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Risk factors for venous thromboembolism in critically ill trauma patients who cannot receive chemical prophylaxis

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ABSTRACT

Background: Standard venous thromboembolism (VTE) prevention for critically ill trauma patients includes sequential compression devices and chemical prophylaxis. When contraindications to anticoagulation are present, prophylactic inferior vena cava filters (IVCF) may be used to prevent pulmonary emboli (PE) in high-risk patients, but specific indications are lacking. We sought to identify independent predictors of VTE in critically-ill trauma patients who cannot receive chemical prophylaxis in order to identify a subset of patients who may benefit from aggressive screening and/or prophylactic IVCF placement.

Methods: All trauma patients in the surgical ICU from 2008 to 2009 were prospectively followed. Patients with an ICU length of stay $\geq$2 days who had contraindications to prophylactic anticoagulation were included. Screening duplex exams were obtained within 48 h of admission and then weekly. CT-angiography for PE was obtained if clinically indicated. Patients were excluded if they did not receive a duplex or if they had a post-injury VTE prior to ICU admission. Data regarding VTE rates (lower extremity [LE] DVT or PE), demographics, past medical history (PMH), injuries, and surgeries were collected. Univariate and multivariable analyses were performed to identify independent predictors of VTE with a $p < 0.05$.

Results: 411 trauma patients with a mean age of 48 (SD 22) years and 8 (SD 9) ICU days were included. 72% were male and the mean ISS was 22 (SD 13). 30 (7.3%) patients developed VTE: 28 (6.8%) with LEDVT and 2 (0.5%) with PE. Risk factors for VTE with a $p < 0.2$ on univariate analysis included: PMH of DVT, injury severity score (ISS), extremity fractures (Fx), and a pelvis or LE extremity Fx repair. After logistic regression, only PMH of DVT (OR = 22.6) and any extremity Fx (OR = 2.4) remained as independent predictors.

Conclusion: VTE occur in 7% of critically injured trauma patients who cannot receive chemical prophylaxis. Aggressive screening and/or prophylactic IVCF placement may be considered in patients with a PMH of DVT or extremity fractures when anticoagulation is prohibited.

Introduction

Deep venous thrombosis (DVT) and pulmonary embolism (PE), collectively known as venous thromboembolism (VTE), continue to significantly impact the morbidity and mortality of hospitalised patients. DVT rates range from 11.8% to 70% in prospectively-screened, critically-injured trauma patients with contraindication for prophylaxis.[1,2] Historically, PE occur in 2% of trauma patients and have been cited as the most common, preventable cause of hospital death.[2,4] In addition, PE represent up to 37% of all post surgical VTEs.[3]

The routine prophylaxis of VTE is part of standard critical care. Low-dose unfractionated heparin (LDH) and low molecular weight heparin (LMWH) are recognised as effective methods of anticoagulation.[4] Mechanical prophylaxis, in the form of sequential compression devices (SCDs), is frequently used in lieu of or in addition to pharmacological prevention. The American College of Chest Physicians suggests early use of LMWH and SCDs for DVT

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prophylaxis in major trauma patients as long as contraindications are not present.[4]

Contraindications for chemical prophylaxis consist of significant bleeding risk (including severe intracranial haemorrhage or critical spinal injury), recent or imminent surgery, renal insufficiency, anaemia, recent history of GI haemorrhage, active peptic ulcer disease, or liver disease.[4,5] Trauma patients frequently present with one or more of these contraindications. In these cases, it is recommended that mechanical prophylaxis be used with chemoprophylaxis commencing as soon as the contraindication resolves.[4] In addition, SCDs are recognised as an acceptable form of DVT prophylaxis when anticoagulants cannot be administered and screening duplex ultrasound exams should be considered in high-risk patients when VTE prophylaxis is considered sup-optimal.[4]

Given that two out of three PEs occur within the first week of injury, withholding chemical prophylaxis due to contraindications compromises the prevention of PE and its associated mortality during the most crucial period.[6] Currently, IVCFs are sometimes used in patients with contraindications to VTE prophylaxis to prevent PE even prior to the development of lower extremity DVT (LEDVT). This practice is referred to as "prophylactic IVCF placement". Despite being used in 4% of trauma patients, studies analysing the safety and efficacy of IVCFs have produced mixed results.[7–13] Although IVCFs have been associated with up to a seven-fold decrease in the occurrence of PE,[14] several studies have shown no benefit.[10,11] Retrieval of temporary IVCFs is also of special concern due to the lifestyle demands of a young trauma population. Whilst the success rate of filter removal has reached 97%, overall filter removal rates range from 22% to 78% due to lack of follow-up and contraindications.[8,9,15] In addition, IVCFs may be associated with complications that include fracture, migration, and the formation of VTE within the filter itself.[5,8,10]

