

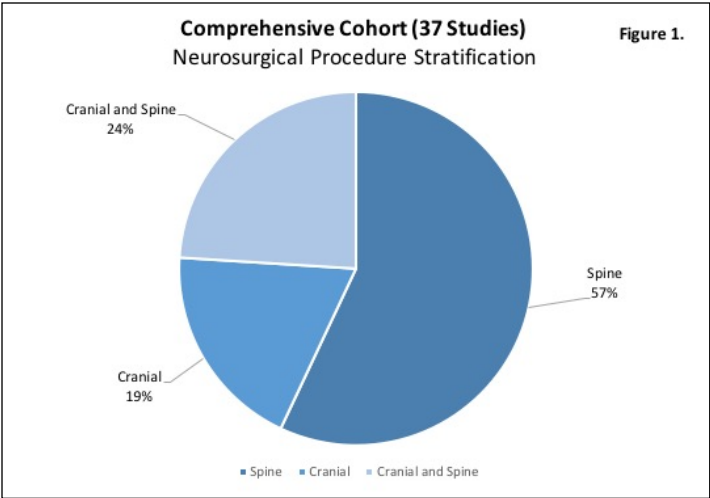


Introduction

Venous thromboembolism (VTE) is a potentially life-threatening complication after neurosurgery. Current recommendations suggest chemoprophylactic, mechanical, or combination therapy to reduce the risk of VTE; however, the literature has been inconclusive as to which strategy is the most effective in reducing the incidence of VTE. We performed a systematic literature review to compare the efficacy and safety of chemoprophylaxis, mechanical prophylaxis, and combination prophylaxis for DVT/PE prevention after cranial and spinal procedures.

Methods

A search was performed of Pubmed, MedlinePlus, JAMA and the National Library of Medicine (NLM) for the following key words: venous thromboembolism, prevention, prophylaxis, unfractionated heparin, mechanical, neurosurgery, spinal surgery. Thirty-seven studies were identified for analysis. A systematic review compared the following cohorts: control (no prophylaxis), chemoprophylaxis (including low molecular weight heparin, low dose unfractionated heparin, and direct Xa inhibitors), mechanical prophylaxis, and combination prophylaxis. Subgroup analysis based on procedure type was also performed (cranial, spinal, or combined - figure 2). Studies were included irrespective of type of neurosurgical procedure or treated pathology. Inclusion criteria for each study varied, but only two studies included patients with previous DVT or thrombophila within their samples. Incidence of deep vein thrombosis (DVT), pulmonary embolism (PE), and postoperative bleeding complications were the primary outcomes evaluated. Postoperative bleeding complications included both intracranial and extracranial hemorrhage.



Results

Thirty-seven studies met inclusion criteria and reported on 9992 patients undergoing common neurosurgical procedures. Qualifying studies were randomized controlled trials (RCTs) or had MINORS (methodological index for non-randomized studies) scores of 8 or greater. The final cohort was comprised of 6 double-blind RCTs, 11 RCTs, 7 prospective studies, 9 retrospective studies, and 4 cohort studies. Results of our systematic review are summarized in figure 1.

NO PROPHYLAXIS			Figure 1.
	Frequency of DVT	Frequency of PE	Frequency of Postoperative Bleeding Complications
Cranial	34.00%	0.00%	4.00%
Spine	12.32%	ns	ns
Cranial and Spine	19.55%	0.00%	2.33%
Comprehensive Cohort	16.40%	0.00%	1.68%
MECHANICAL PROPHYLAXIS			
Cranial	5.63%	1.88%	2.22%
Spine	2.19%	1.17%	0.00%
Cranial and Spine	8.19%	1.12%	2.13%
Comprehensive Cohort	3.42%	1.16%	1.27%
CHEMOPROPHYLAXIS			
Cranial	6.00%	0.00%	2.00%
Spine	1.65%	0.22%	5.27%
Cranial and Spine	3.46%	1.89%	5.97%
Comprehensive Cohort	2.18%	0.68%	4.75%
COMBINATION PROPHYLAXIS			
Cranial	8.91%	0.20%	7.82%
Spine	0.69%	0.36%	4.54%
Cranial and Spine	7.56%	0.00%	2.24%
Comprehensive Cohort	2.39%	0.31%	1.85%

Statistical Analysis

A Chi-square test was performed on all relevant values in MATLAB R2018a, significance defined as $p < 0.05$. All prophylactic interventions significantly reduced the incidence of DVT compared to no prophylaxis. No significant difference in the incidence of PE was found between prophylaxis and control groups, regardless of the mode of treatment. The chemoprophylaxis group had a significantly higher incidence of bleeding complications compared to mechanical and combined prophylaxis. However, this finding may be skewed by the preferential use of preoperative prophylaxis in multiple studies within the chemoprophylaxis group and the inclusion of one study that used a Direct Xa inhibitor, which independently resulted in a higher rate of postoperative bleeding events (6.16%).

Sub-group Analysis Based on Procedure Type

Comprehensive Cohort - 37 Studies

Both chemoprophylaxis and combination prophylaxis were more effective in reducing DVT incidence than mechanical prophylaxis. However, there was no significant difference between them($p < 0.05$, $p = .00034$, $p = .001$).

Cranial Cohort - 7 of 37 Studies

There was no significant difference in DVT incidence among chemoprophylaxis, mechanical prophylaxis, and combination prophylaxis, but all were significantly superior to no prophylaxis. Mechanical prophylaxis had a significantly lower incidence of post-operative bleeding compared to combination prophylaxis($p < 0.05$, $p = 0.026$).

Spine Cohort - 21 of 37 Studies

Combination prophylaxis significantly reduced the incidence of DVT compared to chemoprophylaxis or mechanical prophylaxis($p < 0.05$, $p = 0.0002$, $p = 0$). Mechanical prophylaxis and no prophylaxis had significantly lower rates of post-operative bleeding than chemoprophylaxis or combination prophylaxis($p < 0.05$, $p = 0.001$).

Cranial and Spine Cohort - 9 of 37 Studies

Chemoprophylaxis had significantly lower DVT rates than mechanical prophylaxis ($p = 0.00035$), but no significant difference from combination prophylaxis.

Conclusions

- 1). All modes of VTE prophylaxis are effective in reducing the incidence of VTE when compared to no prophylaxis.
- 2). Chemoprophylaxis and combination prophylaxis are more effective than mechanical prophylaxis alone in reducing the incidence of DVT when cranial and spinal procedures are considered collectively. However, this study was not sufficiently powered to generalize this conclusion to each procedure sub-type.
- 3). Incidence of postoperative bleeding events is significantly increased by the use of chemoprophylaxis, but this may be due to variable timing of anticoagulant administration (pre- vs. post-procedure prophylaxis) or type of anticoagulant used, with direct anti-Xa inhibitors potentially bearing an independently increased risk.