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REVIEW ARTICLE

High preoperative D-dimer increases the risk of venous thromboembolism after gynecological tumor surgeries: a meta-analysis of cohort studies

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Abstract

The role of preoperative D-dimer in the prediction of postoperative venous thromboembolism (VTE) with gynecological tumor remains unclear. This meta-analysis sought to assess the association between preoperative D-dimer and the risk of VTE after gynecological tumor surgeries and to identify prognostic significance of D-dimer in the prediction of postoperative VTE. This study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 statement. Eight electronic databases were searched for cohort studies from the date of inception to April 2024. The Newcastle-Ottawa Scale scoring tool and the Risk of Bias in Non-Randomized Studies–Intervention tool were used to assess the quality of the literature and the risk of bias in cohort studies, respectively. The relative risk and 95% CIs of the highest vs the lowest category and per milligram per liter of D-dimer were pooled relative to the VTE risk after gynecological tumor surgeries. Fifteen studies that met the criteria were included. Among these studies, D-dimer was considered as a continuous variable in 8 studies. The random-effect model results showed that the VTE risk was increased by 42% (15%-69%) per milligram per liter increase in D-dimer. Furthermore, based on the cutoff thresholds of D-dimer, 7 studies that reported the effect estimates of postoperative VTE in women with gynecological tumor by D-dimer were categorized as binary variables. Compared with the reference levels, the pooled relative risk of VTE after gynecological tumor surgeries for the higher level was 2.58 (95% CI, 1.49-4.47). Elevated preoperative D-dimer was associated with higher VTE risks after gynecological tumor surgeries.

KEYWORDS
cohort study, D-dimer, gynecological tumor, meta-analysis, venous thromboembolism

Zeyu Meng and Lu Liu contributed equally to this work and share the first authorship.

Essentials

- Association between D-dimer and postoperative venous thromboembolism (VTE) remains unclear.
- A meta-analysis of cohort studies was conducted from the date of inception to April 2024.
- Elevated preoperative D-dimer was associated with higher risks of postoperative VTE.
- Preoperative D-dimer is a potential indicator for occurrence of postoperative VTE.

1 | INTRODUCTION

Venous thromboembolism (VTE), including pulmonary embolism and deep vein thrombosis (DVT), is a common complication after gynecological tumor surgery. VTE is characterized by high incidence, disability, misdiagnosis, and mortality rates. Studies have shown that without intervention measures, the DVT incidence after gynecological surgery was approximately 9.2% to 40.0%. Among DVT patients, the most alarming and likely complication is pulmonary embolism, which can occur in up to 46.0% of cases [1]. In recent years, despite advancements in surgical techniques and improvements in surgical instruments, DVT remains the most common thrombotic complication following gynecological surgeries [2]. Compared with patients who underwent general surgery, patients with malignant tumors have a higher VTE risk. Surveys with widespread attention paid to VTE in recent years show that the incidence of VTE after gynecological tumor surgery has increased, with approximately 20.0% of them having cancer [3,4]. Meanwhile, VTE also interferes with the patient's nursing and chemotherapy plans, reduces quality of life, and increases the consumption of health resources [5]. Therefore, early predictive biomarkers of VTE in patients with gynecological tumors have long been sought to improve outcomes and help guide clinical decision-making [1].

D-dimer, a molecular complex formed from 2 cross-linked D fragments of fibrin, is a type of soluble fibrin degradation product [6]. It has been found in various tumor types, marking significant fibrinolysis during clot activation and fibrin formation reactions [7]. The coagulation process involves the transformation of blood from liquid to gel, subsequently resulting in clot formation. Fibrinolysis, the breakdown of fibrin, prevents blood clot formation. Thrombin promotes the dissociation of fibrinogen into fibrin monomers and provides a framework for the formation of activated coagulation factors and plasmin. Further, fibrin monomers, when combined with activated coagulation factors, create fibrin polymers with covalent bonds in the D-domain. Subsequently, plasmin degrades the cross-linked fibrin, releasing fibrin degradation products and exposing D-dimer antigens, resulting in D-dimer production [8,9]. In gynecological cancers, both the coagulation and fibrinolytic systems are overactivated. Consequently, elevated plasma D-dimer indicates the ongoing or potential formation of VTE [10].

