New recommendations for the prophylaxis of venous thromboembolism in stroke patients

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Abstract

Deep venous thrombosis (DVT) is one of the most important, potentially preventable, causes of death and morbidity. Stroke confers a high risk of DVT (8-20%) in the absence of prophylactic treatment. Magnetic resonance studies show DVT in 40% of stroke patients, and in 18% of patients within 3 weeks of stroke. Colour Doppler ultrasound (CDU) reveals asymptomatic DVT in 18% of stroke patients.

Guidelines advise the routine assessments of risk of DVT on hospital admission for stroke, and initiation of prophylaxis especially in high-risk patients. Risk factors for DVT after stroke are the stroke severity, whenever immobility is present, as well as some comorbidities such as cardiac heart disease, cancer, increased body weight index, and the presence of elevated D-dimers.

A review of 22 trials with low molecular weight heparin (LMWH) in ischemic stroke showed that, per 1000 patients, it can avoid 9 deaths, 3 pulmonary embolism (PE), 1 symptomatic DVT, although causing 6 major bleedings.

Non-pharmacological measures aiming prophylaxis of venous thromboembolism (VTE) in stroke patients have been investigated in the last years. In CLOTS Trial 1, 2518 immobile stroke patients were allocated thigh-length graduated compression stockings or not, and, in CLOTS Trial 2, 3014 to thigh-length or below-knee graduated compression stockings. In both trials there were no statistically significant differences in VTE events and compression stockings increased the risk of skin breaks. Allocation to thigh-length graduated compression stockings was associated with a nonsignificant increased hazard of death in the first 6 months.

Intermittent pneumatic compression (IPC) has been developed to prevent DVT in stroke patients. A sequential compression allows increasing venous flow through the deep veins of the leg to reduce the likelihood of thrombosis, while it stimulates release of intrinsic fibrinolytic substances.

In intracranial hemorrhage (ICH), a meta-analysis of anticoagulant drugs for thromboprophylaxis that included 1000 ICH patients from 4 trials (2 randomized), revealed that the early use of enoxaparin or heparin (from 1 to 6 days after admission) could reduce PE (1.7% versus 2.9%), having a non-significant effect on mortality reduction (16.1% versus 20.9%), hematoma enlargement (8.0% versus 4.0%) or DVT (4.2% versus 3.3%).

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outcome was DVT in the popliteal or femoral veins within 30 days of randomisation, either asymptomatic as detected on the first or second CDU performed as part of the trial protocol, or symptomatic DVT confirmed on imaging (either CDU or venography). The compression system used in this trial delivered a sequential circumferential compression and incorporated a venous refill technology so that the frequency of compression was tailored to the individual patient. The trial included 2876 acute stroke patients, 376 with ICH. Patients were allocated in a 1:1 basis to routine treatment or routine treatment plus IPC. The routine treatment included in each group 17% patients receiving prophylactic dose and about 14% patients receiving full-dose of anticoagulants. The IPC group had 3.6% less absolute risk of DVT (12.1% vs 8.5%), and a 34% risk reduction when adjusting for confounding factors. This effect was particularly prominent in ICH patients (6.7% versus 17.0% DVT cases). The Cox model showed a reduced probability for death up to 6 months after randomisation in those allocated IPC.

In secondary analyses from CLOTS 3, namely regarding cost-effectiveness of ICP, it was shown that IPC is inexpensive, prevents deep vein thrombosis, improves survival but not functional outcomes, and does not lead to a significant gain in quality-adjusted survival.

The current European Stroke Organization (ESO) recommendations to improve outcome and reduce the risk of DVT in immobile patients with intracranial hemorrhage are against short or long graduated compression stockings, and in favor of IPC; it is pointed that there is insufficient evidence from randomized controlled trials to make strong recommendations about how, when, and for whom anticoagulation should be given to prevent DVT or improve outcome.

Concerning ESO guidelines for prophylaxis of VTE in immobile patients with acute ischaemic stroke, it is also recommended that graduated compression stockings should not be used, while IPC (thigh-length, sequential) and prophylactic-dose anticoagulation can reduce the risk of VTE in those patients, the strongest evidence being for IPC. IPC should not be used in patients with open wounds on the legs and should be used with caution in those with existing DVT, heart failure, severe peripheral vascular disease or confusion where attempts to mobilise when unsupervised could lead to falls and injury. Prophylactic anticoagulation with unfractionated heparin (5000U, 2 or 3 daily), LMWH or heparinoid should be considered in patients whom the benefits of reducing the risk of VTE is high enough to offset the increased risks of intracranial and extracranial bleeding associated with their use.

ESO guidelines state that further research is required to test whether neuromuscular electrical stimulation is effective. Additionally, it is highlighted that better methods are needed to define which stroke patients are at high enough risk of VTE acutely, or during later phases of care, to warrant prophylaxis, as well as to stratify their risk of bleeding on anticoagulants.