Meta-analysis of the Risk Factors of Thrombosis in the Perioperative Period of the Orthopedics Spinal Surgery

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To explore the specific risk factors of thrombosis in the perioperative period of orthopedics spinal surgery, a search was conducted with specific keywords in PubMed, EMbase, the Cochrane Library, China National Knowledge Infrastructure, WanFang Data, very important paper and Web of Science databases between January 2015 and December 2019. Two researchers independently screened the literature, extracted the data and cross-checked. RevMan 5.3 software was used for meta-analysis. A total of 6 articles were included in this study, with a total of 23 106 patients. The results of meta-analysis showed that the age standard mean difference (=0.39, 95 % confidence intervals 0.18, 0.59, p=0.0002), blood loss (mean difference =35.26, 95 % confidence intervals 30.18, 40.34, p=0.00001), and operation time (mean difference =13.49, 95 % confidence intervals 30.18, 40.34, p=0.0001) of the experimental group were significantly higher than those of the control group, and the body mass index mean difference was -1.82, 95 % confidence intervals (-2.79, -0.85, p=0.0002) of the experimental group was significantly lower than that of the control group. There was no significant difference in the number of female (odds ration=2.23, 95 % confidence intervals 0.65, 7.69, p=0.2) and male (odds ration=0.65, 95 % confidence intervals CI 0.32, 1.32, p=0.23) patients between the experimental group and the control group. Age, operation time, blood loss, and body mass index were the risk factors of thrombosis in the perioperative period of orthopedics spinal surgery.

Key words: Spinal operation, perioperative period, thrombosis, risk factors, meta

Many complications often occur during the perioperative period of orthopedic spinal surgery, among which the pulmonary embolism and deep venous thrombosis were one of the common complications^{[1-5].} Previous studies have shown that patients with fracture of hip and knee osteoarthritis were more likely to form such thrombi during the perioperative period, with an incidence of up to 84 %^{[6].} Therefore, clinic should prevent thrombosis actively. However, there were many risk factors of thrombosis in the perioperative period of orthopedic spinal surgery, so it is difficult to grasp the preventive measures. Therefore, it is necessary to study the risk factors of thrombosis. A large number of studies have analyzed the risk factors of thrombosis in the perioperative period of orthopedic spinal surgery^[7-12], but different conclusions were often drawn due to small sample size, deviations in subject selection and other factors. Therefore, this study comprehensively searched the literature on thrombosis in the perioperative period of orthopedic spinal surgery and analyzed the risk factors of venous thrombosis reported through metaanalysis, to make these conclusions more reliable. Studies reporting venous thrombosis in the perioperative

period of orthopedic spinal surgery published at home and abroad were selected without any restriction to the languages. The studies published from January 2015 to December 2019 on the subject patients with venous thrombosis were selected, which included full-text literature and when not available, conference reports, reviews were included. Keywords in English used included spinal surgery, deep venous thrombosis, venous thromboembolism, and risk factors were searched in the PubMed, EMbase, The Cochrane Library, China National Knowledge Infrastructure (CNKI), WanFang Data, very important paper (VIP) and Web of Science databases. There were no restrictions on languages. The searched time was from January 2015 to December 2019. Two researchers independently screened the literature, extracted the data, and cross-checked. If there were differences, these were resolved through discussion or consultation with a third party. When screening the literature, obviously irrelevant literature was eliminated through screening the titles, and then the abstracts and full text were scrutinized to determine whether to include or not. When necessary, the original research author was

contacted to obtain additional information that would be of importance to this study. The risk factors of venous thrombosis in the perioperative period of orthopedic spinal surgery were meta-analysed. Continuous variables such as, age, operation time, blood loss, body mass index (BMI) were analyzed by the mean difference (MD) and 95 % confidence intervals (CI) and the binary variables (gender) were analyzed by odds ratio (OR) and 95 % CI. The heterogeneity among the results was analyzed by the χ^2 test, and the heterogeneity was quantitatively judged by I². If there was no statistical heterogeneity among the results of each study, the fixed effect model was used for metaanalysis. If there was statistical heterogeneity among the results, the source of the heterogeneity was further analyzed. After excluding the obvious clinical heterogeneity, the random effect model is used for meta-analysis. In this paper, a total of 5345 related reports were preliminarily detected by software, and finally 6 reports on 23 106 patients were included in this study^[14-19] grouped into 596 patients in the experimental group and 22 510 patients in the control group. The literature screening process and results were shown in (fig. 1). The basic characteristics of the inclusion study were shown in Table 1. A total of 6 reports^[14-19] were included, which reported data of 23 106 patients. The results of the random effect model meta-analysis showed that the age of the study group was significantly higher than that of the control group standard mean difference (SMD)=0.39, 95 % CI 0.18,