Abnormal elevation of D-dimer is an important indicator of disseminated intravascular clotting. D-dimer offers a wide range of clinical applications, particularly in diagnosis and prognosis, due to its benefits, such as noninvasiveness, affordability, convenience, and rapid result generation [11]. Both coagulation and fibrinolysis systems are hyperactivated in gynecological cancers. Thus, the level of plasma D-dimer is also found to be elevated and associated with the formation of VTE [12]. Xu et al. [11] performed a meta-analysis to determine the association between plasma D-dimer and long-term survival in gynecological cancers, including ovarian, cervical, and endometrial carcinoma and observed that gynecological cancer patients with high D-dimer had a much lower 5-year survival rate and overall survival than those with low D-dimer. VTE has been reported as an important cause of postoperative death in patients with gynecological tumors. Whether there was a role of preoperative D-dimer in the prediction of postoperative VTE with gynecological tumors remains unclear. A prospective study involving 205 patients with gynecological cancer indicated that D-dimer may act as a potential biomarker in identifying the risk of VTE following gynecological cancer surgery [13]. Conversely, Ma et al. [14] reported that there was no association between D-dimer and risk of postoperative VTE in women with ovarian cancer. Samuelson Bannow and Konkle [15] reported that although D-dimer was associated with the risk of VTE, D-dimer only exhibited predictive value at very low or extremely high levels. Thus, a number of studies reported the relationship of D-dimer with postoperative VTE with gynecological tumor, but it has not been formally identified.

Therefore, this meta-analysis aimed to comprehensively and systematically evaluate the relationship between preoperative D-dimer and the incidence risk of VTE following gynecological tumor surgery in order to identify prognostic significance of D-dimer in the prediction of postoperative VTE with gynecological tumor.

2 | METHODS

2.1 | Search strategy

This study adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 statement for systematic reviews and meta-analyses [16]. A comprehensive search of scientific literature was performed across multiple databases, including PubMed, Elsevier, Cochrane Library, Web of Science, Sinomed (http://www.sinomed.ac.cn), Wanfang Data (http://www.wanfangdata.com.cn/index.html), China National Knowledge Infrastructure (http://www.cnki.net), and China Science and Technology Journal Database (http://www.cqvip.com) until April 2024. The following terms were utilized in the literature search: P(a): "Genital Neoplasms, Female," "Uterine Cervical Neoplasms," "Ovarian Neoplasms," "Endometrial

