Thromboembolic Disease After Orthopedic Trauma

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KEYWORDS

• Orthopaedic trauma • Coagulation • Deep venous thrombosis • Pulmonary embolism
• Thromboprophylaxis

KEY POINTS

- Traumatic musculoskeletal injury results in systemic physiologic changes that predispose patients to venous thromboembolism (VTE).
- Combined mechanical and pharmacologic thromboprophylaxis is most efficacious for decreasing VTE incidence.
- Low molecular weight heparin is the preferred agent for pharmacologic thromboprophylaxis.
- Pharmacologic prophylaxis should be initiated as soon as possible, and should be continue for a minimum of 14 days.
- Patients with isolated lower extremity fractures who are ambulatory do not require pharmacologic prophylaxis in the absence of other VTE risk factors.

PHYSIOLOGY AND EPIDEMIOLOGY OF VENOUS THROMBOEMBOLISM IN TRAUMA

Basic Science and Physiology of Trauma and Coagulation

Traumatic injury results in significant physiologic changes. Serum levels of inflammatory cytokines including interleukin-6 (IL-6), IL-8, and tumor necrosis factor-alpha (TNF-α) are increased following traumatic injury and result in a hypercoagulable state.[1] In addition to inflammatory markers, serum levels and activity of procoagulant microparticles are significantly increased following blunt trauma, and peak thrombin levels are correlated to injury severity.[2,3] The systemic inflammatory response triggered by traumatic injury results in a hypercoagulable state that places patients at increased risk of venous thromboembolism (VTE).[4] This hypercoagulability combined with endothelial injury and venous stasis, 2 other conditions often noted in trauma patients, completes the Virchow Triad. The presence of all 3 elements contributes to venous thrombosis.

Venous Thromboembolism Following Major Trauma

Before the implementation of routine thromboprophylaxis, reported rates of VTE following major trauma were extremely high. Using bilateral lower extremity venography, Geerts and colleagues[5] reported a 58% incidence of lower extremity deep vein thrombosis (DVT) in 349 patients admitted for major traumatic injuries who did not receive thromboprophylaxis. DVT rates varied by anatomic region injured, ranging from 50% in patients with major injuries to the face, chest, or abdomen to 80% in patients with femur fractures. The rate of fatal pulmonary embolism (PE) was 0.9%, and independent risk factors for DVT

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identified included age, blood transfusion, surgery, fracture of the femur or tibia, and spinal cord injury. Despite its relatively low incidence, PE is still the third most common cause of in-hospital death among trauma patients.[6]

Thromboprophylaxis for Venous Thromboembolism in Trauma Patients

Both chemical and mechanical thromboprophylaxis has been shown to decrease rates of VTE in the setting of trauma.[7,8] Pharmacologic prophylaxis with low molecular weight heparin (LMWH) was shown to significantly decrease the incidence of both DVT and PE in a large cohort of more than 2200 trauma patients.[9] Mechanical prophylaxis with pneumatic sequential compression devices (SCDs) significantly decreased VTE incidence from 11% to 4% ($P = .02$) in a prospective randomized controlled trial of 300 orthopedic trauma patients compared with no VTE prophylaxis.[10] A growing understanding of the importance of thromboprophylaxis in trauma patients has led to the development of institutional protocols for VTE prophylaxis at trauma centers around the world. Additionally, several professional organizations have published clinical guidelines for thromboprophylaxis in trauma patients, which are summarized in **Table 1**.[8,11–13]

More recent literature using larger patient cohorts and routine thromboprophylaxis protocols has better defined the true incidence of clinically relevant VTE following severe trauma. A retrospective review of a multicenter trauma registry containing nearly 8000 major trauma patients identified a VTE incidence of only 1.8% when institutional thromboprophylaxis protocols were used.[14] Despite the relatively low incidence, the presence of VTE (either DVT or PE) nearly doubled the mortality rate (13.7% vs 7.4%), and among patients who developed a PE, the mortality rate was 25.7%. A single-center retrospective review of more than 1300 major trauma patients treated at a level 1 trauma center revealed a 2.3% incidence of PE.[15] All PEs occurred within 15 days of injury, with most being diagnosed within the first week. Age older than 55 years, multisystem injury, cannulation of central veins, and pelvic fractures (but not long-bone fractures) were independent risk factors for developing a PE. Using a statewide trauma database over a 5-year period, Tuttle-Newhall and colleagues[16] reported an overall PE incidence of 0.3% among more than 300,000 trauma patients receiving standard VTE prophylaxis. Age older than 55 was a significant risk factor for development of PE, with an incidence of 0.7% in this demographic. Increasing Injury Severity Score (ISS) and Abbreviated Injury Scale (AIS) for the extremities, soft tissue, and chest regions were also associated with significantly increased risk of PE.

VENOUS THROMBOEMBOLISM AND ORTHOPEDIC TRAUMA

Compared with the abundance of data relevant to venous thromboembolism in the general trauma population, high-quality evidence specific to VTE prophylaxis and treatment in the orthopedic trauma population is relatively limited. The available literature is summarized as follows and organized by fracture location when possible. In addition, the Orthopedic Trauma Association's Evidence-Based Quality Value and Safety Committee has recently produced a therapeutic algorithm to guide VTE prophylaxis in orthopedic trauma patients. A portion of this algorithm has been presented[13] and publication in its entirety is forthcoming.

Epidemiology and Risk Factors

Using the National Trauma Data Bank (NTDB), Godzik and colleagues[17] investigated the incidence of PE in 200,000 patients with pelvic and lower extremity fractures who received thromboprophylaxis according to the protocols of each institution. The overall incidence of PE was 0.46%, and the in-hospital mortality rate among patients who developed PE was 12%. These investigators also identified independent risk factors for PE in this patient population, including multiple fractures, history of warfarin use, morbid obesity, and emergency department disposition to an intensive care unit or to the operating room. **Table 2** summarizes the literature documenting VTE incidence and risk factors in orthopedic trauma patients.

Thromboprophylaxis

Both mechanical and chemical thromboprophylaxis have been shown to decrease rates of VTE following orthopedic trauma.[7,8,10] Fisher and colleagues[10] conducted a prospective randomized controlled trial comparing pneumatic SCDs with no VTE prophylaxis in 300 orthopedic trauma patients. Mechanical thromboprophylaxis significantly decreased VTE incidence from 11% to 4% ($P = .02$). In another prospective randomized trial, Stannard and colleagues[7] reported equivalent efficacy of mechanical and pharmacologic prophylaxis for DVT prevention following blunt skeletal trauma. The most recent Cochrane database systematic review found that pharmacologic