

EVIDENCE BASED STATEMENT

DOMAIN **04**, Statement **01**
TOPIC: “Deep venous pathophysiology”

SEARCH TERMS & SOURCES

((deep venous) AND (pathophysiology)) AND (lower limb) **INCLUSION CRITERIA**

- English language
- Reviews, Meta-analysis
- Publication < 10 years, only ENG

SEARCH RESULT BEFORE - AFTER SELECTION

53/13

PERTINENT LITERATURE NOT IDENTIFIED BY THE LITERATURE SEARCH

1. Luo P, Xu J, Cheng S, Xu K, et al. Large-scale genetic correlation scanning and causal association between deep vein thrombosis and human blood metabolites. *Sci Rep.* 2022 May 12;12(1):7888
2. Benfor B, Peden EK. A systematic review of management of superficial venous reflux in the setting of deep venous obstruction. *J Vasc Surg Venous Lymphat Disord.* 2022 Jan 20:S2213-333X(22)00003-8.
3. Navarrete S, Solar C, Tapia R, et al. Pathophysiology of deep vein thrombosis. *Clin Exp Med.* 2022 Apr 26.
4. Radaideh Q, Patel NM, Shammam NW. Iliac vein compression: epidemiology, diagnosis and treatment. *Vasc Health Risk Manag.* 2019 May 9;15:115-122
5. Kahn SR. The post-thrombotic syndrome. *Hematology Am Soc Hematol Educ Program.* 2016 Dec 2;2016(1):413-418.
6. Marston W, Fish D, Unger J, et al. Incidence of and risk factors for ilio caval venous obstruction in patients with active or healed venous leg ulcers. *J Vasc Surg.* 2011 May;53(5):1303-8
7. Musil D, Herman J. Prevalence and causes of reflux in deep venous system of the leg in patients with insufficiency of superficial veins. *Vnitr Lek.* 2006 Jun;52(6):596-601.
8. Labropoulos N, Tassiopoulos AK, Kang SS, et al. Prevalence of deep venous reflux in patients with primary superficial vein incompetence. *J Vasc Surg.* 2000 Oct;32(4):663-8.
9. Bradbury A, Evans CJ, Allan P, et al. The relationship between lower limb symptoms and superficial and deep venous reflux on duplex ultrasonography: The Edinburgh Vein Study. *J Vasc Surg.* 2000 Nov;32(5):921-31

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Domain 4; Statement 1

IDENTIFIED REFERENCES

1. Raffetto JD, Ligi D, Maniscalco R, et al. Why Venous Leg Ulcers Have Difficulty Healing: Overview on Pathophysiology, Clinical Consequences, and Treatment. *J Clin Med*. 2020 Dec 24;10(1):29.
2. Williams ZF, Dillavou ED. A systematic review of venous stents for iliac and venacaval occlusive disease. *J Vasc Surg Venous Lymphat Disord*. 2020 Jan;8(1):145-153.
3. Menon D, Onida S, Davies AH. Overview of venous pathology related to repetitive vascular trauma in athletes. *J Vasc Surg Venous Lymphat Disord*. 2019 Sep;7(5):756-762.
4. Naringrekar H, Sun J, Ko C, et al. It's Not All Deep Vein Thrombosis: Sonography of the Painful Lower Extremity With Multimodality Correlation. *J Ultrasound Med*. 2019 Apr;38(4):1075-1089.
5. Moustafa A, Alim HM, Chowdhury MA, et al. Postthrombotic Syndrome: Long-Term Sequela of Deep Venous Thrombosis. *Am J Med Sci*. 2018 Aug;356(2):152-158.
6. Shuster R, Mathew J, Olausen A, et al. Variables associated with pulmonary thromboembolism in injured patients: A systematic review. *Injury*. 2018 Jan;49(1):1-7.
7. Lee DK, Ahn KS, Kang CH, et al. Ultrasonography of the lower extremity veins: anatomy and basic approach. *Ultrasonography*. 2017 Apr;36(2):120-130.
8. Davies HO, Popplewell M, Singhal R, et al. Obesity and lower limb venous disease - The epidemic of phlebesity. *Phlebology*. 2017 May;32(4):227-233.
9. ten Cate-Hoek AJ, Henke PK, Wakefield TW. The post thrombotic syndrome: Ignore it and it will come back to bite you. *Blood Rev*. 2016 Mar;30(2):131-7.
10. Verma H, Tripathi RK. Algorithm-based approach to management of venous leg ulceration. *Semin Vasc Surg*. 2015 Mar;28(1):54-60.
11. Birn J, Vedantham S. May-Thurner syndrome and other obstructive iliac vein lesions: meaning, myth, and mystery. *Vasc Med*. 2015 Feb;20(1):74-83.
12. Ricci S, Moro L, Antonelli Incalzi R. The foot venous system: anatomy, physiology and relevance to clinical practice. *Dermatol Surg*. 2014 Mar;40(3):225-33.
13. Baldwin MJ, Moore HM, Rudarakanchana N, Gohel M, Davies AH. Post-thrombotic syndrome: a clinical review. *J Thromb Haemost*. 2013 May;11(5):795-805.

