Review Article

The prevalence of venous thromboembolism in patients with prophylactic low molecular weight heparin and/or mechanical measures after degenerative lumbar surgery: a systematic review and meta-analysis

Jia Qi Li[1], Bing Yi Zhao[2], Ling De Kong[1], Xian Da Gao[1], Jing Tao Zhang[1], Yong Shen[1]

[1]Department of Spinal Surgery, The Third Hospital of Hebei Medical University, Shijiazhuang, Hebei, People's Republic of China; [2]Department of Reproductive Medicine, The Second Hospital of Hebei Medical University, Shijiazhuang, Hebei, People's Republic of China

Abstract: Purpose: Venous thromboembolism (VTE) includes deep venous thrombosis (DVT) and pulmonary embolism (PE). Consensus had yet to be reached on the prevention for thromboembolic events following degenerative spine surgery. Therefore, we wished to evaluate the efficacy and safety of mechanical measures as well as LMWH on prevention for VTE in patients after degenerative lumbar spinal surgery. Methods: We searched the PubMed, EMBASE, and the Cochrane library databases. A systematic review and meta-analysis were performed according to the following inclusive selection criteria: (a) population: patients with lumbar degenerative diseases. (b) intervention: postoperative VTE prophylaxis with LMWH and/or mechanical methods. We performed a subgroup analysis to explain heterogeneity. In addition, the Egger test and Egger graph were conducted to find publication bias with a P value < 0.05 being statistically significant. Results: Eleven studies met our inclusion criteria with a total of 6993 patients. The pooled prevalence of total DVT was 11.4% (8.7%, 14.5%) and that of distal DVT was 9.6% (7.1%, 12.4%). In contrast, the occurrence rates of symptomatic DVT [0.64% (0.49%, 0.81%)], proximal DVT [1.7% (0.8%, 2.7%)], total PE [1.00% (0.72%, 1.21%)] and symptomatic PE [0.9% (0.64%, 1.1%)] were low. One patient suffered from a postoperative PE was died. No postoperative hematoma was reported. Conclusion: We recommended mechanical prophylaxis for patients after degenerative lumbar open surgery. Routinely postoperative examination with Doppler ultrasound for these patients should be recommended. Further prospective and high-quality studies should be conducted to find a better anticoagulation regime balancing efficacy and safety.

Keywords: Lumbar, surgery, low molecular weight heparin, mechanical prophylaxis, venous thromboembolism

Introduction

Venous thromboembolism (VTE), which includes deep venous thrombosis (DVT) and pulmonary embolism (PE), is a common and life-threatening complication after orthopedic surgery. Numerous prospective studies have indicated a significant decrease in VTE when using mechanical with or without pharmacological prophylaxis in patients undergoing general, urological or orthopedic surgery [1-3]. Mechanical measures include compression stockings (CS) and pneumatic compression devices (PCD). Pharmacological prophylaxis for VTE includes aspirin, low-molecular-weight heparin (LMWH), low-dose unfractionated heparin (UH) and warfarin. LMWH has been more widely used compared with others for fewer nursing time, fewer bleeding complications, and greater efficacy at VTE prophylaxis [2, 4-7]. Therefore, we focused on LMWH in chemical anticoagulation.

Experts have reached an agreement that prophylactic low molecular weight heparin and/or mechanical measures should be used on patients following joint arthroplasty and surgery with trauma [8, 9]. Consensus had yet to be reached on the prevention for thromboembolic events following degenerative spine surgery. Because compared those with trauma and joint arthroplasty, the prevalence of VTE following spinal surgery is lower. In addition, these patients are at risk for neurologic deficit resulting

from postoperative epidural hematomas related to pharmacologic prophylaxis.

Upon the background of preventing thrombotic events following spine surgery, lots of prospective and retrospective studies were performed to find an appropriate anticoagulation regime balancing efficacy and safety. We performed the present systematic review to evaluate the efficacy and safety of mechanical measures or Low Molecular Weight Heparin on prevention for venous thromboembolism in patients after degenerative lumbar spinal surgery. Prior systematic reviews or meta analyses focused on the prevalence of venous thromboembolic disease according to the whole spine stage [10, 11]. However, lumbar surgery or thoracolumbar surgery is quite different from cervical spine surgery in terms of spinal level, surgical trauma, perioperative bleeding, and postoperative bedtime. The prevalence of VTE after elective spinal surgery was different in each spinal levels. Lumbar surgery or thoracolumbar surgery had an associated higher risk than cervical spine surgery [12]. Cervical spine surgery had an associated low risk in particular. Therefore, we concentrated on evaluating the efficacy and safety of mechanical options or LMWH for preventing VTE following degenerative lumbar surgery.

Materials and methods

Search strategy

Two authors independently searched the Pub-Med, EMBAES, and the Cochrane library databases for relevant articles published up to April 21, 2016. Search terms included "lumbar", "surgery", "low molecular weight heparin", "mechanical prophylaxis", and so on. The restriction of language and study type was not imposed to include more articles for selecting suitable studies. We manually checked the reference lists of identified studies and topic related reviews to include other potentially eligible studies. This process was performed interactively until no additional articles could be identified.

Inclusion/exclusion criteria

The following inclusive selection criteria were applied: (a) population: patients with lumbar degenerative diseases (degenerative lumbar spondylosis and/or spondylolisthesis, lumbar canal stenosis, lumbar instability, degenerative lumbar disc disease or facet joint disease) receiving open lumbar spinal surgery; (b) intervention: postoperative VTE prophylaxis with LMWH and/or mechanical methods. Studies were excluded: (a) patients with neoplasm, trauma, infection, and idiopathic deformity; (b) preoperative use of anticoagulant drugs; (c) case reports; (d) lumbar minimally invasive surgery; (e) studies for the whole spine which we could not extract data of the lumbar region.

