



# Comparison of coagulation profile and thromboembolic events among patients undergoing spinal surgery before and after COVID-19 pandemic

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## Abstract

**Background** Impairment of coagulation parameters and increased rate of thromboembolism are known complications of COVID-19 infection. In this study the coagulation profile and rate of thromboembolic events between two groups of patients who underwent spinal surgery before and after the COVID-19 pandemic was compared.

**Patients and method** Clinically and laboratory negative for COVID-19 elective patients before (n: 211) and during COVID-19 pandemic (n: 294) with spinal surgeries were included in this retrospective study. Surgical characteristics, Physiologic parameters, coagulation parameters and thromboembolic events were compared between the two study groups.

**Results** Preoperative coagulation parameters, including PT, PTT, and INR were significantly increased during the COVID-19 pandemic ( $P < 0.001$ ,  $P = 0.001$ , and  $P < 0.001$ , respectively), while the platelet count was significantly reduced ( $P = 0.04$ ). The same differences were observed between the two study groups after the spinal surgery. In addition, respiratory rate and postoperative bleeding of the first postoperative 24 h was significantly more in patients who were operated on during COVID-19 outbreak ( $P = 0.03$  and  $P = 0.002$ , respectively). The rate of thromboembolic events was 3.1% during the COVID-19 pandemic (seven PE, one DVT, and one MI) and 0% before that. This difference was statistically significant ( $P = 0.043$ ).

**Conclusion** The rate of thromboembolic events seems to be increased during the COVID-19 pandemic. These findings urge more stringent monitoring of the patients' coagulation parameters during the COVID-19 outbreak.

**Keywords** COVID-19 · Thromboembolic events · Spine surgery

## Introduction

Thromboembolic events are acknowledged as a common COVID-19 complication [1]. A meta-analysis study showed a 26% pooled incidence of venous thromboembolism (VTE) in 3487 COVID-19 patients from 30 studies [2]. The same finding was reported in a meta-analysis focused on pulmonary embolism (PE) and deep vein thrombosis (DVT). For these reasons, clinical guidelines recommend pharmacological prophylaxis for high-risk COVID-19 patients [3].

Spinal disorders are among the most common musculoskeletal problems with an increased frequency over the last 20 years. A parallel increase is observed in the number of spinal surgeries [4]. Owing to the complexity of spinal surgeries, reducing the risk of postoperative complications is of critical importance [5]. VTEs are among potential complications of spinal surgeries, with a high rate of morbidity and mortality. Preoperative risk assessment is considered a

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key element in preventing thromboembolic events following the spinal surgeries [6].

Asymptomatic or subclinical COVID-19 infection could be seen in up to 45% of patients [7]. Besides, nucleic acid-based testing, which is often called polymerase chain reaction (PCR), is not reliable for the detection of asymptomatic patients [8, 9]. As a result, there is a high probability that a considerable number of patients undergoing spinal surgeries are subclinical COVID-19 patients with a false-negative test. If this is true, we will face an increased rate of thromboembolic events during the COVID-19 pandemic. In that case, preoperative VTE risk assessment might require reconsideration in patients elected for high-risk surgeries like spinal fusions.

In this study, we compared the rate of thromboembolic events between two groups of patients who underwent spinal surgery before and after the COVID-19 pandemic. We hypothesized a potential increase in thromboembolic events after the COVID-19 pandemic as a result of subclinical COVID-19 infection in patients undergoing spinal surgery.

## Patients and methods

This study was approved by the review board of our institute. Medical profiles of the patients who underwent spinal surgeries in 2018 (before the COVID-19 pandemic) and in 2020 (after the COVID-19 pandemic) in our orthopedic hospital were retrospectively reviewed. Patients were included only if they had complete medical records following spine surgeries. During the COVID-19 pandemic, elective surgeries were only performed if the patient had no COVID-19-associated symptoms and provided a negative-PCR test for COVID-19. Patients with the history of COVID-19 infection in the last one year were not operated during the COVID-19 pandemic.

None of the patients received postoperative pharmacologic prophylaxis for VTE. Mechanical prevention of thromboembolic events was applied in all patients using a DVT pump (pneumatic compression pumps).

