EVIDENCE BASED STATEMENT

DOMAIN 06, Statement 09

TOPIC: "**Anticoagulation therapy indication and contra-indication**"

SEARCH TERMS & SOURCES

("venous thrombosis" OR "venous thromboembolism" OR "VTE" OR "DVT") AND
("anticoagulation" OR "anti-coagulation") AND (indication OR contraindication) AND ("meta analysis" OR "systematic review" OR "guidelines")

INCLUSION CRITERIA

Systematic review or meta-analysis (2012-2022)
Focused on anticoagulation for VTE
Last ten years

SEARCH RESULT BEFORE - AFTER SELECTION

200 – 20

PERTINENT LITERATURE NOT IDENTIFIED BY THE LITERATURE SEARCH

1. *Stevens SM, Woller SC, Kreuziger LB, et al. Antithrombotic therapy for VTE disease: second update of the CHEST guideline and expert panel report. Chest. 2021 Dec 1;160(6):e545-608
2. Brenner B, Hull R, Arya R, et al Evaluation of unmet clinical needs in prophylaxis and treatment of venous thromboembolism in high-risk patient groups: cancer and critically ill. Thromb J. 2019 Apr 15;17:6.
3. Mai V, Guay CA, Perreault L, et al. Extended anticoagulation for VTE: a systematic review and meta-analysis. Chest. 2019 Jun 1;155(6):1199-216.
4. Kearon C, Akl EA, Ornelas J, Bet al. Antithrombotic therapy for VTE disease: CHEST guideline and expert panel report. Chest. 2016 Feb 1;149(2):315-52.
5. Lyman GH, Khorana AA, Kuderer NM, et al; American Society of Clinical Oncology Clinical Practice. Venous thromboembolism prophylaxis and treatment in patients with cancer: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol. 2013 Jun 10;31(17):2189-204. doi: 10.1200/JCO.2013.49.1118. Epub 2013 May 13. PMID: 23669224.

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IDENTIFIED REFERENCES

1. Nisly SA, Mihm AE, Gillette C, et al. Safety of direct oral anticoagulants in patients with mild to moderate cirrhosis: a systematic review and meta-analysis. J Thromb Thrombolysis. 2021 Oct;52(3):817-827.
2. Ortega-Paz L, Galli M, Capodanno D, et al. Safety and efficacy of different prophylactic anticoagulation dosing regimens in critically and non-critically ill patients with COVID-19: A systematic review and meta-analysis of randomized controlled trials. Eur Heart J Cardiovasc Pharmacother. 2021 Sep 14:pvab070.
3. Cheung CY, Parikh J, Farrell A, et al. Direct oral anticoagulant use in chronic kidney disease and dialysis patients with venous thromboembolism: a systematic review of thrombosis and bleeding outcomes. Annals of Pharmacotherapy. 2021 Jun;55(6):711-22.
4. Verso M, Di Nisio M. Management of venous thromboembolism in cancer patients: Considerations about the clinical practice guideline update of the American society of clinical oncology. Eur J Intern Med. 2020 Jan;71:4-7.
5. Aursulesei V, Costache II. Anticoagulation in chronic kidney disease: from guidelines to clinical practice. Clinical Cardiology. 2019 Aug;42(8):774-82.
6. Tran HA, Gibbs H, Merriman E, et al. New guidelines from the Thrombosis and Haemostasis Society of Australia and New Zealand for the diagnosis and management of venous thromboembolism. Med J Aust. 2019 Mar;210(5):227-235.
7. Ha JT, Neuen BL, Cheng LP, et al. Benefits and Harms of Oral Anticoagulant Therapy in Chronic Kidney Disease: A Systematic Review and Meta-analysis. Ann Intern Med. 2019 Aug 6;171(3):181-189.
8. Tritschler T, Kraaijpoel N, Le Gal G, et al. Venous Thromboembolism: Advances in Diagnosis and Treatment. JAMA. 2018 Oct 16;320(15):1583-1594.
9. Miller CS, Dorreen A, Martel M, et al. Risk of Gastrointestinal Bleeding in Patients Taking Non-Vitamin K Antagonist Oral Anticoagulants: A Systematic Review and Meta-analysis. Clin Gastroenterol Hepatol. 2017 Nov;15(11):1674-1683.e3.
10. Sterne JA, Bodalia PN, Bryden PA, et al. Oral anticoagulants for primary prevention, treatment and secondary prevention of venous thromboembolic disease, and for prevention of stroke in atrial fibrillation: systematic review, network meta-analysis and cost-effectiveness analysis. Health Technol Assess. 2017 Mar;21(9):1-386.
11. Altiok E, Marx N. Oral Anticoagulation. Dtsch Arztebl Int. 2018 Nov 16;115(46):776-783.
12. Dorobantu M, Bogdan S. Unfractionated heparin or low-molecular-weight heparin in the elderly. Int J Cardiol. 2016 Nov 1;222:1084-1090.
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15. Cohen AT, Hamilton M, Mitchell SA, et al Comparison of the Novel Oral Anticoagulants Apixaban, Dabigatran, Edoxaban, and Rivaroxaban in the Initial and Long-Term Treatment and Prevention of Venous Thromboembolism: Systematic Review and Network Meta-Analysis. PLoS One. 2015 Dec 30;10(12):e0144856.
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18. Toth PP. Direct oral anticoagulants as alternative treatment options for the effective long-term treatment of patients with pulmonary embolism in primary care: a review. Ann Med. 2014 Sep;46(6):341-52.
19. Farge D, Debourdeau P, Beckers M, et al. International clinical practice guidelines for the treatment and prophylaxis of venous thromboembolism in patients with cancer. J Thromb Haemost. 2013 Jan;11(1):56-70.
20. Perez A, Merli GJ. Novel anticoagulant use for venous thromboembolism: a 2013 update. Curr Treat Options Cardiovasc Med. 2013 Apr;15(2):164-72.

