

Prevention of Deep Vein Thrombosis among Patients Having Undergone Neurosurgery: A Systematic Review

Shani SD

Abstract

Deep vein thrombosis (DVT) and pulmonary thromboembolism are high in the setting of neurosurgery causing significant mortality and morbidity. Incidence of venous thromboembolism among neurosurgery patients is very high (approximately 23%) in the absence of prophylaxis. There is no consensus among surgeons regarding the method of prophylaxis to be instituted and the exact timing of starting of prophylaxis. A systematic review following preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines for design, conduct and reporting was conducted to find out the evidences for DVT prophylaxis among neurosurgery patients and to develop an evidence-based protocol for prevention of DVT. Eligibility criteria was to include studies done among adult patients who had undergone craniotomies or spinal cord. Data were summarised in a pre-defined data extraction form. Summarised information on study characteristics such as design and year, author information, sample size, prophylactic method used, outcome, side effects, investigations done and the timing of prophylactic method used. Risk of bias for randomised controlled trials (RCT) were assessed using predefined Cochrane risk of bias tool. Observational studies were assessed for risk of random and systematic bias. All the studies except one are having high risk of bias. The total participants of included studies were 2811. The incidence of symptomatic DVT ranged from 0.01 - 0.6 percent. Asymptomatic DVT incidence ranged from 4-29.4 percent. The prophylactic methods used were pneumatic compression devices, low molecular weight heparin (LMWH), nadroparin, venacaval filter, elastic compression stockings and physiotherapy. There was no significant difference between the chemoprophylactic and mechanical prophylactic group. Chemoprophylaxis was used post-operatively after 12 hours to 5-6 days. The pneumatic compression device and elastic crepe bandage were used peri-operatively. The incidence of post-operative bleeding and haematoma with the use of LMWH and nadroparin was 0.4 to 1.8 percent, which is within the limits of usual post-operative risk of bleeding. The use of compression device was associated with minor skin irritations. These findings suggest that pharmacological and mechanical prophylaxis can be combined to prevent DVT among neurosurgery patients without increased bleeding risk or discomfort.

Deep vein thrombosis (DVT) is an important health care problem causing significant mortality and morbidity. Among neurosurgery patients, in addition to weakness or paralysis, the surgical positions and various other factors make them prone to the development of DVT. Neurosurgical patients constitute a unique group where prophylaxis with anticoagulant and antiaggregant agents are relatively contraindicated due to the natural course of vascular problems such as aneurysms, haemorrhagic tumours or haematomas or increased vulnerability to complex spinal surgeries and trauma. The thrombus can dislodge and occlude vessels causing pulmonary or systemic thromboembolism. Incidence of venous thromboembolism among neurosurgery patients is very high

(approximately 23%) in the absence of prophylaxis. A survey conducted among clinicians showed 73 percent of neurosurgical respondents and 31 percent of orthopaedic surgeons employed low molecular weight heparin ($p < 0.001$). Neurosurgeons also selected anti-embolism stockings more frequently (79% vs 50%) while orthopaedic surgeons preferred mechanical prophylaxis (26% v 9%) (Bryson et al, 2012).

Deep-vein thrombosis and pulmonary embolism (PE) are associated with major morbidity and mortality, with their burden often extending to longer-term complications such as event recurrence and post-thrombotic syndrome. Few data exist on the overall economic burden of DVT and PE and their sequelae. Surveillance studies have found that the absolute risk of DVT is 10 to 20 percent among

The author is Ward Sister at SCTIMST, Thiruvananthapuram (Kerala).

general medical patients and up to 40 percent 80 percent in patients having hip surgery, knee surgery, or major trauma. Fatal pulmonary embolism rates range from 0.1 to 0.8 percent for all patients. A study to assess the economic burden of DVT and subsequent events suggest that the initial acute DVT or PE event is associated with high total health care costs and that these costs are further increased by subsequent events such as recurrent DVT or PE (Mc Dougall et al, 2006). Early detection and appropriate treatment of this high-risk population have the potential for both clinical and economic benefits.

There is no consensus among surgeons regarding the method of prophylaxis to be instituted and the exact timing of starting of prophylaxis. This review was undertaken to assess the evidences for DVT prophylaxis among neurosurgery patients and to develop an intensive care unit protocol for DVT prevention.

