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The Rate of Venous Thromboembolism Before and After Spine Surgery as Determined with Indirect Multidetector CT

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Background: This prospective cohort study investigated the rate of venous thromboembolism (VTE) before and after spine surgery as determined with use of indirect multidetector computed tomography (MDCT).

Methods: We performed a prospective study of 105 patients (36 women and 69 men ranging in age from 38 to 88 years) undergoing spine surgery at 2 institutions. Indirect MDCT was performed before and 3 days after surgery. Patients with a history of dialysis or drug allergy to contrast medium were excluded.

Results: No patient had symptomatic VTE preoperatively or postoperatively. The preoperative and postoperative rates of asymptomatic VTE were 4.8% and 13.0%, respectively; the rates of asymptomatic pulmonary embolism were 2.9% and 8.0%, respectively; and the rates of asymptomatic deep venous thrombosis were 3.8% and 6.0%, respectively. Age, sex, height, weight, body mass index, operative time, volume of intraoperative blood loss, and specific comorbidities (diabetes, hypertension, cardiac disease, previous VTE, and previous anticoagulation treatment) were not found to be risk factors.

Conclusions: Our findings demonstrated a low rate of preoperative VTE but a high rate of postoperative VTE in association with spine surgery. Surgeons need to be aware of the risk of VTE in patients undergoing spine surgery. MDCT is an effective and convenient technology for the early detection of VTE in such patients.

Level of Evidence: Prognostic Level I. See Instructions for Authors for a complete description of levels of evidence.

Venous thromboembolism (VTE), including pulmonary embolism (PE) and deep venous thrombosis (DVT), is a serious complication after spine surgery[1]. PE mortality is important as a complication. The Japanese Society of Anesthesiologists demonstrated that the incidence of symptomatic PE was 5.71 per 10,000 patients after surgery on the hip and lower extremities, whereas the incidence after spine surgery was lower, at 2.74 per 10,000 patients[2]. Spine surgery presents an intermediate risk of PE. In patients undergoing spine surgery, the rate of PE has been reported to range from 0.06% to 18%[2-4] and the rate of DVT has been reported to range from 0.3% to 15.5%[2,3,5-8]. The risks of symptomatic PE and DVT during the first 30 days postoperatively have been reported to be 0.29% and 0.6%[8]. The incidence of fatal PE has been reported to represent 6% of all PE that occur after spine surgery[9]. Therefore, the risk of PE in patients undergoing spine surgery is important.

The rate of symptomatic PE after spine surgery is very low, so the evaluation of new prophylactic therapies requires a large patient cohort in order to detect any effect. Alternatively, the rate of asymptomatic VTE may be a more useful indicator of the effectiveness of prophylactic anticoagulant therapy[10]. To determine the rate of asymptomatic VTE due to spine surgery, we must exclude the patients with asymptomatic VTE before surgery. Most recent studies have evaluated the postoperative rate of asymptomatic VTE while ignoring the presence of asymptomatic VTE before surgery[3,6,7]. Moreover, many studies have evaluated the rate of asymptomatic PE or DVT alone[5-7].

There are few algorithms for determining a patient's risk of VTE. Piper et al. devised a risk scoring system (based on race,

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preoperative comorbidities, and operative characteristics) to predict the postoperative rate of VTE in patients undergoing spine surgery[11]. Three large cohort analyses have examined the risk factors for VTE in patients undergoing spine surgery, which could help to provide individualized recommendations regarding thromboprophylaxis[9,12,13]. However, those analyses failed to assess whether or not patients had a preoperative asymptomatic VTE. The use of thromboprophylaxis is controversial because of the risk of postoperative spinal hematoma. More research is needed to examine preoperative VTE for the useful verification of thromboprophylaxis.

Many doctors have traditionally detected DVT or PE with use of venography or color Doppler ultrasonography, computed tomography (CT), and ventilation-perfusion lung scintigraphy. Recently, multidetector CT (MDCT) has been used as a highly sensitive and specific means of identifying DVT and PE, although there have been problems related to radiation exposure and the use of contrast agent in association with MDCT procedures[14,15]. MDCT has been clinically useful for facilitating the rapid and objective detection of both symptomatic and asymptomatic DVT and PE in a single acquisition[16-18]. Many studies have investigated the rate of VTE after spine surgery[4,8,11,13], but few have investigated the rate of VTE before surgery[2].

In the present study, we examined the rates of DVT and PE with use of MDCT before and after spine surgery and analyzed the risk factors for VTE.