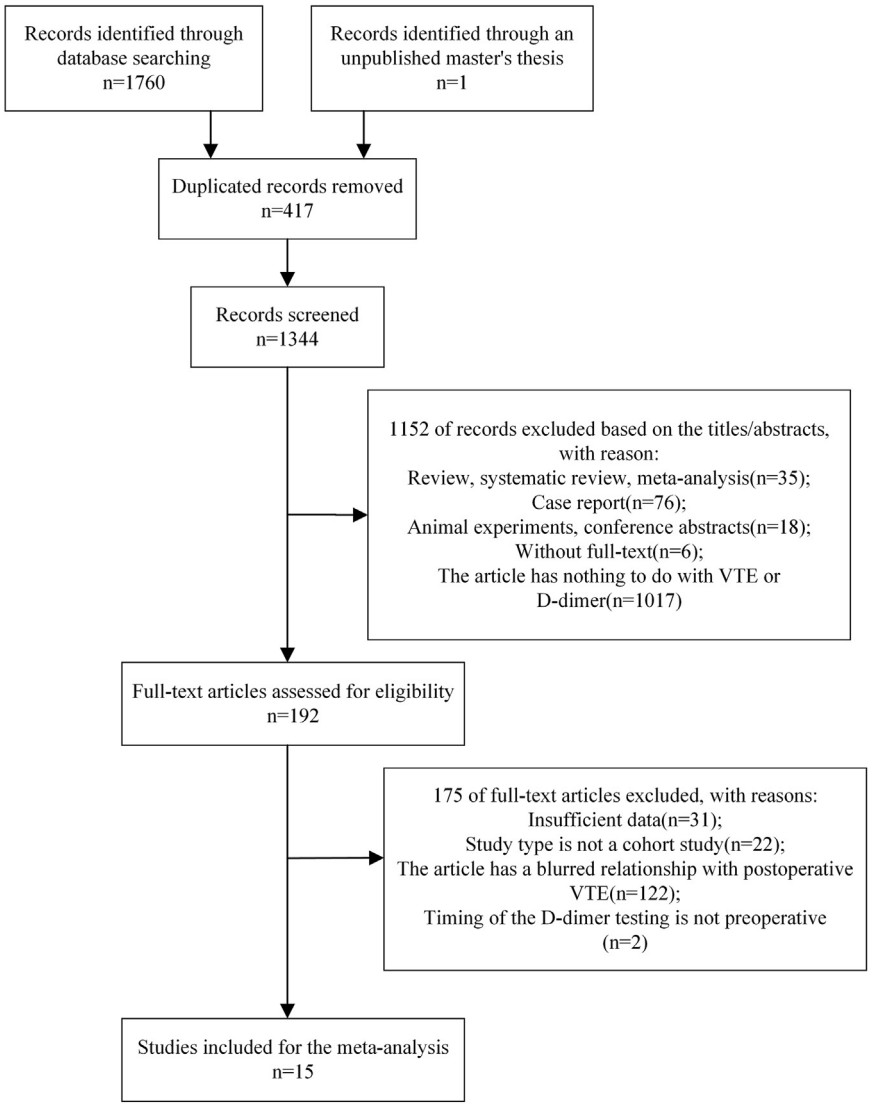

FIGURE 1 Flow diagram of study selection. VTE, venous thromboembolism.

Neoplasms," "Sarcoma, Leiomyoma," "Gynecologic Surgical Procedures"; P(b): "Venous Thrombosis"; I: "Fibrin Fibrinogen Degradation Products"; and C: "Ultrasonography, Doppler, Color" (Supplementary Text S1).

2.2 | Inclusion criteria and study selection

The studies included in this meta-analysis met the following criteria: (1) studies reporting on the association between D-dimer and VTE after gynecological tumor surgery; (2) involving cohort participants without minimum follow-up limitations; and (3) with sufficient data available to calculate relative risks (RRs) with 95% CIs for assessing the VTE risk after gynecological tumor surgery. Studies that did not provide initial data, animal studies, case reports, conference abstracts, letters, guidelines, reviews, and systematic reviews were excluded. Additionally, D-dimer measured after surgery was also excluded. Two investigators independently screened all potentially eligible studies and resolved any discrepancies through discussion until a consensus was reached.

2.3 | Data extraction and assessment of study bias

All relevant studies were systematically reviewed, and the following items were extracted: first author, publication year, country, study sample size, mean age, variable type of D-dimer, D-dimer concentration, D-dimer measurement method, number of patients (VTE/non-VTE), tumor type, operation method, diagnostic criteria of VTE, and effect size RRs and 95% CIs for the most adjusted model. The quality of the literature was evaluated using the Newcastle-Ottawa Scale (NOS) scoring tool. The NOS assigns up to a maximum of 9 points for the least risk of bias in 3 domains: 1) selection of study groups (4 points); 2) comparability of groups (2 points); and 3)

TABLE 1 Characteristics of included studies on D-dimer and risk of venous thromboembolism after gynecological tumor surgeries.

