Recommendations from the ICM-VTE: Spine

The ICM-VTE Spine Delegates*

1 - Is routine screening for DVT required in the pre-operative and/or post-operative period for patients undergoing spine procedures?

Response/Recommendation: There is no role for routine screening for deep venous thrombosis (DVT) in patients undergoing spine procedures. Doppler ultrasonography surveillance may be considered in high-risk surgical patients including those who are older, with spine injury, personal history of VTE, malignancy, cervical spondylotic myelopathy (CSM), and/or non-ambulatory.

Strength of Recommendation: Limited.

Delegates vote: Agree 96.43% Disagree 3.57% Abstain 0.00% (Strong Consensus).

Rationale: Venous thromboembolism (VTE) is a well-known complication of major orthopaedic and spine surgeries. The reported incidence of VTE in patients undergoing spine surgery range from 0.29% – 31%[1-3]. Moreover, the overall rates of pulmonary (PE) and associated fatality after spinal surgery are 1.38% and 0.34%, respectively[2-5].

Although contrast venography has been used for diagnosis of DVT, it is not suitable for the routine screening of asymptomatic patients due to potential complications, technical issues, expense, and invasiveness[6]. Similarly, the use of D-dimer, a byproduct of fibrinolysis[7], as a screening tool lacked sensitivity and specificity in detecting VTE after hip arthroplasty[8-12]. Ultrasonography, on the other hand, has become the primary non-invasive method for investigating suspected DVT of the femoral and popliteal veins[9]. Standard ultrasound showed relatively high sensitivity (> 90%) for proximal or (around 60%) for below-the-knee DVT in a systematic review of diagnostic cohort studies[13]. Duplex ultrasonography (DUS) has also improved precision and efficiency in diagnosing DVT compared to most non-invasive techniques[14]. Furthermore, combined D-dimer and ultrasound screening in patients with acute spinal cord injury have improved the detection of VTE compared to D-dimer screening alone[15].

However, controversy remains regarding the use of routine screening for DVT in the perioperative period for patients undergoing spine procedures. We performed an extensive systematic review of all publications. A total of 26 articles that satisfied all inclusion criteria were selected for data extraction after full review. Information about these studies with respect to year of publication, level of evidence, number of patients, methods of screening, timing of screening, methods of prophylaxis, and incidence of VTE are summarized in Table I. Studies suggest against screening for patients undergoing spine surgery while others recognize that only patients at high risk may benefit. Based on the available literature, the risk factors for an increased risk of VTE in patients undergoing spine surgery may be seen in older patients, long periods of bedrest from paralysis and pain, high D-dimer level, longer duration of operation, intraoperative blood loss and transfusion, previous history of VTE, fracture, comorbid disease burden and tumor surgery[16-44]. Studies reporting DVT and/or PE rates vary in the type of surgery included and the methods used to detect DVT ranging from clinical examination[28,29] to screening DUS[3,22,24-27,30-32,35,38-40,43,44], screening enhanced computer tomography (CT)[34], D-dimer testing combined with DUS and/or enhanced CT[18,33,36,37,41,42], and venography[5].

Five articles recommended preoperative and/or postoperative routine screening for DVT. Liu et al., investigated routine DVT screening in a retrospective cross-sectional study[40]. Of 396 patients with CSM, 16 (4%) had preoperative DVT. They concluded that preoperative screening should be considered for patients with CSM, and in particular those who are older, have had longer duration of CSM, have poor lower limb mobility, and have a heart disease history. Oda et al., evaluated DVT occurrence after posterior spinal surgery[5]. Neither mechanical methods nor anticoagulation medications were used for prophylaxis against VTE in their cohort. Bilateral ascending venography was performed within 14 days after surgery. There were no patients with clinical signs of DVT and PE. However, 17 patients (15.5%) showed venographic evidence of DVT, of whom 16 had distal thrombi, and only one had a proximal thrombus. They suggested that the prevalence of DVT after posterior spinal surgery is higher than generally recognized. Ikeda et al., examined predictable factors of DVT after spine surgery. Postoperative DVT was detected using DUS[18]. Age, sex, body mass index (BMI), operation

*A list of the ICM-VTE Spine Delegates is included in a note at the end of the article.

Disclosure: The **Disclosure of Potential Conflicts of Interest** forms are provided with the online version of the article (http://links.lww.com/JBJS/G863).

TABLE I Summary of the 26 articles selected for inclusion in the review*

First author	Year	Level of Evidence	No cases	Methods of screening	Timing	Prophylaxis	Incidence of VTE
Ferree et al[22]	1993	Level IV	87	DUS	Within 2 weeks; 2-7 days after surgery	CS	6% DVT
Napolitano et al[23]	1995	Level IV	458	DUS	Biweekly	Heparin + PCD	10% DVT
Wood et al[24]	1997	Level II	134	DUS	5 and 7 days after surgery	Mixed	1.5% VTE
Dearborn et al[25]	1999	Level IV	318	DUS and CT	3-20 days after surgery	CS + PCD	2.2% symptomatic PE; 0.9% asymptomatic DVT
Oda et al[5]	2000	Level III	110	Bilateral ascending venography	Within 14 days after surgery	None	15.5% DVT
Lee et al[26]	2000	Level IV	313	DUS	5 and 7 days after surgery	None	0.3% symptomatic DVT
Leon et al[3]	2005	Level IV	74	DUS	weekly	Inferior vena cava filters in high-risk patients	1.3% PE
Epstein et al[27]	2006	Level IV	139	DUS	2 days after surgery	CS	2.8% DVT and 0.7% PE
Platzer et al[28]	2006	Level IV	978	Clinical	-	Mixed	2.2% VTE
Schizas et al[29]	2008	Level IV	270	Clinical and eCT	When clinical suspicion of PE	CS and chemical	2.2% symptomatic PE
Strowell et al[30]	2009	Level III	680	DUS	4 days after surgery	Standard care vs chemical (Epoetin Alfa)	4.7% in the epoetin alfa group and 2.1% in the standard care group
Kaabachi et al[31]	2010	Level IV	40	DUS	Before surgery and 3, 7, 15 days after surgery	None	None
Epstein et al[32]	2011	Level IV	240	DUS, clinical and eCT	1 to 2 days after surgery	CS	3.6-6.7% PE (US negative)
Yoshikawa et al[33]	2011	Level IV	88	DD combined with eCT	Before and 1, 4, 7, 10, and 14 days after surgery	CS and PCD	5.7% DVT
Kim et al[34]	2011	Level IV	130	eCT	NR	CS	25.4% PE only, 3.8% PE and DVT, 2.3% DVT only
Al-Djalili et al[35]	2012	Level IV	158	Clinical + DUS	2 or 3 days after surgery	CS + chemical	0.6% DVT
Takahashi et al[36]	2012	Level IV	1975	Clinical and/or eCT/DD	1 week after surgery	None or CS	1.5% symptomatic PE in non-prophylaxis group and 0.2% symptomatic PE in CS group

continued

TABLE I (*continued*)

First author	Year	Level of Evidence	No cases	Methods of screening	Timing	Prophylaxis	Incidence of VTE
Houl et al[37]	2015	Level IV	5766	Clinical and/or DUS/eCT	NR	PCD	1.5% VTE (0.88% PE and 0.66% PE)
Hamidi et al[38]	2015	Level IV	89	DUS	NR	CA and Chemical or not	3.3% VTE
Weber et al[39]	2016	Level IV	107	Clinical and DUS, and or eCT	4 or 5 days after surgery	Mixed	3.7% VTE (1.9% DVT and 1.9% PE)
Liu et al[40]	2016	Level IV	396	DUS	Before surgery	NR	4% had DVT in patients with CSM preoperatively
Ikeda et al[18]	2017	Level IV	194	DD combined with DUS	US 5 days; DD 1, 3, 7, 10, and 14 days after surgery	CS and PCD	29.4% DVT
Inoue et al[41]	2018	Level IV	72	DD combined with eCT	CT: before and 3 days after surgery; DD: before and 1, 3, and 7 days after surgery	PCD	8.3% asymptomatic PE and 8.3% asymptomatic DVT
Koo et al[42]	2018	Level III	122	DD combined with DUS	7 days after surgery	NR	0.8% DVT in the TXA group and 1.2% DVT in the control group
Cheang et al[43]	2019	Level IV	170	DUS	3 and 7 days after surgery	Chemical	10% DVT
Zhang et al[44]	2021	Level IV	2053	Clinical + DUS	NR	None	2.39% DVT