Materials and Methods

The present study involved patients from Jichi Medical University and Shinkaminokawa Hospital. Ethics approval was obtained from the Ethics Review Board of our university. We prospectively enrolled patients who underwent spine surgery at our 2 institutions between August 2013 and April 2016. Written informed consent was obtained from all participants. The present study was performed in accordance with the principles of the World Medical Association Declaration of Helsinki. We calculated the necessary sample size for an alpha of 0.05 and a power of 0.90 with use of G*Power 3 statistical software[19,20] and found it to be 67.

The exclusion criteria included drug allergy to contrast medium, liver disease, dialysis, congenital clotting factor deficiencies, and treatment with antithrombotic therapy or hemodialysis.

In total, 105 patients (36 women and 69 men) underwent spine surgery. The mean age of the patients was 68.5 years (range, 38 to 88 years). All procedures were performed with the patient under general anesthesia. All patients wore elastic stockings on the legs during surgery. Postoperatively, patients continued to wear the stockings and were managed with an intermittent pneumatic compression device until the initiation of walking practice, according to the Japanese Guidelines for Prevention of Venous Thromboembolism. Patients who were managed with postoperative prophylactic antithrombotic therapy were excluded. All patients with VTE were managed with aggressive antithrombotic therapy.

MDCT

Sixteen-row MDCT was used both preoperatively and 3 days after surgery. The preoperative scans detected any preexisting thrombi, making it possible to show that thrombi detected on the postoperative scans were new, and thus presumably iatrogenic in origin. The time points for testing in the present study were matched to the previous studies[17,21].

All patients were in the supine position during MDCT, and all received an injection of 150 mL (100 mL for those weighing <50 kg) of iohexol (300 mg/mL) (Daiichi-Sankyo) at a rate of 3 mL/sec. The thorax and the area from the diaphragm to the distal crural area were examined craniocaudally. Bolus tracking was performed after setting the target in the main trunk of the pulmonary artery, and scanning began. Then, after 3.5 minutes, the area from the abdomen to the lower limbs was scanned. In the thorax and in the region from the diaphragm to the lower limbs, the MDCT slice thicknesses were 2 and 5 mm, respectively. The radiation dose associated with MDCT was 18.5 mSv for the PE scan and 8.5 to 8.8 mSv for the DVT scan[14,15]. On MDCT scanning, PE was indicated by a sharply delineated pulmonary arterial filling defect that was observed in at least 2 consecutive axial images and located centrally within the vessel or with acute angles at its interface with the vessel wall[22], and DVT was indicated by a low-attenuating partial or complete intraluminal filling defect surrounded by a high-attenuating ring of enhanced blood that was seen on at least 2 consecutive axial images[23]. Proximal DVT was defined as a thrombosis at or proximal to the level of the popliteal vein, and distal DVT was defined as a thrombosis affecting the axial calf veins. A single radiologist assessed the preoperative and postoperative MDCT images in a blinded fashion to determine the presence or absence of PE and/or DVT. Then we divided patients into VTE and no-VTE groups.

Statistical Analysis

Statistical analyses were performed with use of SPSS for Windows (version 17.0; SPSS). Age, volume of intraoperative blood loss, operative time, and other preoperative factors were compared between VTE and no-VTE groups with use of the Mann-Whitney U test. The chi-square test was used for analysis of categorical data. To examine the effect of specific comorbidities on the risk of preoperative VTE, we also categorized patients according to the presence of certain conditions at the time of surgery, such as diabetes, hypertension, cardiac disease (including previous myocardial infarction, congestive heart failure, angina pectoris, arrhythmia, and cardiac valvular disease), previous VTE, and previous anticoagulation treatment. The level of significance was set at $p < 0.05$ for all tests.

Results

Table I shows patient characteristics and risk factors. We prospectively analyzed 105 patients who underwent 23 cervical laminoplasties, 72 lumbar laminectomies, and 10 spinal fusions with instrumentation from August 2013 to April 2016. Five patients with preoperative VTE were excluded from the analysis of postoperative VTE.

