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Nonspecific ST-Segment and T-Wave (NS-STT) on Electrocardiogram is Associated with Increasing the Incidence of Perioperative Deep Vein Thrombosis in Patients with Lower Extremity Fracture Under 75 Years Old

Cheng Ren\* Ming Li\* Teng Ma Yi-Bo Xu Zhong Li Han-Zhong Xue Qian Wang Yao Lu D Liang Sun Kun Zhang

Department of Orthopedic Trauma, Honghui Hospital, Xi'an Jiaotong University, Xi'an, Shaanxi Province, People's Republic of China

\*These authors contributed equally to this work

Correspondence: Kun Zhang Department of Orthopedic Trauma, Honghui Hospital, Xi'an Jiaotong University, Xi'an, Shaanxi Province, People's Republic of China Email hhzhangkun@163.com **Objective:** This study aims to explore the clinical correlation between nonspecific ST-segment or T-wave (NS-STT) changes and perioperative deep vein thrombosis (DVT) in patients with lower extremity fractures.

**Methods:** One thousand four hundred sixty-nine consecutive patients who suffered lower extremity fractures were screened at Xi'an Honghui Hospital between Feb 2016 and Nov 2018. According to the included and excluded criteria, the patients were included in this retrospective study. After collecting the electrocardiogram baseline, the patients were divided into the NS-STT group and the non-NS-STT group. After comparing the demographic and clinical characteristics, multivariate logistic regression models were used to identify the role of NS-STT changes on perioperative DVT. All analyses were performed with R and EmpowerStats software.

**Results:** Nine hundred and sixty-eight patients were included in the study. Ninety-seven patients (10.02%) had NS-STT changes on the electrocardiogram at admission. A total of 303 patients (31.30%) developed perioperative DVT in lower extremities. The univariate analysis showed that NS-STT segment changes were correlated with perioperative DVT significantly (OR = 3.45, 95% CI: 2.25–5.30, P < 0.0001). In addition, age  $\geq$ 50 (P < 0.0001), female (OR = 1.50, 95% CI: 1.14–1.97, P = 0.0038), hypertension (OR = 1.54, 95% CI: 1.08–2.20, P = 0.0161), blood transfusion (OR = 1.78, 95% CI: 1.34–2.37, P < 0.0001), joint prosthesis (OR = 3.26, 95% CI: 2.21–4.81, P < 0.0001), and blood loss  $\geq$ 300 mL (OR = 2.12, 95% CI: 1.50–3.01, P < 0.0001) were associated with perioperative DVT in lower extremities. We identified the confounding factors of age, gender, classification of internal implants, operation time, blood loss, and infusion. After adjustment for potential confounding factors, NS-STT changes were associated with perioperative DVT (OR = 2.13, 95% CI: 1.33–3.42; P = 0.0017). The sensitive analysis showed that the result was stable.

**Conclusion:** The NS-STT changes on electrocardiograms are associated with an increase in the incidence of perioperative DVT by 2.13-fold in patients with lower extremity fractures under 75 years old. In clinical practice, surgeons should pay more attention to these patients.

**Keywords:** nonspecific ST-segment and T-wave, NS-STT, electrocardiogram, DVT, lower extremity fracture, logistic regression

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## Introduction

Deep vein thrombosis (DVT) is an essential complication in patients with lower extremities fractures. However, previous studies have paid more attention to the thrombosis after fracture but ignored the thrombosis after surgery. In patients with lower extremities fracture, the prevalence of postoperative DVT is often higher than the data before surgery.<sup>1</sup> The incidence of postoperative DVT could reach 61.3%.<sup>2</sup> It is also found that 28% of patients would have new DVT after the operation, and most of the thrombosis was preoperative DVT and persisted to post-operation in a recent study.<sup>3</sup>

The perioperative DVT could influence the process of rehabilitation and recovery. Notably, a freshly formed thrombosis is loosely attached to the vein wall, and it is easy to fall off and cause a pulmonary embolism. In addition, the leg swelling, skin changes, pain, and chronic ulceration would affect the patients' psychology. Therefore, perioperative DVT has a higher risk of falling off during functional exercise and should be paid attention to.

