EVIDENCE BASED STATEMENT

DOMAIN 10, Statement 3

TOPIC: "**Lymphedema signs, symptoms and diagnostic work-up**"

SEARCH TERMS & SOURCES

(lymphedema[MeSH Terms]) AND ((signs[MeSH Terms]) OR (symptoms[MeSH Terms]))

INCLUSION CRITERIA

- Lower limb only
- Reviews
- Publication < 10 years, only ENG

SEARCH RESULT BEFORE - AFTER SELECTION

232 (before) - 20 (after selection)

AGREEMENT BETWEEN THE 2 REVIEWERS before DOMAIN WORKING GROUP DISCUSSION & FINALIZATION

(N. of papers triggering disagreement in inclusion/No of papers from the initial search)

4/232

PERTINENT LITERATURE NOT IDENTIFIED BY THE LITERATURE SEARCH

1. Jayaraj A, Raju S, May C, et al. The diagnostic unreliability of classic physical signs of lymphedema. J Vasc Surg Venous Lymphat Disord. 2019 Nov;7(6):890-897.
2. Forte AJ, Huayllani MT, Boczar D, etal. Ultrasound Elastography Use in Lower Extremity Lymphedema: A Systematic Review of the Literature. Cureus. 2019 Sep 5;11(9):e5578
3. Goss JA, Greene AK. Sensitivity and Specificity of the Stemmer Sign for Lymphedema: A Clinical Lymphoscintigraphic Study. Plast Reconstr Surg Glob Open. 2019;7(6):e2295.
4. Keo HH, Gretener SB, Staub D. Clinical and diagnostic aspects of lymphedema. Vasa. 2017 Jul;46(4):255-261.
5. Kayıran O, De La Cruz C, Tane K, Soran A. Lymphedema: From diagnosis to treatment. Turk J Surg. 2017;33(2):51-57.

EVIDENCE BASED STATEMENT

Domain 10; Statement 3

IDENTIFIED REFERENCES

(from the most recent down)

1: Lee E, Biko DM, Sherk W, et al.. Understanding Lymphatic Anatomy and Abnormalities at Imaging. Radiographics. 2022 Mar-Apr;42(2):487-505.

2. Shinaoka A, Kamiyama K, Yamada K, Kimata Y. A new severity classification of lower limb secondary lymphedema based on lymphatic pathway defects in an indocyanine green fluorescent lymphography study. Sci Rep. 2022 Jan 10;12(1):309 2021;40(2):85-93.

3: Mills M, van Zanten M, Borri M, et al. Systematic Review of Magnetic Resonance Lymphangiography From a Technical Perspective. J Magn Reson Imaging. 2021;53(6):1766-1790.

4: Russo S, et al. Standardization of lower extremity quantitative lymphedema measurements and associated patient-reported outcomes in gynecologic cancers. Gynecol Oncol. 2021;160(2):625-632.

5: Guerrini S, Gentili F, Mazzei FG, et al. Magnetic resonance lymphangiography: with or without contrast? Diagn Interv Radiol. 2020 Nov;26(6):587-595.

6: Polomska AK, Proulx ST. Imaging technology of the lymphatic system. Adv Drug Deliv Rev. 2021 Mar;170:294-311.

7: Tan M, Salim S, Beshr M, et al. A methodologic assessment of lymphedema clinical practice guidelines. J Vasc Surg Venous Lymphat Disord. 2020;8(6):1111-1118.e3

8: O'Donnell TF Jr, Allison GM, Iafrati MD. A systematic review of guidelines for lymphedema and the need for contemporary intersocietal guidelines for the management of lymphedema. J Vasc Surg Venous Lymphat Disord. 2020;8(4):676-684.

9: Miseré RML, Wolfs JAGN, Lobbes MBI, et al. A systematic review of magnetic resonance lymphography for the evaluation of peripheral lymphedema. J Vasc Surg Venous Lymphat Disord. 2020;8(5):882-892.e2

10: O'Donnell TF Jr, Allison GM, Melikian R, et al. A systematic review of the quality of clinical practice guidelines for lymphedema, as assessed using the Appraisal of Guidelines for Research and Evaluation II instrument. J Vasc Surg Venous Lymphat Disord. 2020 Jul;8(4):685-692.

11: Bittar S, Simman R, Lurie F. Lymphedema: A Practical Approach and Clinical Update. Wounds. 2020 Mar;32(3):86-92. 13: Dessources K, Aviki E, Leitao MM Jr. Lower extremity lymphedema in patients with gynecologic malignancies. Int J Gynecol Cancer. 2020 Feb;30(2):252-260.

12: Pappalardo M, Cheng MH. Lymphoscintigraphy for the diagnosis of extremity lymphedema: Current controversies regarding protocol, interpretation, and clinical application. J Surg Oncol. 2020 Jan;121(1):37-47.

13. Forte AJ, Huayllani MT, Boczar D, et al. Ultrasound Elastography Use in Lower Extremity Lymphedema: A Systematic Review of the Literature. Cureus. 2019 5;11(9):e5578

14: Bakar Y, Tuğral A. Lower Extremity Lymphedema Management after Gynecologic Cancer Surgery: A Review of Current Management Strategies. Ann Vasc Surg. 2017;44:442-450.

