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Venous Thromboprophylaxis in Spine Surgery

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Abstract

Study Design: Review article.

Objective: A review of the literature on postoperative initiation of thrombophylactic agents following spine surgery.

Methods: A review of the literature and synthesis of the data to provide an update on venous thromboprophylaxis following spine surgery.

Results: Postoperative regimens of venous thromboprophylaxis measures following spine surgery remain a controversial issue. Recommendations regarding mechanical versus chemical prophylaxis vary greatly among institutions.

Conclusion: Postoperative spine surgery initiation of thromboprophylaxis remains controversial regarding optimal timing and agent selection. The benefits of deep vein thrombosis/pulmonary embolism prophylaxis must be weighed against the possible postoperative complications associated with spine surgery.

Keywords

spine surgery, postoperative, deep vein thrombosis, pulmonary embolism, epidural hematoma, prevention

Introduction

Deep vein thrombosis (DVT) and pulmonary embolism (PE) are sources of morbidity and mortality in patients undergoing major spine surgery. Several studies support the use of venous thromboembolism (VTE) prophylactic agents in postoperative patients, yet no consensus has been established regarding the utilization or timing of VTE prophylaxis after elective spine surgery. The risk of VTE in spine surgery is not well described and varies considerably. The risks of these complications need to be weighed against surgical-related complications, such as epidural hematomas (EDHs) and other hematologic complications. EDHs are infrequent complications, with an estimated incidence of less than 1%, but can cause devastating neurologic injury.[1] In comparison, the incidence of postoperative spinal thromboembolic events varies widely, from 0.3% to 31%, gathered from small, heterogenous studies.[1] A variety of factors, including the patient's comorbidities; need for anticoagulation for other medical problems; and type and length of surgery; influence the risk of developing DVT and PE in the postoperative interval and managing these risks with the catastrophic complications of epidural bleeding at the surgical site must be recognized. Incidence is likely influenced by magnitude of the surgery and perioperative mobilization.

The incidence of VTE following spine surgery is poorly defined, with reported rates from 0.3% to 31%, suggesting substantial variability in the literature.[2] There is no established consensus regarding perioperative VTE prophylaxis in patients undergoing elective spine surgery. Nonetheless, the risk of VTE events must be balanced against the risk of postoperative bleeding and epidural hematoma.[2] Recommendations for chemoprophylaxis in spinal surgery remain unclear. In 2009, the North American Spine Society (NASS) group evaluated the use of perioperative VTE chemoprophylaxis in spine surgery

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patients. Regarding the use of chemoprophylaxis following elective spine surgery, the authors found insufficient evidence to recommend the routine use of chemoprophylaxis in patients undergoing elective spine surgery.[3] The Congress of Neurologic Surgeons assessed the use of VTE prophylaxis and treatment of thromboembolic events in thoracolumbar spine trauma patients. The authors concluded there was insufficient evidence to provide specific recommendations regarding use of a specific VTE prophylaxis regimen for minimizing VTE events or complications associated with a specific regimen in patients with thoracic and lumbar spine fractures. Based on the pooled results, the authors recommended the use of thromboprophylaxis to reduce the risk of VTE events in this specific population.[4] Cloney et al[5] evaluated VTE-related events in patients undergoing surgery for spinal fractures. Analysis of 195 patients revealed that compared with other patients undergoing spine surgery, patients with spinal fractures were more likely to receive chemoprophylactic anticoagulation, but experienced higher rates of VTE events. The authors also found that within 30 days of surgery, estimated blood loss and comorbid cardiac disease predicted VTE events in patients with spinal fractures.[5]

Given the paucity of high-quality literature regarding the efficacy and safety of chemoprophylaxis selection and timing, current practice varies widely, and is largely based on surgeons' preference. Proper knowledge regarding available agents and optimal timeframe for initiation of thromboprophylaxis postoperatively following spine surgery is imperative to maximize benefits of thromboembolic events and minimize risks associated with postoperative bleeding complications. Spinal surgeons must balance the risk associated with EDH versus the morbidity and mortality from VTE. The purpose of this review is to evaluate the existing literature regarding the incidence of VTE events following adult spine surgery and the use of thrombophylactic agents and optimal timing for initiation following spine surgery.

