Venous thromboembolism prevention in lower limb trauma – Can we do better?

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Venous thromboembolism prevention in lower limb trauma – Can we do better?

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Trauma is one of the principal causes of death in young people. Each year approximately five million people die as a result of trauma worldwide, responsible for a loss of more than 100 million disability-adjusted life years, a greater loss than that due to all malignant neoplasms combined [1]. In patients who survive beyond the first day, venous thromboembolism (VTE) is a leading cause of preventable mortality [2]. Trauma patients with lower limb fracture are at especially high risk; fracture of the femur or tibia is an independent risk factor for DVT (odds ratio [OR], 4.82; 95% confidence interval [CI], 2.79-8.33) [3]. The incidence of pulmonary embolism (PE) is estimated at between 1.5% and 20%, while the incidence of deep vein thrombosis (DVT) is estimated at between 11.8% and 65% [4]. Although the risk of VTE is clearly heterogeneously distributed amongst the trauma population, these patients are often also at an increased risk of bleeding, with accompanying concerns relating to the use of pharmacological thromboprophylaxis. Additionally, mechanical compression can often be contraindicated in the context of lower limb trauma. These considerations make the optimal method of preventing VTE in this population an important and challenging issue.

The heterogeneous distribution of VTE risk in lower limb trauma is due to a combination of patient-related and injury-related factors. Trauma itself results in a systemic pro-inflammatory and pro-thrombotic state; associated comorbidities, prolonged immobilisation, concomitant spinal or head trauma, and surgical repair of venous injury all contribute and fundamentally exert a pro-thrombotic effect via all arms of Virchow's eponymous triad.

Whilst the risk of VTE is high, there are also concerns about the risk of bleeding in these patients, and the use of pharmacological prophylaxis has been demonstrated to significantly increase bleeding risk (RR 2.04; 95% CI 1.08 to 3.86) [4]. In trials that distinguish between

major and minor bleeding, current evidence only supports an increased risk of minor (RR 2.37; 95% CI 1.13 to 4.98) rather than major (RR 1.03; 95% CI 0.26 to 4.06) bleeding; major bleeding being defined as "use of transfusion or any procedure to control bleeding"[4]. Whilst it is well known that trauma patients are at high risk of bleeding, research has predominantly focused on the point of presentation and probability of requiring massive transfusion. Absolute risk and risk factors for delayed bleeding – that which occurs during admission and thus central to thromboprophylaxis decisions – have not been well investigated and thus make weighing the risks and benefits of prescribing anticoagulation extremely challenging.

The National Institute for Health and Care Excellence (NICE) recommends the use of pharmacological prophylaxis in trauma patients where the risk of VTE outweighs the risk of bleeding [5]. Pharmacological prophylaxis is well established in reducing the risk of VTE, being superior to mechanical prophylaxis alone in preventing DVT (RR 0.48; 95% CI 0.25 to 0.95) and with LMWH being more effective than unfractionated heparins (UH) (RR 0.68; 95% CI 0.50 to 0.94) [4]. The challenge when using these agents, therefore, relates to the individual patient thrombotic and bleeding risk assessment.

Mechanical prophylaxis, such as graduated compression and intermittent pneumatic compression, are established in their ability to reduce the risk of DVT when used alone in trauma patients (RR 0.55; 95% CI 0.34 to 0.90) [4], and to have a superior effect when combined with pharmacological prophylaxis versus pharmacological prophylaxis alone (RR 0.34; 95% CI 0.19 to 0.60) [4]. However, these methods are contraindicated in lower extremity trauma due to detrimental effects on wound and fracture healing in the damaged limb.

Inferior vena cava filters (IVCF) can be useful adjuncts in lower limb trauma where the risk of bleeding and extent of injury contraindicate both pharmacological and mechanical prophylaxis. IVCFs significantly reduce the risk of PE (OR 0.028, P<0.001) [6], however, insertion is invasive, they do not prevent DVT and their impact on mortality is debated. IVCFs can have numerous complications including caval wall penetration or thrombosis, and the frequency of complications increase with filter dwell time. The use of retrievable filters has grown dramatically, however multiple studies have reported that the majority of IVCFs are not being removed, often due to patients being lost to follow up [7].

A method for VTE prophylaxis which has seen a re-emergence of interest is the use of neuromuscular electrical stimulation (NMES). The evidence base for NMES devices is limited; they have been shown to increase venous blood flow in the leg, and to significantly reduce the risk of DVT when compared to no thromboprophylaxis (meta-analysis of 717 patients; OR 0.29, 95% CI 0.13 to 0.65) [8]. However, compared to current practice, their efficacy is less convincing; a recent Cochrane review found no clear benefit of NMES in the prevention of VTE, with the quality of evidence described as low. There was no difference in the total number of VTE events in the NMES group compared to graduated or intermittent pneumatic compression. Compared to heparin, the risk of DVT was higher in the NMES group (194 patients, OR 2.78, 95% CI 1.19 to 6.48), although it should be noted that these studies were in perioperative rather than trauma patients [9]. NICE recognised the limited evidence; nonetheless, it approved the use of the geko™ NMES devices for high risk VTE patients where other forms of prophylaxis are contraindicated or unsuitable[10]. This may make NMES devices suitable in lower limb trauma; however there is limited evidence of

their use in this patient population and the practicalities of employing such a device in traumatic limb injury are yet to be explored.

Venous thromboembolism is an important cause of morbidity and mortality following lower limb trauma, yet it is challenging to prevent in this patient population due to the complex interplay of VTE and bleeding risk factors alongside mechanical considerations relating to the traumatised limb. Further high quality studies are needed to explore several key areas, including predictive factors for delayed haemorrhage, risk thresholds that should contraindicate anticoagulation, and to validate alternative thromboprophylactic methods such as NMES in this specific patient population.

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Re: Disclosure of conflict of interest

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Yours Sincerely,
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