscintigraphy: lymphatic morphology – number and size of lymphatic channels and lymph nodes	70–78%	100%
Quantitative lymphoscintigraphy: lymphatic flow – transport capacity	90–98%	83–100%

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### Supplementary investigations

Lymphoscintigraphy parameters

- "goldstandard"
- no standardization
- varying radiotracers and doses
- different injection-volumes
- intracutaneous vs. subcutaneous injection
- no. of injections




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### Supplementary investigations

Lymphoscintigraphy

- False negative result*  
e.g. early lymphedema phase
- False positive result*  
e.g. erysipelas  
extensive venous dysfunction.
- Repeated lymphoscintigraphy



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### Supplementary investigations

- Lymphangiography
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- patent-blue
- others

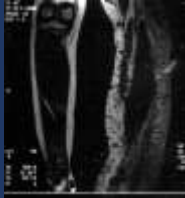
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## Supplementary investigations

Conventional MR

MR

- honeycomb pattern



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## Supplementary investigations

Conventional MR

MR Non contrast MR lymphangiography (NCMRL)  
 technically adapted MR  
 (extensive T2-weighting and fat-suppression)

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## Supplementary investigations

Conventional MR

MR Non contrast MR lymphangiography (NCMRL)

- honeycomb pattern
- muscular abnormalities
- dermal thickening
- distal dilated lymphatics
- inguinal lymph node number
- appearance of iliac lymphatic trunks

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## Supplementary investigations

Conventional MR

MR Non contrast MR lymphangiography (NCMRL)  
 MR lymphography

subcut. injection of paramagnetic contrast  
 direct injection of contrast into lymphnodes  
 qualitativ assessment of lymph vessels  
 quantitativ assessment of function  
 (lymphtransport capacity in cm<sup>3</sup>/min.)

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Supplementary investigations

- Lymphangiography
- Lymphoscintigraphy
- MR
- CT**
- B-mode
- Fluorescent imaging
- Volume-estimations/volumetry
- COP measurements
- patent-blue
- others

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Supplementary investigations

Conventional CT

- lymphedema distribution
- morphology – fat, fibrosis

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Supplementary investigations

Conventional CT

3D contrast CT

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Supplementary investigations

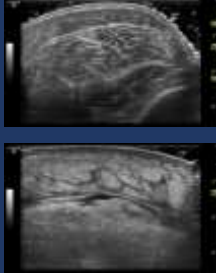
- Lymphangiography
- Lymphoscintigraphy
- MR
- CT
- B-mode**
- Fluorescent imaging
- Volume-estimations/volumetry
- COP measurements
- patent-blue
- others

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Supplementary investigations

B-mode

- honeycomb pattern
- changes in echogenicity
- changes in tissue elasticity




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Supplementary investigations

B-mode

- honeycomb pattern
- changes in echogenicity
- changes in tissue elasticity



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Supplementary investigations

- Lymphangiography
- Lymphoscintigraphy
- MR
- CT
- B-mode
- Fluorescence imaging**
- Volume-estimations/volumetry
- COP measurements
- patent-blue
- others

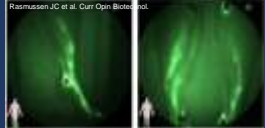
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Supplementary investigations

Fluorescence imaging

Indocyanine-green lymphography (ICG)

- intradermal injection of fluorizing contrast
- lymphatic transport via infrared camera
- qualitative and quantitative info.
- useful pre-operatively
- depth penetratio round 1,5 cm
- primarily superficial lymphatics



Rasmussen, J.C. et al. Curr Opin Biotechnol.

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### Supplementary investigations

- Lymphangiography
- Lymphoscintigraphy
- MR
- CT
- B-mode
- Fluorescence imaging
- Volume-estimations/volumetry**
- COP measurements
- patent-blue
- others


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### Supplementary investigations

**Volume-estimations/volumetry**

- objective measurements
- edema progression
- response to treatment

minimal progression : >5 - <20% volume change  
 moderate progression : 20 - 40% volume change  
 extensive progression : >40% volume change



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### Supplementary investigations

- Lymphangiography
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- MR
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- Fluorescence imaging
- Volume-estimations/volumetry
- COP measurements**
- patent-blue
- others

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### Supplementary investigations

**COP measurements**

Starling:  $F = CFC((P_v - P_e) - \sigma(COP_p - COP_e)) + L$



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**Supplementary investigations**

- Lymphangiography
- Lymphoscintigraphy
- MR
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- Fluorescence imaging
- Volume-estimations/volumetry
- COP measurements
- patent-blue**
- others

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**Supplementary investigations**

**Patent-blue**  
 inter-digital dye injection  
 allergic skin response  
 /anaphylactic reactions  
 intra-operatively (LVA)



Fig. 15. *et al. Ann Plast Surg* 2001

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**Supplementary investigations**

- Lymphangiography
- Lymphoscintigraphy
- MR
- CT
- B-mode
- Fluorescence imaging
- Volume-estimations/volumetry
- COP measurements
- patent-blue
- others**

**Bioimpedance measurements**  
 different electrical tissue conductivity  
 % water, fat, muscle tissue prior to and following treatment

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**Supplementary investigations**

- Lymphangiography
- Lymphoscintigraphy
- MR
- CT
- B-mode
- Fluorescence imaging
- Volume-estimations/volumetry
- COP measurements
- patent-blue
- others**

**Bioimpedance measurements**  
 Tonometry - tissue resistance

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### Supplementary investigations

- Lymphangiography
- Lymphoscintigraphy
- MR
- CT
- B-mode
- Fluorescence imaging
- Volume-estimations/volumetry
- COP measurements
- patent-blue
- others

- Bioimpedance measurements
- Tonometry
- Indirect (water soluble) lymphography
- Fluorescing microlymphangiography
- older methods -  
visualization of lymphatics

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### Supplementary investigations

- Lymphangiography
- Lymphoscintigraphy
- MR
- CT
- B-mode
- Fluorescence imaging
- Volume-estimations/volumetry
- COP measurements
- patent-blue
- others

- Bioimpedance measurements
- Tonometry
- Indirect (water soluble) lymphography
- Fluorescing microlymphangiography
- PET/SPECT lymphangiography

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### Supplementary investigations

#### Genetics

60 genes related to primary lymphedema/vascular anomalies identified increasing

No. of specific inherited syndromes with mutations:

- Milroys – some variants (VEGFR-3)
- lymphedemadisticiasis (FOXO2)
- hypotrichosis-lymphedema-telangiectasia (SOX18)

Genetic/epigenetic risk for secondary lymphedema related to treatment potentially affecting the lymphatics

Lymph-node resection, radiation, trauma, infections etc.

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### End-note

Clinical examination indicates

Lymphoscintigraphy verifies

Supplementary investigation if:

- diagnosis remain unclear
- reconstructive surgery is assessed

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