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TEXT FOR INCLUSION IN THE DOCUMENT

DOMAIN 04, Statement 01, TOPIC: “Deep venous pathophysiology”

Lower limb deep venous insufficiency can be caused by flow obstruction and/or by valve incompetence.

In the first case, an intraluminal thrombosis or external compression (tumor, anatomic variants, aneurysms, etc) can be identified as cause of deep reflux.

This latter can also be the consequence of the vein drainage volume overload by central causes (heart failure for example) and/or of the valve structure compromise by previous insults (thrombotic inflammation, scarring and adhesions).

Patients affected by an active or healed leg venous ulcer showed an ilio-caval obstruction in up to 37%. Risk factors independently associated with a >80% obstruction were female gender, previous deep venous thrombosis and deep reflux.

***[Marston W, Fish D, Unger J, et al. Incidence of and risk factors for ilio-caval venous obstruction in patients with active or healed venous leg ulcers. J Vasc Surg. 2011 May;53(5):1303-8]**

Prompt identification and proper management of deep venous thrombosis is of paramount importance to decrease the post-thrombotic syndrome risk, which is expected in 20% to 50% of patients, with 5% to 10% developing the most advanced stage, including ulceration. Principal risk factors for post-thrombotic syndrome are extensive thrombosis, recurrent ipsilateral events, persistent leg symptoms for more than 1 month after the diagnosis, obesity, and advanced age.

[Kahn SR. The post-thrombotic syndrome. Hematology Am Soc Hematol Educ Program. 2016 Dec 2;2016(1):413-418].

In the population affected by superficial venous reflux, a deep reflux has been reported in more than 40% of cases and mainly associated with obesity. Gender predominance has been reported in a heterogeneous way in the literature.

[Musil D, Herman J. Prevalence and causes of reflux in deep venous system of the leg in patients with insufficiency of superficial veins. Vnitr Lek. 2006 Jun;52(6):596-601].

The main localization of deep reflux in patients with primary superficial venous insufficiency is in the common femoral vein and it's of short duration: a possible explanation of the benefit of superficial reflux abolition on deep venous incompetence restoration.

[Labropoulos N, Tassiopoulos AK, Kang SS, et al. Prevalence of deep venous reflux in patients with primary superficial vein incompetence. J Vasc Surg. 2000 Oct;32(4):663-8].

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STATEMENT FOR PUBLIC EVIDENCE-BASED AWARENESS

DOMAIN 04, Statement 01

“Not only the superficial venous system must be assessed: deep veins of the leg can present a reflux because of spontaneous or post-thrombotic or post-trauma valve damage and/or vein obstruction.”

4 SELECTED REFERENCES

1. * Marston W, Fish D, Unger J, et al. Incidence of and risk factors for ilio caval venous obstruction in patients with active or healed venous leg ulcers. J Vasc Surg. 2011 May;53(5):1303-8
2. Kahn SR. The post-thrombotic syndrome. Hematology Am Soc Hematol Educ Program. 2016 Dec 2;2016(1):413-418
3. Musil D, Herman J. Prevalence and causes of reflux in deep venous system of the leg in patients with insufficiency of superficial veins. Vnitr Lek. 2006 Jun;52(6):596-601
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identified LITERATURE BIAS

Methodology and study population heterogeneity in epidemiology assessment.

SUGGESTED NEXT LINES OF RESEARCH

1. Multiracial CVD burden assessment
2. Obesity induced deep venous hypertension management