*Level I is high-quality randomized control study; Level II, lesser quality randomized control trial, prospective comparative study, prospective study with historical controls; Level III, case control study, retrospective comparative study; Level IV, case series; Level Y, expert opinion, case report. VTE=Venous thromboembolism; DUS=Duplex ultrasonography; CS=Compression stocking; DVT=Deep venous thrombosis; PCD=Pneumatic compression device; PE=Pulmonary embolism; eCT=enhance contrast computed tomography; US=Ultrasound; DD=D-dimer; NR=No record; CSM=Cervical spondylotic myelopathy; TXA=Tranexamic acid.

time, amount of bleeding, preoperative ambulatory status, usage of instrumentation, and preoperative serum levels of D-dimer were compared between the DVT and non-DVT groups to establish predictors for postoperative DVT. Cut-off value of the preoperative level of D-dimer was calculated using receiver operating curve (ROC) analysis. It was suggested that perioperative application of DUS for detecting DVT in the lower extremities should be performed in patients undergoing spine surgery who are female, non-ambulatory, and with higher preoperative D-dimer serum level. Inoue et al., examined changes in blood markers with PE or DVT after low-risk spine surgery, namely cervical laminoplasty or lumbar laminectomy[41]. Elevated D-dimer at postoperative days 3 and 7 was found to be a predictive factor for the early diagnosis of PE after spine surgery. A retrospective study reported an incidence of asymptomatic DVT identified by duplex screening of 10% (45 of 458 trauma patients), significantly higher in older patients, those with major length of stay, higher injury scores and with spinal injury[23]. The authors recommended surveillance in trauma patients with these risk factors.

There are other publications that recommend against routine screening for DVT in patients undergoing spine surgery. Kaabachi et al., investigated asymptomatic DVT and prothrombotic diseases in non-syndromic children undergoing scoliosis surgery[31]. The protocol was designed for active screening of DVT using color DUS on the day before surgery and repeated on the 3rd, 7th, and 15th day postoperatively. Evaluation of prothrombotic disorders included

antithrombin and protein-C activities, and total protein-S antigen level. No patient manifested clinical symptoms of VTE in their study. Preoperative Doppler and ultrasound examinations were normal in all patients. They concluded that VTE events are rare after scoliosis surgery, and routine screening is not justified. Ko et al., investigated the incidence of thromboembolism in patients who received tranexamic acid (TXA) after lumbar spine fusion and explored the diagnostic value of lower limb DUS as a screening test[42]. They found comparable incidence of VTE (0.8%) in the TXA and non-TXA groups, and they concluded that lower limb DUS was not recommended as a screening test of DVT because of high false-positive rate.

Based on the available literature, there does not seem to be a role for routine screening for DVT in patients undergoing spine surgery. Screening should be reserved for patients at high-risk of VTE, as determined by studies on the subject and highlighted above.

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2 - Concerning VTE risk, which surgeries can be considered high-risk, and which surgeries can be considered low-risk in spine surgery?

Response/Recommendation: Concerning venous thromboembolism (VTE) risk in spine surgery, high-risk procedures include those performed for oncologic, traumatic, or infection, as well as those requiring intensive care unit (ICU) admission, multiple stages, or combined approaches. Lumbar procedures including long-segment fusions or procedures utilizing an anterior approach, as well as posterior cervical fusions, should also be considered high-risk. On the other hand, most elective pediatric procedures, microdiscectomies, anterior cervical fusions, and lumbar or cervical decompressions may be considered low-risk procedures.

Strength of Recommendation: Moderate.

Delegates vote: Agree 100.00% Disagree 0.00% Abstain 0.00% (Unanimous Strong Consensus).

Rationale: Patient characteristics (age, obesity, personal history of VTE, etc.), clinical factors (length of hospital stay, operative time, etc.), and neurologic impairment are associated with increased risk of postoperative VTE[45-47]. Nonetheless, there is no consensus regarding the VTE risk profile when it comes to surgical indications, operative techniques, and extent of surgery.

High-risk spine surgeries: Oncologic indication for spinal surgery has been shown to increase the risk of VTE with a reported incidence nearing 11.3%[48-53]. In a National Surgical Quality Improvement Project (NSQIP) database study of 22,434 patients, a diagnosis of tumor resulted in an odds ratio (OR) of 5.07 for postoperative VTE development, whereas a diagnosis of disseminated cancer carried an OR of 6.83[49]. This relationship has also been elucidated separately for cervical and thoracolumbar procedures, with studies reporting OR of 5.2 or 1.8, respectively[50,51]. Furthermore, any surgery for infection or requiring an ICU admission should be considered high-risk[51,54,55]. Infection has been shown to increase VTE risk in multiple studies, with an OR of 18.5 in a 1:2 matched cohort of 85 VTE, and an incidence of 10.7% in a database study of 357,926 patients[51,55]. Similarly, a retrospective study of 6,869 patients with 1,269 postoperative ICU admissions reported a VTE incidence of 10.2% in the ICU group and 2.5% in the non-ICU group despite an increased use of chemoprophylaxis in the former group[54].

Trauma or fracture as an indication for spinal surgery has also been shown to increase the risk of VTE, and these procedures should therefore be considered high-risk[51,53,56-58]. In a retrospective study of 7,156 patients, a diagnosis of fracture was associated with an increased risk of VTE (OR 8.3) despite an increased use of chemoprophylaxis in this group of patients[58]. In another retrospective study of 195 patients, the rate of VTE was 9.2% among fracture patients compared to 2.3% in the non-fracture group (OR 4.5)[57]. Fracture has also been shown to be an independent predictor of pulmonary embolism (PE) (OR 6.9) in a retrospective study of 6,869 patients[53].

Staged procedures and combined surgical approaches have also been shown to increase the risk of VTE[45,51,55,59,60]. A 1:2 matched cohort analysis of 85 postoperative VTE found both staged surgery (OR 28.0) and combined approach (OR 7.5) to increase the risk of VTE[51]. Additionally, multiple studies have shown that lumbar procedures have an increased risk of VTE compared to cervical procedures[46,48,55,58,61-65]. However, an anterior approach to the lumbar spine and a posterior approach to the cervical spine have been shown to increase VTE risk compared to their posterior and anterior counterparts, respectively[45,55,66]. A Nationwide Inpatient Sample (NIS) database study of 273,396 cervical procedures found a postoperative VTE incidence of 2.0% in posterior cervical fusion compared to 0.4% in anterior cervical discectomy and fusion (ACDF)[66].

The number of surgical levels is another factor that could increase the risk of VTE[51,57,67-69]. A 1:2 matched cohort analysis of 85 postoperative VTE identified two or more surgical levels as a risk factor (OR 7.5), and other studies reported an increased risk using various cut-offs for number of levels[51,55,67-69]. Furthermore, one French database demonstrated a "dose-effect" for pedicle screw implantation, with a 40% increased risk of VTE for 1 - 5 screws, 69% for 6 - 9 screws, and 117% for > 10 screws[45].

Low-risk spine surgeries: While most elective pediatric procedures are considered low VTE risk[70,71], patients undergoing surgery for congenital scoliosis, syndromic scoliosis/kyphoscoliosis, thoracolumbar fractures, and the ones requiring ICU admission or prolonged immobilization have a relatively increased VTE risk compared to those undergoing surgery for idiopathic scoliosis[72]. Additionally, microdiscectomy, ACDF, and lumbar or cervical decompression (i.e., laminectomy, hemilaminectomy and laminotomy) have demonstrated a low risk of postoperative VTE, with rates < 0.2% for each procedure[73]. Some studies have suggested that fusion procedures may increase the risk of VTE[55,67,74,75]. However, this claim has been widely disputed, and one retrospective study of 6,869 patients found that fusion actually decreased the risk of 30-day readmission for VTE (OR 0.59). Furthermore, no increased risk has been shown in revision procedures[55]. Consequently, the VTE risk profile of spinal fusion and revision surgery could not be absolutely determined, and surgeons should rather consider the surgical indication, location,

approach, and number of levels when performing VTE risk assessment.

The explanation for these relationships is multifactorial. When evaluating these surgeries, it is important to consider the Virchow's Triad, which constitutes blood flow stasis, endothelial injury, and hypercoagulability[76]. Postoperative immobility may explain the increased risk in traumatic, ICU, multistage, combined approach, and long-segment procedures, while hypercoagulability may explain the increased risk in oncologic, traumatic, and infectious procedures[77,78]. Further research including various surgical procedures and VTE risk assessments should be conducted to further delineate high- and low-risk procedures within spine surgery.

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3 - Does the concern for epidural hematoma influence the choice for VTE prophylaxis after spine surgery?

Response/Recommendation: Epidural hematoma is a feared yet rare postoperative complication after spinal surgery, with symptomatic rates ranging from 0% to 1.8%. Although there is no published evidence to precisely define the safety of chemoprophylaxis, it seems that postoperative anticoagulants in non-therapeutic doses can be administered without an increased risk of spinal epidural hematoma. Prospective studies are required to

better balance the risks and benefits of prophylactic anticoagulants regarding spinal epidural hematomas and Venous thromboembolism (VTE).