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TEXT FOR INCLUSION IN THE DOCUMENT

DOMAIN 06, Statement 09, TOPIC: "**Anticoagulation therapy indication and contra-indication**"

Patients with VTE may be anticoagulated with warfarin (vitamin K antagonist), unfractionated heparin, low molecular weight heparin (LMWH), fondaparinux, or direct oral anticoagulants (DOACs). All patients starting anticoagulation should undergo assessment of their CBC, renal and liver function tests, INR, and PTT (**Kearon C, Akl EA, Ornelas J, Bet al. Antithrombotic therapy for VTE disease: CHEST guideline and expert panel report. Chest. 2016 Feb 1;149(2):315-52**). DOACs are generally contraindicated in patients with creatinine clearance below 30-15 mL/min or significant liver disease. DOACs are first line medications for DVT and PE (***Stevens SM, Woller SC, Kreuziger LB, et al. Antithrombotic therapy for VTE disease: second update of the CHEST guideline and expert panel report. Chest. 2021 Dec 1;160(6):e545-608**). Risk factors for bleeding on anticoagulation include advanced age, bleeding history, cancer, renal or liver failure, thrombocytopenia, stroke, diabetes, anemia, antiplatelet therapy, surgery, falls, alcohol abuse, and NSAIDs. Patients with a DVT in the setting of active bleeding can instead receive an retrievable inferior vena cava filter to prevent embolization to the pulmonary arteries (**Kearon C, Akl EA, Ornelas J, Bet al. Antithrombotic therapy for VTE disease: CHEST guideline and expert panel report. Chest. 2016 Feb 1;149(2):315-52**). Randomized controlled trials in patients with cancer have clearly demonstrated that low molecular weight heparin (LMWH) is superior to warfarin in this patient population. Similarly, oral factor Xa inhibitors (apixaban, edoxaban, rivaroxaban) have lower risk of recurrent VTE compared to warfarin (RR 0.62) without increased major bleeding events. Notably, edoxaban and rivaroxaban may increase gastrointestinal (GI) bleeding in patients with luminal GI malignancies. Current guidelines for cancer patients recommend treatment an oral factor Xa inhibitor over LMWH or warfarin, provided the patient is a candidate for anticoagulation and has a creatinine clearance of greater than 30 mL/min. Treatment should continue for at least 6 months. If patients have a recurrent VTE while on anticoagulation, they should either change their dose or change their medication regimen (**Brenner B, Hull R, Arya R, et al Evaluation of unmet clinical needs in prophylaxis and treatment of venous thromboembolism in high-risk patient groups: cancer and critically ill. Thromb J. 2019 Apr 15;17:6.**
; **Lyman GH, Khorana AA, Kuderer NM, et al; American Society of Clinical Oncology Clinical Practice. Venous thromboembolism prophylaxis and treatment in patients with cancer: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol. 2013 Jun 10;31(17):2189-204**; **Stevens SM, Woller SC, Kreuziger LB, et al. Antithrombotic therapy for VTE disease: second update of the CHEST guideline and expert panel report. Chest. 2021 Dec 1;160(6):e545-608**).

Critically ill patients are at high risk of VTE and should be treated with LMWH if they develop VTE, as this has a lower risk of heparin-induced thrombocytopenia. If patients are at risk of bleeding, IVC filters or unfractionated heparin (given its short half life) can be considered (**Brenner B, Hull R, Arya R, et al Evaluation of unmet clinical needs in prophylaxis and treatment of venous thromboembolism in high-risk patient groups: cancer and critically ill. Thromb J. 2019 Apr 15;17:6**).

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STATEMENT FOR PUBLIC EVIDENCE-BASED AWARENESS

DOMAIN 06, Statement 09

Before starting anticoagulation (blood thinner) therapy, all patients should have a thorough laboratory workup. Patients with severe kidney disease can use warfarin for anticoagulation. Patients with cancer also need a laboratory workup, and may be eligible for treatment with oral anticoagulants or low molecular weight heparin (LMWH).

Why? Apixaban has the same limitation as rivaroxaban of ClCr less 15 mL/min

4 SELECTED REFEREENCES

1. Brenner B, Hull R, Arya R, et al. Evaluation of unmet clinical needs in prophylaxis and treatment of venous thromboembolism in high-risk patient groups: cancer and critically ill. Thromb J. 2019 Apr 15;17:6.
2. Kearon C, Akl EA, Ornelas J, et al. Antithrombotic therapy for VTE disease: CHEST guideline and expert panel report. Chest. 2016 Feb 1;149(2):315-52.
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4. *Stevens SM, Woller SC, Kreuziger LB, et al. Antithrombotic therapy for VTE disease: second update of the CHEST guideline and expert panel report. Chest. 2021 Dec 1;160(6):e545-608.

identified LITERATURE BIAS

Minimal given large number of adequately-powered studies of VTE treatment.

SUGGESTED NEXT LINES OF RESEARCH

Role of factor Xia inhibitors in treatment and prevention of VTE.