TABLE I Demographic Characteristics and Risk Factors for VTE After Spine Surgery

Risk Factors	All Patients (n = 100)	No-VTE Group (n = 87)	VTE Group (n = 13)	P Value
Sex *(no. of patients)*				0.111
Male	66	55	11	
Female	34	32	2	
Age* *(yr)*	68.1 ± 8.9	68.1 ± 8.9	68.5 ± 8.8	0.749
Volume of intraoperative blood loss* *(mL)*	180.9 ± 197.2	170.2 ± 128.7	252.4 ± 442.5	0.372
Operative time* *(min)*	116.3 ± 62.0	115.3 ± 55.5	122.8 ± 97.8	0.279
Height* *(cm)*	160.4 ± 9.2	160.2 ± 9.5	161.5 ± 7.4	0.695
Weight* *(kg)*	64.5 ± 11.3	64.9 ± 11.8	61.3 ± 6.6	0.532
Body mass index* *(kg/m^2)*	25.0 ± 3.2	25.2 ± 3.3	23.6 ± 2.6	0.761
Type of operation *(no. of patients)*				0.845
Cervical laminoplasty	20	18	2	
Lumbar laminectomy	70	60	10	
Spinal fusion	10	9	1	
Specific comorbidities *(no. of patients)*				
Diabetes	20	18	2	0.656
Hypertension	60	51	9	0.466
Cardiac disease	11	11	0	0.198
Previous VTE	4	3	1	0.432
Previous anticoagulation treatment	20	17	3	0.766

*The values are given as the mean and the standard deviation.

Rate of VTE

No patient had symptomatic VTE before or after spine surgery. Preoperative MDCT showed asymptomatic PE in 3 patients (2.9%) and asymptomatic DVT in 4 patients (3.8%), with 2 patients having both DVT and PE (Figure 1, Table II). Postoperative MDCT demonstrated asymptomatic PE in 8 patients (8.0%) and asymptomatic DVT in 6 patients (6.0%), including 1 patient with both. The rates of VTE before and after spine surgery were 4.8% (5 of 105) and 13.0% (13 of 100), respectively. The patients with preoperative VTE showed no VTE on postoperative MDCT. The postoperative VTE cases were thus all iatrogenic.

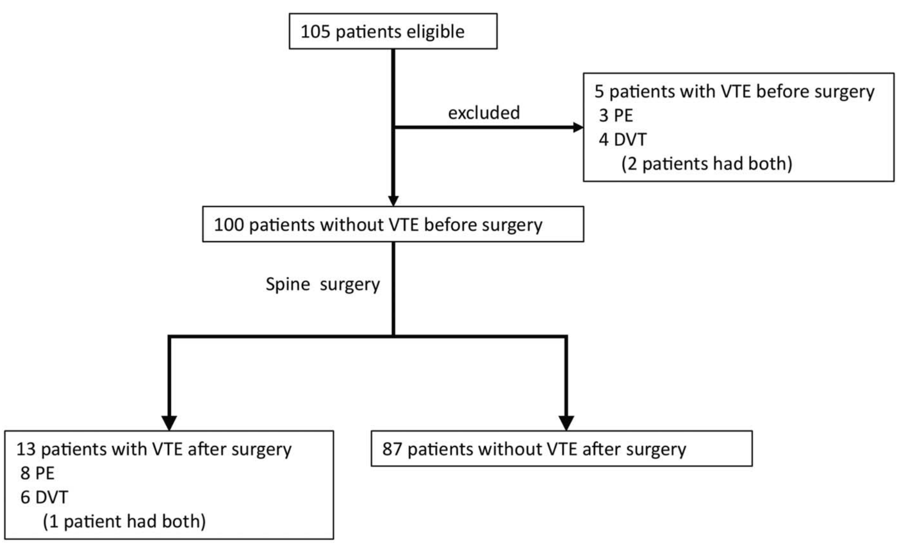

Fig. 1

Study flowchart. VTE = venous thromboembolism, DVT = deep venous thrombosis, and PE = pulmonary embolism.

TABLE II Rates of DVT, PE, and VTE*

	Preop. (n = 105)	Postop. (n = 100)
DVT		
Yes	4 (3.8%)	6 (6.0%)
No	101 (96.2%)	94 (94.0%)
PE		
Yes	3 (2.9%)	8 (8.0%)
No	102 (97.1%)	92 (92.0%)
VTE		
Yes	5 (4.8%)	13 (13.0%)
No	100 (95.2%)	87 (87.0%)

*The values are given as the number of patients, with the percentage in parentheses.

Cervical Laminoplasty Group: Preoperatively, asymptomatic VTE occurred in 3 patients (13.0%), with PE in 2 patients (8.7%) and DVT in 1 patient (4.3%). Three patients with preoperative VTE were excluded. Postoperatively, asymptomatic VTE occurred in 2 patients (10.0%), with PE in 1 patient (5.0%) and DVT in 1 patient (5.0%).

Lumbar Laminectomy Group: Preoperatively, asymptomatic VTE occurred in 2 patients (2.8%), with PE in 2 patients (2.8%) and DVT in 1 patient (1.4%), including 1 patient with both. Two patients with preoperative VTE were excluded. Postoperatively, asymptomatic VTE occurred in 10 patients (14.3%), with PE in 6 patients (8.6%) and DVT in 5 patients (7.1%).