Demographic characteristics of the patients, such as age, sex, and BMI, were extracted from the patients' medical records. Surgical characteristics of the patients, such as the type of surgery, duration of surgery, and intraoperative bleeding amount, were also extracted from the patients' medical records. Physiologic parameters including pulse rate (PR), systolic blood pressure (SBP), diastolic blood pressure, respiratory rate (RR), and oxygen saturation (SaO<sub>2</sub>) were collected in the first 24 h after the operation. Laboratory parameters including blood hemoglobin, platelet count, prothrombin time (PT), partial thromboplastin time (PTT), and International Normalized Ratio (INR) were collected before and 24 h after the operation.

Thromboembolic events that were compared between the two study groups included pulmonary embolism (PE), deep vein thrombosis (DVT), and myocardial infarction (MI). Patients suspected of thromboembolic events were further investigated with complementary diagnostic modalities, including CT angiography, D-dimer level and troponin testing. All patients were checked till the last day of hospital admission and at first follow-up visit nearly one month postoperatively for any sign or symptom of PTE or other thromboembolic events.

## Statistical analysis

The data were analyzed using SPSS for Windows, version 16 (SPSS Inc., Chicago, Ill., USA). Categorical data were presented with numbers and percentages. Quantitative data were presented with mean  $\pm$  standard deviation (SD). A comparison of the mean between the two groups was made using an independent t-test. A comparison of the mean between more than two groups was made using a one-way ANOVA test. A comparison of qualitative variables between the two study groups was made using a chi-squared test or Fisher exact test. A *P*-value  $< 0.05$  was considered significant.

## Results

In total, 505 patients were included in this study, of which 211 patients were operated before the COVID-19 pandemic, and 294 patients were operated during COVID-19 pandemic era. The study population included 189 (37.4%) males and 316 (62.6%) females with a mean age of  $37.2 \pm 21.6$  years (range 5–80). Spinal deformity was the most frequent etiology for spinal surgery ( $n = 174$ , 34.4%). The majority of the surgeries were Posterior Spinal Fusion (PSF) ( $n = 417$ , 82.6%). The characteristic feature of the two study groups is compared in Table 1. The surgical duration was significantly smaller in patients who were operated after COVID-19 pandemic (5.2 vs. 5.7 h,  $P < 0.001$ ). The type of spinal disorder was not significantly different between the two groups ( $P = 0.34$ ). Preoperative coagulation parameters, including PT, PTT, and INR, were significantly increased during the COVID-19 pandemic ( $P < 0.001$ ,  $P = 0.001$ , and  $P < 0.001$ , respectively), while the platelet count was significantly reduced ( $P = 0.04$ ). One patient had impaired PT (0.5%) among pre COVID-19 group, while 30 (10.2%) of the patients had abnormal PT level during the COVID-19 outbreak. Impaired INR test was only identified in two patients and both of them were in after COVID group. PTT was in normal range for both groups.

After the operation, the mean PT and PTT of the patients were significantly prolonged during the COVID-19 outbreak

**Table 1** Comparison of the baseline characteristic features of patients before and during the COVID-19 pandemic

Variable	Before COVID-19 (n=211)	During COVID-19 (n=294)	<i>P</i> -value
Age	34.9 ± 20.8	38.8 ± 22.1	0.05
Sex			0.26
Male	75 (35.5)	114 (38.8)	
Female	136 (64.5)	180 (61.2)	
BMI (Kg/m <sup>2</sup> )	24.6 ± 6.2	24.9 ± 5.9	0.93
Diagnosis			0.34
Canal Stenosis and Disc diseases	47 (22.3)	70 (23.8)	
Spondylolisthesis	23 (10.9)	30 (10.2)	
Spine Deformity	71 (33.7)	103 (35)	
Others	70 (33.1)	91 (31)	
Level of fixation			0.4
0	35 (16.6)	60 (20.5)	
< 4	74 (35.1)	104 (35.4)	
> 4	101 (47.9)	124 (42.2)	
Unknown	1 (0.4)	6 (2.04)	
Type of surgery			0.13
PSF	172 (81.5)	245 (83.3)	
ASF + PSF	35 (16.6)	49 (16.7)	
ASF	4 (1.9)	0	
Surgical duration (hours)	5.7 ± 1.6	5.2 ± 1.5	< 0.001
Intraoperative bleeding (ml)	712.5 ± 600	646.5 ± 624	0.23
Hemoglobin (g/dl)	13.7 ± 1.5	13.5 ± 1.6	0.13
PT (second)	13 ± 0.1	13.1 ± 0.3	< 0.001
PTT (second)	30.5 ± 2.5	31.2 ± 2.3	0.001
INR	1 ± 0.001	1.01 ± 0.03	< 0.001
Platelet (10 <sup>9</sup> /L)	283 ± 159	267 ± 122	0.04