Included studies (author, year)	Study sample	Type of VTE	Age (y), mean or median	Tumor type	No. of patients (VTE/non-VTE)	D-dimer (mg/L), mean ± SD or median (range)	NOS score
Y. Zhang/2023 [19]	137	DVT	VTE: 60.48 ± 8.34 Non-VTE: 54.79 ± 12.68	Ovarian cancer	25/112	VTE: 7.16 ± 6.51 Non-VTE: 3.33 ± 4.34	7
Y. Du/2023 [20]	227	DVT	VTE: 51.96 ± 6.85 Non-VTE: 48.42 ± 6.51	Gynecological malignancy	29/198	VTE: <0.5: 15 (51.72); ≥0.5: 14 (48.28) Non-VTE: <0.5: 145 (73.23); ≥0.5: 53 (26.77)	8
Y. Wang/2022 [21]	208	DVT, PE	VTE: 57.3 (34-83) Non-VTE: 52.6 (23-83)	Ovarian cancer	31/177	VTE: 4.5 (1.9-6.2) Non-VTE: 3.1 (1.0-3.9)	8
Q. Zhou/2022 [22]	233	DVT, PE	VTE: 65 (51-76) Non-VTE: 53 (15-77)	Ovarian cancer	17/216	VTE: 6.2 ± 3.9 Non-VTE: 4.5 ± 3.4	7
G. Wang/2022 [23]	211	DVT	VTE: 51.92 ± 16.88 Non-VTE: 45.52 ± 17.01	Gynecological malignancy	26/185	VTE: <0.5: 14 (53.80) ≥0.5: 12 (46.20) Non-VTE: <0.5: 127 (68.60) ≥0.5: 58 (31.40)	7
H. Ma/2022 [14]	380	DVT, PE	VTE: 59.2 ± 15.0 Non-VTE: 51.1 ± 13.6	Ovarian cancer	52/328	VTE: 1.6 ± 0.4 Non-VTE: 1.2 ± 0.4	8
H. Liang/2022 [24]	493	DVT	VTE: 61.5 ± 4.4 Non-VTE: 58.3 ± 3.2	Myoma of uterus	41/452	VTE: 0.53 ± 0.04 Non-VTE: 0.51 ± 0.03	7
Q. Tian/2021 [2]	355	DVT	VTE: <50: 7 (17.07%); ≥50: 34 (82.93%) Non-VTE: <50: 227 (72.29%); ≥50: 87 (27.71%)	Gynecological malignancy	41/314	VTE: <0.5: 5 (12.20%); ≥0.5: 36 (87.80%) Non-VTE: <0.5: 211 (67.20%); ≥0.5: 103 (32.80%)	8
P. Mu/2021 [25]	98	DVT	NA	Cervical cancer	22/76	VTE: 1.48 ± 0.13 Non-VTE: 0.34 ± 0.08	6
Q. Zhou/2020 [26]	233	DVT, PE	VTE: 65 (51-76) Non-VTE: 53 (15-77)	Ovarian cancer	10/223	VTE: 7.5 ± 7.5 Non-VTE: 2.5 ± 2.9	7
H. Komatsu/2020 [13]	205	DVT, PE	NA	Gynecological malignancy	35/170	VTE: <1.0: 9; ≥1.0: 26 Non-VTE: <1.0: 78; ≥1.0: 92	5
X. Zhang/2020 [27]	51	DVT, PE	VTE: 62.12 ± 10.37 Non-VTE: 54.68 ± 9.49	Ovarian cancer	17/34	VTE: 8.44 (5.61, 17.2) Non-VTE: 3.11 (2.20, 3.76)	7
Q. Zhou/2019 [28]	282	DVT, PE	VTE: 55.31 ± 5.67 Non-VTE: 50.94 ± 6.15	Ovarian cancer	113/169	VTE: 3.69 ± 1.23 Non-VTE: 2.14 ± 0.96	8

(Continues)

TABLE 1 (Continued)

Included studies (author, year)	Study sample	Type of VTE	Age (y), mean or median	Tumor type	No. of patients (VTE/non-VTE)	D-dimer (mg/L), mean ± SD or median (range)	NOS score
K. Nakamura/2016 [29]	129	DVT, PE	VTE: <60: 23 (41.8); ≥60: 32 (58.2) Non-VTE: <60: 43 (58.1); ≥60: 31 (41.9)	Cervical cancer	6/123	VTE: <1.0: 0; ≥1.0: 6 Non-VTE: <1.0: 74; ≥1.0: 49	6
X. Wu/2013 [30]	183	DVT, PE	NA	Ovarian cancer	13/170	VTE: ≥0.788: 6; >0.788: 6; missing: 1 Non-VTE: ≥0.788: 122; >0.788: 35; missing: 13	6