Spinal Fusion Group: Preoperatively, no patient had VTE, so no patients were excluded. Postoperatively, VTE (in the form of PE) occurred in 1 patient (10%).

Risk of VTE

The results of the comparative analyses for VTE are shown in Table I. Age, sex, height, weight, body mass index (BMI), operative time, and the volume of intraoperative blood loss showed no significant differences between the VTE group and the no-VTE group postoperatively. Specific comorbidities such as diabetes, hypertension, cardiac disease, previous VTE, and previous anticoagulation treatment also showed no significant differences between the VTE and no-VTE groups. The types of operations also showed no meaningful differences between the VTE and no-VTE groups.

Discussion

In the present study of patients managed with spine surgery, the preoperative rates of asymptomatic PE and asymptomatic DVT were 2.9% and 3.8%, respectively, and the postoperative rates were 8.0% and 6.0%, respectively. The overall rates of VTE before and after spine surgery were 4.8% and 13.0%. In previous reports, the PE rate after spine surgery has ranged from 0.06% to 18%[2-4] and the DVT rate has ranged from 0.3% to 15.5%[2,3,5-8]. The rates of VTE in the present study were within these ranges and were reasonable results. Venographic studies have indicated that the rates of PE and DVT after total knee arthroplasty range from 0.9% to 28% and from 41% to 85%, respectively, without thromboprophylaxis[24]. Watanabe et al., in a study of patients undergoing total knee arthroplasty, reported that the preoperative and postoperative rates of PE were 1% and 16%, respectively; that the rates of DVT were 8% and 47%, respectively; and that the rates of VTE were 9% and 51%, respectively[10]. Therefore, the PE and DVT risks associated with spine surgery are intermediate compared with those associated with total knee arthroplasty. During spine surgery, PE is an important and potentially fatal complication, and the postoperative rate of VTE is relatively high[25]. Mosenthal et al. found that the rate of PE was 0.7% in patients undergoing spine surgery and that 6% of all PEs (including symptomatic and asymptomatic PEs) were fatal (meaning that the total rate of fatal PE in patients undergoing spine surgery was 0.042%)[9]. Smith et al. showed that the rate of mortality due to PE was 0.034% after spine surgery[26]. Patients undergoing spine surgery need thromboprophylaxis to decrease the risk of death due to PE, but any thromboprophylactic drug increases the risk of a life-threatening epidural hematoma. The use of thromboprophylaxis is therefore controversial[9].

Risk factors for VTE include age[27,28], sex[29], a history of immobility[29-31], obesity[13], smoking[32], oral contraceptive use[33], family history[29,30,34], operative time[13], volume of blood loss[35], and comorbidities such as hypertension[29,36] and diabetes mellitus[13]. The independent predictors of DVT include a BMI of ≥40 kg/m^2, an age of ≥80 years, an operative time of >261 minutes, and an American Society of Anesthesiologists (ASA) classification of ≥3, whereas the independent predictors of PE include a BMI of ≥40 kg/m^2, an operative time of >261 minutes, and male sex[13]. Patient-specific risk factors include an age of >40 years (with increasing risk for each 5-year increment), neurological deficit, reduced mobility, previous thromboembolic disease, cardiovascular disease, a Charlson comorbidity index of ≥3, a BMI of >25 kg/m^2, varicose veins, and resumption of walking later than the second postoperative day[9]. In the present study, age, sex, height, weight, BMI, operative time, volume of intraoperative blood loss, and specific comorbidities (diabetes, hypertension, cardiac disease, previous VTE, and previous anticoagulation treatment) were compared between patients with and without VTE. However, no significant differences were observed. Therefore, we could not determine whether any of these variables is a risk factor.

In the study by Cheng et al., the rate of VTE in the absence of thromboprophylaxis was higher among patients undergoing surgery for the treatment of deformity (5.3%) and trauma (6.0%) than among those undergoing surgery for the treatment of degenerative disease (2.3%)[37]. Mosenthal et al. reported that the direct surgical risk factors include the use of an anterior or combined anterior-posterior surgical approach, surgery for the treatment of malignancy or trauma, and prolonged surgery[9]. Our study mainly involved spinal procedures that were performed for the treatment of degenerative disease, such as cervical laminoplasty or lumbar laminectomy, which are similar types of operations. The preoperative and postoperative rates of VTE were 13.0% and

10.0%, respectively, for cervical laminoplasty; 2.8% and 14.2%, respectively, for lumbar laminectomy; and 0% and 10.0%, respectively, for spinal fusion. However, one of the limitations of the present study is that the number of operations was small; therefore, future studies involving larger numbers of patients undergoing each operation are needed to confirm our findings.