Strength of Recommendation: Limited.

Delegates vote: Agree 96.30% Disagree 0.00% Abstain 3.70% (Strong Consensus).

Rationale: The key words used in our search of PubMed, Cochrane Library, and Embase were "*epidural hematoma*", "*spine surgery*", and "*venous thromboembolism*". Studies were included if they investigated spinal epidural hematomas and chemoprophylaxis of any sort. Studies were not excluded if they did not clearly report VTE or the method of VTE screening. Case reports and series were excluded. References of included studies were checked. Various data was extracted from the included studies including method of chemoprophylaxis, VTE screening, and rates of postoperative symptomatic VTE and epidural hematoma. In total, 14 studies were included for data extraction after full review (Table II).

Spine surgeons must weigh the risks of chemoprophylaxis, which include bleeding and hemorrhagic complications such as spinal epidural hematoma, against the benefits of preventing VTE. Studies report a symptomatic postoperative VTE rate of 1.5% - 31% and symptomatic spinal epidural hematoma of 0% - 1.8%[79-83]. Both rates are noteworthy, especially considering that epidural hematoma can lead to severe neurologic complications. As a result, precise indication, agent, dose, and timing for prophylaxis following spinal surgery is essential[81,84].

In 1998, Agnelli et al.[85], compared in a level I, multicenter randomized controlled trial the use of compression stockings (CS) alone (n = 15) to enoxaparin 40 mg daily started within 24 hours for 7 days and CS (n = 31) following elective spinal cord procedures. No patients developed a spinal epidural hematoma and VTE rate was unknown. Not specific to spinal procedures, the authors concluded that enoxaparin combined with CS was more effective in preventing symptomatic VTE than CS alone and did not increase the risk for excessive bleeding following intracranial and spinal procedures.

In a recent 2021 study by Thota et al.[86], 888 patients who received anticoagulation were propensity score matched to 888 patients receiving no anticoagulation in elective spine surgeries. No difference was found in symptomatic VTE rate; however, unplanned reoperation for hematoma were greater for those who received pharmacological anticoagulation (odds ratio [OR] = 7.5, 95% confidence interval [CI] = 2.0 – 28.3, $p < 0.01$).

Cox et al.[87], compared VTE and epidural hematoma rate before (provider dependent, 24 hours after surgery) and after a protocol change (5,000 U heparin administered subcutaneously 3 times daily, with the first dose given immediately postoperatively). VTE rate decreased in the more aggressive protocol (3.3% vs. 1.5%; $p < 0.01$) and no difference was found in epidural hematoma occurrence (0.6% vs. 0.4%; $p = 0.58$). Gerlach et al.[88], retrospectively included 1,954 spinal procedures on different levels. All patients received routinely 0.3 mL nadroparin within 24 hours of surgery and compression stocking. Only 1 (0.05%) patient had a DVT, and 8 (0.4%) patients developed epidural hematoma, of which 3 patients were discharged with residual neurological impairment. The authors state that early nadroparin is safe and is not associated with an increased risk of postoperative epidural hematoma.

Uribe et al.[89], examined delayed postoperative spinal epidural hematoma, defined as 3 days after surgery, in 4,018 patients that awoke from surgery neurologically unchanged. No standard prophylaxis protocol was used and VTE events were not investigated. Seven (0.2%) patients developed a spinal epidural hematoma of which 4 had received subcutaneous heparin. Dhillon et al., compared 1,904 (28%) patients who received various anticoagulants with 4,965 (72%) patients who received none. The risk of epidural hematomas in both groups was low (both 0.2%; $p = 0.62$). The authors state that administering 5,000 U of heparin, 40 mg of enoxaparin, 2,500 or 5,000 U of dalteparin, or 2.5 mg of fondaparinux within 3 days of surgery was safe for patients undergoing spinal procedures.

Most studies suggested no difference in epidural hematoma rates between postoperative chemoprophylaxis and no prophylaxis[82,83,85,87-96], except for Hohenberger et al.[97]. This retrospective study investigated epidural hematomas in a matched 1:3 case control study of 6,024 patients undergoing spinal decompression surgery. Forty-two patients with an epidural hematoma were matched with 126 patients with the same surgical procedure, year, sex, and age. Anticoagulation use (acetylsalicylic acid, coumadin, and rivaroxaban) were associated with an increased risk of epidural hematomas (OR, 3.32 [1.50 - 7.38]; $p < 0.01$). However, the VTE rate was not provided, and controlling for confounding factors was not performed. In three similar case control studies, use of anticoagulants was not associated with an increased risk for epidural hematomas. (Awad, Kao, and Wang)[98-100]. For instance, a similar 1:3 case control study demonstrated that 32 patients with and 102 matched controls without spinal epidural hematoma received respectively 41% (13/32), and 51% (52/102) anticoagulation[98].

Of interest to note is the study from Cunningham et al.[101], that investigated not the influence of postoperative but preoperative chemoprophylaxis on VTE and epidural hematoma rate. In 3,870 elective spinal procedures, 37% (1,428) received preoperative chemoprophylaxis. Nineteen (0.5%) patients had a VTE of whom 9 (47%) had preoperative chemoprophylaxis ($p = 0.35$). Sixteen (0.4%) patients developed a spinal epidural hematoma, of whom 7 (44%) received preoperative heparin 5,000 units subcutaneously ($p = 0.61$). The authors conclude that preoperative chemoprophylaxis does not influence the rate of VTE and spinal epidural hematomas.

Several studies identified risk factors for development of spinal epidural hematomas, including perioperative transfusion[91], high intraoperative blood loss (> 1 liter)[98], pathologic coagulation values, cigarette smoking[97], intraoperative use of gelfoam for dura coverage, postoperative drain output[100], increased age, obesity, multilevel surgery, and dural tear repair[102]. Although no studies have specifically investigated anticoagulation use in these high-risk patients, one may want to refrain from administering chemoprophylaxis.

TABLE II Characteristics of included studies (n = 14)

Author, year	Level of evidence	Patients	Type of surgery	Chemoprophylaxis	Methods of screening	VTE %(n)	Epidural hematoma %(n)
Agnelli, 1998[85]	I	15	NS	TED	Routinely imaging on day 8	NA	0%
		31		TED + LMWH within 24 hours		NA	0%
Al-Dujaili, 2012[82]	IV	158	NS	CS + LMWH 40 mg within 12h	Clinically + routine US	DVT = 0.6% (1)	1.8% (3)
Amiri, 2013[90]	IV	4,568	Various	Anticoagulant therapy within 24 h	NS	NA	0.2% (10)
Cloney, 2018[91]	IV	6,869	Various	Various 28% (1,904); none 72% (4,965)*	NS	2.5% (170)	0.2% (13)
Cox, 2014[87]	IV	941	NS	CS + 5,000U heparin 3x daily after 24h	NS	3.3% (31); DVT = 2.7% (25); PE = 0.6% (6)	0.6% (6)
		992		Provider dependent 24 h after OR		1.5% (15)	0.4% (4)
Dhillon, 2017[92]	IV	1,904	Various	Chemoprophylaxis#	NS	3.6% (69); DVT = 3.2% (60); PE = 0.8% (15)	0.2% (4)
		4,965		None		2.0% (101); DVT = 1.7% (82); PE = 0.6% (30)	0.2% (9)
Dickman, 1992[93]	IV	104	Posterior pedicle screw fixation	PCS	NS	DVT = 2.9% (3)	1.0% (1)
Gerlach, 2004[88]	IV	1,954	Various, multilevel	LMWH within 24 hours + CS	Clinically	DVT = 0.1% (1)	0.7% (13)
Groot, 2019[85]	IV	637	Spinal metastases	Various 86% (548); none 14% (89)	Clinically	11% (72); DVT = 6.1% (40); PE = 6.0% (38)	1.1% (7)
Park, 2019[94]	IV	2,1261	Various	Various 7.9% (1,678); none 92.1% (19,583)ˆ	NS	2.1% (444); DVT = 1.7% (370): PE = 0.4% (84)	0
Platzer, 2006[95]	IV	978	Trauma	LMWH (792); LMWH + CS (153)	Clinically	2.2% (22); DVT = 1.7% (17); PE = 0.9% (9)	0
Uribe, 2003[89]	IV	4,018	NS	NS; 4 SEH cases with SCH	NS	NA	0.2% (7)
Strom, 2013[96]	IV	367	Cervical and lumbar decompression	LMWH within 36 h	NS	3.8% (14); DVT = 2.7% (10); PE = 1.1% (4)	0
Thota, 2021[86]	IV	888~	Elective	Any anticoagulation	Clinically	0.9% (8); PE = 0.3% (3)	2.0% (18)
		888		None		1.0% (9); PE = 0.3% (3)	0.2% (2)