0.59, p=0.0002, (fig. 2). A total of 5 reports^[14,15,17-19] were included, comprising of 22 972 patients. The results of the random effect model meta-analysis showed that there was no significant difference in the number of female patients between the experimental group and the control group (OR=2.23, 95 % CI 0.65, 7.69, p=0.2, fig. 3). In 5 reports^[14,15,17-19]</sup> that were analyzed on 23 062 patients, the results of which showed that there was no significant difference in the number of male patients between the experimental group and the control group (OR=0.65, 95 % CI 0.32, 1.32, p=0.23, fig. 4). A total of 5 reports^[14-18], which reported 1829 patients, the meta-analysis of the fixed effect model showed that the operation time of the experimental group was significantly longer than that of the control group (MD=13.49, 95 % CI 5.34, 21.64, p=0.001, fig. 5). In 4 studies^[14,15,17-18] on 785 patients. the meta analysis of the fixed effect model showed that the blood loss in the experimental group was significantly higher than that in the control group (MD=35.26, 95 % CI 30.18, 40.34, p=0.00001, fig. 6). In 4 studies^[14,15,17,18] that included 785 patientsm meta analysis of the fixed effect model showed that the BMI of the experimental group was significantly lower than that of the control group (MD=-1.82, 95 % CI -2.79, -0.85, p=0.0002, fig. 7). In recent years, due to the influence of many factors, more and more patients are orthopedic spinal surgery with undergoing а concomitant increase in the incidence especially of thrombus in the perioperative period of orthopedic



Fig. 1: The literature screening process and results

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Control	A	ge	Ger (female)	nder e/male)	Operatio (mi	Blood loss (g)		
group	Experimental group	Control group	Experimental group	Control group	Experimental group	Control group	Experimental group	
421	68.8±13.2	60.7±14.9	27/11	180/241	239.2±123.6	226.9±117.6	517.0±651.1	
60	75±12.5	70.5±10.8	11/9	22/38	212.5±37.7	177.5±40.0	110.0±23.3	
1024	63.5±13.1	53.04±14.3			123.3±34.8	94.05±34.4		
114	75.5±11.3	66.6±14.0	13/2	80/34	145.9±42.2	134.7±36.5	175±33.5	
74	44.9 ± 9.2	43.6±13.2	9/34	34/40	231.7±39.6	239.5±27.6	125.2±17.8	
20817	64.78 ±14.04	61.5±15.97	219/141	11917/8900				

	experii	erimental group control group						Std. Mean Difference		Std. Mean Difference					
Study or Subgroup	Mean SD Total			Mean	SD	Total	Weight	IV, Random, 95% Cl	Year		% CI				
Yoshioka 2015	68.8	13.2	38	60.7	14.9	421	18.0%	0.55 [0.21, 0.88]	2015			- † -			
Tominaga 2015	75	12.5	20	70.5	10.8	60	11.1%	0.40 [-0.11, 0.91]	2015			- t			
Rojas - Tomba 2016	63.5	13.1	20	53.04	14.3	1024	13.2%	0.73 [0.29, 1.18]	2016			- t -			
Kuo Yongzhi Da 2016	75.5	11.3	15	66.6	14	114	10.1%	0.64 [0.10, 1.19]	2016			- t			
Бывальцев В А 2017	44.9	9.2	43	43.6	13.2	74	16.0%	0.11 [-0.27, 0.48]	2017			- t			
Ji Hyun Park 2019	64.78	14.04	460	61.5	15.97	20817	31.7%	0.21 [0.11, 0.30]	2019			•			
Total (95% CI)			596			22510	100.0%	0.39 [0.18, 0.59]							
Heterogeneity: Tau ² = 0.	l ² = 569	6				100	50	<u> </u>		100					
Test for overall effect: Z			exp	erimental g	roup contr	oc ol group	100								