The etiology of perioperative DVT following lower extremity fracture is usually multifactorial, and most of the factors were related to surgery, including blood loss, operation time, and so on.<sup>1</sup> Although the perioperative DVT caused by surgery have increasingly been attracting attention recently, few researchers are concerned about the effects of the preoperative factor on perioperative DVT.

Traditionally, ST-segment or T-wave changes on the electrocardiogram are known predictors of cardiovascular mortality.<sup>4</sup> However, physiological nonspecific ST-segment or T-wave (NS-STT) is also very common and can be seen in any lead of the electrocardiogram. Most clinicians regard isolated, minor, or NS-STT abnormalities to be incidental, often transient, and benign findings in asymptomatic patients.<sup>5</sup> In fact, it is reported that NS-STT changes are related to inflammation diseases.<sup>6</sup> The inflammatory response is involved in thrombus formation, thrombus organization, and the vein recanalization process, and the link between inflammation and DVT has been identified.<sup>7–9</sup> Additionally, the relationship between arrhythmogenesis, inflammation, and coagulation was established early.<sup>10</sup> Thus, the evidence indicates that physiological NS-STT may relate to thrombosis formation.

As far as we know, no preceding work or report has considered the effects of NS-STT changes on perioperative thrombosis. This study aims to explore the clinical correlation between NS-STT changes and perioperative DVT in patients with lower extremity fractures.

# Materials and Methods Study Population

Clinical and surgical data for the cases reviewed were obtained from original medical records. The ethics committee of Xi'an Honghui Hospital approved this retrospective study (No. 2014026). As patient identity remained anonymous, and the requirement for informed consent was waived due to the observational nature of the study, as reported elsewhere.<sup>11,12</sup> All human-related procedures were in concordance with the 1964 Helsinki Declaration and its later amendments.

One thousand four hundred sixty-nine consecutive patients suffered lower extremity fracture at Xi'an Honghui Hospital between Feb 2016 and Nov 2018. The inclusion criteria were as follows: 1). Age of  $\geq$ 18 years; 2) Fresh occurring lower extremity fractures that were receiving surgical treatment; 3) Availability of electrocardiogram; 4) Completing the ultrasonography examination at admission and peri-operation. We excluded data from a patient with coronary heart disease symptoms (n = 28), and with age >75 years (n = 320) and patients receiving the closed reduction and internal fixation (n = 153), and the remaining 968 cases formed the final analysis population finally.

When at admission, the nurses recorded the individual electrocardiogram electrical signals. Professional physicians, diagnosing the reports more than 50,000 cases every year, reported the electrocardiogram results. Their reports were independent and undisturbed. Two trained physicians analyzed each ECG to keep the consistency and resolved disagreements through discussion, and unresolved disagreements were discussed with a third senior physician. The criteria of NS-STT changes included subtle straightening of the ST segment, actual ST-segment depression or elevation, flattening of the T wave, biphasic T waves, or T wave inversion. According to these criteria, a total of 97 patients experienced NS-STT changes following the fracture.

We defined perioperative DVT as the thrombosis occurring before or after the operation, defecting by ultrasonography. Ultrasonography was used to diagnose DVT. Three trained operators performed vascular ultrasonography with a bedside machine. The diagnostic criterion of fresh thrombosis was the presence of a constant intraluminal filling defect.<sup>13</sup> All the patients received the first examination in both lower extremities when at admission.