Review procedure

According to the including criteria, two authors independently reviewed retrieved articles. Firstly, we included some articles after screening the titles and abstracts. Given that our goal was to include prophylactic studies for thrombotic events of lumbar surgery, we temporarily included articles about spine surgery which included different spinal segment. Rather, the purpose was not to omit studies with potentially extractable data. Secondly, potentially relevant full texts were screened according to inclusion/exclusion criteria. Finally, a study was included for systematic review when both reviewers agreed that it could be included.
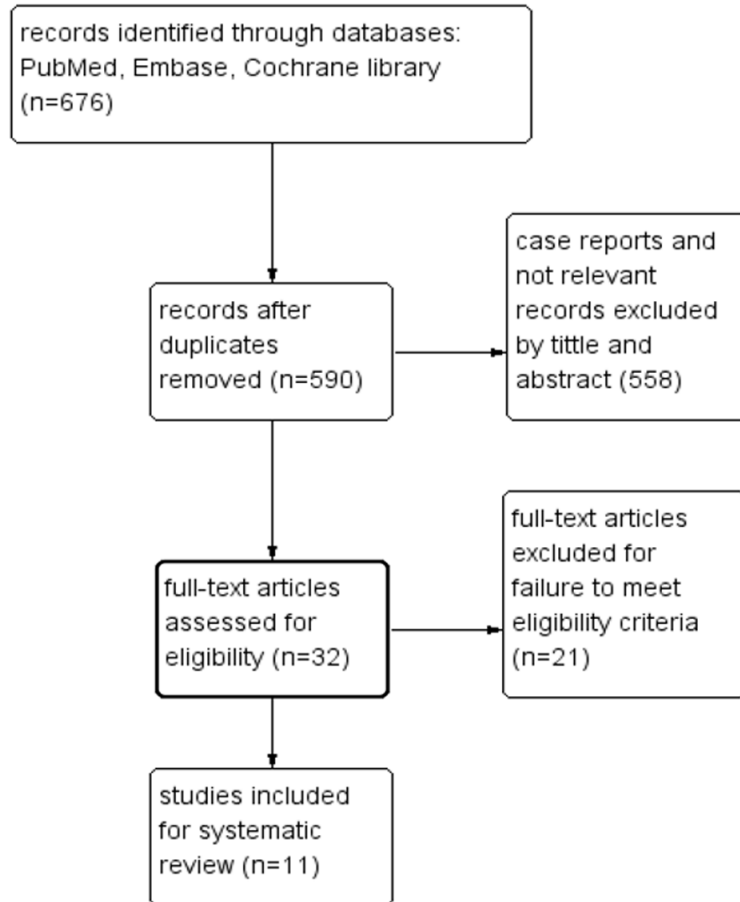
Quality assessment

The risk of bias was assessed by two of the authors. We resolved potential disagreement by a third author. We assessed risk of bias of cohort studies and case-control studies by the Newcastle-Ottawa scale. A case series study was assessed by case series study quality score of the National Institute for Clinical Excellence (NICE). We considered that the risk of bias was low when studies met more than 50% of the criterion for each quality tools or evaluation. We included studies of low risk of bias.

Data extraction

Two authors independently extracted the data according to predetermined forms. When faced with a situation that articles were not just focused on lumbar degenerative disease, we tried to extract the related data of postoperative anticoagulation for lumbar degenerative disease. We extracted the following data: (1) study ID (first author, year of publication). (2) study design/quality evaluation score, patient

Figure 1. Flow diagram of study selection.

and PE. The level of significance was set at *P* < 0.05 (two sided). Meta-analysis is commonly used in RCT, which is a very high level of evidence. However, the present study was to calculate the merged prevalence of thrombotic events with a low event rate. Also, there were few RCTs. Besides, few studies about the comparison between each of LMWH, mechanical methods, and LMWH plus mechanical methods were performed when we strictly refer to the inclusion/exclusion criteria. We obtained some observational case series to perform meta-analyses of a single rate [13]. We further found that the prevalence of thrombotic events was less than 30% in a number of studies. If we directly use the prevalence and standard error to perform meta-analysis, there are two main questions: (1) each of the 95% confidence interval of the prevalence of thrombotic events may be beyond [0, 1]; (2) the variance of each studies will tend to 0. As a result, the research can get a big weight value. Therefore, we used converting formula of double inverse sine to transform the data into normal distribution data for meta-analysis, and then used the formula $[P = (\sin(ES/2))^2]$ to returned to the merged prevalence of thrombotic events and 95% confidence interval (CI). Also, we generated the prevalence equal to 0.0005 when number of thrombotic events was 0. For dichotomous variables, the prevalence (p) and 95% CI was calculated. For continuous variables, means with standard deviations were calculated if data met normal distribution. Otherwise, average (range) was calculated. We estimated heterogeneity with the inconsistency index (I^2) statistic. If I^2 was < 25%, studies were considered to be homogeneous. If I^2 was of 25% to 50%, studies were considered to be lowly heterogeneous. If I^2 was of 50% to 75%, studies were considered to be moderately heterogeneous. If I^2 was > 75%, studies were considered to be highly heterogeneous. If the I^2 statistic (> 50%) indicated heterogeneity

characteristics (sex, years, BMI/weight). (3) study patient inclusion/exclusion criteria. (4) total number of patients. (5) number or incidence of thrombotic events (DVT, PE). (6) primary patient diagnosis. (7) surgical methods. (8) number of lumbar levels performed. (9) anticoagulation program(AP). (10) definition of thrombotic events (DVT, PE). (11) method of thrombotic surveillance (MOTS). (12) follow-up time. (13) operation time. (14) perioperative blood transfusion. (15) intraoperative blood loss. (16) mortality of PE. (17) length of stay. (18) postoperative hematoma. (19) other bleeding complication (type and number). We eliminated duplicate reported data. A third author resolved the disagreement which was reached during extracting data. If wanted, the extra information was obtained from the article author.

