



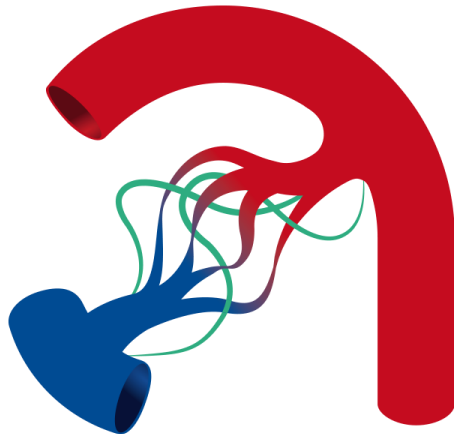
**European  
Reference  
Network**

for rare or low prevalence  
complex diseases



**Network**

Vascular Diseases  
(VASCERN)



# Lymphatic malformation

Final Approved Patient Pathway by the Vascular  
Anomalies (VASCA) Working Group – 29/04/2020

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# Disclaimer

- This document is an opinion statement reflecting strategies put forward by experts and patient representatives involved in the Vascular Anomalies (VASCA) Rare Disease Working Group of VASCERN.
- It is preferable that patients be evaluated in a multidisciplinary center specialized in the diagnosis and management of vascular anomalies.
- This pathway is issued on 29/04/2020 and will be further validated and adjusted as needed.
- Multidisciplinary team should re-evaluate treatment decisions regularly
- Responsibility for care of individual patients remains with the treating physician.



# Lymphatic malformation Diagnostic Work-Up: Overview

## Suspected lymphatic malformation

**Possible clinical signs or symptoms:**

- Prenatal detection of a cyst
- Onset most often in early childhood
- Gradual swelling of a (subcutaneous) non-solid, non-compressible mass
  - Bluish hue on the skin
  - Vesicles
- Recurrent lymph leak/oozing/ bleeding
- Frequent skin infections and inflammations in the mass
- Protein losing enteropathy / pleural- pericardial or abdominal fluid effusion or cysts
  - Most often no pain
  - Incidental finding
  - Edema

- Doppler ultrasound to confirm diagnosis & exclude flow in the lesions
  - MRI if diagnosis unclear or prior to surgery or sclerotherapy
  - CT if suspicion of bone involvement (Gorham-Stout disease)
    - Lymphatic scintigraphy if suspicion of lymphedema
    - Mucosal investigation with endoscopy
- Lymphangiography if suspicion of channel type LM or pleural-, pericardial- or peritoneal chylus effusion
- Coagulation work-up (Chronic localized intravascular coagulopathy?) Kasabach-Merritt Phenomenon (KMP)
  - Biopsy or FNAC occasionally needed for differential diagnosis \*

**\*Histology** is helpful for differential diagnosis : LMs are composed of thin-walled, dilated irregular channels which often appear empty or contain pale eosinophilic amorphous material.

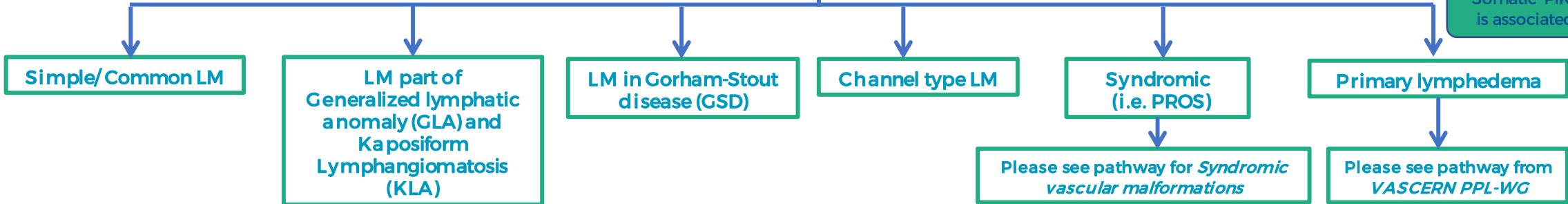
Superficial LM may be associated with overlying epidermal hyperplasia and hyperkeratosis.

Immunostains for lymphatic markers are helpful in differentiating LM from other malformations.

PROX1, VEGFR-3, D2-40 (podoplanin) and LYVE-1 all label lymphatic endothelium.