DVT, deep vein thrombosis; NA, not available; NOS, Newcastle-Ottawa Scale [17]; PE, pulmonary embolism; VTE, venous thromboembolism.

ascertainment of exposure and outcomes (3 points) for cohort studies [17]. Moreover, the risk of bias in cohort studies was assessed using the Risk of Bias in Non-Randomized Studies–Interventions tool [18]. The risk of bias was categorized as "low," "moderate," "serious," and "critical." Two authors independently followed the aforementioned steps, and any discrepancies were resolved through deliberation to achieve consensus.

2.4 | Statistical analysis

This meta-analysis aimed to assess the predictive value of D-dimer for VTE following gynecological tumor surgery. Continuous variables of D-dimer were pooled using effect sizes per milligram per liter, whereas binary variable studies were classified based on the cutoff thresholds of D-dimer. As all included studies were cohort designs, RRs representing the ratio of D-dimer in patients with VTE compared with those without VTE were chosen as the effect size. Random- and fixed-effects models were employed for pooling, ensuring robust statistical analysis. The association between D-dimer and VTE after gynecological tumor surgery was elucidated by presenting a pooled RR with 95% CIs. I^2 statistics were used to assess heterogeneity, where an I^2 value of >50% or $P < .05$ indicated significant heterogeneity. Sensitivity and subgroup analyses were performed to explore potential sources of heterogeneity, including the tumor type, operation method, VTE diagnostic criteria, measurement method of D-dimer, and cutoff thresholds of D-dimer. Funnel plots were utilized to evaluate publication bias. All statistical analyses were performed using Stata 17.0 by StataCorp LLC.

3 | RESULTS

Figure 1 outlines our search and selection process and illustrates the detailed population selection criteria in the original studies. A total of 1760 related articles were pooled from electronic databases, and 1 unpublished master's thesis was also included. A total of 417 duplicate articles were excluded. After reviewing the titles and abstracts, 1152 articles were excluded, leaving 191 articles to be read in full. Ultimately, 15 studies met the predefined inclusion and exclusion criteria and were included in this meta-analysis.

3.1 | Study characteristics and risk of bias

The typical characteristics and data of the included studies are presented in Tables 1 and 2 [2,13,14,19–30], respectively, and other findings of these studies are also summarized in Supplementary Table S1. A total of 15 cohort studies were included, involving a pool of 4041 participants. Among these studies, D-dimer was considered a continuous variable in 8 studies and a binary variable in the remaining 7. The quality assessment of these studies was conducted using the NOS scale, indicating that all studies achieved a

TABLE 2 Relative risk of venous thromboembolism after gynecological tumor surgeries for D-dimer and some other characteristics.