*chemoprophylaxis was defined as 5,000 U heparin, 40 mg enoxaparin, 2,500 U or 5,000 U dalteparin, or 2.5 mg fondaparinux given from 1 day prior to 3 days post operation. #chemoprophylaxis was defined as the following agents given between 1 day before and 3 days after surgery: 5,000 U of heparin, 40 mg of enoxaparin, 2,500 or 5,000 U of dalteparin, or 2.5mg of fondaparinux. ˆChemoprophylaxis was defined as any of the following medications: aspirin, direct thrombin inhibitor, factor Xa inhibitors, low-molecular-weight heparin, unfractionated heparins, and warfarin. ~Propensity score matched starting with 3,536 patients that matched a single patient who did not receive anticoagulation to a single patient who did. All presented VTE rates are symptomatic. n=number; VTE=Venous thromboembolism; NS=Not specified; TED=Thigh length compression; LMWH=Low-molecular-weight heparin; NA=Not available; CS=Compression stockings; US=ultrasound screening; DVT=Deep venous thrombosis; PE=Pulmonary embolism; OR=Operative room; PCS=Pneumatic compression stockings; SHE=Spinal epidural hematoma; SCH=Subcutaneous heparin.

Conclusions from the included studies are difficult given the heterogeneity of methods of prophylaxis and VTE screening, surgical procedures, and patient population. In particular, the timing and dose of chemoprophylaxis vary between studies or are not specified. Furthermore, quality of the individual studies is poor, and the level of evidence is low. The fact that spinal epidural hematomas are relatively rare and potentially life threatening further complicates investigation of this outcome in a meaningful way[81]. For example, a clinical trial design comparing two different prophylaxis strategies would require 18,519 patients (difference 0.2% vs. 0.1%) or 1,002 patients (difference 3.6% vs. 1.8%) for 80% power.

In view of these limitations, future research should provide granular data on type, dosage and timing of anticoagulants and stratified epidural hematoma results by indication and chemoprophylaxis usage. Given the severe neurologic complications of epidural hematoma, prospective studies are also needed to delineate the safe use of various anticoagulants after surgery as well as their ideal timing and dosage.

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4 - When can VTE chemoprophylaxis, if to be used, be started following spine procedures?

Response/Recommendation: Venous Thromboembolism (VTE) chemoprophylaxis can probably be started within 24 - 48 hours following elective lumbar fusions, and within 48 hours following patients considered to be higher risk with bleeding. Chemoprophylaxis benefits should be carefully weighed against the risks of bleeding and hematoma formation.

Strength of Recommendation: Limited.

Delegates vote: Agree 88.46% Disagree 0.00% Abstain 11.54% (Strong Consensus).

Rationale: VTE is a significant adverse event after spine surgery that might be minimized with the use of appropriate prophylaxis regimen. However, the use of prophylaxis needs to be balanced by the risks associated with any intervention, such as bleeding, wound issues, etc. In spine surgery, there is particular concern about the possibility of hematoma which could cause compression of the spinal cord/nerves and the potential of neurologic sequelae.

The risk/benefit considerations of using VTE prophylaxis are dependent on understanding the incidence of this adverse outcome, as well as the associated risks; unfortunately, both of these factors are reported with variable numbers in the literature. Other subgroups are evaluating which specific agents for VTE chemoprophylaxis that should be considered following spine surgery, what screening is recommended, and if there are surgical/procedural/presentation variables that should influence the decision. This sub-group is asked to evaluate the literature regarding when VTE chemoprophylaxis can be started following spine procedures, if it is to be used.

Evaluation of the literature: If pursued, VTE chemoprophylaxis is most relevant during the time of greatest risk. An evaluation of the National Surgical Quality Improvement Program (NSQIP) database revealed that deep venous thrombosis (DVT) was diagnosed a median of 10.5 days after anterior cervical surgery and 8 days after posterior lumbar surgery[103]. The first days were not high incidence, but there could be a delay from onset to detection, so it is difficult to know what to conclude from this information.

A recent survey study of 370 neurosurgeons highlighted the variation in thoughts on the posed question regarding safe timing of chemoprophylaxis following spine surgery[104]. For uncomplicated elective spine surgery, most respondents are comfortable starting chemical prophylaxis on postoperative day 1 (59.1%), followed by day 2 (23.5%) and day 3 (9.4%), with a range of 0 – 14 days (mean 1.6 days). Those who were more senior in their careers recommended later start of chemoprophylaxis.

Another survey study of 193 orthopaedic and neurosurgical spine surgeons asked similar questions for timing of starting chemoprophylaxis after high-risk spinal surgery[105]. The most common response was 48 hours after surgery (21 of 94, 22%). However, individual responses varied widely: 12% chose less than 24 hours, 15% chose 24 hours, 13% chose 72 hours, and 10% chose 96 hours. Some indicated they would start chemoprophylaxis before surgery, whereas others responded they would never use it. The most common basis for this decision was noted to be personal experience.

In terms of retrospective reviews, one group evaluated patients who underwent elective one- or two-stage lumbar spinal fusions at a high-volume single institution[106]. This group found the odds of developing a VTE within 30 day was reduced in those who received chemoprophylaxis withing 24 hours of surgery (odds ratio = 0.189, p = 0.025) with no difference in bleeding rates. In a trauma population, one study suggested starting chemoprophylaxis within 48 hours of surgery[107].

Another retrospective, single-institution study found higher prevalence of 30-day VTE in those who received chemoprophylaxis 1 day before to 3 days after surgery to be higher than the non-chemoprophylaxis group (presumably related to differential in populations who were not randomized) but no difference in the rates of epidural hematoma[108]. Other studies have also found no increase in epidural hematoma with chemoprophylaxis[108,109], but at least one found the rate of epidural hematoma to be increased[110]. Unfortunately, these studies did not specifically assess the variable of when the chemoprophylaxis was started.

Conclusions: There are probably different risk/benefit considerations for chemoprophylaxis based on the risk inherent to patient sub-populations of patients undergoing spine surgery. This becomes a balance of minimizing VTE and avoiding epidural hematoma. No prospective study is identified to help answer this question. Retrospective studies seem to suggest that VTE chemoprophylaxis can be started within 24 or 48 hours. Survey studies were mixed by many respondents suggested postop day one, based on experience.

In the absence of more defined data, the current evidence/opinions are interpreted to suggest stating VTE chemoprophylaxis postoperative day one after spine surgery. However, this needs to be assessed based on individual situations and balanced by mixed suggestion of at least some evidence of increased risk of epidural hematoma.

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5 - If VTE prophylaxis is to be administered, does the number of levels, and/or the anatomical location, and/or surgical approach (i.e., minimally invasive) influence the choice of VTE prophylaxis for patients undergoing spinal surgery?

Recommendation: There is some evidence suggesting that chemoprophylaxis should be considered in patients undergoing multi-level lumbar spine surgery, especially when performed through an anterior approach.

Strength of Recommendation: Limited.

Delegates vote: Agree 96.30% Disagree 0.00% Abstain 3.70% (Strong Consensus).

Rationale: There are many thromboprophylaxis methods used in spinal surgery, including elastic compression stockings (CS), pneumatic sequential compression devices (SCD), low-molecular-weight heparin (LMWH), heparin, and inferior vena cava (IVC) filters. However, the lack of clear clinical evidence of superiority has led to a wide variability in surgeon preference compared to those for other orthopaedic procedures, such as lower extremity trauma or knee/hip arthroplasty, where the clinical evidence is more robust[111]. The American College of Chest Physicians (ACCP) recommended against routine prophylaxis for elective spinal surgeries in patients with no significant risk factors, and a combination of mechanical and chemoprophylaxis in patients with multiple risk factors[112].

One obvious confounding variable is that multi-level surgeries have a longer operative time, which is a known independent risk factor for venous thromboembolism (VTE)[113-115]. Despite this, in a prospective trial comparing the effect of SCD on 100 patients undergoing single level anterior cervical corpectomy and fusion (ACCF) to 100 patients undergoing multilevel ACCF/posterior fusion, Epstein et al., found one VTE event in the former group and 7 in the latter group[116]. Additionally, in a case-control study, Hohl et al., observed that when treated with mechanical compression alone, patients undergoing elective degenerative thoracolumbar surgery involving ≥ 5 segment fusion exhibited a 2.3% prevalence of pulmonary embolism (PE)[117]. Patients at high risk of VTE, namely those undergoing surgery on more than 5 segments, combined anterior-posterior approaches and iliocaval manipulation, have been observed to have a lowered rate (odds ratio [OR] 3.7) of PE when receiving IVC filter and post-operative chemoprophylaxis with LMWH[118,119]. A few other studies have found that placement of IVC in high-risk patients was protective against VTE[120-122].