15: O'Donnell TF Jr, Rasmussen JC, Sevick-Muraca EM. New diagnostic modalities in the evaluation of lymphedema. J Vasc Surg Venous Lymphat Disord. 2017 Mar;5(2):261-27317. Todd M. Best practice: Doppler assessment in lymphoedema. Br J Community Nurs. 2016 Dec 2;21(12):612-613.

16: Iwersen LF, Sperandio FF, Toriy AM, Palú M, Medeiros da Luz C. Evidence-based practice in the management of lower limb lymphedema after gynecological cancer. Physiother Theory Pract. 2017 Jan;33(1):1-8.

17: Mitsumori LM, McDonald ES, Wilson GJ, Neligan PC, Minoshima S, Maki JH. MR lymphangiography: How i do it. J Magn Reson Imaging. 2015 Dec;42(6):1465-77.

18. Mihara M, Hara H, Narushima M, Todokoro T, Iida T, Ohtsu H, Murai N, Koshima I. Indocyanine green lymphography is superior to lymphoscintigraphy in imaging diagnosis of secondary lymphedema of the lower limbs. J Vasc Surg Venous Lymphat Disord. 2013 Apr;1(2):194-201

EVIDENCE BASED STATEMENT

Domain 10; Statement 3

TEXT FOR INCLUSION IN THE DOCUMENT
(300 words, not counting the references)
DOMAIN 10, Statement 3, **TOPIC**: "**Lymphedema signs, symptoms and diagnostic work-up**"

Lymphedema diagnosis starts from a careful assessment of the patient history, signs and symptoms. Family predisposition, previous trauma, inflammatory or infective conditions affecting the lymphatic system must be promptly reported. Chronic swelling, skin infections and progressive trophic changes suggest the diagnosis. *[**O'Donnell TF Jr, Rasmussen JC, Sevick-Muraca EM. New diagnostic modalities in the evaluation of lymphedema. *J Vasc Surg Venous Lymphat Disord*. 2017;5(2):261-273**].
The Kaposi-Stemmer sign (impossibility to pinch the skin on the foot or hand) has a good sensitivity for lymphedema prediction. Yet, its specificity is moderate, therefore instrumental diagnostic is recommended to make an objective diagnosis.
[**Jayaraj A, Raju S, May C, Pace N. The diagnostic unreliability of classic physical signs of lymphedema. J Vasc Surg Venous Lymphat Disord. 2019 Nov;7(6):890-897**].
The limb volume can be measured by tape, water displacement (gold-standard) or perometry. The fibrosis degree can be assessed by a tonometer, while bioimpedance can detect the tissue texture. Ultrasound scanning can detect the fluid and fibrotic components both at the dermal and subdermal levels, in a simple and cost-effective modality. Ultrasound elastography represents a valuable improvement in moderate-to-advanced lymphedema stages characterization.
[**Forte AJ, Huayllani MT, Boczar D, Cinotto G, McLaughlin SA. Ultrasound Elastography Use in Lower Extremity Lymphedema: A Systematic Review of the Literature. Cureus. 2019 Sep 5;11(9):e5578**].
Computed tomography (CT) and magnetic resonance imaging (MRI) are indicated for a better imaging sensitivity and specificity. Moreover, CT offers the advantage of identifying also possible causes of secondary lymphedema, while MRI lymphangiography provides details of the lymphatic system.
The detailed function of the lymphangions can be depitected by Near Infra-Red Fluoresence using indocyanine green, which is limited in its tissue penetration depth though.
[**Shinaoka A, Kamiyama K, Yamada K, Kimata Y. A new severity classification of lower limb secondary lymphedema based on lymphatic pathway defects in an indocyanine green fluorescent lymphography study. Sci Rep. 2022 Jan 10;12(1):309**].
A careful evaluation of clinical and instrumental data by an expert lymphologist is then needed for a proper diagnostic work-up.

EVIDENCE BASED STATEMENT

Domain 10; Statement 3

STATEMENT FOR PUBLIC EVIDENCE-BASED AWARENESS

DOMAIN 10, Statement 3

"**Lymphedema can manifest as swelling, redness, skin infections, abnormal tissue proliferation. At least ultrasound scanning must be performed, eventually together with more advanced techniques based on the specific case**"

4 SELECTED REFEREENCES

1. Jayaraj A, Raju S, May C, Pace N. The diagnostic unreliability of classic physical signs of lymphedema. J Vasc Surg Venous Lymphat Disord. 2019 Nov;7(6):890-897
2. Forte AJ, Huayllani MT, Boczar D, et al. Ultrasound Elastography Use in Lower Extremity Lymphedema: A Systematic Review of the Literature. Cureus. 2019 Sep 5;11(9):e5578
3. *O'Donnell TF Jr, Rasmussen JC, Sevick-Muraca EM. New diagnostic modalities in the evaluation of lymphedema. *J Vasc Surg Venous Lymphat Disord*. 2017;5(2):261-273
4. Shinaoka A, Kamiyama K, Yamada K, et al. A new severity classification of lower limb secondary lymphedema based on lymphatic pathway defects in an indocyanine green fluorescent lymphography study. Sci Rep. 2022 Jan 10;12(1):309

identified LITERATURE BIAS

Lack of signs and symtpoms objective quantification tools.

SUGGESTED NEXT LINES OF RESEARCH

Diagnostic options cost-effectiveness analysis