

EVIDENCE BASED STATEMENT

DOMAIN **06**, Statement **02**

TOPIC: “**Venous thrombosis Diagnostic Work-Up**”

SEARCH TERMS & SOURCES

((“venous thrombosis” OR “venous thromboembolism” OR “VTE”) AND (“diagnosis” OR “workup”) AND (“meta analysis” OR “systematic review”))

INCLUSION CRITERIA

Systematic review or meta-analysis
Focused on diagnosis from 2012 to 2022

SEARCH RESULT BEFORE - AFTER SELECTION

531 – 20

PERTINENT LITERATURE NOT IDENTIFIED BY THE LITERATURE SEARCH

1. Manganelli D, Palla A, Donnamaria V, et al. Clinical features of pulmonary embolism: doubts and certainties. Chest. 1995 Jan 1;107(1):25S-32S.
2. Silveira PC, Ip IK, Goldhaber SZ, et al. Performance of Wells score for deep vein thrombosis in the inpatient setting. JAMA internal medicine. 2015 Jul 1;175(7):1112-7.

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IDENTIFIED REFERENCES

1. Di Minno MN, Calcaterra I, et al. Diagnostic accuracy of D-Dimer testing for recurrent venous thromboembolism: A systematic review with meta-analysis.: VTE recurrence and D-dimer. *European Journal of Internal Medicine*. 2021 Apr 29.
2. Wang Q, Yuan L, Ding X, et al. Prediction and Diagnosis of Venous Thromboembolism Using Artificial Intelligence Approaches: A Systematic Review and Meta-Analysis. *Clinical and Applied Thrombosis/Hemostasis*. 2021 Jun 28;27:10760296211021162.
3. Stals MA, Takada T, Kraaijpoel N, et al. Safety and Efficiency of Diagnostic Strategies for Ruling Out Pulmonary Embolism in Clinically Relevant Patient Subgroups. *Annals of Internal Medicine*. 2021 Dec 14.
4. Bhatt M, Braun C, Patel P, et al. Diagnosis of deep vein thrombosis of the lower extremity: a systematic review and meta-analysis of test accuracy. *Blood advances*. 2020 Apr 14;4(7):1250-64.
5. Kraaijpoel N, Carrier M, Le Gal G, et al. Diagnostic accuracy of three ultrasonography strategies for deep vein thrombosis of the lower extremity: A systematic review and meta-analysis. *PLoS one*. 2020 Feb 11;15(2):e0228788.
6. Chopard R, Albertsen IE, Piazza G. Diagnosis and treatment of lower extremity venous thromboembolism: a review. *Jama*. 2020 Nov 3;324(17):1765-76.
7. Parpia S, Takach Lapner S, et al. Clinical pre-test probability adjusted versus age-adjusted D-dimer interpretation strategy for DVT diagnosis: A diagnostic individual patient data meta-analysis. *Journal of Thrombosis and Haemostasis*. 2020 Mar;18(3):669-75.
8. Takada T, van Doorn S, Parpia S, et al. Diagnosing deep vein thrombosis in cancer patients with suspected symptoms: An individual participant data meta-analysis. *Journal of Thrombosis and Haemostasis*. 2020 Sep;18(9):2245-52.
9. Patel P, Braun C, Patel P, et al. Diagnosis of deep vein thrombosis of the upper extremity: a systematic review and meta-analysis of test accuracy. *Blood advances*. 2020 Jun 9;4(11):2516-22.
10. Lee JH, Lee SH, Yun SJ. Comparison of 2-point and 3-point point-of-care ultrasound techniques for deep vein thrombosis at the emergency department: a meta-analysis. *Medicine*. 2019 May;98(22).
11. Lim W, Le Gal G, Bates SM, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: diagnosis of venous thromboembolism. *Blood advances*. 2018 Nov 27;2(22):3226-56.
12. Nybo M, Hvas AM. Age-adjusted D-dimer cut-off in the diagnostic strategy for deep vein thrombosis: a systematic review. *Scandinavian journal of clinical and laboratory investigation*. 2017 Nov 17;77(8):568-73.
13. van Es N, van der Hulle T, van Es J, et al. Wells rule and D-dimer testing to rule out pulmonary embolism: a systematic review and individual-patient data meta-analysis. *Annals of internal medicine*. 2016 Aug 16;165(4):253-61.
14. Da Costa Rodrigues J, Alzuphar S, Combescure C, et al. Diagnostic characteristics of lower limb venous compression ultrasonography in suspected pulmonary embolism: a meta-analysis. *Journal of Thrombosis and Haemostasis*. 2016 Sep;14(9):1765-72.
15. Abdalla G, Matuk RF, Venugopal V, et al. The diagnostic accuracy of magnetic resonance venography in the detection of deep venous thrombosis: a systematic review and meta-analysis. *Clinical radiology*. 2015 Aug 1;70(8):858-71.
16. Geersing GJ, Zuithoff NP, Kearon C, et al. Exclusion of deep vein thrombosis using the Wells rule in clinically important subgroups: individual patient data meta-analysis. *Bmj*. 2014 Mar 10;348.
17. Schouten HJ, Geersing GJ, Koek HL, et al. Diagnostic accuracy of conventional or age adjusted D-dimer cut-off values in older patients with suspected venous thromboembolism: systematic review and meta-analysis. *Bmj*. 2013 May 3;346.
18. Pomero F, Dentali F, Borretta V, et al. Accuracy of emergency physician-performed ultrasonography in the diagnosis of deep-vein thrombosis. *Thrombosis and haemostasis*. 2013;109(01):137-45.
19. Xiang Q, Zhang HX, Wang Z, et al. The predictive value of circulating microRNAs for venous thromboembolism diagnosis: A systematic review and diagnostic meta-analysis. *Thrombosis research*. 2019 Sep 1;181:127-34.
20. Zhang Y, Begum HA, Grewal H, et al. Cost-effectiveness of diagnostic strategies for venous thromboembolism: a systematic review. *Blood advances*. 2021 Oct 6.