When the nurses collected electrocardiogram and blood samples at admission, the surgeons assessed the thromboembolism risk for every patient using the Risk Assessment Profile for Thromboembolism score.<sup>14</sup> For the patients without contraindications, low-molecularweight heparin (LMWH; 3800 IU/0.4 mL, once per day; Fraxiparine, Glaxo Wellcome Production, GlaxoSmithKline) was subcutaneously injected to prevent DVT, according to the guidelines in CHEST 2012.<sup>15</sup> The anticoagulant therapy was discontinued 12 h before operation and resumed 24 h after operation. In addition, we used a mechanical pressure pump (20 min, twice per day) to promote blood reflux. For the patients without thrombosis, LMWH was continuously subcutaneously injected. For the patients with thrombosis, physicians from the vascular surgery department prescribed the DVT treatment, and LMWH (3800 IU/0.4 mL, twice per day; Fraxiparine, Glaxo Wellcome Production, GlaxoSmithKline) was subcutaneously injected. If needed, we used an inferior vena cava filter to prevent fatal pulmonary embolism before the operation. After the operation, the protocol of anticoagulant strategy was continued. The patients received the second ultrasonography examination in both lower extremities on the third to fifth day after the operation.

### Statistics Analysis

Firstly, we compared the data distribution of each covariate between the NS-STT group and the non-NS-STT group, using the *t*-test or Kruskal-Wallis rank sum test for continuous variables and  $c^2$  tests for categorical data. Secondly, univariate and subgroup analysis and multivariate logistic regression models were used to examine whether NS-STT changes on electrocardiogram and other covariates had an independent effect on perioperative occurring lower extremity DVT following lower extremities fracture separately. Thirdly, we explored the relationship between NS-STT changes on electrocardiogram and perioperative DVT in patients with lower extremity fracture by the smoothing plot, with an adjustment for potential confounders. All analyses were performed with R (http://www.R-project.org) and EmpowerStats software (www.empowerstats.com, X&Y solutions, Inc. Boston, MA).

### **Results** Patient Characteristics

Among the 968 patients included in the study, 97 (10.02%) underwent NS-STT changes on electrocardiogram at admission. The demographic and clinical characteristics, including comorbidities, factors associated with injuries and operation are shown in Table 1. The mean age of the NS-STT group was 65.05±8.41, compared to 47.93±15.34 in the non-NS-STT group (P < 0.001). As for the fracture type, there were more femur fractures in NS-STT group than non-NS-STT group. In the comorbidities, there were more hypertension in NS-STT group and more associated injuries in non-NS-STT group. In addition, in the factors related to the operation, the operation time and operative blood loss in NS-STT group were more than non-NS-STT group. Still, fewer patients were using a tourniquet in NS-STT group. More patients were using an intramedullary nail and joint prosthesis in NS-STT group.

A total of 303 patients (31.30%) developed perioperative DVT in lower extremities in this study. The univariate regression analysis showed that ST-T segment changes on ECG significantly correlated with perioperative DVT (OR = 3.45, 95% CI: 2.25–5.30, P < 0.0001). In addition, age  $\geq$ 50 years, female, hypertension, blood transfusion, joint prosthesis, blood loss  $\geq$ 300 mL might also be associated with perioperative DVT in lower extremities (Table 2).

The subgroup analysis of risk factors contributing to perioperative DVT was shown in Table 3. In these factors, the results in different subgroups were comparable.

At the beginning of the analysis, we identified two confounding factors of age and classification of internal implants. To identify other important confounding factors, we explore the potential factors. Because age, operation time, blood loss, and infusion were continuous variables, the smoothing curve fitting of these factors between perioperative DVT was drawn, shown in Figure 1. As for the curve relationship to perioperative DVT, these factors were considered into the following adjust factors. In addition, we also explore the relationship to NS-STT changes, and we found that the gender (reference to male, female (OR = 4.05, 95% CI: 2.54-6.44, P < 0.0001)) was an essential factor. Thus, we identified the factors needed to control.