Review of Literature

Deep vein thrombosis and pulmonary embolism are frequently encountered in surgical patients and associated with high morbidity and mortality during hospitalisation. There is evidence that many venous thrombi are initiated by blood pooling in the venous sinuses of the calf, which promotes thrombosis by both causing anoxic damage to adjacent endothelial cells and by allowing the products of activated blood coagulation to accumulate (Gerlache et al, 2013). Conventional practice includes use of elastic bandage, surgical stockings or intermittent pneumatic compression. Pharmacological prophylaxis with lowered LMWH is reported to be a safer alternative but the use of these agents might also be hazardous. Vena cava filters (VCF) offer an alternative-adjuvant treatment option for prevention of the pulmonary embolism in high risk patient groups where pharmacological prophylaxis is risky or contraindicated.

In an RCT which included 161 patients, the intermittent pneumatic compression device reduced the incidence of silent DVT compared with no prophylaxis (1.5% vs 23.5%, RR 0.07; 95% CI 0.009 to 0.49) (Turpie et al, 1985). It was confirmed in a second RCT of 95 patients (8.3% vs 25%, RR 0.33; 95% CI 0.11 to 0.94) (Skillman et al, 1978).

A study conducted among spinal surgery patients, to compare the effectiveness of venacaval filter and heparin therapy showed no difference between these two therapies (Akmangit et al, 2015). A study to determine the risk of post-operative haemorrhage during a 3-year period of early post-operative administration of nadroparin (Fraxiparin) plus compression stockings in a large cohort of patients who underwent spinal surgery confirms that early post-operative pharmacological

thromboembolic prophylaxis using nadroparin in patients with spinal surgery is not associated with an increased risk of post-operative haemorrhage (Gerlach et al, 2013).

Methodology

It was a systematic review following Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines for design, conduct and reporting. It was sought to identify evidence-based recommendations for DVT prophylaxis among neurosurgery patients.

Objectives

The objectives of the study were to:

1. Assess the evidences for DVT prophylaxis among neurosurgery patients.
2. Develop an evidence-based ICU protocol for prevention of DVT.

Search Strategy and Study Selection

The search key words include 'deep vein thrombosis', 'prevention' and 'neurosurgery patients'. It was focussed on MeSH terms and other controlled vocabulary. The search strategy was confirmed by a colleague of this author to make sure of reproducibility. The database searched were google scholar and pubmed. On initial search 98 articles came which include 17 RCT and 28 systematic reviews; 28 articles were published within five years. Initially, titles were reviewed and possibly eligible articles were listed for abstract review. Articles with free full text were included for final review. There were 15 articles with free full text; amongst these, nine articles not meeting the inclusion criteria were removed.

Eligibility criteria: Studies done among adult patients who had undergone craniotomies or spinal cord surgeries were included. Studies done among patients in general surgeries, studies done among paediatric patients and elderly patients bedridden for long time because of conditions other than neurosurgical were excluded. Review articles and guidelines were also excluded.

Data Extraction

Data were summarised in a pre-defined data extraction form. Summarised information on study characteristics such as design and year, author information sample size, prophylactic method used, outcome, side effects, investigations done and the timing of prophylactic method used (preoperatively, post-operatively or peri-operatively).

Data synthesis and analysis: The prevention of DVT among neurosurgery patients is described using narrative review.

Results

Search was completed on 22 June 2018 and a total of 98 titles were reviewed. Abstracts were reviewed for 46 studies. Full text articles were reviewed for 15 studies. Of these 9 articles were discarded because of not meeting the inclusion criteria. Identified six studies met our inclusion criteria. The PRISMA flow diagram is shown in Figure 1.

Assessment of risk and bias in studies

Risk of bias for randomised controlled trials (RCTs) were assessed using pre-defined Cochrane risk of bias tool. Observational studies were assessed for risk of random and systematic bias. Studies were considered of high quality if they met the criteria for all the assessment mains (selection, performance, attrition, reporting and confounders). Only one study was having fair risk of bias (Sabri et al, 1971). All the other studies we are having high risk of bias.

