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# Association Between Early Chemoprophylaxis versus No Chemoprophylaxis and Risk of Venous Thromboembolism and Bleeding Complications after Same-Day Spine Surgery for Central Cord Syndrome: A Retrospective Cohort Analysis

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## Abstract

***Study Design***

Retrospective cohort study

***Objectives***

To examine whether early chemoprophylaxis, compared with no chemoprophylaxis, is associated with a reduced risk of venous thromboembolism (VTE) and bleeding complications after spine surgery for acute central cord syndrome (CCS).

***Setting***

Multi-site academic centers

***Methods***

This pre-registered study using the TriNetX database included adults who underwent primary cervical spine surgery the same day they sustained a CCS. After excluding those with very high VTE risk or prior VTE, we divided participants into cohorts depending on the administration of chemoprophylaxis (heparin or enoxaparin; chemoprophylaxis cohort) versus no chemoprophylaxis (no chemoprophylaxis cohort) within the first three days after surgery. Outcomes through three months included the incidence and risk ratio (RR) of VTE (primary), pulmonary embolism (PE), deep venous thrombosis (DVT), and deceased status. Cohorts were propensity matched according to key risk factors.

***Results***

There were 2,417 participants per matched cohort with high follow-up retention (98%). Between cohorts, there was no statistically significant or clinically meaningful difference in the risk of VTE (p=0.375) over three months' follow-up. Furthermore, there was no statistically significant difference in the risk of PE (p=0.762) or DVT (p=0.384). We were unable to assess the risk of epidural hematoma or severe postoperative bleeding as both outcomes were rare.

***Conclusion***

Early postoperative chemoprophylaxis was not associated with reduced VTE risk compared with no chemoprophylaxis after spine surgery for acute CCS in adults. These findings do not provide evidence supporting routine chemoprophylaxis use in CCS participants after surgery. However, clinical decisions should remain individualized.


# INTRODUCTION

Central cord syndrome (CCS) is a common incomplete spinal cord injury (SCI) syndrome, making up 9–14% of traumatic SCIs [1, 2]. CCS most commonly results from a hyperextension injury in those with underlying cervical spondylosis and results in motor and sensory deficits that are more pronounced in the upper extremities versus the lower extremities [3]. Management for CCS includes surgical and non-surgical options; however, recent recommendations suggest early surgical intervention to decompress the cervical spinal cord [4, 5]. Surgical modalities vary, including fusion, discectomy, and decompression, depending on the pathophysiology of CCS [6]. Regardless of modality of surgical intervention, it has been demonstrated that early versus delayed surgery for CCS results in more favorable outcomes and less complications, including venous thromboembolism (VTE) [6, 7]. VTE, including pulmonary embolism (PE) and deep vein thrombosis (DVT), are relatively infrequent complications after surgery for CCS, with incidence ranging from 1.1% to 5.2% after early spine surgery [6–8]. However, considering VTE may be fatal in 0.34% of affected participants after surgery, there is a need for research into prevention strategies [9].

Research regarding efficacy and safety of chemoprophylaxis initiated shortly after surgical intervention for CCS is fairly limited with no strong consensus on utilization, which agent is most effective, and timing of initiation. A shortened clinical

practice guideline by Fehlings et al. (2017) suggested that anticoagulants, in the form of low-molecular-weight heparin (LMWH) or fixed, low-dose unfractionated heparin, initiated within 72 hours of SCI could sufficiently reduce the risk of VTE, however no specific recommendations were made for CCS [10]. In the full clinical practice guideline, Fehlings et al. (2017) discussed the ongoing debate whether patients with CCS should follow the same VTE chemoprophylactic protocol as patients with complete SCI, primarily because individuals with CCS generally demonstrate greater mobility and preserved motor function [5]. Additionally, the recommendation to provide early VTE chemoprophylaxis put forth by Fehlings et al. is labeled as a weak recommendation based on a low quality of evidence.

A recent retrospective cohort study by Baumann et al. (2025) compared early enoxaparin versus heparin and their effectiveness in preventing VTE and safety profile after surgery for CCS [11]. The study found no statistically significant or meaningful difference in three-month VTE incidence between cohorts (i.e., 4.8% vs. 4.3% in the enoxaparin and heparin cohorts, respectively) [11]. Likewise, safety profiles were similar between enoxaparin and heparin, with no statistically significant difference in incidence of epidural hematoma (EDH) or severe postoperative bleeding (SPOB). Due to the relatively low incidence of VTE after surgery for CCS, clinical practice remains inconsistent regarding long-term risks and benefits.

Research evaluating the comparative VTE incidence and safety of chemoprophylaxis versus no chemoprophylaxis following spine surgery for CCS is non-existent. Given these literature gaps, the purpose of this study will be to investigate the risk of VTE in patients receiving chemoprophylaxis (enoxaparin or unfractionated heparin) within three days after same-day spine surgery for CCS compared to those that received no VTE chemoprophylaxis. We will evaluate participants for three months after surgery for CCS, as previous research has demonstrated that most VTE events occur within the three-month postoperative period [12]. We will also use enoxaparin and heparin both in the chemoprophylaxis cohort as recent evidence has cautiously suggested equivalence [11]. Lastly, we will examine the risk of adverse events associated with postoperative anticoagulation, including EDH and SPOB. We hypothesize that early postoperative chemoprophylaxis will not be associated with a lower risk of VTE compared with no chemoprophylaxis after surgery for CCS, without a meaningful increase in bleeding complications.

# METHODS

*Study Registration and Design*

This retrospective propensity-matched cohort study adhered to a preregistered protocol on Open Science Framework (https://osf.io/2jvwz). The University Hospitals Institutional Review Board (IRB) considers de-identified data from TriNetX (TriNetX, LLC., Cambridge, MA, US) to meet criteria for “Not Human Subjects” research. Thus, this study was exempt from IRB review. The query date was January 19, 2026.