After adjustment of potential confounding factors, the independent effect of NS-STT changes on perioperative DVT was confirmed, shown in Table 4. In the models I to IV, the results were close to each other. Also, to explore

Table I	The	Demographic	and	Clinical	Characteristics
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	Non-NS-STT Group (n=871)	NS-STT Group (n=97)	P-value
Age group (year)			<0.001
<50	464 (53.27%)	4 (4.12%)	
≥50, <60	168 (19.29%)	19 (19.59%)	
≥60	239 (27.44%)	74 (76.29%)	
Gender			<0.001
Male	531 (60.96%)	27 (27.84%)	
Female	340 (39.04%)	70 (72.16%)	
Fracture site			<0.001
Pelvis and acetabulum	(12.74%)	6 (6.19%)	
Femur	320 (36.74%)	70 (72.16%)	
Patella	84 (9.65%)	6 (6.19%)	
Tibial and fibular	219 (25.14%)	12 (12.37%)	
Foot and ankle	137 (15.73%)	3 (3.09%)	
Hypertension	124 (14.24%)	33 (34.02%)	<0.001
Diabetes	77 (8.84%)	7 (7.22%)	0.590
Arrhythmia	47 (5.40%)	9 (9.28%)	0.120
Stroke	43 (4.94%)	9 (9.28%)	0.072
Associated injuries	148 (16.99%)	6 (6.19%)	0.006
Time from injury to admission (days)			0.808
<	572 (65.67%)	63 (64.95%)	
≥I, <3	149 (17.11%)	15 (15.46%)	
≥3	150 (17.22%)	19 (19.59%)	
Time from injury to operation (days)			0.749
<2	63 (7.23%)	5 (5.15%)	
≥2, <4	432 (49.60%)	49 (50.52%)	
≥4	376 (43.17%)	43 (44.33%)	
Operation time (mins)	136.628 ± 80.994	116.753 ± 59.403	0.019
Tourniquet	442 (50.75%)	22 (22.68%)	<0.001
Blood transfusion	275 (31.57%)	38 (39.18%)	0.129
Classification of internal implants			<0.001
Plates and screws	450 (51.66%)	21 (21.65%)	
Intramedullary nail	214 (24.57%)	41 (42.27%)	
Joint prosthesis	115 (13.20%)	29 (29.90%)	
Tension band	92 (10.56%)	6 (6.18%)	
Blood loss (mL)			0.024
<100	258 (29.62%)	17 (17.53%)	
≥100, <300	305 (35.02%)	35 (36.08%)	
≥300	308 (35.36%)	45 (46.39%)	
Infusion (mL)			0.261
<1600	127 (14.58%)	14 (14.43%)	
≥1600, <2100	342 (39.27%)	46 (47.42%)	
≥2100	402 (46.15%)	37 (38.15%)	