In terms of anatomic location, Oda et al., found in a trial of 134 patients a higher incidence of venographic deep venous thrombosis (DVT) during lumbar surgery (26.5%) compared to cervical (5.6%) and thoracic (14.3%) surgeries. It is important to note that no patients in this cohort received any VTE prophylaxis, nor did any of the patients develop clinical signs of PE; all VTE events were detected by routine venography[123]. Rokito et al., conducted a randomized control trial investigating the use of CS, CS + SCD, and SCD + warfarin in a study population of 329 patients undergoing major reconstructive spinal procedures in the cervical, thoracic, and/or lumbar spine. There was no benefit to using warfarin and that CS + SCD were adequate for most procedures regardless of spinal level being operated on[124]. The reported rate of DVT after spine surgery, ranging from 0.6% - 6% is very low[117,122,125-127].

Anterior and combined anterior/posterior approaches are one of the high-risk factors for VTE according to the 7th ACCP venous thrombosis prevention guidelines[112]. It becomes difficult to elucidate causality associated to these approach-specific risk factors from other high-risk patient factors. It is thought that the risk associated with anterior and anterior/posterior approaches is related to intraoperative manipulation of the iliac and great vessels[118,119,122,128,129]. Oda et al., found a 15.5% incidence of asymptomatic DVT (by venography screening) after posterior spinal surgery without any prophylaxis[123]. Dearborn et al., found in their retrospective cohort a 6.1% PE incidence in spine patients undergoing anterior and posterior approaches compared to a 0.5% in the posterior approach group[130]. These patients had only mechanical prophylaxis. Pateder et al., conducted a similar study with the addition of pharmacologic prophylaxis using warfarin, LMWH or heparin, according to availability and surgeon judgement. They observed a PE incidence of 3% with anterior and combined approaches, and 0.65% with posterior approaches. The apparent decrease in anterior incidence compared to Dearborn et al., was attributed to the chemoprophylaxis preventing thrombi formation after endothelial injury to the great vessels[129]. This mechanism is supported by the posterior approach incidence of 0.65%, similar to Dearborn et al., suggesting a posterior approach may not equally benefit from the added pharmacologic prophylaxis. Interestingly, Pateder et al., also noted that right-side anterior approaches, which require manipulation of the vena cava, had a higher rate of PE compared to left-side approaches, which require manipulation of the aorta (13.3% vs. 2.3%)[129].

Adding to the debate, McLynn et al., compared the National Surgical Quality Improvement Program (NSQIP) database to a retrospective cohort and found conflicting evidence for the necessity of prophylaxis, demonstrating no associated increased risk of VTE with multi-level procedures or due to a specific surgical approach[125]. They also did not find a reduction in VTE with pharmacologic prophylaxis (relative risk [RR] = 1.32 p = 0.421) but did find an increase in the occurrence of hematoma requiring reoperation with prophylaxis compared to without (0.62% vs. 0.08%; RR = 7.80, p = 0.020). Pendharker et al., found a decreased rate of VTE in microscopic lumbar discectomy group in a study on 42,025 patients which was compared outcomes of lumbar macro discectomy versus micro discectomy[131].

The risk associated with undue pharmacologic VTE prophylaxis is excessive bleeding, specifically epidural hematomas, due to the potential for devastating neurologic injury. Thus, the risk of possible VTE needs to be weighed against the risk of administration of VTE prophylaxis to patients undergoing spine procedures.

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6 - Is aspirin a viable chemoprophylaxis for VTE in patients undergoing spine surgery?

Response/Recommendation: While aspirin (ASA) may reduce venous thromboembolism (VTE) after orthopaedic procedures, there are no high-quality studies addressing this issue in patients undergoing spine surgery. We recommend surgeons weigh the potential benefits of chemoprophylaxis with known risks of increased bleeding.

Strength of Recommendation: Consensus.

Delegates vote: Agree 96.43% Disagree 0.00% Abstain 3.57% (Strong Consensus).

Rationale: VTE following orthopaedic procedures is a feared complication as it may lead to fatal pulmonary embolism (PE). The incidence of VTE following spine surgery is not well established with published rates varying from 0.3 - 31%[132-138]. Currently, no specific protocol exists for VTE prophylaxis in patients undergoing spine surgery likely due to the heterogeneity of cases performed by spine surgeons. Another reason is that VTE chemoprophylaxis in spine surgery may increase the risk of bleeding and hematoma formation, which can result in cord impingement and paralysis[139]. Although the efficacy of ASA chemoprophylaxis following hip and knee joint arthroplasty is robust[140-144], evidence in spine surgery is extremely limited. Previous studies are heterogeneous to allow drawing strong conclusions regarding the use of ASA for VTE prevention.

The only prospective deep venous thrombosis (DVT) chemoprophylaxis study in spine surgery found no incidence of acute DVT in 117 patients who underwent posterior lumbar spine fusion and were treated with 600 mg ASA twice a day (*bis in die* [BID][145].

Another study, retrospective, evaluated two cohorts consisting of no prophylaxis vs. 150 mg ASA daily for VTE prophylaxis in patients undergoing spine surgery. The no prophylaxis group consisted of 697 procedures, 554 of these were described as laminotomies, decompressions, or disc enucleations, and the remaining 143 were posterolateral spinal fusions. This group has two cases of DVT and no PE for an overall VTE rate of 0.29%. The ASA prophylaxis group consisted of 414 procedures, 272 of these were non-fusion, as described previously and the remaining 142 were fusions. This group had one case of DVT and no cases of PE for a VTE occurrence of 0.24%. Thus, no difference was observed in the rates of VTE when prophylactic ASA was used[146].

A retrospective study of 637 patients who underwent surgery for spinal metastasis were given various VTE chemoprophylaxis starting 48 hours after surgery including low-molecular-weight heparin (LMWH), subcutaneous heparin, ASA, and warfarin. Symptomatic VTE developed in 11% of the patients that used any chemoprophylaxis and in 11% who received no chemoprophylaxis[147].

A retrospective review of a prospectively collected data on 200 patients who underwent anterior lumbar interbody fusion (ALIF) were given LMWH and tinzaparin the evening before surgery and then daily for 3 to 5 days while inpatient, and then ASA daily for 4 weeks on an outpatient basis. No VTE or bleeding occurred in any of these 200 patients[148].

Lastly, a retrospective study of 83,839 patients who underwent anterior cervical discectomy and fusion (ACDF), or posterior lumbar fusion (PLF) were given either ASA, regular heparin, or LMWH on the day of surgery. About 1,872 patients (2.23%) received ASA. No difference was found in the incidence of VTE between these group. However, patients receiving ASA had increased odds of requiring a blood transfusion (1.48 [1.17 - 1.86])[149].

Conclusion: There is a dearth of studies investigating the use of ASA as a VTE prophylaxis in patients undergoing spine surgery. The studies that exist are low in quality and are not conclusive. Although ASA has been shown to be effective for prevention of VTE following other orthopaedic procedures, its efficacy as a VTE prophylaxis in patients undergoing spine surgery remains unproven.

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7 - What is the optimal protocol for management of patients who are on aspirin for a non-spine related disorder prior to spine surgery?

Response/Recommendation: Prior to spine surgery, low dose-aspirin (LD-ASA) (81 mg - 500 mg) used for primary and secondary cardiovascular prevention, can be stopped for one to three days. For ASA doses > 1 g per day, ASA should be stopped for at least seven days prior to surgery. However, in patients with extensive cardiac history, it is reasonable to maintain LD-ASA (81 mg) throughout spine surgery.

Strength of the Recommendation: Moderate.

Delegates vote: Agree 89.29% Disagree 10.71% Abstain 0.00% (Strong Consensus).

Rationale: ASA is commonly used for patients with cardiovascular disease. ASA irreversibly inhibits platelet aggregation, with platelets typically requiring seven to ten days to fully regenerate[150]. ASA discontinuation prior to non-cardiac surgery has been associated with a rebound hypercoagulation effect and a 5- to 10-fold increase in the mortality rate related to acute myocardial infarction[151,152].