Data analysis and synthesis

We used stata/SE 12.0 for windows to calculate meta-analyses of the prevalence of DVT

Table 1. Characteristics of included studies

Study	Design	Year	No. of patient (M:F)	Quality evaluation	Age(yr)	BMI (kg/m²)	Operating time (min)	Blood loss (ml)
Epstein et al. [1]	Case series	2006	139 (78:61)	6	53 (25-75)	N/A	5.0 h (3.5-8)	N/A
Yoshioka et al. [2]	Case series	2013	169 (82:87)	7	61.5±16.5	23.8±4.0	239.1±1147.8	N/A
Ferree et al. [3]	Case series	1994	60	7	N/A	N/A	N/A	N/A
Sun et al. [4]	Case series	2011	78 (29:49)	6	62.4±10.6	N/A	174.24±62.8	441±364.7
Moayer et al. [5]	Case series	2016	93	6	44.8±12.6	24.6±6.8	206.5±49.6	460.9±197.2
Yoshioka et al. [6]	Case series	2015	292 (159:133)	7	62.7±15.5	24.1±11.8	259.9±1044.4	308.1±2020.5
Justin et al. [7]	Case series	2015	5766 (2708:3057)	6	60.3	N/A	N/A	N/A
Yoshioka et al. [8]	Case series	2010	28	7	N/A	N/A	N/A	N/A
Kumar et al. [9]	Case series	2012	76 (30:46)	6	N/A	N/A	115 (31-369)	N/A
Ferree et al. [10]	Prospective cohort	1993	185	7*	47	N/A	N/A	N/A
Weber B et al. [11]	Prospective cohort	2014	117	8*	58 (±12)	29.8 (±6.1)	279 (162-426)	N/A

N/A indicates not available; BMI, Body Mass Index; *, we assessed risk of bias of the two prospective cohorts by the Newcastle-Ottawa scale and the full mark was 9 stars.

between studies, a random effects model was calculated. Otherwise, a fixed effects model was used. Subgroup analyses were further performed to explore possible explanations for heterogeneity. The Egger test and Egger graph were conducted to find potential publication bias with a *P* value < 0.05 being statistically significant.

Results

Initial search criteria

A total of 676 articles were obtained by the initial database search. We identified 590 articles after removing duplicated studies. On the basis of the titles and abstracts, 558 articles were excluded because they were case reports or article topics were not relevant to the objective of this systematic review. We reviewed the remaining 32 full text articles for more detailed evaluation. Three articles were excluded because of minimally invasive surgery [14-16]. Two articles were excluded because only abstract [17, 18]. Seven articles which could not extract the data of lumbar spine surgery were excluded [19-25]. Three articles were excluded because of trauma or tumor [26-28]. Three articles were excluded because of pre-operative anticoagulation or unclear anticoagulation regimens [29-31]. Two articles were excluded because one's anticoagulation regimens included unfractionated heparin and the other included aspirin [32, 33]. One article was excluded because the type of lumbar disease was unknown [34]. Finally, eleven studies which met our inclusion criteria were included in the present systematic review [12, 35-44]. The

selection process for studies included is shown in **Figure 1**.

Study description

The eleven articles included 9 case series and 2 prospective cohort studies. Basic characteristics of the 11 articles were shown in **Table 1**. Seven of 9 case series studied postoperative mechanical anticoagulation [12, 35-37, 39, 42, 43]. In contrast, two of the nine case series used LMWH for postoperative thrombosis prevention [38, 40]. A total of 6993 patients were included in the 11 articles with 6701 participants in case series and 292 participants in prospective cohort studies. Each patient included was underwent open lumbar operation for lumbar degenerative diseases (degenerative lumbar spondylosis and/or spondylolisthesis, lumbar canal stenosis, lumbar instability, degenerative lumbar disc disease or facet joint disease).

Risk of bias

Newcastle-Ottawa scales in two prospective Cohort studies were 7* and 8* of 9*. The scores of the NICE in 9 case series ranged from 5 to 7 of 8 (**Table 1**). We considered them low risk of bias.

Venous thromboembolism (DVT and PE)

The eleven included articles all concerned DVT and PE. We divided them into three parts to present the results of thrombotic events according to different study design and anticoagulation program: 1. Venous thromboem-

Table 2. Summary of thrombotic events of included studies (9 case series)

Author year	Design	tDVT	pDVT	dDVT	sDVT	tPE	sPE	DVT+PE	Total	AP	MOTS for DVT	MOTS for PE
Yoshioka K 2013	Prospective	22	4	18	0	5	2	3	169	CS+PCD	1*(POD7-10)	1*(POD7-10)
Yoshioka K 2015	Prospective	30	4	26	0	4	1	1	292	CS+PCD	1*(POD7-10)	1*(POD7-10)
Yoshioka K 2010	Prospective	3	1	2	0	1	0	1	28	CS+PCD	1*(POD7-10)	1*(POD7-10)
Epstein N.E 2006	Prospective	4	1	3	3	1	1	1	139	PCD	1*(POD2-3)	2*
Ferree BA 1994	Prospective	3	0	3	0	0	0	0	60	CS	1*(POD2-3)	2*
Justin BH 2015	Retrospective	38	N/A	N/A	38	51	51	9	5766	CS+PCD	3*	3*
Kumar A 2012	Retrospective	3	N/A	N/A	N/A	0	0	0	76	CS	3*	3*
Sun Z 2011	Prospective	0	0	0	0	0	0	0	78	LMWH	2*	2*
Moayer AF 2016	Prospective	0	0	0	0	0	0	0	93	LMWH	2*	2*

tDVT indicates total deep venous thrombosis; *pDVT*, Proximal deep venous thrombosis; *dDVT*, distal deep venous thrombosis; *sDVT*, symptomatic deep venous thrombosis; *tPE*, total pulmonary embolus; *sPE*, symptomatic pulmonary embolus; *AP*, anticoagulation program; *MOTS*, method of thrombotic surveillance; *CS*, compression stockings; *PCD*, pneumatic compression devices; *LMWH*, low-molecular-weight heparin; *1*, all patients were examined to find DVT with Doppler ultrasound or PE with lung perfusion scintigraphy several days after surgery and the patient was examined immediately when symptomatic DVT or PE was suspected; *2*, the patient underwent examination with Doppler ultrasound or chest computed tomography only when symptomatic DVT or PE was suspected; *3*, reviewed medical records systems; *N/A*, not available; *POD*, postoperative day.

bolism of 7 case series with postoperative mechanical anticoagulation; 2. Venous thromboembolism of 2 case series with LMWH; 3. Venous thromboembolism of 2 prospective cohort studies.