*Data Source and Study Setting*

Data was acquired from TriNetX, a large online multicenter database that is based on electronic health records of healthcare organizations throughout the United States. The database represents greater than 161 million participants across 113 healthcare organizations. TriNetX utilizes International Classification of Disease (ICD) and Current Procedural Terminology (CPT) codes, as well as RxNorm for medications. TriNetX is compliant with the Health Insurance Portability and Accountability Act (HIPAA). Data displayed are in the aggregate form and de-identified as defined in Section §164.514(a) of the HIPAA Privacy Rule. Participating healthcare organizations remain anonymous in order to protect patient privacy.

*Participants and Cohort Creation*

Participants were adults ≥18 years old undergoing same-day spine surgery for first-time CCS between three months and twenty years prior to the query (2005-2023), with the surgical date representing the index date. Surgical modalities vary, including fusion, discectomy, and decompression, depending on the pathophysiology of CCS [6], thus, our study included participants undergoing multiple types of cervical spine surgery for CCS to expand sample size and generalizability. Participants were excluded if they had VTE, EDH, or SPOB within the preceding six months, or any history of inferior vena cava

filter or spinal neoplasms. To minimize selection bias related to administration of enoxaparin or heparin in the early postoperative period, participants with a diagnosis of chronic kidney disease prior to surgery or through three days postoperative were excluded. Similarly, participants with a diagnosis of acute kidney injury or use of dialysis within six months prior or three days after surgery were also excluded. Participants were divided into two cohorts dependent on the chemoprophylaxis administration: those receiving heparin or enoxaparin (chemoprophylaxis cohort; **Supplementary Table 1**) or receiving no anticoagulation (no chemoprophylaxis cohort; **Supplementary Table 2**) within the first three days after surgery for CCS. Administration of anticoagulants within 72 hours was chosen based on the recommendation by Fehlings et al. (2017), that anticoagulation after SCI should occur in the first 72 hours [10]. To ensure participants in the chemoprophylaxis cohort received only heparin or enoxaparin, participants that received other anticoagulant and antiplatelet agents in this timeframe were also excluded. This included aspirin, direct oral anticoagulants (DOACs [dabigatran, rivaroxaban, apixaban, edoxaban]); vitamin K antagonists (warfarin, phenprocoumon); direct thrombin inhibitors (desirudin, argatroban, lepirudin, bivalirudin); antithrombotic agents (defibrotide); heparin, porcine; low-molecular-weight heparin other than enoxaparin (fondaparinux, dalteparin); as well as drugs like glycoprotein IIb/IIIa inhibitors (tirofiban, eptifibatide).

*Propensity Matching Variables*

We utilized propensity score matching to control for risk factors associated with VTE after SCI, using an assessment window of one year preceding and including the index date of surgery [10]. Propensity matched factors and codes utilized are shown in **Supplementary Table 3** [13-19]. Additionally, we controlled for VTE between six months and one year before surgery, polytrauma, history of shock, prior use of DOACs (rivaroxaban and apixaban) as another proxy for baseline VTE risk [20], as well as bed confinement and wheelchair bound status [21]. The use of generalized risk factors for VTE overlapped with those of our secondary outcomes of DVT and bleeding risks, thereby minimizing confounding. Additionally, participants were matched by a common multilevel fusion code for both anterior and posterior approaches to control for surgical approach/extent [8].

*Primary and Secondary Outcomes*

The primary outcome of this study were the incidence and risk ratio (RR) for VTE through three months after surgery for CCS [11]. Secondary outcomes included the incidence and RR for EDH, DVT, PE, and SPOB through three months (**Supplementary Table 4**). Rare events of less than 10 cases for an outcome are not displayed in TriNetX for patient privacy. We also represented the cumulative incidence graphically.

*Power Analysis for Sample Size*

A required sample size of 1,059 participants per cohort was calculated using assumptions of 5% risk of VTE in the chemoprophylaxis cohort and 8% risk of VTE in the no chemoprophylaxis cohort through three months after surgery for SCI in adults. This was based on the 4.3% and 4.8% incidence of VTE in after heparin and enoxaparin administration following surgery for CCS in our prior study [11]. This was similar to the 5.2% incidence of VTE for patients with CCS within an unspecified time frame [8]. This power analysis utilized a two-tailed alpha-error of 0.05, an allocation ratio of one, and a power of 0.95 using GPower (Kiel University, DE) software with the z-testing function for our statistical analysis.

*Statistical Analysis*

Initial statistical analysis was completed within the TriNetX online statistical software. For comparisons of patient baseline characteristics, this study utilized standardized mean difference (SMD), using a threshold of SMD>0.1 to represent meaningful asymmetry in baseline characteristics. TriNetX uses Python (scikit-learn version 1.3 [Python Software Foundation, Delaware, USA]) to conduct logistic regression and compute propensity scores, using 1:1 greedy nearest-neighbor matching with a caliper of 0.1 pooled standard deviations. To explore data quality, we reported the mean and median follow-up duration, as well as the proportion of participants having at least three months follow-up. We also calculated the RR for negative control outcomes to determine if meaningful between-cohort differences in high-energy trauma or patient care could account for our findings, evaluating the RR point estimates around the null as balanced (i.e., values of 0.8 to 1.2) [22]. These included major

trauma diagnoses of “injuries of multiple body regions” (ICD-10: T07) and physical therapy evaluations. For primary and secondary outcomes, this study used RRs with [95% confidence intervals (CIs)], set the statistical significance at $p<0.05$, and explored cumulative incidence with 95% CIs for VTE. We utilized R (version 4.2.2, Vienna, AT) [23] to calculate 95% CIs and ggplot2 [24] to graph propensity densities and cumulative incidences.