Included studies (author, year)	Risk estimates on the basis of D-dimer	RR (95% CI)	*P* value	Prospective/ retrospective cohort study	Follow-up time	Timing of the D-dimer testing
Y. Zhang/2023 [19]	Per mg/L	1.091 (1.007-1.175)	.04	Retrospective cohort study	NA	Preoperative
Y. Du/2023 [20]	Highest quartile (>0.5 mg/L) vs lowest (<0.5 mg/L)	5.272 (2.312-12.021)	<.05	Retrospective cohort study	NA	Preoperative
Y. Wang/2022 [21]	Per mg/L	1.144 (1.020-1.283)	.02	Retrospective cohort study	6 mo	Preoperative
Q. Zhou/2022 [22]	Highest quartile (>4.215 mg/L) vs lowest (<4.215 mg/L)	1.182 (1.006-1.387)	.04	Prospective cohort study	NA	Preoperative
G. Wang/2022 [23]	Highest quartile (>0.5 mg/L) vs lowest (<0.5 mg/L)	2. 353 (1.443-8.375)	.04	Retrospective cohort study	NA	Preoperative
H. Ma/2022 [14]	Per mg/L	0.452 (0.170-1.201)	.11	Retrospective cohort study	NA	Preoperative
H. Liang/2022 [24]	Per mg/L	4.141 (1.925-8.909)	.00	Retrospective cohort study	4 y	Preoperative
Q. Tian/2021 [2]	Highest quartile (>0.5 mg/L) vs lowest (<0.5 mg/L)	3.914 (1.083-5.229)	.008	Retrospective cohort study	NA	NA
P. Mu/2021 [25]	Per mg/L	2.054 (1.349-3.128)	.008	Retrospective cohort study	NA	NA
Q. Zhou/2020 [26]	Per mg/L	1.182 (1.006-1.387)	.04	Retrospective cohort study	NA	Preoperative
H. Komatsu/2020 [13]	Highest quartile (>1.0 mg/L) vs lowest (<1.0 mg/L)	2.45 (1.083-5.538)	.03	Prospective cohort study	3 mo	Preoperative
X. Zhang/2020 [27]	Per mg/L	2.227 (1.342-3.694)	<.001	Retrospective cohort study	NA	NA
Q. Zhou/2019 [28]	Per mg/L	2.946 (1.983-11.307)	.009	Retrospective cohort study	30 d	NA
K. Nakamura/2016 [29]	Highest quartile (>1.0 mg/L) vs lowest (<1.0 mg/L)	2.33 (1.121-5.504)	.04	Retrospective cohort study	NA	Preoperative
X. Wu/2013 [30]	Highest quartile (>0.788 mg/L) vs lowest (<0.788 mg/L)	3.49 (1.06-11.49)	.04	Retrospective cohort study	5 mo	Preoperative

NA, not available; RR, relative risk.

medium-to-high level of quality, with an average score of 7. Furthermore, an evaluation regarding the risk of bias was performed using the Risk of Bias in Non-Randomized Studies–Interventions tool, which indicated that all studies exhibited either a moderate or severe risk of bias. Detailed results from this risk-of-bias assessment are shown in Figure 2.

3.2 | Association between D-dimer as a continuous variable and VTE

D-dimer in 8 studies was considered a continuous variable between per milligram per liter increase. Figure 3 presents the random-effects model results, ie, the risk of VTE was significantly increased by 42% (15%-69%) per milligram per liter increase in D-dimer after gynecological tumor surgery (RR, 1.39; 95% CI, 1.15-1.69; $P < .001$), with substantial heterogeneity ($I^2 = 79.7\%$; $P < .001$).

3.3 | Association between D-dimer as a binary variable and VTE

Based on the diverse cutoff thresholds of D-dimer, 7 studies reported that the effect estimates of VTE after gynecological tumor surgeries by D-dimer were categorized as binary variables. Figure 4 indicates that compared with the reference levels, the random-effects model also showed that elevated D-dimer significantly increased the VTE risk after gynecological tumor surgery (high vs low: RR, 2.58; 95% CI, 1.49-4.47; $P < .001$), with substantial heterogeneity (high vs low: $I^2 = 78.4\%$; $P < .001$).