Postoperative Epidural Hematoma

The utility of prophylactic anticoagulation to prevent clinically significant VTE events following spine surgery must be balanced against the risk of postoperative bleeding issues. In a systematic review conducted by Glotzbacker et al,[6] the authors reported a 0.2% overall incidence of postoperative epidural hematoma. Of 16 studies evaluated, 6 included chemical prophylaxis consisting of low-molecular-weight heparin (LMWH) or unfractionated heparin (UFH), while 10 studies did not implement chemoprophylaxis. In comparison, no notable difference in EDH incidence was found in these 2 groups. The authors concluded that though EDH is a rare and devastating complication, further studies were needed to identify risk factors associated with occurrence.[6] A multicenter, retrospective study evaluated over 16 000 patients from 23 institutions who underwent cervical spine surgery and found a 0.09% incidence of EDH. However, in patients with EDH, 33% demonstrated continued neurologic deficit at 6-week follow-up visit despite prompt diagnosis and intervention. The incidence of EDH was low (<1.0%) in these studies, yet substantial morbidity was associated with this complication.[7]

Mechanical Prophylaxis

External Compression Devices

External compressions devices consisting of intermittent pneumatic compression devices (IPC), sequential compression devices (SCDs), and thrombosis embolic deterrent (TED) are effective noninvasive methods for VTE prophylaxis. These modalities provide circumferential compression to the patient's leg, preventing venous stasis and improving blood flow. Their use and efficacy following joint arthroplasty has been well documented, but the efficacy of such devices for VTE prevention is less well accepted after spine surgery.[8,9] Rokito et al[10] reported a prospective evaluation of the incidence of DVT after elective adult spine surgery. A total of 329 patients in total were included and randomized to 1 of 3 groups. Group 1 (42 patients) received thrombosis embolic deterrent (TED) compression stocking, group 2 (33 patients) received TED stockings and thigh-length cuffs for sequential pneumatic compression of the calf and thigh, and group 3 (35 patients) received TED stockings and low-dose coumadin. The remaining 219 patients not randomized received either TED stockings alone or TED stockings plus pneumatic compression boots.[10] The authors found that 1/329 patients (0.3%) were diagnosed with a DVT, and 5.7% of patients receiving coumadin experienced bleeding complications. Given the risk of hemorrhage associated with coumadin, mechanical prophylaxis with graduated compression stockings and pneumatic compression boots without Coumadin was the preferred treatment.

Akeda et al[11] prospectively evaluated the incidence of venous thromboembolic events during the perioperative period in patients who underwent spinal surgery and were managed with mechanical prophylaxis postoperatively, unless a documented VTE occurred. Patients underwent ultrasonographic assessments of both lower extremities before and after surgery. Of 209 patients evaluated, 9 patients (4.3%) had VTE before surgery and 14 patients developed new-onset VTE (2 with PE with DVT, 12 with DVT only) in the postoperative period. The authors concluded DVT assessment with ultrasonography is vital in the perioperative spine surgery period and mechanoprophylaxis using pneumatic sequential compression devices and compression stockings is effective.[11]

In a retrospective study conducted by Epstein,[12] 139 patients undergoing posterior laminectomy and instrumented fusion were treated with compression stockings only to assess their efficacy in VTE prevention. Results demonstrated a DVT rate of 2.8% and PE rate of 0.7%, which is comparable to rates associated with LMWH regimens.[12]

A systematic review and meta-analysis conducted by Mosenthal et al[1] revealed a nonsignificant difference between the mechanoprophylaxis group (DVT 1%, PE 0.81%) and the chemoprophylaxis group (DVT 0.85%, PE 0.58%). When complications were assessed, 6% of PE were fatal and the rate of