# RESULTS

*Patient Characteristics*

There were 2,833 participants in the chemoprophylaxis cohort and 3,936 participants in the no chemoprophylaxis group before matching. After matching, there were 2417 participants in each cohort. Once matched, participants in the chemoprophylaxis cohort had a mean (standard deviation (SD)) age at the time of same-day surgery to be 57.9 (13.4) years and 74% were male. Individuals within the no chemoprophylaxis cohort had a mean (SD) age at the time of same-day surgery to be 57.8 (13.6) years and 73% were male. The chemoprophylaxis and no chemoprophylaxis had near-identical proportions of multilevel posterior fusion (30% versus 30%; SMD=0.006) and multilevel anterior fusion (10% versus 10%; SMD=0.015). Once the two cohorts were matched, they had similar attributes across at baseline (SMD<0.1) (**Table 1; Figure 1**).

| Variable (n (%) or mean (SD)) | Before Matching | | | After Matching | | |
|---|---|---|---|---|---|---|
| | Chemoprophylaxis | No Chemoprophylaxis | SMD | Chemoprophylaxis | No Chemoprophylaxis | SMD |
| Participents (n) | 2833 | 3936 | - | 2417 | 2417 | - |
| Black or African American | 668 (24%) | 739 (19%) | **0.118** | 533 (22%) | 532 (22%) | 0.001 |
| Slipping, tripping, stumbling and falls | 1577 (56%) | 1609 (41%) | **0.299** | 1257 (52%) | 1259 (52%) | 0.002 |
| Ischemic heart diseases | 330 (12%) | 469 (12%) | 0.008 | 286 (12%) | 284 (12%) | 0.003 |
| Apixaban | 33 (1%) | 56 (1%) | 0.023 | 32 (1%) | 31 (1%) | 0.004 |
| Age at Index | 58.1 (13.4) | 58 (13.3) | 0.012 | 57.9 (13.4) | 57.8 (13.6) | 0.005 |
| Dependence on wheelchair | 22 (1%) | 40 (1%) | 0.025 | 21 (1%) | 20 (1%) | 0.005 |
| Not Hispanic or Latino | 2296 (81%) | 3060 (77%) | 0.082 | 1945 (80%) | 1939 (80%) | 0.006 |
| Posterior arthrodesis, each additional interspace (CPT: 22614) | 1000 (35%) | 917 (23%) | **0.266** | 729 (30%) | 736 (30%) | 0.006 |
| Paraplegia | 109 (4%) | 114 (3%) | 0.053 | 86 (4%) | 83 (4%) | 0.007 |
| Persons with potential health hazards related to socioeconomic and psychosocial circumstances | 195 (7%) | 159 (4%) | **0.125** | 133 (6%) | 137 (6%) | 0.007 |
| Hispanic or Latino | 145 (5%) | 198 (5%) | 0.004 | 123 (5%) | 119 (5%) | 0.008 |
| White | 1766 (62%) | 2507 (64%) | 0.028 | 1534 (63%) | 1543 (64%) | 0.008 |
| Other chronic obstructive pulmonary disease | 236 (8%) | 313 (8%) | 0.014 | 195 (8%) | 201 (8%) | 0.009 |
| Other forms of heart disease | 793 (28%) | 873 (22%) | **0.134** | 614 (25%) | 623 (26%) | 0.009 |
| Unspecified multiple injuries | 137 (5%) | 195 (5%) | 0.005 | 115 (5%) | 120 (5%) | 0.010 |
| Current Age | 63.8 (13.5) | 64.8 (13.3) | 0.076 | 63.9 (13.5) | 63.7 (13.5) | 0.010 |
| Intracranial injury | 400 (14%) | 435 (11%) | 0.093 | 325 (13%) | 315 (13%) | 0.012 |
| Overweight and | 477 (17%) | 589 (15%) | 0.051 | 398 (16%) | 410 (17%) | 0.013 |