Park et al., evaluated the timing of ASA cessation prior to one- or two-level lumbar fusion (three to seven days vs. seven to ten days prior to surgery)[153]. They evaluated three groups: ASA naïve patients vs. patients who stopped ASA three to seven days pre-surgery, vs. patients who stopped ASA seven to ten days pre-surgery[153]. Patients who stopped ASA three to seven days prior to surgery experienced more surgical drainage and longer time of surgical drainage compared to the other two groups[153]. They also found that if ASA was stopped more than seven days before spine surgery, there was no significant difference in bleeding risk compared to the other two groups[153]. On the other hand, Kang et al., compared two groups of patients undergoing spinal fusion: ASA naïve patients vs. patients who stopped LD-ASA (100 mg) at least seven days prior to surgery[154]. The ASA group experienced significantly increased rates of postoperative hemorrhage, higher transfusion requirements, and wound complications even when ASA was stopped at least seven days prior to surgery[154]. Nonetheless, they recommended stopping LD-ASA seven days preoperatively[154]. In another study, Park et al., divided patients who underwent two or more level lumbar fusions into three groups: ASA naïve (group I, 38 patients) vs. patients who stopped ASA one week prior to surgery (group II, 38 patients), vs. patients who continued LD-ASA throughout surgery (group III, 30 patients)[155]. They found that LD-ASA significantly increased bleeding for groups II and III compared to ASA naïve patients[155]. Furthermore, the additional utilization of non-steroidal anti-inflammatory (NSAID) medication was a confounding variable that increased perioperative blood loss in all three groups[155]. Therefore, it is also suggested to stop NSAID in the perioperative phase.

On the other hand, Cuellar et al., retrospectively analyzed 200 patients with cardiac stents who were randomized to either a group that underwent spine surgery while taking ASA (81 mg or 325 mg; 100 patients) or a group that stopped ASA five days prior to spine surgery (100 patients)[156]. They demonstrated that patients who did not stop ASA had shorter length of hospitalization, reduced operative time, similar blood loss, and comparable overall complication and readmission rates to the patients who stopped ASA five days before surgery[156]. Importantly, there was no major increase in the rate of epidural hematoma formation in patients who continued ASA[156]. Similarly, Soleman et al., conducted a retrospective analysis of 102 patients undergoing non-instrumented lumbar decompression surgery[157]. They compared perioperative risks of bleeding and cardiovascular complications of patients on daily ASA 100 mg (40 patients) vs. a control group who stopped ASA (62 patients)[157]. They demonstrated that ASA continuation was safe, and did not lead to higher risk of morbidity, perioperative blood loss, surgical time, or length of hospitalization[157]. Nevertheless, one patient remaining on LD-ASA developed an epidural hematoma, resulting in irreversible paralysis[157]. This complication challenges the safety of continuing perioperative ASA in spine surgery.

More recently, the American Society of Regional Anesthesia (ASRA) published its guidelines on managing anticoagulation in patients undergoing interventional spine and

pain procedures. The ASRA concluded that surgery can be performed safely after ASA cessation as follows: after 12 hours if LD-ASA (< 1 g) is used for secondary prevention, and after three days if ASA is used for primary prevention[158]. This cessation time is extended to one week preoperatively for ASA doses greater than 1 g per day[158]. The ASRA also suggested that 81 mg ASA can be reasonably maintained in patients with extensive cardiac history (i.e., drug eluting stents), with its potential benefits outweighing the risk of major surgical bleeding[158]. This recommendation was supported by other recent studies, suggesting the safety of continuing antiplatelet drugs throughout spine surgery[159,160].

Despite the mixed and contrasting data, prophylactic LD-ASA (81 mg - 500 mg) can typically be stopped for one to three days prior to spine surgery, but for one week if the ASA dose is greater than 1 g per day. In patients with extensive cardiac history, it is reasonable to maintain LD-ASA (81 mg) throughout spine surgery.

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8 - What is the optimal protocol for management of patients who are being treated with warfarin for a non-spine related disorder prior to spine surgery?

Response/Recommendation: Warfarin (Coumadin) should be discontinued at least 5 days before spine surgery, and the international normalized ratio (INR) goal should be 1.2 or less.

Strength of the Recommendation: Moderate.

Delegates vote: Agree 92.86% Disagree 3.57% Abstain 3.57% (Strong Consensus).

Rationale: Warfarin, a vitamin K antagonist (36 - 42 hours half-life), reduces the function of clotting factors II, VII, IX, and X by blocking the vitamin K epoxide reductase enzyme[161]. It is a commonly used anticoagulant for treatment of deep venous thrombosis (DVT) and pulmonary embolism (PE), and prevention of cerebrovascular accidents in patients with atrial fibrillation, valvular heart disease, or artificial heart valves. Perioperative continuation of warfarin can be associated with increased risk of bleeding[162]. Rokito et al., reported that in patients undergoing major reconstructive spinal surgery, the perioperative use of warfarin can be associated with major blood loss (> 800 mL), while adding no benefit in DVT prevention compared to the use of compression stocking and sequential compression devices[163]. Benzon et al., studied the remaining anticoagulation effect of warfarin five days after its discontinuation. In the majority of patients (n = 21), the international normalized ratio (INR) normalized to less than 1.2, which was considered adequate for safe neuraxial procedures[164]. A small number of patients (n = 2) had INR values of 1.3 or 1.4. However, the safety of this INR range for neuraxial injections was considered inconclusive[164]. Narouze et al., and the American Society of Regional Anesthesia (ASRA) published guidelines recommending stopping warfarin five to six days before interventional spine and pain procedures, with a goal INR of 1.4 or less[165]. While most available data suggest withholding warfarin for a minimum of five preoperative days to be reasonably safe in patients undergoing spinal surgeries, there is concern for increased operative blood loss even after seven days of warfarin discontinuation. Young et al., evaluated 263 patients undergoing elective lumbar spine surgery including laminectomy with and without instrumented posterolateral fusion[166]. All patients on warfarin had their anticoagulation stopped seven days prior to surgery[166]. They noted that patients on warfarin (n = 13) had significant increase in intraoperative blood loss (839 mL vs. 441 mL) and postoperative blood transfusions (23% vs. 7.4%, p = 0.04) compared to patients not on warfarin (n = 250)[166]. Despite the limited data on neurologic and spinal surgery, warfarin discontinuation is recommended for a minimum of five preoperative days. Additionally, while a goal INR of 1.4 or less is acceptable, a more conservative range of 1.2 or less is adequate for safe spinal surgeries.

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9 - In patients on anticoagulants for a non-spine disorder, is perioperative bridging therapy necessary following cessation of anticoagulation prior to spine surgery?

Response/Recommendation: Perioperative bridging anticoagulation therapy is not superior to placebo in preventing thromboembolic events following cessation of anticoagulation prior to spine surgery. Additionally, bridging anticoagulation therapy can be associated with higher risk of major bleeding.

If a bridging therapy is contemplated in high-risk patients, and at the discretion of the treating physician, unfractionated heparin and low-molecular-weight heparin (LMWH) are reasonable options.

Strength of the Recommendation: Limited.

Delegates vote: Agree 89.29% Disagree 3.57% Abstain 7.14% (Strong Consensus).

Rationale: Preoperative discontinuation of anticoagulation is commonly practiced mitigating the risks of bleeding and the formation of neuraxial hematoma[167-170]. However, anticoagulant cessation may promote thromboembolic events in high-risk patients with valvular heart disease, atrial fibrillation, ischemic stroke, or venous thromboembolism (VTE).

The concept of bridging anticoagulation therapy was therefore hypothesized to minimize the risk of thromboembolic events in the perioperative period after discontinuation of anticoagulation. In a randomized double blinded study, Douketis et al., reported comparable risk of arterial thromboembolic events with or without the use of perioperative bridging therapy LMWH vs. placebo, following cessation of warfarin in patients with atrial fibrillation[171]. They recommended against the use of bridging therapy due to a lack of superiority in preventing thromboembolic events, and the associated risk of major bleeding[171]. This study was not specific to spine surgery, however, and excluded patients with a history of mechanical heart valve, stroke, or VTE within 12 weeks prior to surgery[171].

In another study, Steinberg et al., reported a higher rate of bleeding if bridging anticoagulation therapy (LMWH or unfractionated heparin [UFH]) was implemented during perioperative interruption of anticoagulation therapy (odds ratio [OR] = 3.84)[172]. As a result, they recommended against the use of routine bridging therapy[172]. This study was also not specific to patients undergoing spine surgery[172]. In 2009, the North American Spine Society (NASS) issued clinical guidelines for the use of antithrombotic therapy in spine surgery, and the published consensus did not support an ideal perioperative bridging anticoagulation therapy[173]. The workgroup also suggested that the ideal time to withhold anticoagulation prior to surgery is unique to each drug's clearance half-life[173]. If a bridging therapy is contemplated in high-risk patients, despite the limited evidence, the workgroup suggested that either intravenous UFH or LMWH is a reasonable bridging anticoagulation agent following warfarin[173]. They argued, however, that intravenous heparin is more controllable and predictable than LMWH[173]. A bridging-intravenous-heparin-therapy should be stopped 4 - 6 hours (based on a half-life of 1 - 2 hours) prior to surgery and can be resumed 24 hours postoperatively[169,174]. Alternatively, bridging enoxaparin should be stopped 24 hours (based on a half-life of 4 - 7 hours) prior to surgery and can be resumed 12 - 24 hours postoperatively[169].

