

This is the peer reviewed version of the following article:

Secondary lymphatic insufficiency in chronic varicose veins / Manenti, Antonio; Farinetti, Alberto; Manco, Gianrocco; Mattioli, Anna Vittoria. - In: ANNALS OF VASCULAR SURGERY. - ISSN 0890-5096. - (2020), pp. 1-2. [10.1016/j.avsg.2020.08.099]

Terms of use:

The terms and conditions for the reuse of this version of the manuscript are specified in the publishing policy. For all terms of use and more information see the publisher's website.

01/05/2024 20:12

Correspondence

Secondary Lymphatic Insufficiency in Chronic Varicose Veins

Antonio **Manenti**

antonio.manenti@unimore.it

Alberto **Farinetti**

Gianrocco **Manco**

Department of Surgery, University of Modena, Polyclinic Hospital, Modena, Italy

Annavittoria **Mattioli**

Department of Cardiology, University of Modena, Polyclinic Hospital, Modena, Italy

To the Editor,

The interesting research of Sukirot et al.¹ offers an important contribution to understand the leg edema secondary to chronic venous stasis from varicose veins. Inside the pathophysiology of this complication, we recognize as relevant also the dysfunction of the lymphatic microcirculation. In fact, an increased pressure in the main venous trunks of the lower limbs directly reflects on the blood capillaries, favoring the leakage into the interstitial space of fluids, water, and solutes, but also of larger protein molecules, such as albumin, fibrinogen, and fibrin. Normally they move along ‘low-resistance’ ways, represented by the connective fibers of the interstitial tissue, toward the lymphatic capillaries. However, in condition of prolonged venous stasis, the abnormal amount of interstitial fluid and molecules exceeds the drainage capacity of this system, although in a first stage, the lymphatic capillaries enlarge, thanks to the compensatory mechanism activated by the stretched fibrils connected to their walls.²⁻⁴ Therefore, the pressure inside the lymphatic capillaries increases in a nonlinear relation, and beyond a physiological limit, hinders the lymph drainage. At the same time, the valves of the overloaded lymphatic precollectors lose their competence, further increasing the upstream congestion.⁵ This mechanism is self-feeding for the damage induced on the endothelial glycocalyx of the blood and lymphatic capillaries, which increase their permeability and the escape of large molecules. They, progressively accumulating in the interstitial tissue, decrease the osmotic gradient between capillaries and interstitial fluid.⁶ All these change the characteristics of the interstitial tissue environment, leading to an inflammatory-like condition, which becomes progressively more evident and irreversible.^{4,7} This cascade of pathological events outlines the edema as an important complication of the lower limb varicose veins. In the routine clinical practice, its evaluation can be performed through a careful study of the soft tissue by Doppler ultrasound, but, with a more precision and at an earlier stage, measuring the extracellular fluid resistance and content through a bioimpedance analysis.^{1,7}

References

1. K. Suchiro, N. Morikage, T. Harada, et al., Extracellular fluid content in the legs of patients with chronic venous disease, *Ann Vasc Surg* 2020, <https://doi.org/10.1016/j.avsg.2020.07.046>.
2. J.W. Breslin, Y. Yang, J.P. Scallan, et al., Lymphatic vessel network structure and physiology, *Compr Physiol* **9**, 2019, 207-299.
3. D. Negrini and A. Moriondo, Lymphatic anatomy and biomechanics, *J Physiol* **589**, 2011, 2927-2934.
4. H. Wiig and M.A. Swartz, Interstitial fluid and lymph formation and transport: physiological regulation and roles in inflammation and cancer, *Physiol Rev* **92**, 2012, 1005-1060.
5. B.O. Ikhimwin, C.D. Bertram, S. Jamalian, et al., A computational model of a network of initial lymphatics and pre-collectors with permeable interstitium, *Biomech Model Mechanobiol* **19**, 2020, 661-676.
6. O. Yilmaz, B. Afsar, A. Ortiz, et al., The role of endothelial glycocalyx in health and disease, *Clin Kidney J* **12**, 2019, 611-619.
7. A. Caggiati, Ultrasonography of skin changes in legs with chronic venous disease, *Eur J Vasc Endovasc Surg* **52**, 2016, 534-542.

Queries and Answers

Query: If there are any drug dosages in your article, please verify them and indicate that you have done so by initialing this query

Answer: No drug dosage in this article.

Query: Please update page range and volume number for the ref. [1].

Answer: Reference [1] concerns a paper still 'online ahead of print'.

Query: Refs. [4] and [7] were identical, the latter has been removed from the reference list and subsequent references have been renumbered.

Answer: I agree and thank you.

Query: Please confirm that given names and surnames have been identified correctly and are presented in the desired order and please carefully verify the spelling of all authors' names.

Answer: Yes