Narrative review

Description of included studies: Six studies were included for review, four uncontrolled trials and two RCTs. Details of the study characteristics can

be found in Table 1. The total participants of included studies were 2811. The participants were mainly those who had undergone cranial and spinal surgeries. The outcome used was the incidence of symptomatic and asymptomatic DVT and pulmonary embolism (PE). The outcome was measured with clinical evaluation alone in two studies (symptomatic DVT). Other studies used Doppler ultrasonography and venography for assessing asymptomatic DVT.

The incidence of deep vein thrombosis both symptomatic and asymptomatic ranged from 0.01 to 29.4 percent. The incidence of symptomatic DVT ranged from 0.01 to 0.6 percent. Asymptomatic DVT incidence ranged from 4 to 29.4 percent. Two studies assessed the incidence of pulmonary embolism, but none of the patients developed such an event. The outcome PE was defined positive pulmonary angiography in symptomatic patients. Two studies assessed the factors associated with increased risk of DVT (Sabri et al, 1971; Teague et al, 2012). They found out immobility and increased duration of surgery more than 4.5 hours were associated with increased risk of DVT.

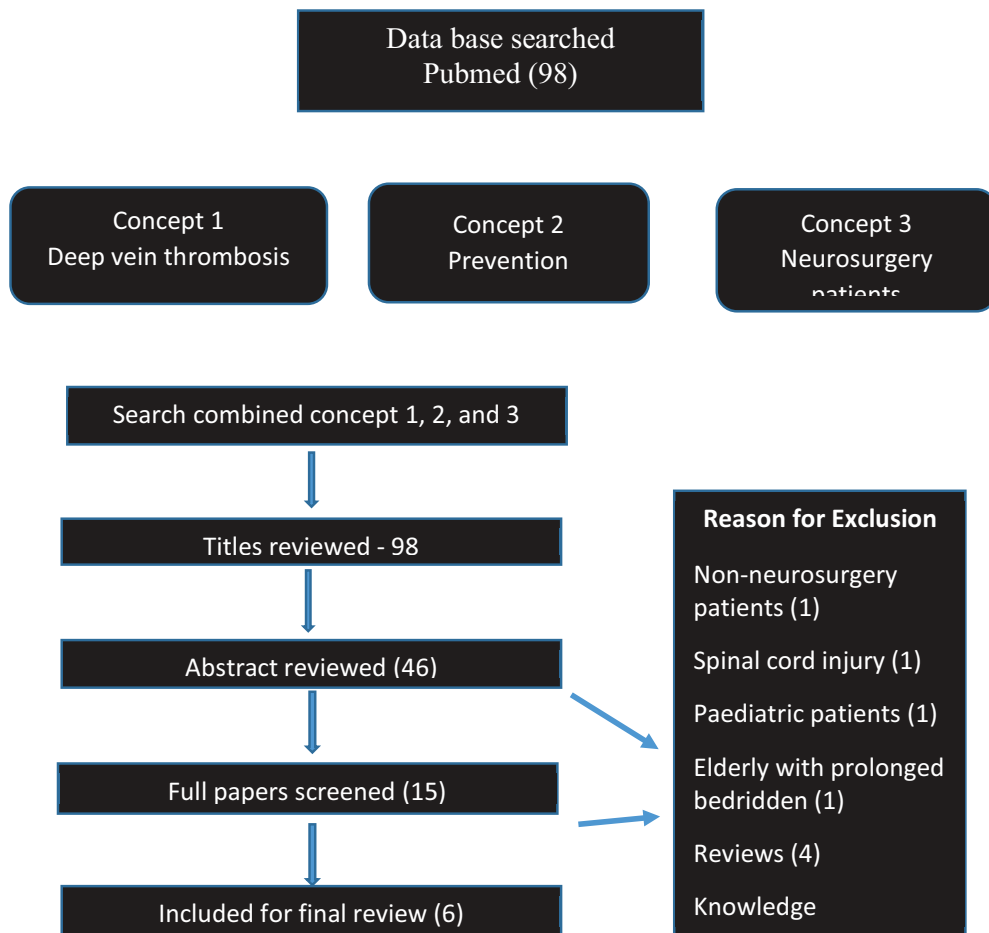


Figure 1: PRISMA flow diagram.