In conclusion, despite the limited evidence related to spine surgery, perioperative bridging anticoagulation therapy is not superior to placebo in preventing thromboembolic events following cessation of anticoagulation prior to surgery. Additionally, bridging therapy can be associated with higher risk of major bleeding. If a bridging therapy is contemplated in high-risk patients, UFH and LMWH are reasonable options.

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10 - Do patients with spine trauma require routine VTE prophylaxis before and after surgery?

Response/Recommendation: Patients suffering from traumatic spine injury are at an increased risk for venous thromboembolism (VTE). Recommendations for VTE prophylaxis before and after surgery in spine trauma varies based on pertinent factors such as presence of spinal cord injury (SCI), segment of the spine involved and age.

Strength of Recommendation: Moderate.

Delegates vote: Agree 100.00% Disagree 0.00% Abstain 0.00% (Unanimous Strong Consensus).

Rationale: Understanding the use VTE prophylaxis in surgical spinal trauma is very important in clinical practice as it aids in surgical planning and management. The current literature is lacking in terms of a standard of practice and future research is warranted.

VTE which includes deep venous thrombosis (DVT), and pulmonary embolism (PE) is one the most common complications following major joint surgery, with an incidence between 2.9% and 3.7%[175]. While there has been a focus on the incidence of VTE in other major orthopaedic procedures such as emergency hip fracture care and total hip/knee arthroplasty, there exists a gap in the literature in examining the incidence of VTE after spinal surgery. The range of VTE in spinal surgery ranges from 3% to 31% based on the patient population and diagnostic methodology[176,177]. To date there is no clear consensus or standard of practice with regards to VTE prophylaxis in spinal trauma surgery. In a major study conducted by Glotzbecker et al., in 2008, 94 orthopaedic and neurological spine surgeons with established clinical interest and volume in spine trauma surgery responded to questions focused on varying issues that included the perceived risk of DVT, PE, postoperative epidural hematoma, preferred chemoprophylactic agents, the safe time point for initiation of chemoprophylaxis, and use of inferior vena cava (IVC) filters. The authors concluded that there is wide variability in practices regarding thromboprophylaxis in spinal trauma surgery, which likely occurred due to the paucity of scientific evidence in the literature[178,179].

VTE prophylaxis in spinal trauma surgery can be stratified based on the presence or absence of SCI. In patients without significant SCI, there is preservation of neurologic function with mobility of the extremities and decreased venous blood stasis. The reported incidence of VTE in patients with SCI has a wide range of 2% to 45.2%[180-183]. In a large population study of a total of 47,916 Taiwanese patients with SCI, the authors found a 2.5-fold increased risk of DVT and a 1.6-fold increased risk of PE when compared with controls[184]. Also, in an analysis by Ploumis et al., the authors found that the prevalence of DVT was significantly lower in patients without SCI as compared to patients with SCI (odds ratio [OR] = 6.0; 95% confidence interval [CI] = 2.9 - 12.7). Furthermore, patients with an acute SCI who were receiving oral anticoagulants had significantly fewer episodes of PE (OR = 0.1; 95% CI = 0.01 to 0.63) than those who were not receiving oral anticoagulants. Starting thromboprophylaxis within the first two weeks after the injury resulted in significantly fewer DVT events than delayed initiation did (OR = 0.2; 95% CI = 0.1 to 0.4)[185]. In spine trauma patients with associated SCI, the recommendation is to start VTE prophylaxis as early as possible and once it is deemed safe.

Risk factors for VTE in patients with SCI include increased age, obesity, flaccid paralysis, and cancer. Age as a risk factor is very important, several studies have shown that among patients with SCI, older patients are more likely to develop VTE[186,187]. In a study conducted by Jones T. et al., with a total of 16,240 SCI patients, the authors concluded that patients with age < 30 years had a lower risk of developing a thromboembolic event[188]. The risk is greatest in the first three months post-injury. In elderly SCI patients, VTE prophylaxis should be administered rigorously pre- and post-operatively.

In addition to the presence or absence of SCI, the segment of the spine also plays an important role in deciding whether DVT prophylaxis should be administered before and after surgery. In another article by Ploumis et al,. the authors surveyed twenty-five spine trauma surgeons pertaining to the management of VTE prophylaxis in patients with spine fractures (with and without concomitant SCI). It was concluded that in most surgical cases of cervical spine trauma with associated SCI and thoracolumbar spine trauma with or without SCI, postoperative VTE prophylaxis is necessary. However, postoperative VTE prophylaxis after cervical spine injuries without SCI was agreed not to be needed. VTE prophylaxis is recommended to be started as early as possible in SCI cases or any cases with surgical delay. The current recommendation is that pharmacologic VTE prophylaxis needs to be administered for at least three months post-injury[189].

Even though patients with spinal fractures are likely to receive VTE prophylaxis pre- and post-operatively, it has been shown in the literature that these patients still have a high rate of VTE when compared to patients undergoing elective spine surgery[190]. One of the major reasons why many spine trauma surgeons may be reluctant to initiate VTE prophylaxis in the early stages of injury or even immediately after surgery is the possible increased risk of bleeding (especially epidural hematoma), neurologic and wound healing complications that may occur in certain patients[191,192]. In a study by Kim DY et al., the authors analyzed 206 patients who underwent operative fixation for spine fractures. Forty-eight (23%) patients received early (< 48 hours) VTE prophylaxis, and 158 patients (76.7%) received late (> 48 hours) VTE prophylaxis. They found no difference in bleeding or neurologic complications between the two groups. In fact, none of the patients developed any bleeding complications in either group[193]. In a more recent study by Zeeshan M. et al., the authors found similar results. A total of 3,554 patients were equally matched (1,772, early VTE prophylaxis; 1,772 late). Patients who received early VTE prophylaxis (< 48 hours) had decreased rates of DVT versus those who did not (2.1% vs. 10.8%, p < 0. 01) in operative spinal trauma without increasing the risk of bleeding and mortality[194]. Despite the research, there remain a wide variation in VTE prophylaxis for patients with spine trauma, based on the survey of spine surgeons[178,179].

In spinal trauma patients with concomitant SCI, low-molecular-weight heparin (LMWH) is more effective in preventing DVT than unfractionated heparin with fewer bleeding complications. Use of vitamin K antagonist was also more effective in preventing PE[185,195]. Furthermore, according to Glotzbecker MP et. Al., the majority of surgeons surveyed selected LMWH as their agent of choice for chemoprophylaxis, with subcutaneous

heparin and coumadin as the second and third most common choices, respectively. In many cases in the post-operative period, chemical anticoagulation may be delayed due to concerns of bleeding or neurologic complications. Instead, IVC filters may be used in preventing a PE[179].

As previously mentioned, there is no clear standard of practice regarding the administration of VTE prophylaxis to patients suffering from spine trauma. There is a wide variability of practice regarding thromboprophylaxis in spinal trauma surgery. Further research examining the epidemiology of VTE in spinal surgery and the risks-benefit relationship of thromboprophylaxis is warranted.

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11 - Does the presence of a dural tear influence the choice for VTE prophylaxis after spine surgery?

Response/Recommendation: Following spine surgery, the rate of venous thromboembolism (VTE) is significantly higher in patients with incidental durotomy (almost 1.5 times) compared to patients without. Therefore, in patients with dural tears post spine surgery, vigorous VTE prophylaxis therapies should be considered.

Strength of Recommendation: Limited.

Delegates vote: Agree 92.31% Disagree 3.85% Abstain 3.85% (Strong Consensus).