Fig. 2: Meta-analysis of the age comparison of venous thrombosis patients Meta-analysis of the age comparison of venous thrombosis patients in the perioperative period of orthopedic spinal surgery between the experimental group and the control group

	experimental group control group Odds Ratio							Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	r M-H, Random, 95% Cl
Tominaga 2015	11	20	22	60	19.5%	2.11 [0.76, 5.89]	2015	5 +
Yoshioka 2015	27	38	180	421	20.9%	3.29 [1.59, 6.80]	2015	5 –
Kuo Yongzhi Da 2016	13	15	80	1024	16.9%	76.70 [17.01, 345.85]	2016	6
Бывальцев В А 2017	9	43	34	74	20.3%	0.31 [0.13, 0.74]	2017	7 —•
Ji Hyun Park 2019	219	460	11917	20817	22.4%	0.68 [0.56, 0.82]	2019	9 🔸
Total (95% CI)		576		22396	100.0%	2.23 [0.65, 7.69]		-
Total events	279		12233					
Heterogeneity: Tau ² = 1.	77; Chi ² = 61.10							
Test for overall effect: Z	= 1.27 (P = 0.20)		experimental group control group					

Fig. 3: Meta-analysis of female patients comparison of venous thrombosis patients Meta-analysis of female patients comparison of venous thrombosis patients in the perioperative period of orthopedic spinal surgery between the experimental group and the control group

spinal surgery. Due to the high incidence of thrombosis in the perioperative period, the prognosis of patients undergoing orthopedic spinal surgery was affected along with the quality of life of patients. Therefore, many studies focused on the risk factors of thrombosis in the perioperative period of orthopedic spinal surgery, to further prevent the formation of thrombus in the clinic through the analysis of the influencing factors of thrombosis. The results of this study found that the age, operation time, blood loss, and BMI were related to thrombosis in the perioperative period of orthopedic spinal surgery. Age, blood loss, and BMI were the high risk factors for thrombosis in the perioperative period of orthopedic spinal surgery. The results of meta-

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analysis showed that the age of the experimental group was significantly higher than that of the control group. The blood loss in the experimental group was significantly higher than that of the control group. The BMI of the experimental group was significantly lower than that of the control group. This showed that the age of the patients, blood loss, and BMI were positively correlated with the rate of thrombosis, which is consistent with the previously reported conclusions^[20]. However, Yoshioka *et al.*^[14], Rojas-Tomba *et al.*^[15] and other workers pointed out that the gender should be considered in the perioperative risk factors of orthopedic spinal surgery. However, according to the meta-analysis of the gender related factors, there was no significant difference in the number of female and male patients between the experimental group and the control group. Gender factors have little effect on the thrombosis in perioperative period of orthopedic spinal surgery, which



Fig. 4: Meta-analysis of male patients comparison of venous thrombosis patients
Meta-analysis of male patients comparison of venous thrombosis patients in the perioperative period of orthopedi
spinal surgery between the experimental group and the control group

	experir	rimental group control group						Mean Difference		Mean Difference					
Study or Subgroup	Mean	lean SD Total Mean SD Total Weight IV, Fixed, 95% Cl Yea					Year	IV, Fixed, 95% CI							
Tominaga 2015	212.5	37.7	20	177.5	40	60	17.7%	35.00 [15.62, 54.38]	2015						
Yoshioka 2015	239.2	123.6	38	226.9	117.6	421	4.0%	12.30 [-28.57, 53.17]	2015						
Rojas – Tomba 2016	123.3	34.8	20	94.05	34.4	1024	28.0%	29.25 [13.85, 44.65]	2016						
Kuo Yongzhi Da 2016	145.9	42.2	15	134.7	36.5	114	13.3%	11.20 [-11.18, 33.58]	2016	+-					
Бывальцев В А 2017	231.7	39.6	43	239.5	27.6	74	37.0%	-7.80 [-21.20, 5.60]	2017						
Total (95% CI) 136 1693								13.49 [5.34, 21.64]		•					
Heterogeneity: Chi² = 18.50, df = 4 (P = 0.0010); l² = 78%															
Test for overall effect: Z =	: 3.24 (P =	= 0.001)		experimental group control group											



	experimental group control group							Mean Difference	Mean Difference					
Study or Subgroup	Mean SD Total			Mean	SD	Total	Weight	IV, Fixed, 95% CI	Year		% CI			
Tominaga 2015	110	23.3	20	60	14.4	60	21.9%	50.00 [39.16, 60.84]	2015				-	
Yoshioka 2015	517	651.1	38	148	167.9	421	0.1%	369.00 [161.36, 576.64]	2015					•
Kuo Yongzhi Da 2016	175	33.5	15	126.8	46.6	114	7.2%	48.20 [29.21, 67.19]	2016				_	
Бывальцев В А 2017	125.2	17.8	43	96.1	12.5	74	70.8%	29.10 [23.07, 35.13]	2017				•	
Total (95% CI)			116			669	100.0%	35.26 [30.18, 40.34]					•	
Heterogeneity: Chi² = 22 Test for overall effect: Z =			-100	-50		50	100							