Venous thromboembolism of 7 case series with postoperative mechanical anticoagulation (Table 2)

Total deep venous thrombosis (tDVT) and symptomatic deep venous thrombosis (sDVT): Seven moderate-quality studies of postoperative physical anticoagulation were used in the data synthesis for the prevalence of tDVT [12, 35-37, 39, 42, 43]. We considered that studies were highly heterogeneous because I^2 score was 95.7%. The overall estimate demonstrated that the prevalence of tDVT was 6.1% (95% CI, 1.7% to 13.1%). Then we performed a subgroup analysis by method of thrombotic surveillance (MOTS) for DVT. A random effect model was calculated when I^2 score > 50%. Otherwise we used a fixed effect model. Consequently, the subtotal estimate of prevalence was 11.4% (95% CI, 8.7% to 14.5%) for the subgroup [1*(POD7 to POD10)] with all patients examined postoperative day (POD) 7 to POD10. No significant heterogeneity was showed (I-squared = 0.0%, P = 0.658). Also, the subtotal pooled prevalence of subgroup [1*(POD2 to POD3)] with all patients examined POD2 to POD3 was 3.9% (95% CI, 1.7% to 7.1%). No significant heterogeneity existed (I-squared = 0.0%, *P* = 0.424). But, the subgroup (3*) that definite DVT was obtained by reviewing medical records systems showed highly heterogeneity (I-squared = 81.3%, P = 0.021). The subtotal pooled prevalence was

1.8% (95% CI, 0.01% to 6.9%) with a random effect model (**Figure 2A**). A statistically significant publication bias was indicated by Egger's test [(*P* > |t| = 0.026 < 0.05) (**Figure 3A**).

At the same time, six of 7 above case series focused on sDVT [12, 35, 37, 39, 42, 43]. Heterogeneity test demonstrated there was low heterogeneity in the prevalence of sDVT among studies (I-squared = 35.9%, *P* = 0.168). The pooled prevalence of sDVT was 0.64% (95% CI, 0.49% to 0.81%) with a fixed effect model (**Figure 2B**). Egger's test indicated no statistically significant publication bias for prevalence of sDVT [(*P* > |t| = 0.781 > 0.05) (**Figure 3B**).

Distal deep venous thrombosis (dDVT) and proximal deep venous thrombosis (pDVT): dDVT was defined as thrombi involving the calf only. Thrombi involving the popliteal or a more proximal vein was called pDVT. In addition, we put those into pDVT when patients with both a proximal and a distal thrombus. As we all know, pDVT is more dangerous than dDVT for patients. Therefore, it is of great clinical significance to distinguish them. Five of seven case series reported dDVT and pDVT [12, 35, 39, 42, 43]. The overall pooled prevalence of dDVT was 7.1% (95% CI, 3.9% to 11.1%) with a moderate Heterogeneity (I-squared = 65.4%, *P* = 0.021). Furthermore, a subgroup analysis was performed by MOTS. Thus, the pooled prevalence of dDVT was 9.6% (95% CI, 7.1% to 12.4%) for the subgroup [1*(POD7 to POD10)] and 3.4% (95% CI, 1.3% to 6.4%) for the subgroup [1*(POD2 to POD3)]. Heterogeneity test indicated homogeneous for both subgroups with I^2
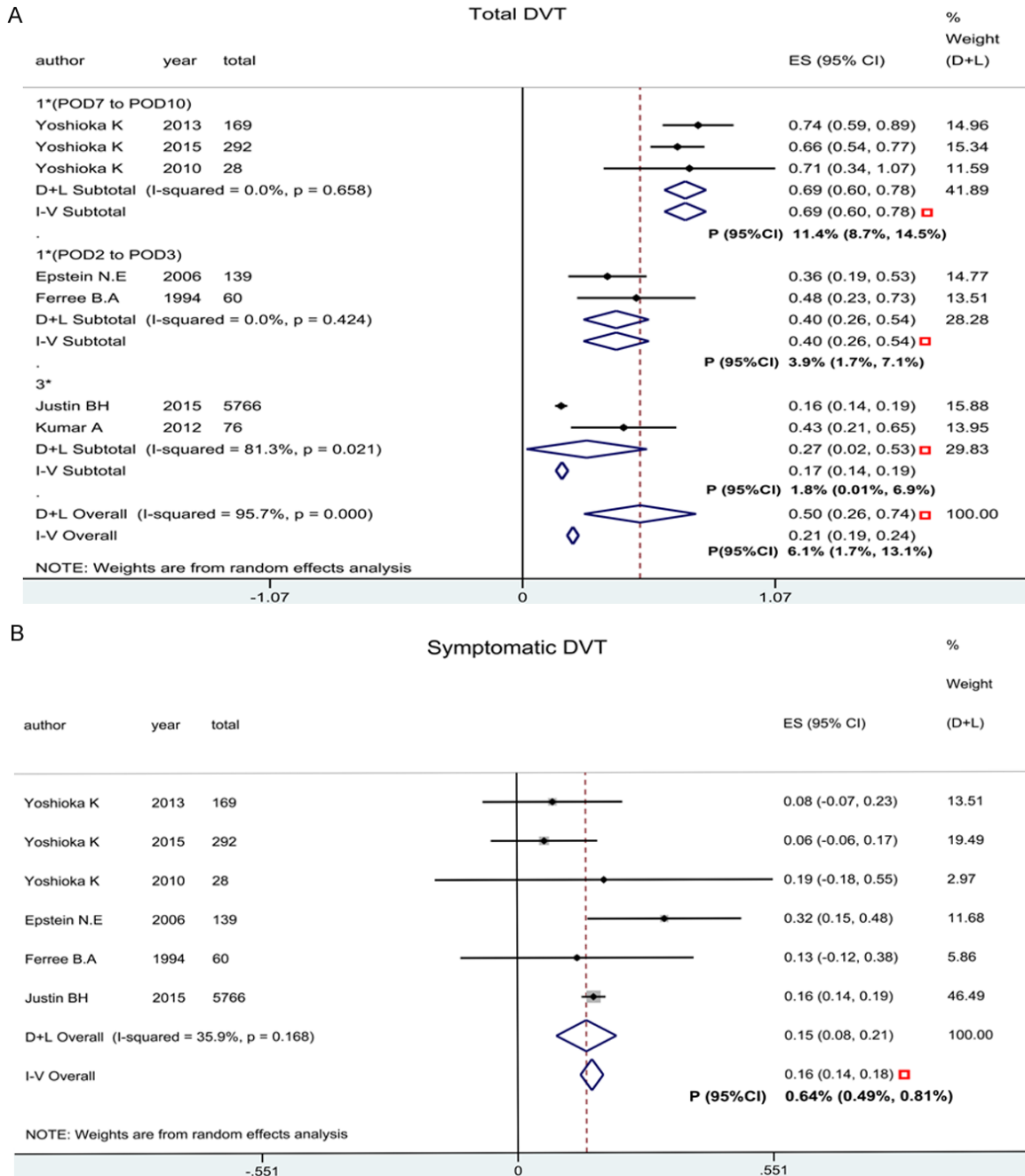
Figure 2. Forest plot of the merged prevalence for tDVT and sDVT. The merged prevalence and its 95% CI were acquired after putting the subtotal or overall ES (95% CI) marked with a small square into the formula [P = $(sin(ES/2))^2$].

score being 0.0% (P = 0.799) and 14.4% (P = 0.280) (**Figure 4A**). Egger's test indicated no statistically significant publication bias for prevalence of dDVT [(P > |t| = 0.683 > 0.05) (**Figure 3C**).