*BMI* Body mass index, *AIS* Adolescent Idiopathic Scoliosis, *ASF* Anterior Spinal Fusion, *PSF* Posterior Spinal Fusion, *PT* Prothrombin Time, *PTT* Partial Thromboplastin Time, *INR* International Normalized Ratio

Data are presented as mean ± SD or number (%)

*P* < 0.05 is considered significant

(*P* < 0.001 for both). Accordingly, the INR of the patients was significantly more in the corresponding group of patients (*P* < 0.001). In addition, the respiratory rate of the first 24 h after the operation was significantly increased in patients who were operated on during COVID-19 outbreak (*P* = 0.03). Postoperative bleeding in the first 24 h was also significantly higher during the COVID-19 pandemic (*P* = 0.002) (Table 2).

Before the COVID-19 pandemic, no case of PE, DVT, and MI was recorded in our patients. After the COVID-19 pandemic, PE and DVT were recorded in 7 (2.4%) and 1 (0.34%) patients respectively and confirmed with CT-angiography and Color-Doppler Sonography. Two out of seven

PE patients and patient with MI expired during COVID-19 pandemic. Accordingly, the rate of thromboembolic events was 3.1% during the COVID-19 pandemic and 0% before that. This difference was statistically significant (*P* = 0.012).

## Discussion

In this study, we compared the coagulation indices and rate of thromboembolic events in patients undergoing spinal surgeries before and after the COVID-19 pandemic. The pre and postoperative PT, PTT, and INR of the patients were significantly higher during the COVID-19 pandemic compared with the pre-pandemic period. The preoperative platelet count of the patients was significantly lower during the COVID-19 outbreak. After the operation, the respiratory rate was significantly more in patients who operated during the COVID-19 pandemic. Moreover, postoperative bleeding was significantly more after the COVID-19 pandemic. The rate of a thromboembolic event, including PE and DVT, was also significantly increased following the COVID-19 outbreak.

Coagulation disorders and thromboembolic events are common COVID-19 associated complications. Alteration coagulation profiles, including D-dimer, PTT, PTT, platelet count, and fibrinogen, generally occur 7–11 days after the onset of COVID-19 symptoms [10, 11]. Impaired coagulation profile in COVID-19 patients predisposes the occurrence of thromboembolic events such as PE and DVT [12, 13]. The extent of coagulation impairment has been attributed to the severity of COVID-19 infection, so platelet count and d-dimer level were identified as significant predictors of COVID-19 severity on meta-regression analysis [14]. Coagulopathy and thromboembolism are predictors of COVID-19 mortality. Accordingly, the rate of coagulopathy was significantly more in non-survivor COVID-19 patients compared to the survivors (76.3% vs. 56.2%) [15].

Coagulation impairment has been less investigated in patients with non-severe COVID-19 because it generally does not complicate the COVID-19 outcome. For this reason, subclinical thrombosis tends to be missed in patients with asymptomatic COVID-19 [16, 17]. Caesario et al. reported a sudden elevation of D-dimer in an asymptomatic COVID-19 patient, which became normal with three days of heparin administration and rebounded back some days after anticoagulant therapy was stopped. They concluded that asymptomatic COVID-19 patients might also be at risk of a coagulopathy impairment [18]. Mahardhika et al. also reported a high D-dimer level in an asymptomatic woman who was later confirmed to be positive for COVID-19 [19].