**\*Cytology** and cyst chemistry is used to rule out cysts of other origin such as pseudocysts from parenchymal organs

Somatic PIK3CA mutation is associated to most LM



LEGEND:

- Clinical evaluation
- Investigations
- Treatment
- Associated genes
- Particular cases



# Lymphatic malformation: Management/Treatment Overview

## Common management LM:

All LM

Micro cystic LM

Macro cystic LM

Mixed LM

GLA/KLA

Channel Type

### Overall treatment strategy:

**Overall treatment options are:**  
Watchful waiting ,compression garments, antibiotics, corticosteroids, sclerotherapy, surgery and Sirolimus. The decision must be made within multi-disciplinary teams with good knowledge of all treatment modalities, the treatments must be re-evaluated regularly

In case of signs of infection, always start early with antibiotics. Consider corticosteroids after systemic bacterial infection has been ruled out.

- Reduce risk of infections and inflammations
- Treat oozing, bleeding and causes of protein loss
- Reduce risk of compromise of vital function if sudden swelling occurs in the malformation, protect vital functions
- Improve quality of life and treat malformation which give psychosocial burden to the patient

## Specialized treatments per type of LM:

Micro cystic LM

Macro cystic LM

Mixed LM

GLA/KLA/GSD

Channel Type

- Sclerotherapy often first line of treatment: OK-432, Bleomycin, Doxycyclin etc.
- Consider primarily surgery if excision can be made or after more than four attempts of unsatisfactory sclerotherapy sessions

- Antibiotics due to recurrent infections.
- Topical corticosteroids
- Surgery if excisable lesions.
- Consider sclerotherapy (Bleomycin)
- Consider Sirolimus

- Dietary adjustment to lower chylus circulation
- Consider MR lymphangiography- a new emerging diagnostic tool which opens new treatment options i.e. embolization treatment

- Coagulation work-up prior to treatment. Associated with higher risk of chronic Localized Intravascular Coagulopathy (LIC) and Kasabach Merritt Phenomenon (KMP)
- Consider surgery prior to sclerotherapy when malformation is in contact with vital structures and functions.
- Consider Sirolimus if there are contraindication to other treatments
- Consider MR lymphangiography and embolization treatment

LEGEND:

Clinical evaluation

Investigations

Treatment

Associated genes

Particular cases



Part A

**Lymphatic malformation: Diagnosis, Management and treatment (Simple LM, Common LM)**

Suspected lymphatic malformation

- 1) Ultrasound/ Doppler :
  - No flow in cysts?
  - Size of cysts?
- 2) MRI if suspicion of extension to vital structures and organs, and/or prior to treatment
- 3) Mucosal investigation with endoscopy if signs of protein losing enteropathy

Localized lesions, limited to the skin, subcutaneous tissue or mucosa

Diffuse and extensive lesions, verified deep extension or fluid /lymph effusions in deep cavities on MRI

- Common Macrocytic LM
- Common Microcystic LM
- Common Mixed LM

See Part B

Somatic PIK3CA mutation?

**Therapeutic options**, depending on the characteristics of the lesion and the **multidisciplinary team** decision, treatments require **re-evaluation regularly**

**Watchful waiting** if no symptoms, no risk of relevant physical complications nor psychosocial impairment

**Sclerotherapy**, first line of treatment for most LM. OK-432, Bleomycin, Doxycycline depending on cyst type and location. May require several treatment sessions.

**Surgery**, if the lesion is considered resectable, part of a debulking procedure or after several (>4 sessions) attempt of insufficient sclerotherapies.

**Laser**, in cases of oozing vesicles in skin or mucosa

**Sirolimus**, if other treatment options are considered inadequate.

If signs of local infections / cellulitis or septicemia start with **systemic antibiotics** and, consider short term of **glucocorticoids**

LEGEND:

Clinical evaluation

Investigations

Treatment

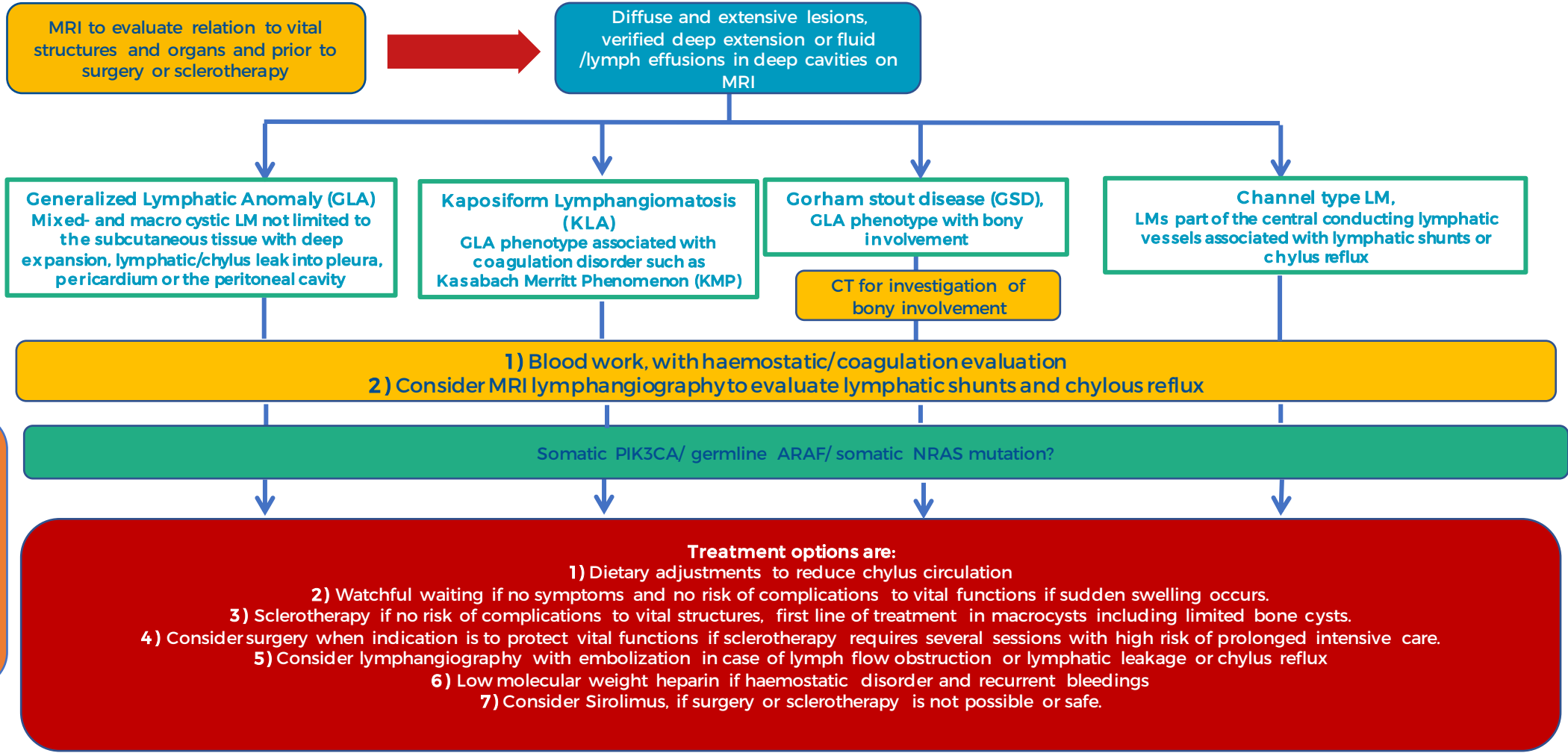
Associated genes

Particular cases



Part B

**Lymphatic malformation: Management and treatment (Diffuse and extensive LM)**



Always individualized treatments tailored to reduce risk of life threatening complications, improving life quality including prevention of psychosocial impairment.



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VASCERN

Gathering the best expertise in Europe  
to provide accessible cross-border healthcare  
to patients with rare vascular diseases



VASCERN, the European Reference Network on Rare Multisystemic Vascular Diseases, is dedicated to gathering the best expertise in Europe in order to provide accessible cross-border healthcare to patients with rare vascular diseases (an estimated 1.3 million concerned). These include arterial diseases (affecting aorta to small arteries), arterio-venous anomalies, vascular malformations, and lymphatic diseases.

VASCERN currently consists of 30 highly specialised multidisciplinary Healthcare Providers (HCPs) from 11 EU Member States and of various European Patient Organisations and is coordinated in Paris, France.

Through our 5 Rare Disease Working Groups (RDWGs) as well as several thematic WGs and the ePAG – European Patient Advocacy Group, we aim to improve care, promote best practices and guidelines, reinforce research, empower patients, provide training for healthcare professionals and realise the full potential of European cooperation for specialised healthcare by exploiting the latest innovations in medical science and health technologies.

More information available at: <https://vascern.eu>

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