EVIDENCE BASED STATEMENT

DOMAIN 10, Statement 7

TOPIC: "**Lymphedema differential diagnosis**"

SEARCH TERMS & SOURCES

(lymphedema[MeSH Terms]) AND (differential diagnosis[MeSH Terms])
(lymphedema[MeSH Terms]) AND (diagnosis[MeSH Terms])

INCLUSION CRITERIA

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

SEARCH RESULT BEFORE - AFTER SELECTION

280 (before) - 17 (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
4/280

PERTINENT LITERATURE NOT IDENTIFIED BY THE LITERATURE SEARCH

1. Rockson SG. Bioimpedance Analysis of Lower Extremity Lymphedema. Lymphat Res Biol. 2020 Apr;18(2):98.
2. Steele ML, Janda M, Vagenas D, et al. A Bioimpedance Spectroscopy-Based Method for Diagnosis of Lower-Limb Lymphedema. Lymphat Res Biol. 2020 Apr;18(2):101-109
3. Greene AK, Goss JA. Diagnosis and Staging of Lymphedema. Semin Plast Surg. 2018;32(1):12-16. doi:10.1055/s-0038-1635117

EVIDENCE BASED STATEMENT

Domain 10; Statement 7

IDENTIFIED REFERENCES

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

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

3: 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 Sep;8(5):882-892.e2.

4: Li CY, Kataru RP, Mehrara BJ. Histopathologic Features of Lymphedema: A Molecular Review. Int J Mol Sci. 2020 Apr 6;21(7):2546.

5: Bittar S, Simman R, Lurie F. Lymphedema: A Practical Approach and Clinical Update. Wounds. 2020 Mar;32(3):86-92. PMID: 32163039.

6: Chamnanchanunt S, Svasti S, Fucharoen S, Umemura T. Neglected Tropical Diseases: The Potential Application of microRNAs for Monitoring NTDs in the Real World. Microrna. 2020;9(1):41-48.

7: 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.

8: Moffatt C, Keeley V, Quere I. The Concept of Chronic Edema-A Neglected Public Health Issue and an International Response: The LIMPRINT Study. Lymphat Res Biol. 2019 Apr;17(2):121-126.

9: Moffatt C, Franks P, Keeley V, et al. The Development and Validation of the LIMPRINT Methodology. Lymphat Res Biol. 2019 Apr;17(2):127-134.

10: Jones GE, Mansour S. An approach to familial lymphoedema. Clin Med (Lond). 2017 Dec;17(6):552-557.

11: Todd M. Best practice: Doppler assessment in lymphoedema. Br J Community Nurs. 2016 Dec 2;21(12):612-613.

12: Greene AK. Diagnosis and Management of Obesity-Induced Lymphedema. Plast Reconstr Surg. 2016 Jul;138(1):111e-118e.

13: Mulasi U, Kuchnia AJ, Cole AJ, et al. Bioimpedance at the bedside: current applications, limitations, and opportunities. Nutr Clin Pract. 2015 Apr;30(2):180-93.

14: Dixon JB, Weiler MJ. Bridging the divide between pathogenesis and detection in lymphedema. Semin Cell Dev Biol. 2015 Feb;38:75-82.

15: Johnson KC, Kennedy AG, Henry SM. Clinical measurements of lymphedema. Lymphat Res Biol. 2014 Dec;12(4):216-21.

16: Keast DH, Despatis M, Allen JO, Brassard A. Chronic oedema/lymphoedema: under-recognised and under-treated. Int Wound J. 2015 Jun;12(3):328-33.

17: Trayes KP, Studdiford JS, Pickle S, Tully AS. Edema: diagnosis and management. Am Fam Physician. 2013 Jul 15;88(2):102-10. PMID: 23939641.

EVIDENCE BASED STATEMENT

Domain 10; Statement 7

TEXT FOR INCLUSION IN THE DOCUMENT
(300 words, not counting the references)
DOMAIN 10, Statement 7, **TOPIC**: "**Lymphedema differential diagnosis**"

In order to perform a proper differential diagnosis first of all a proper lymphedema definition is needed: it can be identified as a chronic disease characterized by increased lymphatic fluid accumulation lasting for more than three months, causing swelling, leading to progressive tissue fibrosis and damage.
Histology is not providing any pathognomonic finding, but it may include dermal infiltration, hyperkeratosis, epidermal papillomatosis, dermal vessel walls hypertrophy, fibroblasts hyperplasia.
[**Li CY, Kataru RP, Mehrara BJ. Histopathologic Features of Lymphedema: A Molecular Review. Int J Mol Sci. 2020 Apr 6;21(7):2546**]
A detailed history and physical examination are mandatory for properly guiding the diagnosis.
Laboratory exams can identify eventual renal or hepatic causes of lymphedema, together with eventual infections.
Ultrasound scanning can detect a venous origin of the edema (chronic venous disease and/or thrombosis), while also depicting the subcutaneous fluid infiltration and the eventual lymphnodes involvement.
[**Todd M. Best practice: Doppler assessment in lymphoedema. Br J Community Nurs. 2016 Dec 2;21(12):612-613**].
Lymphoscintigarphy can confirm the diagnosis, while computed tomography and magnetic resonance can also identify causes of secondary lymphedema origin (masses) while investigating the soft tissue compromission.
Bioimpedance represents a valuable opportunity to measure in an objective way the fluid shift in the edema differential diagnosis
[**Polomska AK, Proulx ST. Imaging technology of the lymphatic system. Adv Drug Deliv Rev. 2021 Mar;170:294-311**]
Systemic causes of lower limb edema include idiopathic cyclic edema, heart/liver/renal failure and malnutrition states. Venous system insufficiency is tightly interconnected with the lymphatic system function and can mutually influence the limb drainage.
Infections, inflammatory states (for example arthritis), ischemia, lipedema, vascular malformations, tumors and trauma can lead to leg edema.
*[**Moffatt C, Franks P, Keeley V, et al. The Development and Validation of the LIMPRINT Methodology. Lymphat Res Biol. 2019 Apr;17(2):127-134**].
The heterogeneity of the above described clinical scenario clearly indicates the need of a multi-specialty approach.

EVIDENCE BASED STATEMENT

Domain 10; Statement 7

STATEMENT FOR PUBLIC EVIDENCE-BASED AWARENESS

DOMAIN 10, Statement 7

"In the diagnosis of lymphedema always exclude heart and renal conditions, malnutrion, malformations, tumors, lipedema, arterial and venous disease and post-traumatic swelling"

4 SELECTED REFEREENCES

1. Li CY, Kataru RP, Mehrara BJ. Histopathologic Features of Lymphedema: A Molecular Review. Int J Mol Sci. 2020 Apr 6;21(7):2546
2. Todd M. Best practice: Doppler assessment in lymphoedema. Br J Community Nurs. 2016 Dec 2;21(12):612-613
3. Polomska AK, Proulx ST. Imaging technology of the lymphatic system. Adv Drug Deliv Rev. 2021 Mar;170:294-311
4. Moffatt C, Franks P, Keeley V, et al. The Development and Validation of the LIMPRINT Methodology. Lymphat Res Biol. 2019 Apr;17(2):127-134

identified LITERATURE BIAS

Lack of precise methodology to discriminate between purely venous and lymphatic edema

SUGGESTED NEXT LINES OF RESEARCH

Identification of pathognomonic findings of venous vs lymphatic edema