Rationale: Complications in spine surgery tend to occur in clusters as complex spinal pathologies lead to higher rate of successive undesirable events. Inadvertent dural tears during spine surgery are associated with increased in-hospital complications, health care burden, and readmission rates[196-198]. In a retrospective analysis, Alluri et al., found that VTE occurred in 1.3% of patients with a dural tear in contrast to 0.9% of patients without (odds ratio [OR] 1.46, $p < 0.001$)[199]. Similarly, deep venous thrombosis (DVT) and pulmonary embolism (PE) occurred in 1% and 1% of patients with a dural tear and only in 0.7% and 0.7% of patients without durotomy (OR 1.36, $p = 0.03$ for DVT, OR 1.48, $p = 0.01$ for PE) respectively. This relationship was seen after matching specific demographic and comorbidity variables that were associated with VTE complications. Another observational cohort study by Durand et al., studied 86,212 patients who underwent spine surgery using the National Surgical Quality Improvement Program (NSQIP) dataset from 2012 to 2015[200]. The authors identified late-presenting dural tears (LPDT) using reoperation or readmission procedures defined by durotomy-specific Current Procedural Terminology (CPT) codes. After adjusting for patient and procedure-level factors, patients with LPDT had higher rates of surgical site infection (OR 2.54, $p < 0.0001$), wound disruption (OR 2.24, $p < 0.0001$), sepsis (OR 2.19, $p < 0.0001$), and VTE (OR 1.71, $p < 0.0001$). The authors suggested that predisposition of LPDT patients to wound infection and subsequent bacteremia may lead to higher risks of thromboembolic events[201]. Although the underlying pathogenesis of VTE development in sepsis remains unclear, the etiology is thought to be the result of several factors associated with dural tears including immobility and activation of thrombo-inflammatory pathways[202-204]

In another retrospective study using the Nationwide Inpatient Sample (NIS) database, Yoshihara et al., analyzed patient

outcomes after incidental durotomies in cervical spine surgery[196]. In this study, the mean hospital stay was 1.4 days longer in patients with dural tears than in those without (4.6 vs. 3.0 days, $p < 0.001$). Rates of neurologic (3.0 vs. 0.4%, $p < 0.001$) complications (including transitory ischemic attack [TIA]/stroke) and PE (1.8 vs. 0.2%, $p < 0.001$) were significantly higher in the dural tear group.

Current postoperative managements of dural tears include subarachnoid lumbar drainage and/or postoperative bed rest, which can lead to extended immobilization and subsequent venous stasis, thereby increasing the odds of VTE[196,198,205-207]. In a study investigating bedrest greater or less than 24 hours for incidental lumbar dural tear after laminectomy, there was a statistically significant increase in the incidence of medical complications in the bed rest group > 24 hours ($p = 0.0003$), which included greater rates of DVT (4.2 vs. 0%)[208]. However, this study was underpowered to statistically compare DVT rates.

In addition to postoperative immobility, increased rates of VTE in patients with dural tears may be attributed to increase in operative times. In a prospective cohort study of patients undergoing discectomy or laminectomy procedures, Smorgick et al., found that intraoperative repair of an incidental durotomy significantly increased operative duration (146 ± 59 vs. 110 ± 54 minutes; $p = 0.0025$)[209]. Another prospective, observational study by Weber et al., showed that an incidental dural tear prolonged surgical duration from 116 to 153 minutes ($p < 0.0001$) in patients undergoing elective spinal surgery for degenerative disorders of the cervical, thoracic, or lumbar spine[210]. Inflammation and endothelial damage that occurs during surgery, in combination to immobility associated with prolonged surgical duration, can initiate the clotting cascade, and increase thrombus formation[211-215]. It has been shown that ischemia and venous stasis, which occur during surgery, can also lead to DVT formation via the upregulation of P-selectin and local prothrombotic microparticles[216,217]. Few studies within the spine literature have investigated the direct effect of longer operative times on VTE risk[218]. A prospective cohort study by Inoue et al., using indirect multidetector computed tomography (MDCT) in 100 patients undergoing spine surgery found that operative duration was not significantly different in patients that did (87) and did not (13) develop VTE[219]. However, this study was limited in cohort size and surgical durations. Schoenfeld et al., using the NSQIP dataset investigating 27,730 patients determined that operative time exceeding 261 minutes was associated with risk of developing DVT (OR: 3.1 95% confidence interval [CI]: 2.3 – 4.1) and PE (OR: 3.15 95% CI: 2.1 – 4.7); however, this operative time is significantly higher than those found in previous incidental durotomy studies[220]. Further studies focusing on the relationship between operating time and VTE risk in spine surgery are needed to determine a threshold duration of surgery.

The relationship between dural tears and VTE development is likely multifactorial and can be attributed to more complex pathology, longer operative duration, prolonged postoperative immobility, and risk for post-surgical infection. As such, a standardized approach to VTE prophylaxis in patients undergoing elective spine surgery must consider these risk factors as well as preexisting individual risk factors and comorbidities to guide appropriate post-operative prophylaxis. Currently, risk stratification tools such as the Rogers and Caprini scores do not adequately factor in intraoperative variables, such as the complexity of the procedure, especially in the event of a dural tear[221,222]. Data in dural tear studies were also limited to in-hospital events which may underestimate the true incidences of complications and mortality. In view of these limitations, clinicians should factor in identifiable preoperative and intraoperative risk factors in the event of a dural tear to guide prophylactic measures such as more aggressive and evidence-based anticoagulation therapy for patients at risk.

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12 - Should pediatric patients undergoing major spine procedures require routine VTE prophylaxis?

Response/Recommendation: Routine administration of pharmacologic venous thromboembolism (VTE) prophylaxis for major spinal procedures in pediatric patients is not supported by current evidence. Chemoprophylaxis should be limited to patients with multiple risk factors. Controversy exists on the utility of mechanical prophylaxis although poses minimal risk.

Strength of Recommendation: Limited.

Delegates vote: Agree 96.30% Disagree 3.57% Abstain 0.00% (Strong Consensus).

Rationale: Currently, there is no widely accepted guideline for VTE prophylaxis in pediatric orthopaedic patients and a majority of pediatric orthopaedic surgeons are unaware of their own institution's VTE prophylaxis protocol[223]. In a multi-national study on critically ill children, 17.6% of 2,484 patients met the criteria of the American College of Chest Physicians (ACCP) guidelines for pharmacologic prophylaxis, however, almost 2/3 of those patients did not receive prophylaxis due to lack of evidence[224].

The incidence of VTE in pediatric orthopaedic patients primarily derives from three main existing registries (Canada, Germany, and the Netherlands) and is reported to be 5.3 per 10,000 hospital admissions and 0.7 per 100,000 children. Previously documented risk factors for VTE in pediatric patients include intubation, intensive care unit (ICU) admission, blood transfusion, major surgery, central venous catheter placement, and longer length of ICU stay[225]. The estimated incidence of VTE following spinal fusion in children is 0.21% and risk factors include adolescent children and children with diagnoses of congenital scoliosis, syndromic spinal deformities, kyphoscoliosis, or thoracolumbar fractures[226]. In a 28-year follow up study on pediatric scoliosis surgery, Erkilinc et al., found a lower extremity deep venous thrombosis (DVT) rate of 0.13% in 1,471 patients and zero patients were diagnosed with pulmonary embolism (PE)[227].

There is a paucity of data on the utility of VTE prophylaxis in pediatric patients undergoing major spine procedures. However, due to the extremely low incidence of VTE in pediatric patients, no studies have identified a clear benefit thus far. In a retrospective review of 73 patients aged 14 - 19 undergoing posterior spinal fusion for adolescent idiopathic scoliosis (AIS), there were no DVT, or PE identified in any patients, regardless of whether chemoprophylaxis was used[228]. In a 2020, multi-center retrospective study, the incidence of VTE after elective spine and lower-extremity surgery in children with neuromuscular complex chronic conditions was 4 per 10,000, and only 4% used chemoprophylaxis. Moreover, only 10% used compression devices, raising the question whether mechanical prophylaxis should even be recommended in this cohort[225]. Asian literature also has shown that except for spinal cord injury patients the routine use of anticoagulation for spine surgery in children is not recommended[229-231].

There is minimal research on potential complications of chemoprophylaxis in pediatric spinal patients. A 2019 study on VTE chemoprophylaxis in AIS patients showed a higher but statistically non-significant difference in post-operative drain output as well as the amount of wound oozing in patients who received post-operative chemoprophylaxis compared to those who didn't. Length of stay was significantly shorter in the non-chemoprophylaxis group. The authors did not find a correlation between when chemoprophylaxis was initiated and the reported complications[228].

To evaluate standard of care among experts, forty-seven spine surgeons (orthopaedic spine surgeon and neurosurgeon) were surveyed on current trends in the perioperative administration of thromboprophylaxis in spinal surgery. Pharmacologic prophylaxis was used for spinal cord injury (SCI) by 91% of surgeons compared to 62% for non-SCI. Similar results were seen in anterior thoracolumbar procedures vs. posterior thoracolumbar surgeries. Almost half of the surgeons experienced complications with low-molecular-weight heparin (LMWH) including epidural hematomas, retropharyngeal hematoma, thrombocytopenia, and wound hematoma[232].

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Appendix

eA Supporting material provided by the authors is posted with the online version of this article as a data supplement at jbjs.org (http://links.lww.com/JBJS/G864).

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