Table1: Summary of the included studies

Study	Design	Sample	Sample size	Prophylactic method used	Timing of prophylaxis	Investigations	Outcome	Factors associated	Side effects
Teague MS et al	RCT	Cranio and spinal surgery patients	75- experimental 75- control	Experimental group- intermittent calf compression device control- physiotherapy and stockings	Post-operatively 4 hrs after surgery	Compression Ultrasound and venography, CT angiography	DVT (4.0% vs. 18.7%) PE- 0%	Immobility	Minor skin aberrations
Al-Dulajji et al	Non-controlled clinical trials	Spinal surgeries	158	LMWH and below knee compression stockings	12 hrs after surgery- LMWH Perioperative- stockings	Signs and symptoms and confirmatory doppler ultrasonography	DVT incidence 0.6%	Duration of surgery >4.5 hrs	Haematoma 1.8%
Akmangit I. et al	Non-controlled clinical trial	Neuro surgery	40- experimental 27- control	Venacaval filter- experimental LMWH- control	Post-operative day 5-7	Doppler ultrasonography and pulmonary CT angiography	DVT (0.05 in filter group and 0.03 in LMWH) PE (0% in both groups)	Not done	Sepsis, heart failure, cerebral haemorrhage- filter group LMWH- Nil
Nicol et al	Non- controlled clinical trial	Spinal surgery	414	LMWH	First post- operative day	Clinical evaluation	DVT (0.24%)	Not assessed	Not assessed
Gerfache et al	Non-controlled clinical trials	Spinal surgery	1954	Nadroparin and compression stockings	Post-operative nadroparin Intraoperative and post- operative compression stockings	Clinical evaluation	DVT (0.01%)	Not assessed	Haematoma (0.4%)
Koo et al	RCT	Spinal surgery	34- experimental 34- control	Alternate sequential compression device (ASCD) vs a simultaneous sequential compression device (SSCD).	Peri-operative	Duplex ultrasonography on 4th and 7th POD	DVT (11.6 vs 29.4) No significant difference between groups	Not assessed	Nil

Prophylactic Methods Used

The prophylactic methods used were pneumatic compression devices, LMWH, nadroparin, vena caval filter, elastic compression stockings and physiotherapy. The timing of the prophylactic (chemoprophylaxis) was, post-operatively at 12 hour and 5-6 days. The pneumatic compression device, elastic crepe bandage was used peripherally.

The side effects were more associated with chemoprophylaxis. The incidence of post-operative bleeding and haematoma with the use of LMWH and nadroparin was 0.4 to 1.8 percent (Akmangit et al, 2015; Teague et al, 2015). One study showed no incidence of bleeding associated with use of LMWH. The use of compression device was associated with minor skin irritations. The use of venacaval filter was associated with sepsis, heart failure and cerebral haemorrhage.

Discussion

The findings of this review suggest that pharmacological and mechanical prophylaxis can be combined to prevent DVT among neurosurgery patients without increased bleeding risk or discomfort. These findings are comparable with other international studies and it is concluded that combined antithrombotic, mechanical and chemoprophylaxis is effective in decreasing post-spinal surgery DVT incidence to a minimum and, at the same time, without significant increase in the rate of bleeding complications.

The incidence of DVT and pulmonary thromboembolism is high in the setting of neurosurgery. Different methods prevent the development of DVT among neurosurgery patients. The ideal timing of use of prophylactic method and the risk benefit of pharmacological prophylactic methods are still controversial. High quality studies are lacking. Many studies support the use of prophylactic pharmacological methods, but some do not support it because bleeding risk and the neurological deficit caused by it can offset the morbidity caused by DVT.

A survey conducted among spinal surgeons shows that 73 percent of neurosurgical respondents and 31 percent of orthopaedic surgeons employed low molecular weight heparin ($p < 0.001$). Neurosurgeons also selected anti-embolism stockings more frequently (79% vs 50%) while orthopaedic surgeons preferred mechanical prophylaxis (26% vs 9%). The incidence of symptomatic post-operative epidural haematoma is 0.1 to 3 percent (Kebaish & Award, 2004). The use of prophylactic LMWH or mini dose heparin is not associated with increased risk of post-operative bleeding (Akmangit et al, 2015; Gruber et al, 1984). The initiation of chemoprophylaxis pre-operatively can have high risk for patients 12 hours prior surgery. It can be restarted

safely 72 hours post operatively or on an individual case to case basis (Bryson et al, 2012; Skillman et al, 1978; Akmangit et al, 1984).