| | | | | | | |
|---|---|---|---|---|---|---|
| obesity | | | | | | |
| Other venous embolism and thrombosis | 41 (1%) | 55 (1%) | 0.004 | 37 (2%) | 33 (1%) | 0.014 |
| Focal traumatic brain injury | 34 (1%) | 37 (1%) | 0.025 | 27 (1%) | 31 (1%) | 0.015 |
| Anterior arthrodesis, each additional interspace (CPT: 22552) | 248 (9%) | 455 (12%) | 0.093 | 240 (10%) | 251 (10%) | 0.015 |
| Contraceptives, systemic | 133 (5%) | 112 (3%) | 0.097 | 99 (4%) | 92 (4%) | 0.015 |
| Nicotine dependence | 905 (32%) | 1007 (26%) | **0.141** | 739 (31%) | 722 (30%) | 0.015 |
| Coagulation defects, purpura and other hemorrhagic conditions | 200 (7%) | 208 (5%) | 0.074 | 162 (7%) | 152 (6%) | 0.017 |
| Posterior arthrodesis, cervical below C2, single (CPT: 22600) | 1041 (37%) | 951 (24%) | **0.276** | 769 (32%) | 747 (31%) | 0.020 |
| Male | 2081 (73%) | 2877 (73%) | 0.008 | 1780 (74%) | 1758 (73%) | 0.021 |
| Female | 751 (27%) | 1058 (27%) | 0.008 | 636 (26%) | 658 (27%) | 0.021 |
| Inflammatory polyarthropathy | 161 (6%) | 276 (7%) | 0.055 | 148 (6%) | 136 (6%) | 0.021 |
| Shock, not elsewhere classified | 208 (7%) | 123 (3%) | **0.190** | 124 (5%) | 113 (5%) | 0.021 |
| Tetraplegia | 607 (21%) | 543 (14%) | **0.201** | 452 (19%) | 431 (18%) | 0.022 |
| Chemotherapy | 68 (2%) | 96 (2%) | 0.003 | 54 (2%) | 63 (3%) | 0.024 |
| Other incomplete lesions of thoracic spinal cord | 18 (1%) | 30 (1%) | 0.015 | 14 (1%) | 19 (1%) | 0.025 |
| Diabetes mellitus | 604 (21%) | 837 (21%) | 0.001 | 525 (22%) | 499 (21%) | 0.026 |
| Hypotension | 537 (19%) | 410 (10%) | **0.243** | 380 (16%) | 357 (15%) | 0.026 |
| Traumatic shock | 84 (3%) | 53 (1%) | **0.112** | 61 (3%) | 49 (2%) | 0.033 |
| Asian | 130 (5%) | 255 (6%) | 0.083 | 120 (5%) | 103 (4%) | 0.034 |
| Anterior arthrodesis, cervical below C2, single (CPT: 22551) | 607 (21%) | 965 (25%) | 0.074 | 553 (23%) | 590 (24%) | 0.036 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Other and unspecified injury of lumbar and sacral spinal cord | 182 (6%) | 339 (9%) | 0.083 | 163 (7%) | 197 (8%) | 0.054 |
| Other and unspecified injuries of thoracic spinal cord | 212 (7%) | 393 (10%) | 0.089 | 183 (8%) | 235 (10%) | 0.077 |
| Other incomplete lesions of cervical spinal cord | 325 (11%) | 266 (7%) | **0.164** | 258 (11%) | 200 (8%) | 0.082 |
| Primary thrombophilia | 16 (1%) | ≤10 | 0.049 | 13 (1%) | ≤10 | - |
| Pulmonary embolism | ≤10 | 31 (1%) | - | ≤10 | ≤10 | - |
| Rivaroxaban | ≤10 | 19 (<1%) | - | ≤10 | ≤10 | - |
| Traumatic subdural hemorrhage | ≤10 | 14 (0%) | - | ≤10 | ≤10 | - |
| Systemic lupus erythematosus | ≤10 | 12 (<1%) | - | ≤10 | ≤10 | - |

**Table 1:** Baseline patient characteristics amongst the chemoprophylaxis and no chemoprophylaxis cohorts within this study organized by ascending post-match standardized mean difference (SMD). Patient counts of less than or equal to 10 cases for a specific attribute were not reported for de-identification purposes. SMD of >0.1 are bolded. For variables having ≤10 participants, SMD was not calculated (dash). Other abbreviations: Current Procedural Terminology (CPT).

[Insert Figure 1].

*Primary Outcome: Risk of Venous Thromboembolism through Three Months*

With regards to the risk of VTE between participants in the chemoprophylaxis cohort versus the participants in the no chemoprophylaxis cohort through three months after same-day spine surgery, there was no statistically significant or clinically meaningful difference (RR:1.14 [95% CI: 0.85 to 1.56]; p=0.375). There were 85 (3.5%) occurrences in the chemoprophylaxis cohort and 74 (3.1%) occurrences in the no chemoprophylaxis cohort experiencing VTE through three months after same-day spine surgery for CCS. The total incidence of VTE across both cohorts was 3.3% (n=159 occurrences out of 4,834 participants). The cumulative incidence for the two cohorts displayed a sharp initial curve succeeded by a gradual curve and 95% CIs overlapped at all time points amongst both cohorts (**Figure 2**).

| Primary and Secondary Outcomes | After Propensity Matching | |
|---|---|---|
| | Chemoprophylaxis Cohort | No Chemoprophylaxis Cohort |
| Participants, N | 2,417 | 2,417 |
| Venous Thromboembolism, N (%) | 85 (3.5) | 74 (3.1) |
| RR ([95% CI]; p) | 1.15 ([0.85, 1.56]; p=0.375) | (reference) |
| Pulmonary Embolism, N (%) | 21 (0.8) | 23 (1.0) |
| RR ([95% CI]; p) | 0.91 ([0.51, 1.65]; p=0.762) | (reference) |
| Deep Venous Thrombosis, N (%) | 47 (1.9) | 39 (1.6) |
| RR ([95% CI]; p) | 1.21 ([0.79, 1.84]; p=0.384) | (reference) |
| Abbreviations: Risk Ratio (RR), 95% confidence intervals (95% CI). | | |

**Table 2:** Outcomes for the chemoprophylaxis and no chemoprophylaxis cohorts, respectively, after propensity score matching. Estimates for epidural hematoma and severe postoperative bleeding could not be calculated as these had ≤10 participants per cohort.

[Insert Figure 2]

*Secondary Outcomes: Risk of Pulmonary Embolism through Three Months*

There was no statistically significant difference in the risk of PE between participants in the chemoprophylaxis cohort versus the participants in the no chemoprophylaxis cohort through three months after spine surgery for CCS (RR:0.91 [95% CI: 0.51 to 1.65]; p=0.762). There were 21 (0.8%) cases and 23 (1.0%) cases of PE in the chemoprophylaxis and no chemoprophylaxis cohorts through three months, respectively (Table 2). The overall incidence of PE at three months post-surgery for CCS, amongst both cohorts, was 0.9% (n=44 cases out of 4,834 participants).

*Secondary Outcomes: Risk of Deep Vein Thrombosis through Three Months*

With regards to the risk of DVT between participants in the chemoprophylaxis cohort versus the participants in the no chemoprophylaxis cohort through three months after same-day spine surgery, there was no statistically significant or clinically meaningful difference (RR:1.21 [0.79 to 1.84]; p=0.384). There were 47 (1.9%) occurrences in the chemoprophylaxis cohort and 39 (1.6%) occurrences in the no chemoprophylaxis cohort experiencing DVT through three months after same-day spine surgery for CCS. The total incidence of DVT at three months post same-day surgery for CCS amongst both cohorts was 1.8% (n=86 occurrences out of 4,834 participants).

