EVIDENCE BASED STATEMENT

DOMAIN 01, Statement 10

TOPIC: "venous thrombosis genetic predisposition burden"

SEARCH TERMS & SOURCES

inherited thrombophilia

INCLUSION CRITERIA

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

SEARCH RESULT BEFORE - AFTER SELECTION

214/33

PERTINENT LITERATURE NOT IDENTIFIED BY THE LITERATURE SEARCH

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2. Connors JM. Thrombophilia Testing and Venous Thrombosis. N Engl J Med. 2017 Sep 21;377(12):1177-1187.
3. Baglin T, Gray E, Greaves M, et al. Clinical guidelines for testing for heritable thrombophilia. Br J Haematol. 2010 Apr;149(2):209-20.
4. Roldan V, Lecumberri R, Munoz-Torrero JF, et al. Thrombophilia testing in patients with venous thrombo- embolism. Findings from the RIETE registry. *Thromb Res* 2009; 124: 174–177.
5. Buchanan GS, Rodgers GM, Branch DW. The inherited thrombophilias: genetics, epidemiology, and laboratory evaluation. Best Pract Res Clin Obst Gynecol. 2003. 138:128-34.
6. Seligsohn U, Lubetsky A. Genetic susceptibility to venous thrombosis. N Engl J Med. 2001 Apr 19;344(16):1222-31.
7. Maessen-Visch MB, Hamulyak K, Tazelaar DJ, et al. The prevalence of factor V Leiden mutation in patients with leg ulcers and venous insufficiency. Arch Dermatol. 1999 Jan;135(1):41-4

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IDENTIFIED REFERENCES

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2. Darlow J, Mould H. Thrombophilia testing in the era of direct oral anticoagulants. Clin Med (Lond). 2021 Sep;21(5):e487-e491.
3. Chopard R, Albertsen IE, Piazza G. Diagnosis and Treatment of Lower Extremity Venous Thromboembolism: A Review. JAMA. 2020 Nov 3;324(17):1765-1776.
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7. Dautaj A, Krasi G, Bushati V, et al. Hereditary thrombophilia. Acta Biomed. 2019 Sep 30;90(10-S):44-46.
8. Bravo-Pérez C, Vicente V, Corral J. Management of antithrombin deficiency: an update for clinicians. Expert Rev Hematol. 2019 Jun;12(6):397-405.
9. Trasca LF, Patrascu N, Bruja R, et al. Therapeutic Implications of Inherited Thrombophilia in Pregnancy. Am J Ther. 2019 May/Jun;26(3):e364-e374
10. Campello E, Spiezia L, Adamo A, Simioni P. Thrombophilia, risk factors and prevention. Expert Rev Hematol. 2019 Mar;12(3):147-158.
11. Carroll BJ, Piazza G. Hypercoagulable states in arterial and venous thrombosis: When, how, and who to test? Vasc Med. 2018 Aug;23(4):388-399.
12. Rybstein MD, DeSancho MT. Hypercoagulable States and Thrombophilias: Risks Relating to Recurrent Venous Thromboembolism. Semin Intervent Radiol. 2018 Jun;35(2):99-104.
13. Arachchillage DRJ, Makris M. Inherited Thrombophilia and Pregnancy Complications: Should We Test? Semin Thromb Hemost. 2019 Feb;45(1):50-60.
14. Montagnana M, Lippi G, Danese E. An Overview of Thrombophilia and Associated Laboratory Testing. Methods Mol Biol. 2017;1646:113-135.
15. Middeldorp S. Inherited thrombophilia: a double-edged sword. Hematology Am Soc Hematol Educ Program. 2016 Dec 2;2016(1):1-9.
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21. Franchini M, Martinelli I, Mannucci PM. Uncertain thrombophilia markers. Thromb Haemost. 2016 Jan;115(1):25-30.
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23. Bleker SM, Coppens M, Middeldorp S. Sex, thrombosis and inherited thrombophilia. Blood Rev. 2014 May;28(3):123-33.
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TEXT FOR INCLUSION IN THE DOCUMENT

DOMAIN 01, Statement 10, TOPIC: "venous thrombosis genetic predisposition burden"

Last decades have been characterized by a significant increase in the knowledge of inherited thrombophilia.

Inherited hypercoagulable states can be divided into 5 main categories:

1. qualitative or quantitative deficit of coagulation (for example, Antithrombin, Protein C, Protein S deficiency).
2. increased activity of coagulation factors (for example, Activated protein C resistance and factor V Leiden, Prothrombin gene mutation (G20210A)
3. hyperhomocysteinemia
4. fibrinolytic system deficit
5. altered platelet function.

[Seligsohn U, Lubetsky A. Genetic susceptibility to venous thrombosis. N Engl J Med. 2001 Apr 19;344(16):1222-31].

In the general population, the prevalence of inherited hypercoagulation is reported to be 1 in 2500-5000 subjects and it increases to more than 10% in patients with a past history of thrombosis.

[Darlow J, Mould H. Thrombophilia testing in the era of direct oral anticoagulants. Clin Med (Lond). 2021 Sep;21(5):e487-e491].

Due the multitude of variables, the real prevalence is yet to be identified.

A large registry evaluation reported at least 7% of the population presenting inherited thrombophilia. Interestingly, in this population no difference was reported between provoked and unprovoked thrombosis.

The most frequently encountered thrombophilia in the registry was Factor V Leiden (26%) followed by antiphospholipid antibodies (20%) and prothrombin gene mutation (18%).

[Roldan V, Lecumberri R, Munoz-Torrero JF, et al. Thrombophilia testing in patients with venous thrombo- embolism. Findings from the RIETE registry. *Thromb Res* 2009; 124: 174–177].

Sparse investigations dealt with the ethnical differences on inherited thrombophilia distribution. Further studies should be addressed to this topic.

In general, testing should be considered in subjects belonging to families with a significant <50 yo unprovoked VTE history.

Testing should not be performed in case of clearly provoked events and in case of no changes in the anticoagulation strategies associated with the test result.

***[Carroll BJ, Piazza G. Hypercoagulable states in arterial and venous thrombosis: When, how, and who to test? Vasc Med. 2018 Aug;23(4):388-399].**

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STATEMENT FOR PUBLIC EVIDENCE-BASED AWARENESS

DOMAIN 01, Statement 10: venous thrombosis genetic predisposition burden

"**Up to 8% of the population presents genetic predisposition to thrombosis**"

SELECTED REFEREENCES

1. **Seligsohn U, Lubetsky A. Genetic susceptibility to venous thrombosis. N Engl J Med. 2001 Apr 19;344(16):1222-31**
2. **Darlow J, Mould H. Thrombophilia testing in the era of direct oral anticoagulants. Clin Med (Lond). 2021 Sep;21(5):e487-e491**
3. **Roldan V, Lecumberri R, Munoz-Torrero JF, et al. Thrombophilia testing in patients with venous thrombo- embolism. Findings from the RIETE registry. *Thromb Res* 2009; 124: 174–177**
4. ***Carroll BJ, Piazza G. Hypercoagulable states in arterial and venous thrombosis: When, how, and who to test? Vasc Med. 2018 Aug;23(4):388-399**

identified LITERATURE BIAS

Possible selection bias in the study populations

SUGGESTED NEXT LINES OF RESEARCH

Multi-ethnicity inherited thrombophilia analysis