Meanwhile, meta-analysis for the same five case series regarding the prevalence of pDVT demonstrated that the pooled prevalence was 1.7% (95% CI, 0.8% to 2.7%). Heterogeneity test

indicated homogeneous (I-squared = 0.0%, P = 0.502) (**Figure 4B**). No statistically significant publication bias was indicated by Egger's test [(P > |t| = 0.816 > 0.05) (**Figure 3D**).

Total pulmonary embolus (tPE) and symptomatic pulmonary embolus (sPE): Seven studies provided data on tPE of postoperative physical anticoagulation [12, 35-37, 39, 42, 43]. The I[2] statistic indicated that the studies were lowly
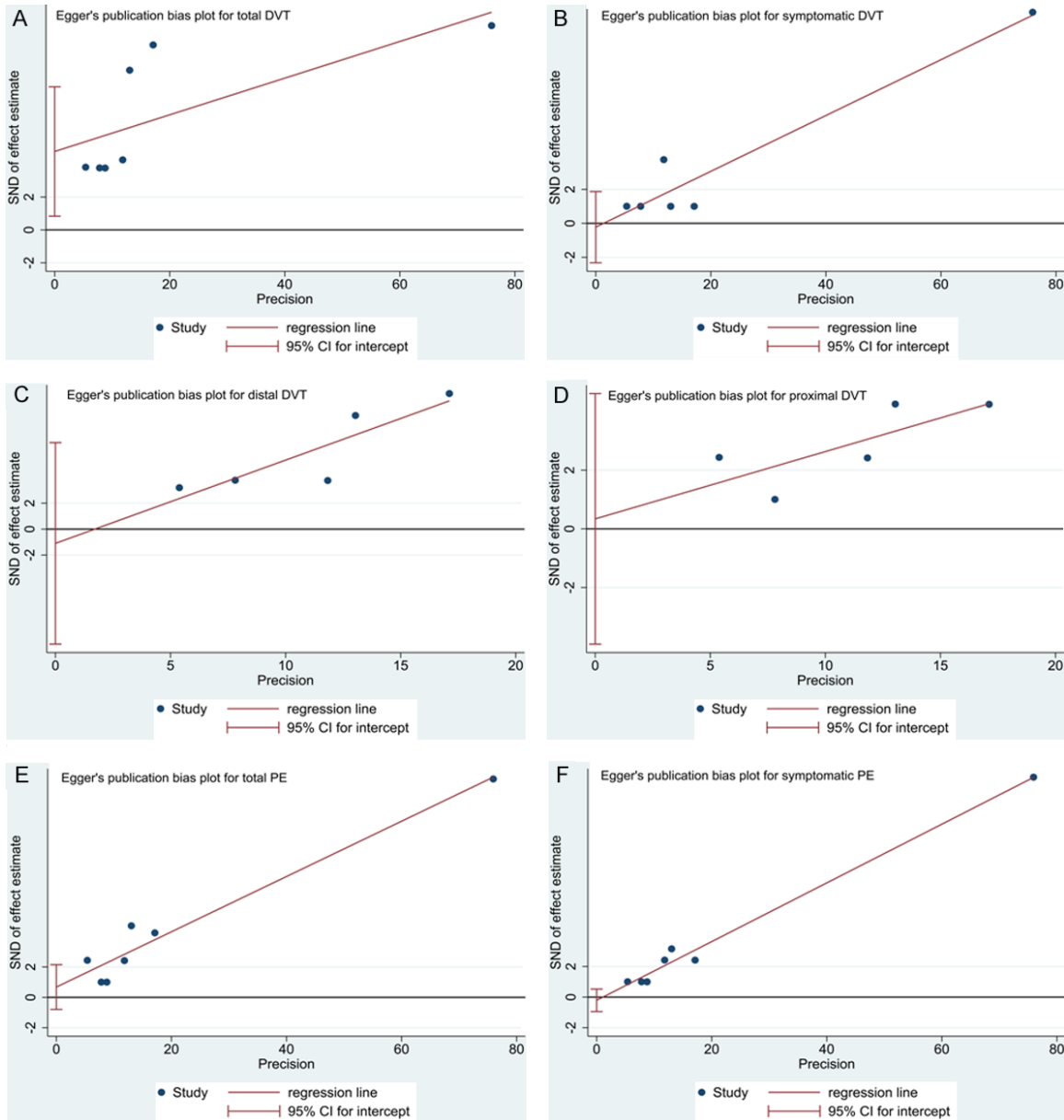
Figure 3. Egger's test illustrating the publication bias of the prevalence for different types of DVT or PE.

heterogeneous (I-squared = 28.7%, P = 0.209). The pooled prevalence of tPE was 1.00% (95% CI, 0.72% to 1.21%) with a fixed effect model (**Figure 5A**). No statistically significant publication bias was indicated by Egger's test [(P > |t| = 0.291 > 0.05) (**Figure 3E**).

Meanwhile, we were focused on sPE reported by the same seven articles [12, 35-37, 39, 42, 43]. The I^2 statistic indicated that the studies were homogeneous (I-squared = 0.0%, P = 0.936). The pooled prevalence of sPE was 0.90% (95% CI, 0.64% to 1.10%) with a fixed

effect model (**Figure 5B**). Egger's test indicated no statistically significant publication bias for prevalence of sPE [(P > |t| = 0.499 > 0.05) (**Figure 3F**).