Fig. 6: Meta-analysis of blood loss comparison of venous thrombosis patients Meta-analysis of blood loss comparison of venous thrombosis patients in the perioperative period of orthopedic spinal surgery between the experimental group and the control group www.ijpsonline.com

	experim	cont	rol gro	up		Mean Difference			ice					
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% Cl	Year		IV, I	ixed, 95%	CI	
Tominaga 2015	21.2	11	20	22.4	12.2	60	2.9%	-1.20 [-6.92, 4.52]	2015			±		
Yoshioka 2015	21.8	3.3	38	23.7	3.8	421	76.4%	-1.90 [-3.01, -0.79]	2015					
Kuo Yongzhi Da 2016	23.7	9.8	15	23.8	8.4	114	3.5%	-0.10 [-5.29, 5.09]	2016			+		
Бывальцев В А 2017	21.6	6.4	43	23.5	5.9	74	17.2%	-1.90 [-4.24, 0.44]	2017			1		
Total (95% CI) Heterogeneity: Chi ² = 0.4	19. df = 3 (F	P = 0.92	116); ² = 09	6		669	100.0%	-1.82 [-2.79, -0.85]			<u> </u>		-	
Test for overall effect: Z =			-100 expe	-50 erimental gr	0 oup cont	50 rol group	100							

Fig. 7: Meta-analysis of BMI comparison of venous thrombosis patients

Meta-analysis of the BMI comparison of venous thrombosis patients in the perioperative period of orthopedic spinal surgery between the experimental group and the control group

is contrary to the conclusions of the previous studies^[18]. It is believed that the reasons for the inconsistent conclusions could be related to the small number of samples selected in this paper and the untimely return visit after operation. In addition, the results of the meta analysis showed that the operation time of the experimental group was significantly higher than that of the control group, indicating that the surgery time was one of the main factors of thrombosis in the perioperative period of orthopedic spinal surgery and long operation times might lead to a high incidence of thrombosis in orthopedic spinal surgery. However, the risk of thrombosis can be decreased by initiating factor Xa inhibitors immediately after the surgery thus preventing venous thromboembolism. Although this paper puts forth these conclusion which is basically consistent with the previous research, it still has some limitations. First of all, more comprehensive research literatures were obtained by the literature retrieval in a large number of databases, and the final literatures were obtained through the literature screening by the professionals. However, there was still a certain selective bias. Secondly, there were many results of meta-analysis on the perioperative risk factors of orthopedic spinal surgery, but due to the different research methods and evaluation methods in different research teams, the risk factors of thrombosis were quite different, resulting in the biased conclusions. Finally, through the investigation, it was found that although there were many literatures related to the orthopedic spinal surgery, there were relatively few literatures about the risk factors of thrombosis in the perioperative period of orthopedic spinal surgery, especially high-quality papers. And there were few references used in this paper, which limits the authenticity of the research, and affect the analytical 148

conclusions. Therefore, the author believes that a joint study and the cooperation of multiple teams should be adopted to comprehensively evaluate the risk factors of thrombosis in the perioperative period of orthopedic spinal surgery. Finally, obtain the real risk factors of thrombosis in the perioperative period of orthopedic spinal surgery more effectively. To sum up, the risk factors of thrombosis in the perioperative period of orthopedic spinal surgery such as age, operation time, blood loss, gender and BMI have little effect on thrombosis. Despite the BMI has negligible effect to cause the thrombosis it is believed that obesity and less physical activity could be inter-related and the sedentary life style of obese patients could cause thrombosis. The age, blood loss, and BMI, operation time were positively correlated with thrombosis in the perioperative period of orthopedic spinal surgery.

Author's contributions:

Yang Wu conceived and designed the experiments. Xiongzhong Li and Jun Xuan performed the experiments. Hao Cheng analyzed the data and wrote the paper.

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Conflict of interests:

The authors declared no conflict of interest.

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