#### Table 2 Effects of Risk Factors on Perioperative DVT by Univariate Analysis

Variables	Total	Odds Ratio (95% CI)	P	
ST-T segment changes on ECG	97 (10.02%)	3.45 (2.25, 5.30)	<0.0001	
Age group (year)				
<50	468 (48.35%)	1		
≥50, <60	187 (19.32%)	3.70 (2.55, 5.36)	<0.0001	
≥60	313 (32.33%)	3.24 (2.34, 4.48)	<0.0001	
Gender				
Male	558 (57.64%)	1		
Female	410 (42.36%)	1.50 (1.14, 1.97)	0.0038	
Fracture site				
Pelvis and acetabulum	117 (12.09%)	1		
Femur	390 (40.29%)	1.35 (0.88, 2.08)	0.1697	
Patella	90 (9.30%)	0.96 (0.54, 1.72)	0.8975	
Tibial and fibular	231 (23.86%)	0.52 (0.32, 0.85)	0.0093	
Foot and ankle	140 (14.46%)	0.38 (0.21, 0.68)	0.0012	
Hypertension				
No	811 (83.78%)	1		
Yes	157 (16.22%)	1.54 (1.08, 2.20)	0.0161	
Diabetes				
No	884 (91.32%)	1		
Yes	84 (8.68%)	0.87 (0.53, 1.42)	0.5726	
Arrhythmia				
No	912 (94.21%)	1		
Yes	56 (5.79%)	1.34 (0.77, 2.34)	0.3042	
Stroke				
No	916 (94.63%)	I		
Yes	52 (5.37%)	1.52 (0.86, 2.70)	0.1490	
Associated injuries				
No	814 (84.09%)	I		
Yes	154 (15.91%)	1.23 (0.85, 1.76)	0.2726	
Time from injury to admission (days)				
<1	635 (65.60%)	I		
≥I, <3	164 (16.94%)	1.00 (0.69, 1.45)	0.9875	
≥3	169 (17.46%)	1.22 (0.85, 1.75)	0.2785	
Time from injury to operation (days)				
<2	68 (7.02%)	1		
≥2, <4	481 (49.69%)	1.37 (0.76, 2.49)	0.2929	
≥4	419 (43.29%)	1.70 (0.94, 3.09)	0.0801	
Operation time (mins)	134.64 ± 79.30	1.00 (1.00, 1.00)	0.3161	
<90	237 (24.48%)	1		
≥90, <140	389 (40.19%)	0.92 (0.65, 1.29)	0.6267	
≥140	342 (35.33%)	0.80 (0.56, 1.14)	0.2187	
Tourniquet				
No	504 (52.07%)	I		
Yes	464 (47.93%)	0.51 (0.39, 0.68)	<0.0001	

(Continued)

Variables	Total	Odds Ratio (95% CI)	Р	
Blood transfusion				
No	655 (67.67%)	1		
Yes	313 (32.33%)	1.78 (1.34, 2.37)	<0.0001	
Classification of internal implants				
Plates and screws	471 (48.66%)	1		
Intramedullary nail	255 (26.34%)	1.53 (1.09, 2.14)	0.0135	
Joint prosthesis	144 (14.88%)	3.26 (2.21, 4.81)	<0.0001	
Tension band 98 (10.12		1.68 (1.06, 2.68)	0.0288	
Blood loss (mL)				
<100	275 (28.41%)	1		
≥100, <300	340 (35.12%)	1.31 (0.91, 1.88)	0.1478	
≥300	353 (36.47%)	2.12 (1.50, 3.01)	<0.0001	
Infusion (mL)				
<1600	4  ( 4.57%)	1		
≥1600, <2100	388 (40.08%)	1.00 (0.66, 1.51)	0.9852	
≥2100	439 (45.35%)	1.09 (0.72, 1.64)	0.6818	

#### Table 2 (Continued).

the stability of the result, we continued to complete the sensitivity analysis. When the subgroups were divided as above-identified factors one by one, the results in different subgroups were very close. Therefore, NS-STT changes were associated with perioperative DVT (OR = 2.13, 95% CI 1.33-3.42; P = 0.0017).

## Discussion

In this study, we have found that NT-STT change on electrocardiogram is associated with an increase in the incidence of perioperative DVT by 2.13-fold in patients with lower extremity fracture under 75 years old. In clinical practice, when there is an NT-STT change at admission in patients with lower extremity fracture under 75 years old, surgeons should pay more attention to prevent the perioperative DVT. As we know, it is the first correlation analysis that illustrates the relationship between characteristics of electrocardiograms and thrombosis.

To date, studies have investigated so many risk factors for developing perioperative DVT after lower extremity fracture. It is now clear that in addition to Virchow's triad (blood flow disturbance, hypercoagulability, and vessel wall changes), inflammation has a crucial role in triggering DVT.<sup>8</sup> ST and T wave changes may represent cardiac pathology or be a normal variant. NS-STT abnormalities are associated with benign factors such as food ingestion, posture, emotional stressors, hyperventilation, electrolyte disturbances, and use of antiarrhythmic or psychotropic drugs, in addition to being prevalent in middle-aged men, women, and blacks.<sup>16–28</sup> Furthermore, inflammation might also be associated with NS-STT on electrocardiograms.<sup>6</sup> Therefore, we explore the relationship between perioperative DVT and NS-STT changes on electrocardiograms.