Venous thromboembolism of 2 case series with LMWH (Table 2)

We included two case series regarding to preventing venous thromboembolism only with LMWH. The method of thrombotic surveillance for the two studies was not a routine examination with Doppler ultrasound or lung perfusion
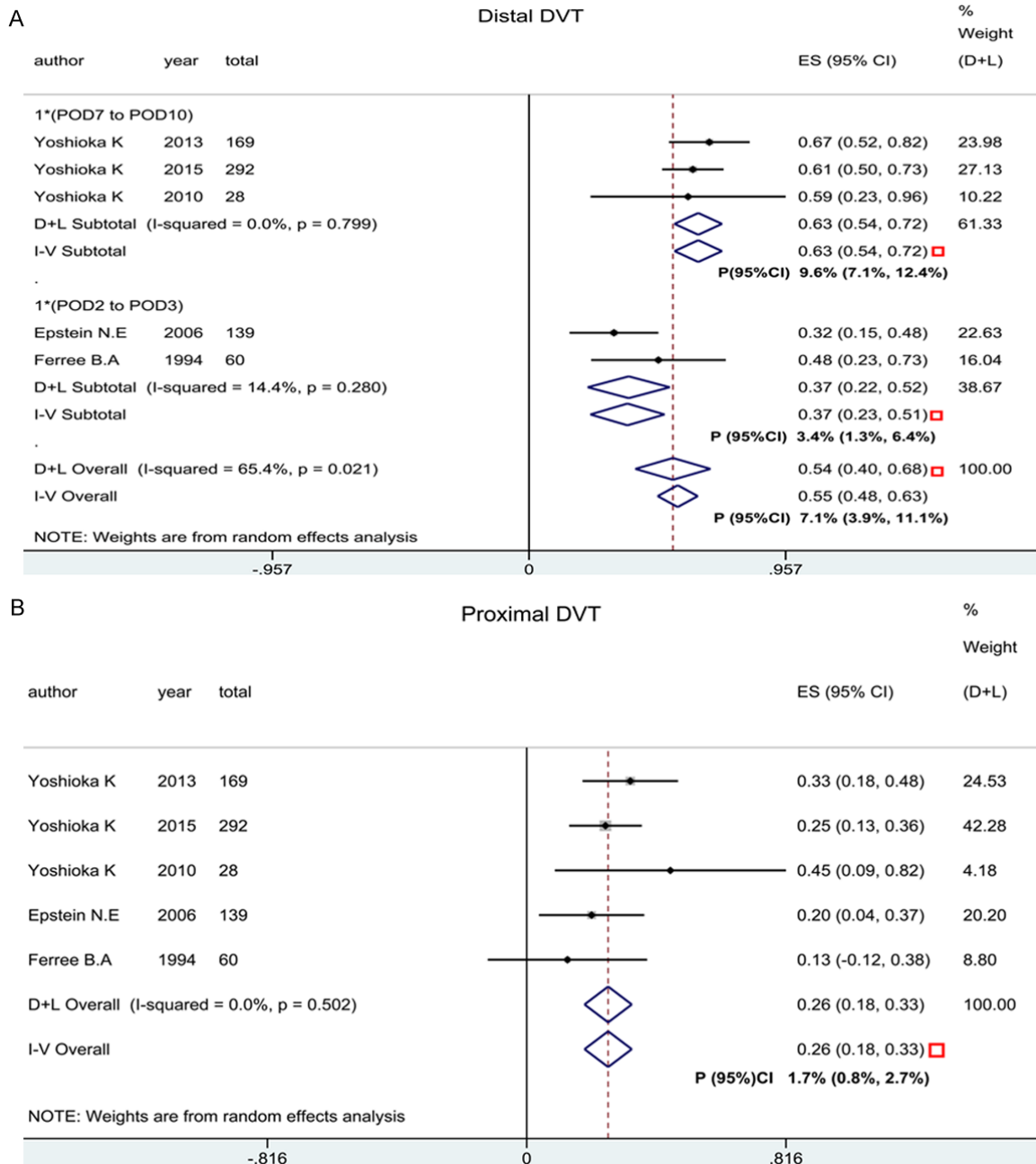
Figure 4. Forest plot of the merged prevalence for dDVT and pDVT. The merged prevalence and its 95% CI were acquired after putting the subtotal or overall ES (95% CI) marked with a small square into the formula [P = $(\sin(ES/2))^2$].

scintigraphy, but daily reviewing their clinical status or laboratory test. Sun et al. [40] and Moayer et al. [38] both reported no DVT and PE.

Venous thromboembolism of 2 prospective cohort studies

In their own cohort studies, Weber et al. [44] and Ferree et al. [41] indicated that there were no statistically significant differences in gen-

