Research – Venous Thromboembolism (Deep Vein Thrombosis and Pulmonary Embolism): Evidence Based Treatment

Brief	Evidence Based Treatments for ***Venous Thromboembolism (Deep Vein Thrombosis and Pulmonary Embolism)***
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The Research Team are unable to ensure that the information listed below provides an accurate & up-to-date snapshot of these matters.

1 Contents

2 Summary

- ***Venous Thromboembolism*** (VTE) is a disease which includes ***Deep Vein Thrombosis*** (DVT) and ***Pulmonary Embolism*** (PE). DVT and PE are both forms of VTE, but they're not the same condition
- The treatment for DVT depends on its anatomical extent (proximal or distal)
- Initial treatment for DVT are anticoagulation medications used to prevent blood clots
- Severe VTE requires additional invasive/surgical measures

3 Introduction

This document summarizes the evidence based research detailed in the 2019 guidelines produced by the Thrombosis and Haemostasis Society of Australia and New Zealand (THANZ) which aims to promote evidence based optimal management of VTE [1, 2].

In the development of the guidelines, a Venous Thromboembolism (VTE) writing group was established within THANZ and comprised of experts in the field of thromboembolic disorders in Australian and New Zealand. All members undertook a detailed literature review and critically appraised existing evidence on the diagnosis and treatment of VTE. Drafts of evidence-based recommendations, practice points and a background manuscript were developed. The recommendations follow the National Health and Medical Research Council levels of evidence and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system to determine the strength of the recommendations [1].

4 What is Venous Thromboembolism (VTE)?

VTE is a chronic and frequently recurrent disease that includes deep vein thrombosis (DVT) and pulmonary embolism (PE). DVT and PE are both forms of VTE, but are not the same thing [3]. It is a potentially preventable disease, however, can result in complications such as post-thrombotic syndrome, pulmonary hypertension, recurrent thrombosis, or death.

In DVT a blood clot usually forms in the deep veins of the calf, thigh, or pelvis which may or may not cause symptoms such as swelling, redness or pain. In some people, clots resolve spontaneously, however there is a risk that some or all of the clot may break away and travel to the lungs, resulting in PE. This can cause respiratory symptoms, heart failure or death [4].

VTE can be fatal if untreated; long term morbidity includes post-thrombotic syndrome (PTS) and pulmonary hypertension. Symptoms of VTE are non-specific, and the diagnosis should actively be sought once considered. A diagnosis of VTE has an impact on subsequent pregnancies, oestrogen use, surgery, life insurance and, occasionally, long-haul travel [5].

VTE is the third most common cardiovascular disease, with an annual incidence of more than 10 million people globally [6]. In Australia, at least 17,000 people develop VTE each year (annual incidence, 0.83 per 1,000 population) [7]. The lifetime risk of VTE is 8%, with 1% of people aged over 80 years experiencing their first VTE. This disease is a major cause of health-related economic loss for patient's and the community (estimated to be $1.7 billion for Australia in 2008) [8].

5 Treatment of Venous Thromboembolism

5.1 Overview

- The spectrum of VTE ranges from distal DVT, which may not require anticoagulation (medications that help prevent blood clots), through to proximal DVT to potentially life-threatening PE requiring additional invasive strategies. The treatment for DVT depends on its anatomical extent: in proximal DVT, thrombus is present in the popliteal (and its trifurcation) or a more proximal vein; in distal DVT, thrombus only occurs in the tibial, peroneal, gastrocnemius and soleal veins [9].

- Anticoagulation is indicated in most cases of VTE because it is highly effective in preventing thrombus extension or recurrence by at least 80% [10].

5.2 Anticoagulant therapy for deep vein thrombosis and pulmonary embolism

- Direct oral anticoagulants (DOACs) and warfarin are equally effective and can be prescribed to most patients. GRADE: Strong; Evidence: High [10, 11].

- DOACs do not require routine monitoring, have no known food interactions and few drug interactions, and are favoured in most instances. However, DOACs should not be used during pregnancy or breastfeeding, in which case low molecular weight heparin is indicated [10].

- Edoxaban and rivaroxaban have been shown to be as efficacious as dalteparin in cancer-related thrombosis, but are associated with an increased risk for major bleeding or clinically relevant non-major bleeding (CRNMB) and, therefore, can be considered when appropriate [12, 13].

- Oral factor Xa inhibitors (eg, apixaban, rivaroxaban) are preferred to dabigatran or warfarin to treat proximal DVT and PE because they do not require parenteral anticoagulation for initiation. GRADE: Strong; Evidence: High [10].

5.2.1 Duration of anticoagulation

5.2.1.1 Proximal deep vein thrombosis and pulmonary embolism

- All patients with proximal DVT and PE should receive anticoagulant therapy for at least 3 months. GRADE: Strong; Evidence: Strong [10].

- Patients whose proximal DVT or PE were provoked by major surgery or major trauma can cease anticoagulation at this time [10].

5.2.1.2 Distal deep vein thrombosis

- Uncertainty exists about the value of anticoagulation for distal DVT. In general, anticoagulation is used for proximal DVT and PE, but serial duplex ultrasound (two duplex ultrasound scans over 2 weeks) is reasonable (GRADE: Strong; Evidence: Moderate), especially if the risk of bleeding is increased. Most distal DVT can be treated for 6 – 12 weeks. GRADE: Strong; Evidence: Moderate [14].

5.2.1.3 Extended anticoagulation for deep vein thrombosis and pulmonary embolism (beyond 3–6 months)

- For patients whose events were unprovoked or associated with transient risk factors (non-surgical), decide whether to stop or to continue with extended anticoagulant therapy after 3 months of anticoagulation. Continuing therapy for longer than 3 months reduces the risk of VTE recurrence during therapy by at least 80% but is associated with a major bleeding risk of < 1% per year. Once anticoagulant therapy is stopped, the risk of recurrence is the same as for patients who cease treatment after 3 – 6months when followed up over time [13].

- Aspirin (100 mg daily) reduces the rate of VTE recurrence to a much lesser extent than oral anticoagulants but is associated with similar rates of bleeding to rivaroxaban 10 mg daily [15, 16]. Therefore, aspirin should be avoided, unless anticoagulation cannot be used. GRADE: Strong; Evidence: High

6 Invasive strategies for VTE management

- Invasive treatment modalities for acute removal of thrombosis have been investigated, with the goals of rapidly relieving acute right ventricular pressure overload in PE and thereby improving survival or rapidly relieving venous obstruction to prevent vein dysfunction and PTS and reduce VTE recurrence [5].

- The following strategies have been investigated with variable results [17-20]:
    - Systemic administration of thrombolytic agents
    - Catheter-directed thrombolysis, which uses lower thrombolytic doses with or without the addition of mechanical clot disruption
    - Acute surgical thrombectomy

7. References

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