In including patients, we only limit fresh occurring lower extremity fractures that received surgical treatment to control the baseline of included patients and avoid the confounding factors from delayed fracture and conservative treatment. In addition, we identified two crucial factors. As we know, ST and T wave changes had a close relationship to coronary heart disease.<sup>29,30</sup> It is a robust confounding factor to our result. We excluded patients with coronary heart disease symptoms and patients with age >75 years in this study. The percentage of coronary heart disease of age >75 years was nearly 40% (127/320) in the fracture patients. Thus, we excluded the patients with pathological ST and T wave changes, and most of the rest patients were physiological NS-STT. In addition, the ways of reduction (open reduction or closed reduction) were another confounding factor.<sup>31,32</sup> As most of the patients received the open procedure, we excluded the patients receiving the closed reduction and internal fixation. The age, operation time, and operative blood loss in NS-STT group were more than non-NS-STT group in the demographic and clinical characteristics. Also, the

#### Table 3 Subgroup Analysis of Potential Risk Factors Contributing into Perioperative DVT

Subgroups	N	Odds Ratio (95% CI)	Р	
Age group (years)				
<50	468	4.52 (0.63, 32.58)	0.1340	
≥50, <60	187	2.23 (0.84, 5.95)	0.1088	
≥60	313	2.17 (1.28, 3.69)	0.0040	
Gender				
Male	558	4.14 (1.88, 9.14)	0.0004	
Female	410	2.83 (1.67, 4.78)	0.0001	
Fracture site				
Pelvis and acetabulum	117	4.17 (0.73, 23.82)	0.1086	
Femur	390	2.53 (1.49, 4.30)	0.0006	
Patella	90	4.46 (0.77, 25.91)	0.0957	
Tibial and fibular	231	2.84 (0.86, 9.38)	0.0866	
Foot and ankle	140	2.61 (0.23, 30.09)	0.4409	
Hypertension				
No	811	3.17 (1.89, 5.32)	<0.0001	
Yes	157	3.54 (1.59, 7.90)	0.0020	
Diabetes				
No	884	3.42 (2.19, 5.34)	<0.0001	
Yes	84	3.80 (0.78, 18.47)	0.0980	
Arrhythmia				
No	912	3.36 (2.14, 5.26)	<0.0001	
Yes	56	4.27 (0.94, 19.42)	0.0606	
Stroke				
No	916	3.21 (2.05, 5.02)	<0.0001	
Yes	52	7.25 (1.33, 39.53)	0.0221	
Associated injuries				
No	814	3.56 (2.28, 5.56)	<0.0001	
Yes	154	3.92 (0.69, 22.14)	0.1220	
Time from injury to admission (days)				
<	635	3.49 (2.05, 5.94)	<0.0001	
≥I, <3	164	5.45 (1.76, 16.92)	0.0034	
≥3	169	2.29 (0.87, 6.00)	0.0917	
Time from injury to operation (days)				
<2	68	2.33 (0.35, 15.37)	0.3784	
≥ <u>2,</u> <4	481	4.04 (2.20, 7.43)	<0.0001	
≥4	419	3.00 (1.58, 5.71)	0.0008	
Operation time (mins)				
<90	237	3.97 (1.72, 9.14)	0.0012	
≥90, <140	389	3.25 (1.73, 6.09)	0.0002	
≥140	342	3.19 (1.38, 7.39)	0.0068	
Tourniquet				
No	504	2.69 (1.63, 4.45)	0.0001	
Yes	464	4.16 (1.74, 9.91)	0.0013	

(Continued)