Due to uncertainty regarding the efficacy, safety, and retrievability of IVCFs, it is imperative that vena cava filtration be used only in high-risk patients. The Eastern Association for the Surgery of Trauma (EAST) Practise Management Guidelines Work Group established a level-3 recommendation for prophylactic IVCF only in "very-high-risk trauma patients" who are not candidates for DVT prophylaxis and present with immobilizing injuries.[16] At present, there are no level-1 or level-2 recommendations for prophylactic vena cava filtration (prior to the development of a VTE) in critically injured patients. Guidelines from the Institute for Clinical Systems Improvement state that IVCFs are not appropriate for routine use but are indicated in any type of patient with a VTE and contraindications to anticoagulation, failure of adequate anticoagulation to treat a progressive VTE, or a history of pulmonary hypertension.[5] Given this, it is fair to say that a trauma patient who develops a LEDVT or PE and can not receive therapeutic anticoagulation would have an indication for IVCF insertion. This study was designed to find independent predictors of LEDVT or PE in critically-injured trauma patients who cannot receive chemical prophylaxis in order to identify a subset of patients with a significantly increased risk of VTE who may benefit from aggressive screening and/or prophylactic IVCF placement. Whilst only aggressive screening is recommended in these cases by the American College of Chest Physicians,[4] practise patterns vary in trauma centers and some centers do employ the use of prophylactic IVCF under similar circumstances.[15] The ability to elucidate risk factors for VTE in trauma patients who cannot receive adequate chemical prophylaxis may help centers to focus these additional resources on the patients who have the greatest chance to benefit from them.

Methods

All adult patients on the surgical intensive care unit (SICU) service at an academic, level-1 trauma center were prospectively followed from January 2008 to December 2009. VTE prophylaxis was administered according to a pre-established protocol. This included SCDs, which were applied bilaterally to the lower extremities as early as possible. When indicated, 30 mg LMWH [Enoxaparin, Sanofi-aventis, Bridgewater, NJ] was subcutaneously administered twice-daily. LMWH was held due to the following contraindications: bleeding risk, renal insufficiency, early mobilization, or thrombocytopenia (<100,000 platelets/μL). In the case of renal insufficiency, LDH (5000 units subcutaneously administered three times a day) was substituted for LMWH. Screening ultrasound duplexes were routinely obtained for the bilateral upper and lower extremities within 48 h of admission and weekly thereafter. Weekly screening continued in the wards after discharge from the SICU to ensure that all inpatient VTE were documented. When clinically suspected, PE was diagnosed via CT angiography. An IVCF was introduced at the discretion of the attending physician in patients with any of the following indications: contraindication for anticoagulation in the presence of an LE DVT or PE, high risk for VTE with contraindication for chemical prophylaxis, or failure of anticoagulation to prevent progression of a VTE.

Data regarding age, gender, body mass index (BMI), amount of blood products received in the first 24 h after admission, injury severity score (ISS), abbreviated injury scores (AIS), specific injuries, comorbidities, complications, surgical interventions, ICU length of stay (LOS), and ventilator days were collected. Types of injuries recorded included ICH, spinal cord injury, cervical spine fracture, thoracolumbar spine fracture, pelvic fracture, upper extremity fracture, and lower extremity fracture. In addition to listing spine and extremity fractures by specific region of the body, "any spine fracture" and "any extremity fracture" variables were also analysed as risk factors. The "any extremity fracture" variable did not include pelvic fracture. Comorbidities recorded included outpatient warfarin therapy and a past medical history (PMH) of any of the following: cancer, intravenous drug abuse (IVDA), renal insufficiency, DVT, and PE. DVT PMH and PE PMH were also grouped as "VTE PMH." Complications recorded included systemic inflammatory response syndrome (SIRS) and sepsis within the first 5 days of ICU admission. Patients with SIRS had two or more of the following: temperature <36 °C or >38 °C, respiratory rate >20 breaths per minute or pCO2 <32 mmHg, heart rate >90 beats per minute, or a white blood cell count <4000 or >12,000 per μL of blood. Sepsis was defined as having a diagnosis of SIRS with a known or presumed infection. Lastly, surgical interventions recorded included craniotomy, spine surgery, abdominal surgery, pelvic fracture repair, upper extremity fracture repair, and lower extremity fracture repair.

The primary outcome measure was the occurrence of a documented LEDVT or PE. LE DVT was defined as a DVT in the popliteal vein or more proximal. Upper extremity (UE) DVTs were not included in this study because a PE originating from an upper extremity would not be prevented with an IVCF.

All patients cared for by the SICU service were enrolled and selection criteria were applied (Fig. 1). Patients were excluded if they were non-traumas, had an ICU LOS <2 days, or if they did not receive an ultrasound duplex. Patients with an ICU LOS <2 days were thought to be at low risk for VTE due to minor injury and the potential for early mobilization. Lastly, of the remaining patients, only those with a contraindication to chemical prophylaxis that had no anticoagulation for at least the first five days of ICU admission were included. This cutoff of five days was determined by consensus at our institution as it was felt that if a patient could not receive prophylactic anticoagulation for five days, IVCF placement would be considered depending on the patient's risk factors for VTE.

Patient characteristics, VTE risk factors, and the proportions of patients with LE DVT or PE were compared to find variables that