EDHs was 0.3%.[1] The authors concluded that the overall incidence of DVT and PE was relatively low regardless of prophylaxis type chosen; however, it was difficult to draw meaningful conclusions due to the heterogenous nature of the studies included. However, PE in these patients has been associated with a relatively high rate of mortality, which suggests a role for chemoprophylaxis in select patients who have undergone spine surgery. The NASS guideline concluded that mechanical prophylaxis of any form (pneumatic sequential compression boots or compression stockings) should be considered following inpatient spine surgery due to documented efficacy and low complication rates.[3] Despite the paucity of high-quality studies demonstrating the efficacy of external compression devices in spine patients, their routine use should be strongly considered in standard postoperative spine care as they are easy to apply, noninvasive, low risk, and may reduce VTE events by reducing venous stasis.

Inferior Vena Cava Filters

Inferior vena cava (IVC) filters are endovascular devices designed to prevent thrombi from propagating to the pulmonary vasculature. Despite requiring an invasive procedure for device placement, IVC filters have shown efficacy in reducing the risk of PE. A retrospective review identified 74 patients as being high risk for VTE events who received IVC filters prior to thoracolumbar surgery. Patients were considered high risk for VTE events if they demonstrated a history of VTE, malignancy, thrombophilia, staged procedure, and anesthesia time over 8 hours. The authors found 27 DVTs (31%), with 18 (24.3%) documented above the popliteal fossa, and 1 PE (1.3%) during weekly doppler ultrasonography of the lower extremities in this cohort. One complication related to failed IVC filter deployment occurred. The authors concluded that despite a high incidence of DVT in high-risk patients undergoing spine surgery, prophylactic IVCF placement appeared beneficial.[13]

McClendon et al[14] retrospectively reviewed prophylactic IVC filature placement in 219 patients considered high risk for major spinal reconstructive surgery. Indications for IVC filter placement included prior history of DVT or PE, malignancy, hypercoagulability, prolonged immobilization, staged procedure or greater than 5 operative levels, combined approaches, and anesthetic time greater more than 8 hours. The authors found that the incidence of DVT was 18.7% (41/219) and PE was 3.7% (82/219), and paradoxical embolus rate was 0.5% (1/219). Prophylactic IVC filter reduced the odds ratio of PE development (odds ratio = 3.7, $P < .05$) compared with population controls. Results also showed that patients receiving Greenfield filters had significantly higher VTE incidence than those receiving retrievable filters (odds ratio = 2.8, $P = .08$) and anesthesia time more than 8 hours increases VTE incidence ($P = .029$). The authors concluded that prophylactic IVC filter placement significantly lowers VTE events.[14] Therefore, in patients considered high risk for spinal surgery, prophylactic IVC filter placement may serve as a useful adjunct in VTE prevention.

Early Ambulation After Surgery

Early ambulation following spine surgery is a safe and effective modality to reduce the risk and incidence of VTE in the immediate postoperative interval. It has been shown that prolonged immobilization after surgery can result in functional decline along with increased risk of hospital-associated complications aside from VTE.[15] Early ambulation after surgery has also been shown to significantly reduce perioperative complications, decrease length of stay, and contribute to improved perioperative functional status in elderly patients.[16]