*Secondary Outcomes: Risk of Epidural Hematoma or Severe Postoperative Bleeding*

Less than or equal to 10 participants per cohort experienced postoperative EDH and SPOB. Considering de-identification requirements for small participant counts to protect patient privacy (i.e., ≤10 participants), RRs and other results could not be calculated.

*Propensity Matching Diagnostics and Data Quality*

With regards to the chemoprophylaxis cohort, there was a median follow-up time of 90 days and mean (SD) of 82.0 (21.6) days with 97.8% of participants following up within three months post-surgery. For the no chemoprophylaxis cohort, there was a median of 90 days and a mean (SD) of 83.5 (20.2) days with 98.1% of participants retained to follow-up. Comparing chemoprophylaxis to no chemoprophylaxis, two of three negative control outcome RR effect sizes, as well as deceased status during follow-up were in the predefined zone indicative of balance (0.8 to 1.2), while the remaining negative control approximated this zone (Figure 2), suggesting that between-cohort differences in multiple injuries or other unmeasured

confounders would be unlikely to explain our findings. After matching, the propensity score density plots between the two cohorts overlapped closely, further indicating similarities amongst the cohorts (Figure 3). Accordingly, matched characteristics, patient attrition, and further traumatic exposure likely did not confound the results of this study.

[Insert Figure 3]

# DISCUSSION

In the first study to examine the incidence of VTE with chemoprophylaxis compared to no chemoprophylaxis after spine surgery for CCS, we found no statistically significant difference in the risk of VTE within the first three months post same-day surgery. These findings support our hypothesis that early postoperative chemoprophylaxis will not be associated with a lower risk of VTE compared with no chemoprophylaxis after surgery for CCS, without a meaningful increase in bleeding complications. There are relatively limited clinical data regarding prevention of VTE via chemoprophylaxis in patients with CCS, prompting this follow-up study to a recently published retrospective analysis by Baumann et al. (2025) that investigated VTE chemoprophylaxis after surgery for CCS utilizing early enoxaparin versus heparin [11]. In the study by Baumann et al. (2025), no clinically meaningful difference was observed between early (≤ 3 days) enoxaparin versus heparin anticoagulant administration [11].

The AO spine 2017 guideline did not provide definitive recommendations on whether chemoprophylaxis should be used versus no prophylaxis in the CCS population [5]. Our study similarly found no benefit of chemoprophylaxis (heparin or enoxaparin) compared to no chemoprophylaxis in the CCS population, adding to the evidence that the decision to use chemoprophylaxis and if so, which strategy is optimal, remains unclear. The incomplete status of CCS, typically classified as lower extremity score – upper extremity score ≥ 10 [2], allows for the preservation of lower limb function which may improve mobility recovery outcomes post-surgery, but the similar risk of post-operative complications compared to SCI surgeries may remain. Furthermore, our study helps provide further context on clinical guideline suggestions by comparing multiple anticoagulant chemoprophylaxis against no chemoprophylaxis which should cautiously be considered by clinicians electing to not pursue chemoprophylaxis for patients after surgery for CCS. Nonetheless, definitive clinical recommendations must await further investigation.

The VTE incidence of 3.3% within three months after same-day spine surgery for CCS demonstrated by this analysis is similar to reported incidences ranging from 1.1% to 5.4% [6–8, 16]. However, it is imperative to note that many of these studies did not include a time frame for their assessment. Bortz et al. (2021) demonstrated that incidence of VTE is significantly lower in patients that undergo same-day spine surgery [6]. We can extrapolate on our VTE incidence results which reflect a profound ambiguity amongst the broader context of spinal trauma literature. The use of a 3-month time frame producing an incidence of 3.3% aligns with the SCI literature VTE incidence of 5.4% recorded amongst the same time frame [16]. Our results closely mirror Anaspure et al. (2025), which found no statistically significant difference between chemoprophylaxis (3.88%) versus no chemoprophylaxis (5.68%) for spinal trauma surgery patients [25]. Our study took a more tailored approach into CCS spinal surgery risk of VTE based on the recommendations of early spine surgery, discretionary use of chemoprophylaxis, and timing of anticoagulant administration. [5]

In the present study, patient characteristics were consistent with previous CCS studies, supporting the generalizability of our findings. Specifically, mean age (57.9 vs 57.8 years) and sex distribution (74% vs 73% male) in the chemoprophylaxis and no chemoprophylaxis cohorts aligned with published literature (mean age 52-62.5 years, 63-74.5% male) [6–8]. There was limited ability to stratify by the number of fusion levels and the approach of surgery that was enacted amongst participants, but propensity matching was utilized for posterior multilevel fusion and, anterior multilevel fusion. There were roughly equal proportions of multilevel anterior fusion (10% versus 10%) and multilevel posterior fusion (30% versus 30%) in the chemoprophylaxis and no chemoprophylaxis cohorts, respectively. Conversely, Smith et al. (2023) incorporated anterior versus posterior surgical approach for CCS in their study's parameters but did not discuss single level versus multilevel surgical intervention [7]. Furthermore, Bortz et al. (2021) reported that 52% of CCS surgical cases involved fusion most commonly involving the length of 2 to 3 spinal levels (62.4% of fusions) [6]. Additionally, Bortz et al. (2021) did not mention

information regarding the surgical approach that was used when compiling their data [6]. Our study was able to account for patient characteristics pertaining to both, the approach and multilevel condition of spinal fusion which are seen amongst various studies in the literature reporting on either.