The prevention of VTE may require mechanical prophylaxis and chemoprophylaxis after spine surgery. Mechanical prophylaxis is an easy-to-use, low-cost, low-risk intervention with proven efficacy that can prevent the morbidity and mortality associated with DVT and PE. The North American Spine Society Evidence-Based Clinical Guideline on Antithrombotic Therapies in Spine Surgery recommends the use of mechanical prophylaxis and chemoprophylaxis for patients undergoing elective spine surgery[12]. Preoperative mechanical prophylaxis may have merit for the prevention of postoperative VTE without adding more risk of perioperative blood loss in elderly patients with hip fracture[38]. In the future, we need to (1) determine which combination of risk factors should indicate the use of chemoprophylaxis and (2) elucidate the optimal chemoprophylaxis or mechanical prophylaxis, timing of initiation, and treatment duration.

Doppler ultrasound is frequently used to assess for DVT, and many studies have demonstrated the occurrence of DVT with use of ultrasound[5,6]. Doppler ultrasound is noninvasive and easy to repeat but is dependent on the skill of the examiner. Although the specificity of ultrasound for the detection of asymptomatic DVT is high (94% to 97%), the sensitivity is low (47% to 62%)[39]. Moreover, Doppler ultrasound is unable to detect PE[39]. In contrast, MDCT is able to detect symptomatic or asymptomatic PE at the location of the subsegmental pulmonary arteries[40-42]. MDCT also can measure the thrombus size and can detect both PE and DVT in 1 acquisition. MDCT is useful because of its high sensitivity (100%) and specificity (96.6%) and moderate-to-high interobserver reliabilities, with κ values ranging from 0.59 to 0.94 for the detection of symptomatic PE[43-45]. Therefore, we decided to have a single radiologist evaluate preoperative and postoperative MDCT scans in a blinded fashion. Furthermore, Bounameaux et al. demonstrated that the D-dimer level was significantly elevated in patients with asymptomatic DVT on the third postoperative day after total knee arthroplasty[46]. In that study, the rate of DVT as detected with venography was 39.8%. In the present study, the rates of postoperative asymptomatic PE and asymptomatic DVT were 8.0% and 6.0%, respectively, on the third postoperative day after spine surgery. MDCT examination costs 15,200 yen in Japan (approximately 138 USD), and most patients are covered by the National Health Insurance system. MDCT is available, but it cannot be used for all patients because of costs, allergy to contrast medium, liver damage, and renal failure. Inoue et al. showed that the D-dimer level was significantly elevated in patients with asymptomatic PE on the third and seventh postoperative days after spine surgery[21]. We suggest that patients undergo a predictor test such as evaluation of the D-dimer level. If the D-dimer level is high, the patients should receive MDCT.

The present study had several limitations. First, none of the patients had severe liver disturbance, severe renal disturbance, congenital clotting factor deficiencies, or a history of antithrombotic therapy or hemodialysis; patients with such risk factors may have higher rates of PE, DVT, or VTE than those patients in the present study. Second, MDCT was performed before surgery and on the third day after surgery; therefore, the results reflect the state of asymptomatic thrombi at those time points. As MDCT was not performed continuously from the preoperative period to the fourth postoperative day, we may not have detected all thrombi during spine surgery. Thus, VTE rates may be underestimated after surgery, and the timing of MDCT in preventing VTE during surgery must be further verified in larger studies. Third, this approach of using MDCT has problems, such as radiation exposure, invasive administration of contrast medium, potential for drug allergy, the cost of equipment, and the frequent imaging required to detect VTE, the occurrence of which is unpredictable. Fourth, in our study, the types of operations consisted mainly of cervical laminoplasty and lumbar laminectomy. Therefore, both operative time and blood loss tended to be minimal. Finally, the sample size was small, and therefore our findings should be confirmed in a larger cohort.

In conclusion, MDCT is a useful technology for detecting VTE before and after spine surgery, thereby reducing risk of mortality. We found that the preoperative and postoperative rates of asymptomatic VTE were 4.8% and 13.0%, respectively; that the rates of asymptomatic PE were 2.9% and 8.0%, respectively; and that the rates of asymptomatic DVT were 3.8% and 6.0%, respectively. There were no risk factors for VTE based on age, sex, height, weight, BMI, operative time, volume of intraoperative blood loss, or specific comorbidities (diabetes, hypertension, cardiac disease, liver and kidney disease, previous VTE, and previous anticoagulation treatment). ■

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