der, age, body mass index (BMI), operation time, blood transfusion and time to mobilization between two compared groups studies. Compared anticoagulation program (AP), method of thrombotic surveillance (MOTS) and thrombotic events of the two studies were shown in **Table 3**. The four DVTs reported by Ferree et al. [41] and the two DVTs reported by Weber et al. [44] were all distal DVTs. Obviously,
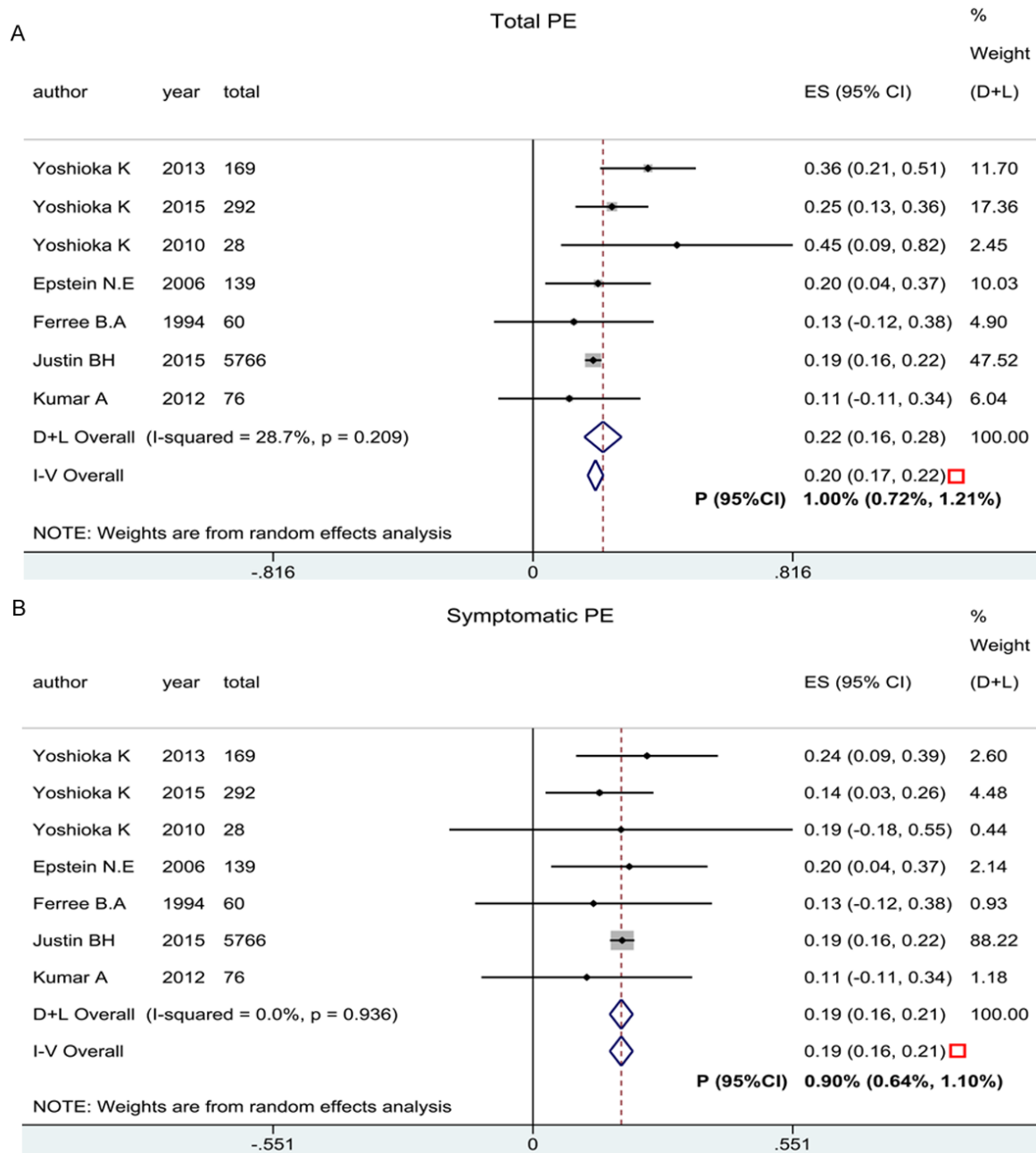
Figure 5. Forest plot of the merged prevalence for tPE and sPE. The merged prevalence and its 95% CI were acquired after putting the overall ES (95% CI) marked with a small square into the formula $[P = (\sin(ES/2))^2]$.

compared anticoagulation programs were different between the two cohort studies, so we could not make a meta-analysis. Ferree et al. [41] found that pneumatic compression devices (PCD) plus compression stockings (CS) significantly decreased the prevalence of dDVT ($P < 0.05$). Weber et al. [44] found that there was no difference in the prevalence of DVT or PE between group (CS+PCD) and group (CS+PCD+LMWH) ($P > 0.05$).

Complications and other results

Three of the 11 articles were focused on postoperative hematoma and no postoperative hematoma was found [38, 40, 44]. Justin et al. [37] reported that 1 patient diagnosed with a postoperative PE was died. In a study of 78 patients, Sun et al. [40] reported 4 cases of mild elevation in aminotransferase level and 1 case of suspicious allergic reaction.

Table 3. Summary of thrombotic events of the included studies (2 prospective cohort studies)

Study ID	AP	No. Cases	No. DVT	No. PE	MOTS for DVT	MOTS for PE
Weber B2014	CS+PCD	67	2	2	4*	2*
	CS+PCD+LMWH	40	0	0		
Ferree BA1993	CS	74	4	0	1*	2*
	CS+PCD	111	0	0		

AP indicates anticoagulation program; *MOTS,* method of thrombotic surveillance; *CS,* compression stockings; *PCD,* pneumatic compression devices; *LMWH,* low-molecular-weight heparin; *1**, all patients were examined to find DVT with Doppler ultrasound or PE with lung perfusion scintigraphy several days after surgery and the patient was examined immediately when symptomatic DVT or PE was suspected; *2**, the patient underwent examination with Doppler ultrasound or Chest computed tomography only when symptomatic DVT or PE was suspected; *4**, patients were observed for clinical evidence of VTE and two-thirds were screened for DVT on day 4 or day 5 post-surgery with Doppler ultrasound.

Discussion

We included 9 case series and 2 cohort studies in the present systematic review and meta-analysis, in order to assess effectiveness and safety of postoperative anticoagulation with physical method or low molecular weight heparin for patients with lumbar degenerative diseases. Meta-analysis of a single rate for the 7 case series indicated that the incidence of tDVT [11.4% (8.7%, 14.5%)] and dDVT [9.6% (7.1%, 12.4%)] were relatively high, and the heterogeneity was very high. However, Subgroup analyses performed by the method of thrombotic surveillance (MOTS) could well explain the heterogeneity of the sources (**Figures 2A** and **3A**). In contrast, the occurrence rates of sDVT [0.64% (0.49%, 0.81%)], pDVT [1.7% (0.8%, 2.7%)], tPE [1.00% (0.72%, 1.21%)] and sPE [0.9% (0.64%, 1.1%)] were low. The two case series of postoperative LMWH anticoagulation (171 patients) found no postoperative thrombosis. Moayer et al. [38] and Sun et al. [40] both used clinical status as a method of thrombotic surveillance, so that they missed asymptomatic DVT and PE. In addition, the two novels of no thrombotic event reported might be due to the small sample size. For the two cohort studies, Ferree et al. [41] found that pneumatic compression devices (PCD) plus compression stockings (CS) significantly decreased the prevalence of dDVT (*P* < 0.05) and Weber et al. [44] found that there was no difference in the prevalence of DVT or PE between group (CS+PCD) and group (CS+PCD+LMWH) (*P* > 0.05).