This current study found no statistically significant or clinically meaningful difference in the risk of PE (p = 0.762; 0.8% versus 1.0%) or DVT (p = 0.384; 1.6% versus 1.9%) between the chemoprophylaxis versus the no chemoprophylaxis cohorts. Bleeding complications including EDH and SPOB were rare (< 0.4%) in both groups, precluding statistical comparison but suggesting low absolute risk. These findings are consistent with rates reported by Baumann et al. (2025) of a 1.5–1.6% incidence of SPOB [11]. The present findings must be interpreted within the context of the study population. To minimize selection bias and confounding, our study excluded participants at highest risk for VTE, including those with prior VTE, inferior vena cava filters, kidney disease, or requiring other anticoagulants, which represent populations that could benefit from chemoprophylaxis. Therefore, while our results suggest that chemoprophylaxis may not provide clear benefit in lower-risk CCS patients without contraindications, they should not be extrapolated to higher-risk populations or interpreted as evidence against chemoprophylaxis use. Clinical decision-making should remain individualized based on patient-specific risk factors, and further prospective research is needed to clarify which CCS patients benefit most from early chemoprophylaxis, including examination of dosing, timing, and patient selection criteria.

Further research is needed on the topic. First, studies should examine chemoprophylaxis in higher-risk CCS populations, including participants with prior VTE, kidney disease, or other comorbidities. Given the rarity of such high-risk CCS surgical cases, alternative study designs such as multicenter registries, case-control studies, or longer time windows may be necessary to achieve adequate statistical power. Second, the risk of VTE should be examined based on variables that can quantify the time to surgery after CCS onset, estimated blood loss, and operative time utilizing more granular measurements. Lastly, future high quality cohort studies should investigate the timing, dosing, and type of anticoagulation on the risk of VTE and bleeding complications while stratifying by fusion length and approach, as well as other variables that we could not account for in this study that can impact VTE.

# Strengths and Limitations

Strengths of this study include an appropriate assessment window with the highest risk of VTE based on the literature [11, 12], a robust propensity matching, an adequately large sample size with power analysis, and the first study in the literature to date to compare anticoagulants and no chemoprophylaxis after spine surgery for CCS, allowing enhanced decision-making. However, there are also study limitations that merit consideration. First, being a retrospective study, certain biases are unavoidable. Despite rigorous eligibility criteria and propensity score matching methods, confounding by indication and selection bias could influence our results. This study is unable to provide detailed data regarding medication dose or adherence. Similarly, we are unable to comment on the mechanism or etiology of the CCS, which could be a potential confounder. Additionally, variables such as time from injury to surgery were unavailable; however, restricting inclusion to participants with a same-day diagnosis and surgical code was intended to partially mitigate this limitation. Furthermore, while enoxaparin and heparin provide similar efficacy, their indications and contraindications differ, which may result in different outcomes. For instance, unfractionated heparin is typically preferred in patients with renal insufficiency. We attempted to account for this difference by excluding participants with acute kidney injury, history of chronic kidney disease, or dialysis dependence. Due to the nature of large de-identified database studies, this analysis is unable to determine more granular information including the length of fusion, surgical technique, surgical approach, exact timing of anticoagulation in the 3-day window, or operative time; all of which may exist and impact outcomes. Similarly, we are unable to evaluate specific types of concomitant trauma in different regions of the body, which could affect risk of VTE as well as choice of VTE prophylaxis. In an attempt to mitigate this confounder, we examined the incidence of polytrauma between cohorts. Lastly, we were unable to perform statistics on EDH and SPOB due to < 10 participants in each cohort experiencing each outcome. Until data from large high-quality studies that examine anticoagulation in patients after spine surgery for CCS become available, this study can aid in decision-making and patient education.

## CONCLUSIONS

The present study found no statistically significant or clinically meaningful differences in risk of VTE or bleeding complications between chemoprophylaxis and no chemoprophylaxis cohorts through three months after same-day spine surgery for acute CCS in adults. However, these findings must be interpreted cautiously in light of our limitations. Our cohort excluded participants at highest risk for VTE, such as those with prior VTE. While our results suggest chemoprophylaxis does not provide clear benefit in lower-risk CCS patients, clinical decisions should remain individualized based on patient-specific risk factors. Prospective studies are needed to establish optimal thromboprophylaxis strategies after CCS surgery.

## Declarations


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# Data Availability Statement

All data analyzed during this study can be found within the published article and its supplementary files.

# Authorship Statement

All authors conceived and/or designed the work that led to the submission, acquired data, and/or played an important role in interpreting the results. Additionally, all authors drafted or revised the manuscript, approved the final version, and agreed to be accountable for all aspects of the work

# Competing Interests

All authors report they have no declaration of interest in terms of this study or its publication.


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# *Declaration of Interest*

Dr. Anthony N. Baumann, Nathan Cuttica, Harris Skaramagas, Dr. Robert J. Trager, Dr. Davin Gong, and Dr. Gregory Hawryluk report that they have no declarations of interest.