Chemical Prophylaxis

Subcutaneous Heparin

UFH, delivered subcutaneously, binds to and activates antithrombin III, which results in inhibition of thrombin, (factor Xa) along with other proteases in the direct clotting cascade. Regarding postoperative chemoprophylaxis in the spine population, there are limited studies evaluating the efficacy and risks associated with UFH administration. Cox et al[17] evaluated a protocol for early VTE prophylaxis consisting of combined mechanoprophylaxis (compressive devices) and chemoprophylaxis (subcutaneous heparin 5000 units 3 times daily, except in patients older than 75 years or weighing less than 50 kg, who received twice daily dosing) initiated either preoperatively or on the same day of surgery and compared outcomes prior to protocol implementation. The authors reported following protocol implementation, 10 DVT (1%), 5 PE (0.5%), and 4 postoperative EDH (0.4%) were encountered in 992 patients compared with the preprotocol cohort, which demonstrated 25 DVT (2.7%), 6 PE (0.6%), and 6 postoperative EDH (0.6%) in 941 patients. Reduction in DVT occurrence was statistically significant after protocol implementation ($P = .009$) without an increase in postoperative EDH. The authors concluded that early VTE prophylaxis after spine surgery decreases VTE occurrence without increased risk of postoperative EDH.[17] The routine use of UFH in patients undergoing spine surgery may reduce the risk of VTE events without increasing surgery-related complications, such as wound infection and EDH, but further, more robust studies are needed to assess the safety of UFH in this population.

Low-Molecular-Weight Heparin

LMWH are derivates of UFH that provide more predictable anticoagulant response and require less frequent monitoring. Similar to UFH, they bind antithrombin III, inhibiting factor X and indirectly inhibiting thrombin. Literature suggests indirect inhibition of thrombin results in lower risk of bleeding associated with prophylactic use. The main advantage of LMWH is its longer half-life, which allows for daily dosing and potentially improving patient compliance. Zeng and

Peng[18] retrospectively evaluated the effectiveness and safety of LMWH in preventing VTE complications after spine surgery in 2 cohorts. The therapeutic group, 947 patients, received LMWH daily after surgery while the control group, 814 patients, did not receive heparin. Compared with the control group, the therapeutic group showed a lower rate of postoperative thromboembolic complications (therapeutic group, 0.21%; control group, 1.6%; $P = .002$). The overall rate of bleeding complications was higher in the therapeutic group compared with the control group, although this did not reach statistical significance (therapeutic group, 1.8%; control group, 0.74%; $P = .051$) with larger volume of drainage (therapeutic group, 292 $\pm$ 137 mL; control group, 179 $\pm$ 121 mL; $P = .023$) and seven spinal EDH in the treatment group. Of the 7 EDH, 6 required surgical evacuation. The authors concluded that the use of LMWH significantly reduced the incidence of VTE complications after spine surgery, but increased surgical bleeding, leading to an increased risk of symptomatic spinal EDH.[18]

Strom and Frempong-Boadu[19] retrospectively evaluated the safety and efficacy of prophylactic LMWH following cervical and lumbar laminectomy initiated 24 to 36 hours after degenerative spine surgery. Mechanical prophylaxis was implemented throughout admission and prophylactic LMWH was started postoperative day 1 at 10 PM. The authors evaluated the incidence of hemorrhage, DVT, and PE. Analysis of 367 patients revealed no incidence of postoperative hemorrhage (95% CI; 0%-0.8%). Acute VTE was diagnosed in 14 patients (3.8%; 95% CI 2.1-6.3) of the study population by ultrasonography or chest computed tomography. The authors concluded LMWH was associated with a very low risk of hemorrhage when started 24 to 36 hours after spine surgery.[19] DiGiorgio et al[20] evaluated the safety and effectiveness of early chemical DVT prophylaxis with LMWH within 24 hours after spinal cord injury in a prospective observational study. The authors evaluated the incidence of DVT, PE, and hemorrhagic complications. Of 49 patients reviewed, 3 DVTs (6.1%), 2 PEs (4.1%), and no hemorrhagic complications were identified. There was no association between VTE complications and age, ASIA (American Spinal Injury Association) grade, race, or having undergone a neurosurgical procedure. The authors concluded that initiation of LMWH to patients with spinal cord injury within 24 hours of injury is effective.[20]

Vitamin K Antagonist

Warfarin is an oral anticoagulant that competitively inhibits the vitamin K epoxide reductase complex (VKORC), which is a necessary enzyme for activating vitamin K and promoting coagulation. As a result, warfarin depletes vitamin K reserves and reduces the synthesis of vitamin K-dependent coagulation factors II, VII, IX, and X as well as regulatory factors protein C and protein S. Data on the use of warfarin following spine surgery is limited. In 2009, NASS reviewed antithrombotic therapies and concluded the bleeding risk associated with warfarin use outweighed its potential benefit in VTE prevention.[3]