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TEXT FOR INCLUSION IN THE DOCUMENT

DOMAIN 06, Statement 02, TOPIC: “Venous thrombosis Diagnostic Work-Up”

For patients with clinically suspected VTE but no personal history of VTE, the rate of VTE diagnosis is just 20%. Therefore, diagnostic work-up for VTE must balance the importance of ruling out this highly morbid condition with the need to minimize excessive diagnostic investigations for low-risk patients. The symptoms with the highest predictive value for lower extremity DVT are swelling, cramping, or discomfort in the thigh or calf. Other common symptoms include warmth (calor), erythema (rubor), a palpable cord, and visibly bulging leg veins (**Chopard R, Albertsen IE, Piazza G. Diagnosis and treatment of lower extremity venous thromboembolism: a review. Jama. 2020 Nov 3;324(17):1765-76**). Symptoms for PE are less specific, but include tachypnea, tachycardia, shortness of breath, chest pain, and hemoptysis (**Manganelli D, Palla A, Donnataria V, et al. Clinical features of pulmonary embolism: doubts and certainties. Chest. 1995 Jan 1;107(1):25S-32S**).

Clinicians should rely on validated clinical decision tools, such as the Wells (DVT or PE) and Geneva (PE) Scores, that evaluate patient symptoms and physical examination findings to determine pre-test probability of DVT or PE. In patients with low pre-test probability of DVT or PE, age-adjusted D-dimer is a highly sensitive test to rule out a diagnosis, but it lacks specificity to confirm diagnosis (***Bhatt M, Braun C, Patel P, et al. Diagnosis of deep vein thrombosis of the lower extremity: a systematic review and meta-analysis of test accuracy. Blood advances. 2020 Apr 14;4(7):1250-64**). The exceptions to this rule are hospitalized patients and patients with a history of DVT or PE, in whom the Wells and Geneva scores have not been validated for predicting VTE. Therefore, these patients should undergo duplex imaging to rule out deep venous thrombosis when suspected (**Lim W, Le Gal G, Bates SM, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: diagnosis of venous thromboembolism. Blood advances. 2018 Nov 27;2(22):3226-56**).

In patients with intermediate-to-high pre-test probability of DVT or elevated D-dimer, compression ultrasonography of the extremity is the preferred diagnostic test, as it is both sensitive and highly specific. However, venography remains the gold standard for DVT diagnosis and is much more accurate in patients without DVT symptoms. For patients with intermediate-to-high pre-test probability of PE or elevated D-dimer, CT pulmonary angiography and ventilation-perfusion scans are the diagnostic approaches of choice. In cancer patients with suspected DVT, compression ultrasonography is the first-line diagnostic modality (**Chopard R, Albertsen IE, Piazza G. Diagnosis and treatment of lower extremity venous thromboembolism: a review. Jama. 2020 Nov 3;324(17):1765-76**).

It is debatable and better to be excluded. DUS is a gold standard for DVT confirmation according to all guidelines.

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STATEMENT FOR PUBLIC EVIDENCE-BASED AWARENESS

DOMAIN 06, Statement 02

“Symptoms of a deep venous thrombosis in the arms or legs include pain, swelling, redness, tenderness, fever, bulging veins, and skin discoloration. Symptoms of a pulmonary embolism include chest pain, fast heart rate, coughing up blood, and shortness of breath”.

4 SELECTED REFERENCES

1. *Bhatt M, Braun C, Patel P, Patel P, Begum H, Wiercioch W, Varghese J, Wooldridge D, Alturkmani HJ, Thomas M, Baig M. Diagnosis of deep vein thrombosis of the lower extremity: a systematic review and meta-analysis of test accuracy. Blood advances. 2020 Apr 14;4(7):1250-64.
2. Chopard R, Albertsen IE, Piazza G. Diagnosis and treatment of lower extremity venous thromboembolism: a review. Jama. 2020 Nov 3;324(17):1765-76.
3. Lim W, Le Gal G, Bates SM, Righini M, Haramati LB, Lang E, Kline JA, Chasteen S, Snyder M, Patel P, Bhatt M. American Society of Hematology 2018 guidelines for management of venous thromboembolism: diagnosis of venous thromboembolism. Blood advances. 2018 Nov 27;2(22):3226-56.
4. Manganelli D, Palla A, Donnamaria V, Giuntini C. Clinical features of pulmonary embolism: doubts and certainties. Chest. 1995 Jan 1;107(1):25S-32S.

identified LITERATURE BIAS

Many risk scores specifically exclude patients with a personal history of VTE from consideration.

SUGGESTED NEXT LINES OF RESEARCH

Future research should consider the most sensitive tools to rule out recurrent VTE among hospitalized patients and patients with prior VTE.