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## Figures

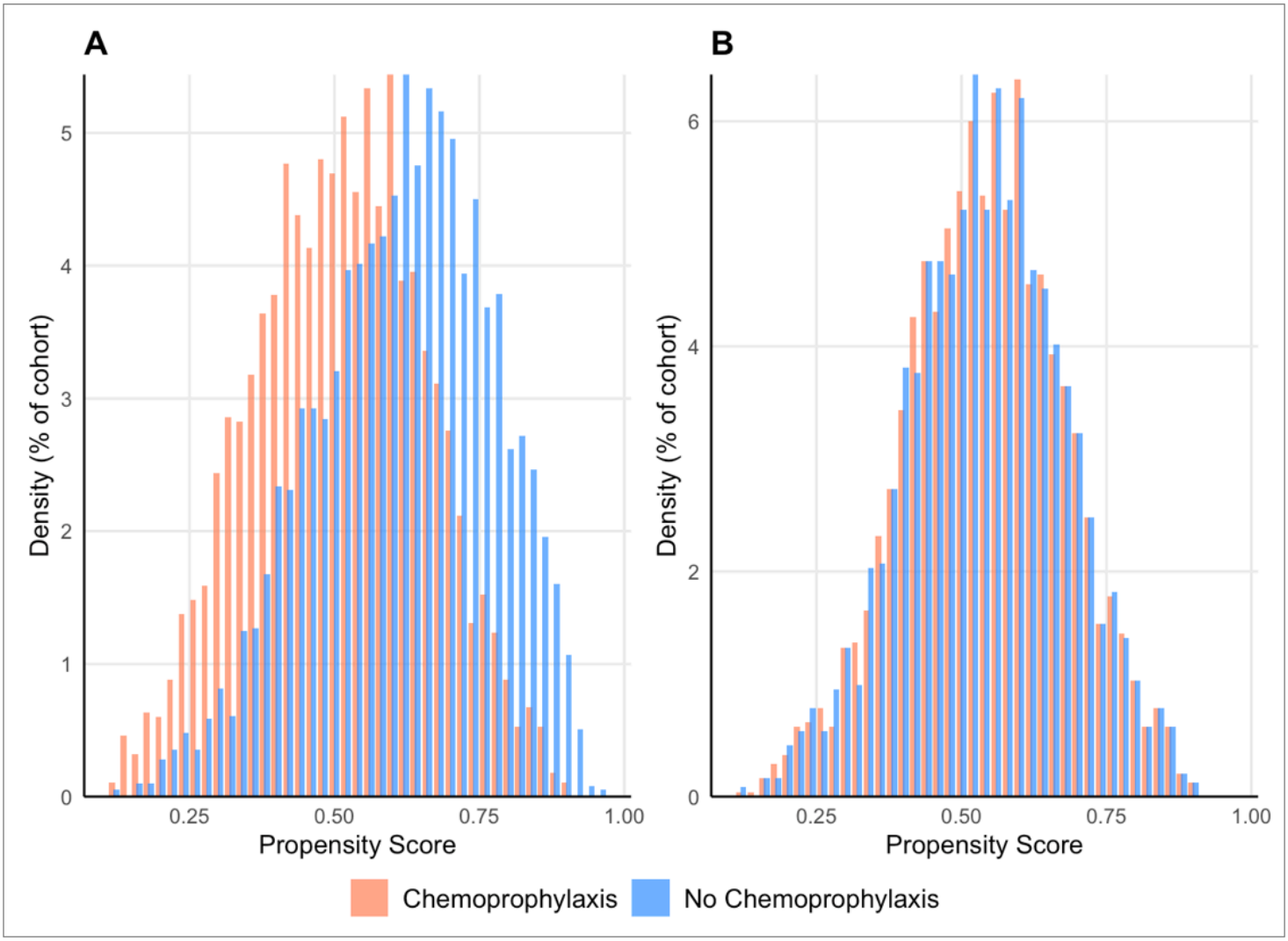



**Figure 1**

Propensity score density graph. The chemoprophylaxis (orange) and no chemoprophylaxis (blue) cohorts with overlap (gray), are shown before matching (A) and after matching (B).