In the present study, we compared the coagulation parameters and thromboembolic events before and after the COVID-19 pandemic, which showed impaired coagulation profile and increased thromboembolic events during the

**Table 2** Comparison of the laboratory indices and physiologic parameters of patients before and during the COVID-19 pandemic

Variable	Before COVID-19 (n = 211)	After COVID-19 (n = 294)	P-value
Hemoglobin (g/dl)	10.9 ± 1.5	11.2 ± 1.6	0.05
PT (second)	13 ± 0.37	13.7 ± 1.5	<0.001
PTT (second)	30.5 ± 4.5	34.4 ± 8.4	<0.001
INR	1.01 ± 0.4	1.09 ± 0.19	<0.001
Platelet (10 <sup>9</sup> /L)	217 ± 62	205 ± 80	0.07
Respiratory rate of first 24 h (breath per min)	19 ± 1.2	20 ± 7.3	0.03
Pulse rate of first 24 h (number per min)	89.2 ± 13.9	88.9 ± 14.9	0.84
SBP first 24 h (mmHg)	118 ± 11	118 ± 15	0.91
DBP first 24 h (mmHg)	72 ± 8	72 ± 9	0.89
O <sub>2</sub> Sat (%)	96.2 ± 1.5	95.9 ± 1.5	0.06
Postoperative bleeding of first 24 h (ml)	198.1 ± 223	272 ± 297	0.002

*BMI* Body mass index, *AIS* Adolescent Idiopathic Scoliosis, *ASF* Anterior Spinal Fusion; *PSF*, Posterior Spinal Fusion; *PT* Prothrombin Time, *PTT* Partial Thromboplastin Time, *INR* International Normalized Ratio, *SBP* Systolic Blood Pressure, *DBP* Diastolic Blood Pressure, *O<sub>2</sub>Sat* Oxygen Saturation

Data are presented as mean ± SD or number (%)

*P* < 0.05 is considered significant

COVID-19 outbreak. We cannot directly relate the observed Coagulation disorders to the COVID-19 infection because the patients had no COVID-19 symptoms, and the COVID-19 PCR testing was negative. However, several scenarios could be established. The first scenario is the subclinical involvement of patients undergoing spinal surgery during COVID-19 patients. In that case, an asymptomatic COVID-19 and a false negative PCR test [20] might be an underlying cause for the coagulation impairment during the COVID-19 pandemic and thereby increasing the risk of thromboembolic events. The second scenario is the sustained coagulation activation during the post-COVID-19 infection. We routinely checked patients for COVID-19 thorough evaluation of the clinical symptoms and PCR testing; however, asymptomatic COVID-19 infection during the last one year could not be evaluated. The study of Willems et al. revealed increased in vivo coagulation activity in a post-COVID-19 cohort 6–20 weeks after recovery from acute COVID-19 [21]. Therefore, the impaired coagulation profile of the patients who underwent spinal surgery during the COVID-19 period could be in part associated with a history of previous COVID infection.

Whatever the reason, the impaired coagulation parameters and a higher rate of thromboembolic events following the COVID-19 pandemic urge the need for more stringent monitoring of the coagulation profile of the patients undergoing surgery, namely spinal surgery, during and after the COVID-19 outbreak.

The present study was not without limitations. The main limitation of the study was its retrospective design and subtle differences between the baseline characteristics of the two study groups, such as in the surgical type and etiology of spinal disorder. Moreover lack of data regarding

the history of smoking and blood transfusion rate following the surgery among these two study groups is another limitation of this study. Evaluation of other coagulation parameters such as D-dimer would have better represented the coagulation status of the patients. Therefore, future complementary studies are required to confirm the present findings.

## Conclusion

In patients who underwent spinal surgery, the pre and postoperative coagulation parameters, including PT, PTT, and INR, were significantly higher during the COVID-19 pandemic compared with the pre-pandemic period. The preoperative platelet count of the patients was significantly lower during the COVID-19 outbreak. Postoperatively, the rate of bleeding and thromboembolic event was also significantly increased following the COVID-19 outbreak. These observations urge a more stringent evaluation of the patients' coagulation profile during the COVID-19 pandemic.

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## Declarations

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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