Factor X Inhibitors

Factor X inhibitors, including apixaban (Eliquis) and rivaroxaban (Xarelto), directly antagonize factor Xa in the clotting cascade. Advantages of these agents include daily oral dosing without need for routine monitoring. However, the lack of existing reversal agents is problematic in the setting of hemorrhage. Factor Xa inhibition has demonstrated efficacy in prevention of VTE events without increased postoperative bleeding in the orthopedic literature, but data regarding their use after spine surgery is minimal.

In a single center, retrospective review conducted by Zhang et al,[21] the authors compared the safety and efficacy of apixaban and rivaroxaban as anticoagulants after lumbar spine surgery. A total of 480 patients were included, with 240 patients allocated to the apixaban group and 240 patients in the rivaroxaban cohort. Patients in the apixaban group were administered 2.5 mg orally twice daily for 14 days, commencing at 8 AM on the morning of surgery. Patients in the rivaroxaban group began daily oral treatment with 10 mg 6 to 8 hours after surgery for a total of 14 days. All patients were also provided with graduated compression stockings for 6 weeks and intermittent pneumatic compression devices while in-hospital. Bilateral lower-extremity Doppler ultrasonography was performed between postoperative day 3 and 7. The authors assessed VTE events, bleeding, and D-dimer changes. Results demonstrated 12 thrombotic events (5%) in the apixaban group, consisting of 4 pulmonary emboli (2 fatal, 2 nonfatal) and 8 deep vein thromboses (2 symptomatic, 6 identified by ultrasonography only). In the rivaroxaban group, 9 thrombotic events occurred (3.75%). There were 3 pulmonary emboli (1 fatal, 2 nonfatal) and 6 deep vein thromboses (1 symptomatic, 5 identified by ultrasonography). There was no significant intergroup difference found in the incidences of VTE events between the groups ($P > .05$). Regarding blood loss and D-dimer results, the authors found that compared with rivaroxaban, postoperative D-dimer values, total bleeding (1397 $\pm$ 99 vs 1535 $\pm$ 77; $P = .02$), and invisible bleeding (842 $\pm$ 17 vs 855 $\pm$ 22; $P = .02$) were significantly lower in the apixaban group. The authors concluded that apixaban and rivaroxaban were equally effective anticoagulant therapies that demonstrated similar preventive effects against postoperative VTE. However, the authors acknowledge their study is limited by retrospective nature, small sample size, and single center.[21]

Antiplatelet Agents

Antiplatelet agents, including acetylsalicylic acid (aspirin) and clopidogrel cause an irreversible effect on platelet aggregation that exerts its affect for approximately 7 to 10 days. Existing orthopedic surgery literature supports the use of acetylsalicylic acid over other available chemoprophylactic agents in the reduction of clinically significant VTE and wound drainage in patients undergoing lower extremity joint replacement surgery. Historically, antiplatelet agents are not considered for postoperative VTE chemoprophylaxis in spine patients because

their irreversible effect on platelet function results in hemostasis issues and possible postoperative hematoma. It is common practice to discontinue antiplatelet agents as early as one week prior to surgical intervention because of the risks regarding postoperative spinal epidural hematoma. In a recent systematic review and meta-analysis conducted by Zhang et al,[22] the authors assessed the effect of continuing aspirin administration during the perioperative spine surgery period on bleeding and cardiovascular events. Following analysis of four articles, continuation of aspirin did not increase the risk of blood loss during surgery (95% CI, −111.72 to −0.59; $P = .05$), operative time (95% CI, −33.29 to −3.89; $P = .01$), or postoperative blood transfusion (95% CI, 0.00-0.27; $P = .05$). The authors concluded that patients undergoing spine surgery with continued aspirin administration are not at increased risk of bleeding. This study is limited by multiple factors, including differing anesthetic and surgical techniques amongst patients, various surgical locations (cervical, thoracolumbar, lumbar) and unequal number of patients allocated between study cohorts.[22] Because of the risk of postoperative epidural hematoma in patients undergoing spine surgery, additional large studies evaluating the safety of antiplatelet agents as chemoprophylaxis are necessary.