Subgroups	Ν	Odds Ratio (95% CI)	P
Blood transfusion			
No	655	4.27 (2.46, 7.39)	<0.0001
Yes	313	2.30 (1.15, 4.57)	0.0180
Classification of internal implants			
Plates and screws	471	3.06 (1.27, 7.41)	0.0131
Intramedullary nail	255	3.28 (1.65, 6.51)	0.0007
Joint prosthesis	144	2.15 (0.92, 5.02)	0.0778
Tension band	98 4.13 (0.72, 23.84)		0.1125
Blood loss (mL)			
<100	275	3.13 (1.16, 8.49)	0.0247
≥100, <300	340	4.44 (2.15, 9.16)	<0.0001
≥300	353	2.59 (1.37, 4.91)	0.0036
Infusion (mL)			
<1600	141	3.50 (1.13, 10.83)	0.0293
≥1600, <2100	388	3.19 (1.70, 5.97)	0.0003
≥2100	439	3.91 (1.94, 7.85)	0.0001

#### Table 3 (Continued).

percentage of female, femur fracture, hypertension, and associated injuries in NS-STT group were higher than non-NS-STT group, but the portion of using the tourniquet was lower in NS-STT group. These characteristics were different in the two groups.

The mean age in NS-STT group was 65.05. The age was near the boundary of older people. In the previous studies, elderly age was related to hypertension,<sup>33</sup> associated injuries,<sup>34</sup> and hip fracture.<sup>35</sup> A higher incidence of hip fracture means lower percentage of using tourniquets. Thus, age was the crucial factor to control. In the subgroups of age  $\geq 60$  years, the NT-STT change on electrocardiogram was associated with perioperative DVT. There was no relationship in subgroups of age <60 years. We considered the reason was the samples in subgroups of age <60 years were small. In addition, we also found the female took 72.16% of patients in the NS-STT group, compared to 39.04% in non-NS-STT group, that the gender was related to NS-STT changes on electrocardiogram. In the previous studies, the female related to hip fracture<sup>36</sup> has been identified. Thus, gender was another confounding factor. In the subgroups, the males (OR = 4.14) had a closer relationship between NT-STT change and perioperative DVT than females (OR = 2.83).

In the subgroup analysis and sensitivity analysis, the results in different subgroups were close to each other. Thus, we finally found that patients with NS-STT changes on electrocardiogram were associated with an increase in the incidence of perioperative DVT by 2.13-fold in patients with lower extremity fracture under 75 years. In clinical practice, when a patient with NS-STT changes is at admission, surgeons should be paid more attention to DVT formation in the lower extremity and screen the ultrasonography more.

Although our analysis suggested that NS-STT changes at admission are associated with perioperative DVT, this study has several limitations that should be noted. Firstly, the result is suitable for the patients under 75 years and excluding the diagnosis of coronary heart disease, so the patients with age more than 75 years or coronary heart disease could not adopt this conclusion. Secondly, the causes of NS-STT changes were too much: including functional and physiologic variants, myocardial ischemia, any cardiomyopathy, myocarditis, pericarditis, post-cardiac surgery, pulmonary emboli or intrinsic pulmonary disease, fever, anemia, acidosis or alkalosis, electrolyte or other metabolic abnormalities, endocrine abnormalities, endogenous catecholamines, acute abdominal process, cerebrovascular accidents. We think the critical point linking NS-STT changes and perioperative DVT is inflammation, but the evidence was insufficient. It is needed to research the relationship in the future. Thirdly, due to the limitations of a retrospective study, possible selection bias and the sample size from a single center might have been presented in this study.