The intraoperative risk of DVT among neurosurgery patients is also a significant problem because of the surgical positions. Pneumatic compression device is now used increasingly because it is a good alternative to anticoagulation chosen primarily in patients at high risk of bleeding. It can be won peri-operatively without significant patient discomfort (McDougall et al, 2006). Venous emptying of at least 12 hours a day can reduce thrombus risk. The intermittent and simultaneous compression devices are equally effective (Koo et al, 204).

Duplex scanning has 100 percent sensitivity and 98 percent specificity in symptomatic patients for proximal DVT, and 94 percent sensitivity and 75 percent specificity for distal venous thrombosis. It is safer than other invasive techniques, such as contrast venography, and also provides a more timely diagnosis in a more efficient manner than most non-invasive techniques. Routine screening is not advised, in symptomatic patients duplex scanning can be done to confirm the diagnosis.

Limitations

This review has many limitations. There is heterogeneity among included studies, single researcher conducted the review and only six studies were covered for final review. Meta-analysis was not done as the primary objective was not to find out the incidence of DVT, but to find out the evidences for DVT prophylaxis among neuro surgery patients.

Recommendations

Following recommendations are made for neurosurgical care practice.

- In craniotomy patients at particularly high risk for venous thromboembolism, initiate mechanical thromboprophylaxis with intermittent pneumatic compression device preoperatively with addition of low molecular weight heparin (LMWH) post-operatively when the risk of bleeding is presumed to be decreased.
- If intermittent pneumatic compression (IPC) is used, it should be applied before the surgical procedure or on admission and continued intra-operatively and post-operatively.
- In patients with non-traumatic intracranial haemorrhage, thromboprophylaxis with IPC should be initiated. Start heparin as the rebleed risk subsides, hold it for 12 hours before surgery.
- Continue thromboprophylaxis until full mobilisation of the patient.
- For patients undergoing spinal surgery with additional risk factors, start mechanical

thromboprophylaxis with IPC and add LMWH post-operatively when the risk of bleeding is presumed to be decreased.

High quality studies are lacking, most of the studies are having high risk of bias. More randomised controlled trials are to be undertaken with sufficient sample size to find out the optimal timing of starting chemoprophylaxis without additional risk of bleeding and observational studies to document the natural course of asymptomatic venous thrombosis.

Conclusion

Neuro surgery patients require particular attention to prevent DVT and venous thromboembolism to decrease the added mortality and morbidity associated with it. All the patients should receive chemoprophylaxis and mechanical prophylaxis after assessing the risk of bleeding. The combined prophylactic methods can reduce the risk of DVT without any additional risk of bleeding. The prophylactic method should be continued till the patient is ambulated. Routine screening for DVT is not recommended. In symptomatic patients duplex ultrasonography can be done to confirm the diagnosis.

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डीप वेन थ्रोम्बोसिस से कैसे निजात पाएं

शरीर के किसी हिस्से खासकर एक टांग में अक्सर दर्द, सूजन का कारण डीप वेन थ्रोम्बोसिस (डीवीटी) हो सकता है। इस बीमारी में खून के थक्के (ब्लड क्लॉट) बन जाते हैं। साठ वर्ष के बाद यह समस्या अधिक होती है। डी-डिमेर टेस्ट, वेनोग्राम, अल्ट्रासाउंड आदि से डीवीटी की पुष्टि हो जाती है। इलाज बतौर एंटीकोगुलेंट्स (खून पतला करने की दवाएं) छह माह तक देते हैं तथा दबाव वाले मोजे पहनने होते हैं। डीवीटी से बचाव के लिए शारीरिक गतिविधि, खासकर चलना चालू रखें, ऑपरेशन आदि के बाद चल न सकें तो एड्रियों का व्यायाम करते रहें।