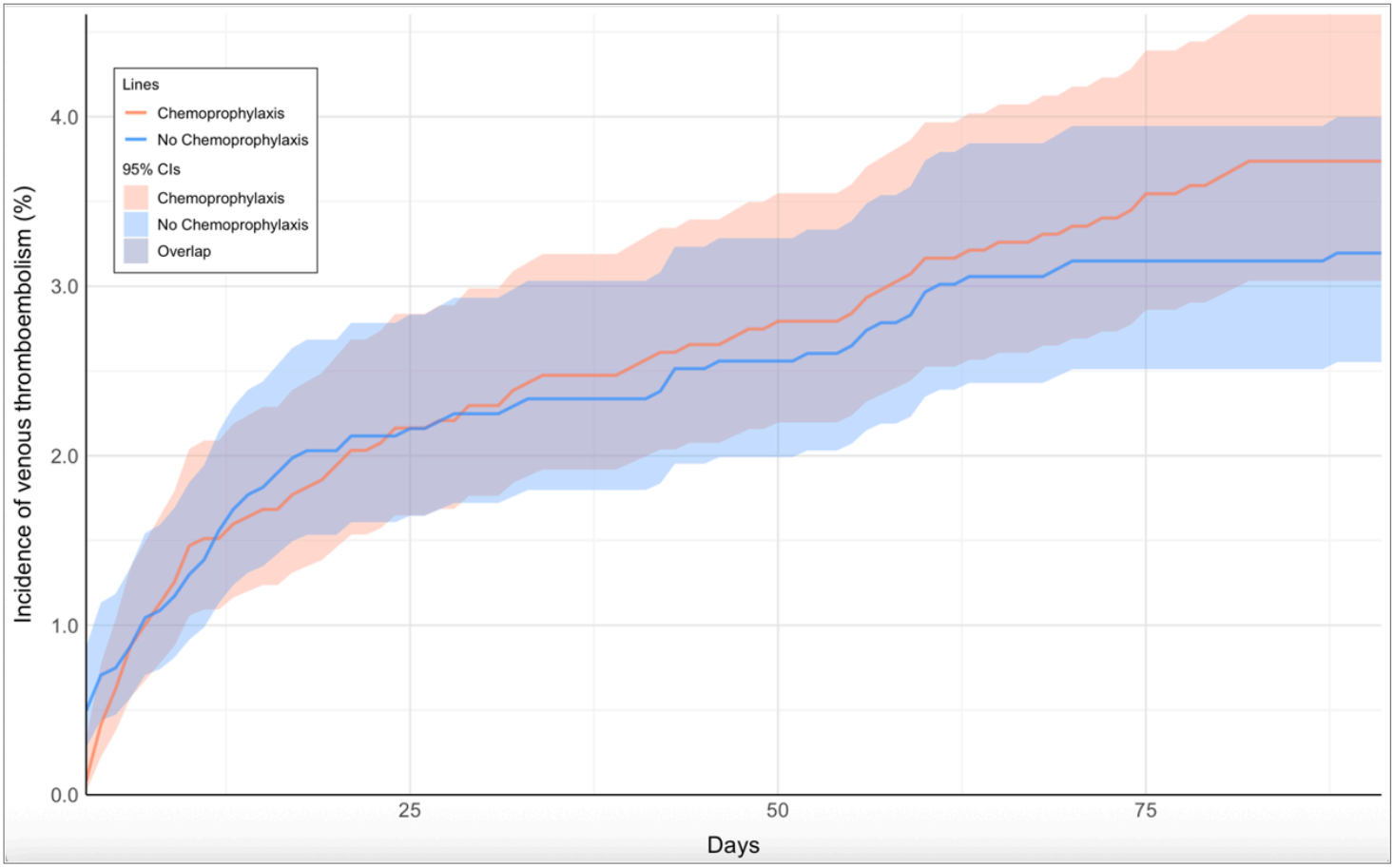



**Figure 2**

The cumulative incidence of venous thromboembolism in both cohorts through three months after spine surgery for central cord syndrome. Shown are the chemoprophylaxis (orange) and no chemoprophylaxis (blue) cohorts, with respective shaded regions indicating 95% confidence intervals (CI) and CI overlap shown in gray-blue.

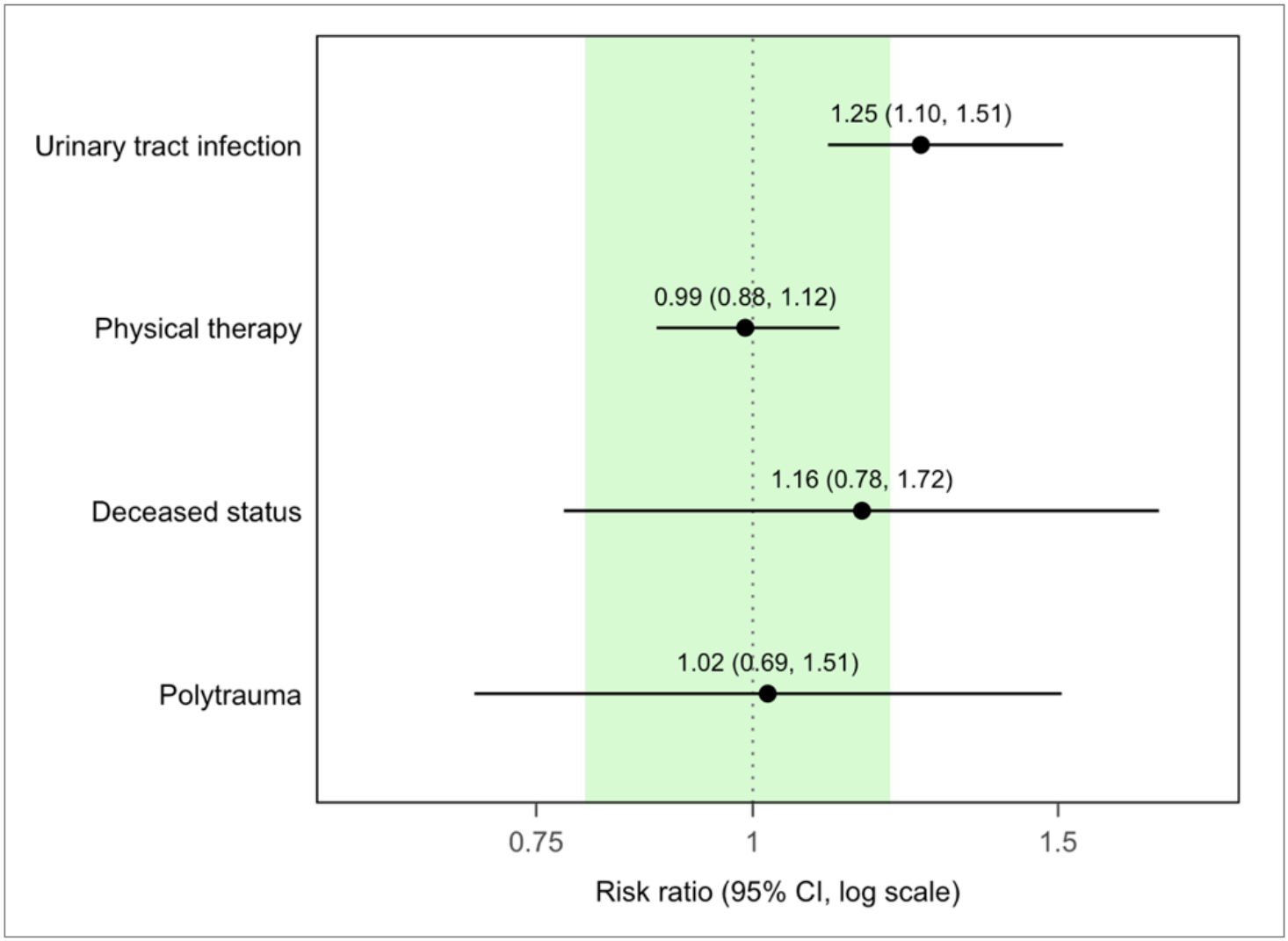



**Figure 3**

Negative control outcomes: Point risk ratio estimates and 95% confidence intervals (CI; whiskers) are shown. The green area represents estimates from 0.8 to 1.2, indicating the predefined region for negative control outcome balance while the vertical gray dotted line indicates the null association of 1.0.

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- ChemoppxSupplementalMaterial.pdf