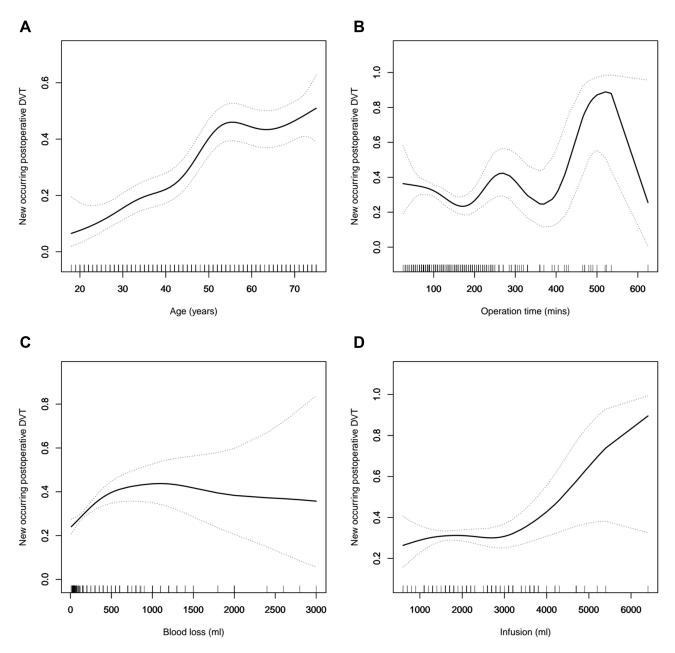


Figure I The curve correlation between age (A), operation time (B), blood loss (C) and infusion (D) and perioperative DVT.

### Conclusions

The NS-STT changes on electrocardiograms are associated with an increase in the incidence of perioperative DVT by

2.13-fold in patients with lower extremity fractures under 75 years old. In clinical practice, surgeons should pay more attention to these patients.

Table 4 R	elationship E	Between NS-ST	T Changes c	n Electrocardiogr	am and Perio	perative DVT

	Crude	Adjust I	Adjust II	Adjust III	Adjust IV
NS-STT segment	3.45 (2.25, 5.30)	2.20 (1.38, 3.49)	2.16 (1.35, 3.45)	2.20 (1.38, 3.50)	2.13 (1.33, 3.42)
changes	<0.0001	0.0008	0.0013	0.0009	0.0017

Notes: Data in table:β (95% CI) P value/OR (95% CI) P value. Outcome variable: Postoperative DVT. Exposed variables: ST-T segment changes on ECG. Adjust I adjust for: Age (smooth); Classification of internal implants (Plates and screws, Intramedullary nail, Joint prosthesis, Tension band). Adjust II adjust for: Age (smooth); Classification of internal implants (Plates and screws, Intramedullary nail, Joint prosthesis, Tension band); Blood loss (smooth); Infusion (smooth). Adjust III adjust for: Age (smooth); Gender; Classification of internal implants (Plates and screws, Intramedullary nail, Joint prosthesis, Tension band). Adjust IV adjust IV adjust for: Age (smooth); Gender; Classification of internal implants (Plates and screws, Intramedullary nail, Joint prosthesis, Tension band). Adjust IV adjust for: Age (smooth); Gender; Classification of internal implants (Plates and screws, Intramedullary nail, Joint prosthesis, Tension band); Operation time (smooth); Blood loss (smooth); Infusion (smooth); Gender; Classification of internal implants (Plates and screws, Intramedullary nail, Joint prosthesis, Tension band); Operation time (smooth); Blood loss (smooth); Infusion (smooth).

### Abbreviations

NS-STT, nonspecific ST-segment or T-wave; DVT, deep vein thrombosis.

## **Data Sharing Statement**

The datasets generated during and/or analyzed during the current study are not publicly available due to data privacy but are available from the corresponding author on reasonable request.

## **Ethics Approval**

The study was approved by the ethical board of Xi'an Honghui Hospital (No. 2014026).

## **Author Contributions**

All authors contributed to data analysis, drafting or revising the article, have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

## Funding

This study was supported by the Social Development Foundation of Shaanxi Province under grant 2017ZDXM-SF-009 and 2019ZDLSF01-09.

## Disclosure

The authors report no conflicts of interest.

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