Timing of Chemoprophylaxis

There is no consensus on the optimal timing to initiate chemoprophylaxis in patients undergoing spine surgery. The Congress of Neurologic Surgeons assessed the use of VTE prophylaxis and treatment of thromboembolic events in thoracolumbar spine trauma patients. The authors concluded there was insufficient evidence to provide specific recommendations regarding use of a specific VTE prophylaxis regimen for minimizing VTE events or complications associated with a specific regimen in patients with thoracic and lumbar spine fractures. Based on the pooled results, the authors recommended the use of thromboprophylaxis to reduce the risk of VTE events in this specific population.[4]

In a retrospective cohort study, the impact of initiating early (<48 hours) versus late (>48 hours) chemical prophylaxis on outcomes and complications in trauma patients undergoing operative intervention was evaluated by Kim et al.[23] In total, 206 patients were included of which 48 patients (23.3%) received early prophylaxis and 158 (76.7%) received late prophylaxis. There was no incidence of epidural hematoma or excessive postoperative bleeding requiring intervention. Thirteen patients (6.2%) developed VTE events, 12 which were in the late VTE group. Additionally, age (>45 years) and traumatic brain injury were associated with increased risk of VTE events. The authors concluded that initiation of VTE prophylaxis within 48 hours of operative fixation were not associated with increased risk of bleeding or neurologic complications.[23]

Cloney et al[5] evaluated VTE-related events in 195 patients undergoing surgery for spinal fractures. They found that compared with other patients undergoing spine surgery, patients with spinal fractures were more likely to receive chemoprophylactic anticoagulation and also experienced higher rates of VTE events. The authors also found that within 30 days of surgery, estimated blood loss, and comorbid cardiac disease predicted VTE events in patients with spinal fractures.[5] Thus, timing of VTE prophylaxis must be evaluated on an individual patient basis with thorough consideration of underlying medical comorbidities and risk factors that impact the chance of encountering a VTE-related event. Limited evidence suggests that patients with spinal cord injury may have a higher VTE risk and thus warrant earlier chemoprophylaxis treatment to negate the effects of venous stasis. In contrary, patients undergoing elective spine surgery may have underlying risk factors that influence form (mechanical versus chemical) of VTE prophylaxis utilized.

Conclusion

Management of thromboprophylaxis following spine surgery presents a challenge in regard to balancing potential VTE events related to withholding thromboprophylaxis versus the potential risks associated with perioperative complications. There is no obvious single risk factor in spinal surgery identified that predisposes patients to VTE complications. This issue is further clouded due to the heterogeneity of patient populations and surgical approaches employed in existing studies. Currently, it is not feasible to recommend a standard thromboprophylaxis regimen for elective spinal surgery, as has been designated in hip and knee surgery. The use and agent of choice for chemoprophylaxis is largely physician or institution dependent.

In conclusion, a standardized approach to VTE prophylaxis in patients undergoing elective spine surgery must consider individual patient risk factors, surgical approach and duration, choice of agent and timing. Patients undergoing elective spine procedures must have preexisting comorbidities and risk factors considered to determine appropriate prophylaxis. Large, randomized controlled trials evaluating the optimal timing of VTE prophylaxis are warranted. Ultimately, postoperative chemoprophylaxis should be considered for spine procedures that are long and complex, including combined anterior-posterior approaches, and in patients with known thromboembolic risk factors, such as paralysis, malignancy, spinal cord injury, and hypercoagulable disorders. Additional studies are warranted to address both the efficacy of chemoprophylaxis and to provide detailed rates of postoperative complications following initiation of chemoprophylaxis after elective spine surgery.

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