A former systematic review by Glotzbecker et al. [11] indicated the prevalence of DVT and PE was 2.2% and 0.3%. Moreover, a former meta-analysis by Sansone et al. [10] showed the prevalence of DVT and PE were 1.09% (0.54%, 1.64%) and 0.06% (0.01%, 0.12%). These two studies were both focused on the incidence of thrombotic events after surgery of various spinal regions. Also, the variability between the included studies is large. Variability existed in different patient/surgery, anticoagulation program, and thrombus detection method. However, the present systematic review and meta-analysis only included patients with open surgery for lumbar degenerative diseases. And we analyzed postoperative thrombotic events according to the different types of postoperative anticoagulation and study. Also, we performed a subgroup analysis by MOTS for the first time. In the article of Glotzbecker et al. [11], the pooled prevalence of DVT and PE was determined by using a simple summation because that there was a great heterogeneity between the included studies. Sansone et al. [10] pooled overall rates of DVT with a random effect model with heterogeneity (*P* < 0.0001) and PE with a fixed-effects model (*P* = 0.427). As we know, the prevalence of thrombotic events in a number of studies was less than 30%, so we could not directly use the prevalence and standard error to perform meta analyses. Therefore, we used converting formula of double inverse sine to transform the data into normal distribution data for meta analyses, and then used the formula [$P = (\sin(ES/2))^2$] to return to the merged prevalence of thrombotic events and 95% confidence interval (CI), which was more proper and accurate.

We were strict in removing the lumbar trauma, tumor patients. Also, we only concentrated on postoperative anticoagulation with mechanical method or low molecular weight heparin. In addition, studies of postoperative anticoagula-

tion for lumbar degenerative disease were insufficient, so we included fewer articles than previous systematic review by Glotzbecker et al. [11] and meta-analysis by Sansone et al. [10]. However, included studies of the present review were of lower variability than the previous studies because of the strict inclusion criteria. About our included articles, we could find that researches on LMWH anticoagulation and compared studies both were less. Therefore, we performed a meta-analysis on the prevalence of VTE for patients with postoperative physical anticoagulation. We synthesized prevalence of tDVT, sDVT, pDVT, dDVT, tPE, and sPE. The occurrence rate of tDVT was significantly higher than that of sDVT, which showed that a lot of asymptomatic DVT were found. Results of the present meta-analysis also showed that the pooled incidence of tDVT in subgroup [1*(POD7 to POD10)], subgroup [1*(POD2 to POD3)] and subgroup (3*) decreased in turn. So we speculated that the delay in detection of thrombosis after surgery or multiple detection of thrombosis found more asymptomatic thrombosis, which could attract the attention of clinicians to carefully monitor patients. The prevalence of dDVT was much higher than that of pDVT, which showed that the thrombus was mainly distal thrombus. In addition, the pooled incidence of tPE and sPE is similar, which may be related to the clinical detection of PE after surgery only. The present meta-analysis showed a low incidence of sDVT and sPE, which indicated that the patient with physical anticoagulation could make the postoperative thrombotic events at a low level.

LMWH is used to prevent postoperative thrombosis, especially fatal PE. And patients with tumors or trauma Benefit from postoperative LMWH prophylaxis. However, it can increase the incidence of epidural hematoma, and then cause neurological injury [11]. The review of 16 articles by Glotzbecker et al. [11] reported a prevalence of epidural hematoma from 0 to < 1%. The pooled prevalence of epidural hematoma was 0.39% and 3 of 2071 patients suffered a permanent neurological deficiency in the meta-analysis by Sansone et al. [10]. The present systematic review found no occurrence of epidural hematoma, which might because the majority of the studies included in the review were postoperative physical anticoagulation. A review of Cheng et al. [45] in spine surgery found no fatal PE from 29 studies. The

meta-analysis of 14 articles written by Sansone et al. [10] reported one fatal PE. In our present systematic review of 6993 patients, Justin et al. [37] reported that 1 patient diagnosed with a postoperative PE was died. All above showed that the incidence of fatal PE after spinal surgery was very small. The two studies of our systematic review on LMWH prophylaxis found no VTE, but it was not very persuasive because of insufficient sample size. Therefore, weighing the neurological injury and fatal PE, we did not recommend routine LMWH anticoagulation after degenerative lumbar surgery.

As mentioned above, we performed the meta-analysis for the first time on postoperative VTE in view of degenerative lumbar open surgery. Furthermore, we successfully synthesized the rates of different types of PE or DVT. In addition, we performed subgroup analyses by the method of thrombotic surveillance (MOTS) to explain heterogeneity. However, the present systematic review and meta-analysis had some deficiency. Our research topic did not include adequate articles, resulting in insufficient sample size. Besides, 11 included articles were short of randomized controlled trials, cohort studies and case-control studies with high levels of evidence. Thus, we could not perform a meta-analysis on compared studies. And, operative types for lumbar degenerative diseases in our studies were not completely consistent, which might also be one of the sources of heterogeneity.

Future research can focus on the following aspects. Firstly, when performing a meta-analysis on postoperative VTE, someone should include studies of the same operation method, anticoagulation regimen, and thrombus detection method. Secondly, we should conduct more prospective studies on efficacy and safety of low molecular weight heparin for VTE prophylaxis in these patients. Thirdly, multi-center and large sample randomized controlled trials on compared anticoagulation regimens are needed.

Conclusion

The prevalence of tDVT was significantly higher than that of sDVT and the prevalence of tPE was similar to the prevalence of sPE. Also, dDVT was more often happened than pDVT. Compared with patients routinely examined POD2 to POD3 for DVT, patients routinely ex-

amined POD7 to POD10 with Doppler ultrasound showed a significantly higher prevalence of tDVT or asymptomatic DVT. Obviously, the prevalence of sDVT or sPE was low with mechanical prophylaxis. Therefore, given the risk of neurologic deficit resulting from postoperative epidural hematomas related to pharmacologic prophylaxis, we recommended mechanical prophylaxis for patients after degenerative lumbar open surgery. Routinely postoperative examination with Doppler ultrasound for these patients should be recommended to find more asymptomatic DVT. Further prospective and high-quality compared studies should be carried out to find a better appropriate anticoagulation regime balancing efficacy and safety.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Yong Shen, Department of Spinal Surgery, The Third Hospital of Hebei Medical University, No. 139 Ziqiang Road, Shijiazhuang 050051, Hebei, People's Republic of China. Tel: 0086-0311-88602016; Fax: 0086-0311-87023626; E-mail: shenyongat430@sina.com

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