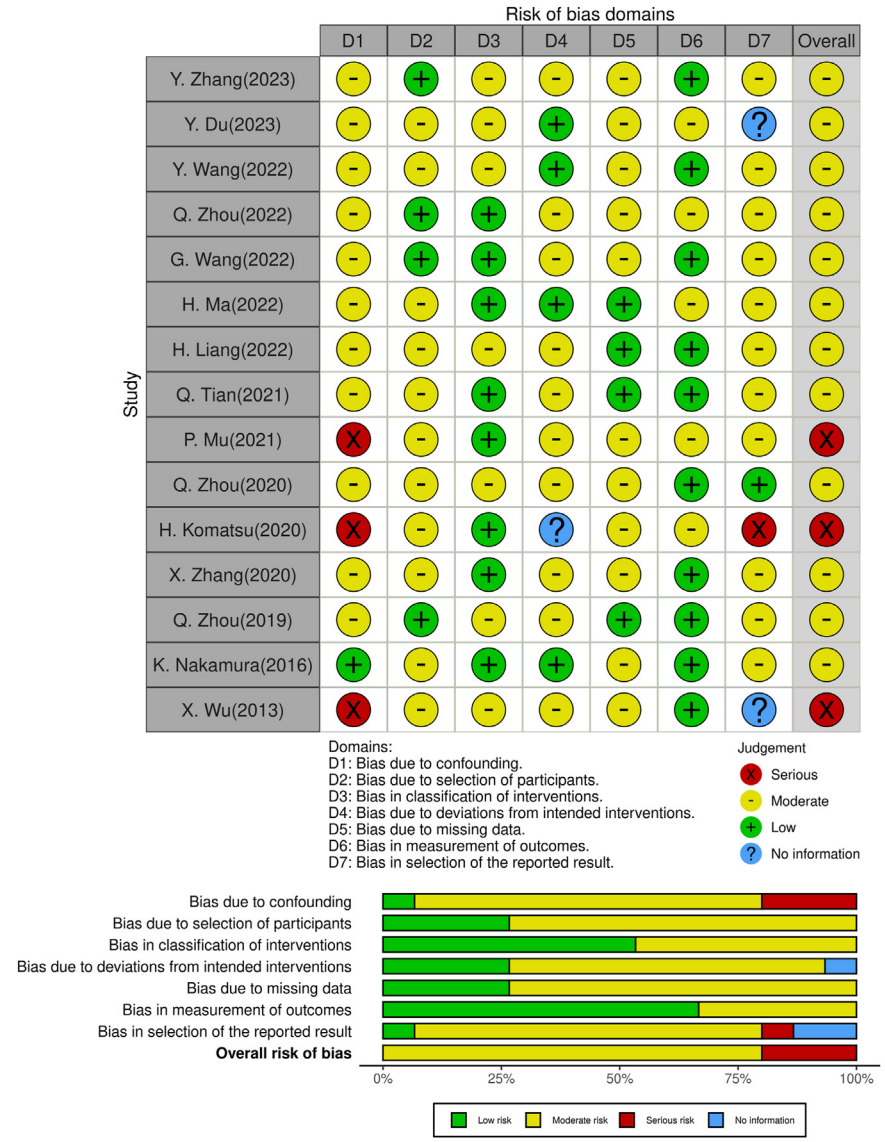

FIGURE 2 Using the Risk of Bias in Non-Randomized Studies–Intervention tool to assess the risk of bias in cohort studies.

3.4 | Subgroup analysis

Substantial heterogeneity still existed among the included continuous variables (I^2 = 79.7%; $P < .001$; Figure 3). To investigate the sources of heterogeneity, subgroup analyses were conducted to evaluate the impact of the tumor type, type of VTE, time of D-dimer testing, method of operation, diagnostic criteria of VTE, and the measurement method of D-dimer. The results showed that subgroup analyses by these classifications resulted in the highest level of I^2 decline in patients with postoperative VTE diagnostic criteria using Doppler ultrasound (RR, 1.12; 95% CI, 1.05-1.19; I^2 = 0.0%; P = .61), those undergoing laparoscopic surgery (RR, 3.57; 95% CI, 2.01-6.34; I^2 = 0.0%; P = .57), and those that did not specify the time of D-dimer testing (RR, 2.21; 95% CI, 1.63-2.99; I^2 = 0.0%; P = .77), indicating that these are likely the main sources of heterogeneity (Figure 5, Supplementary Figure S1, and Supplementary Table S2). No statistically or clinically significant differences were observed in the other subgroup results.

Furthermore, subgroup analysis of binary variables was indicated based on the tumor type, type of VTE, method of operation, cutoff threshold of D-dimer, and diagnostic criteria of VTE. The results showed that subgroup analysis by these classifications resulted in the highest level of I^2 decline in patients with gynecological malignancy (RR, 3.35; 95% CI, 2.21-5.05; I^2 = 0.0%; P = .48), with DVT as the type of VTE (RR, 3.72; 95% CI, 2.31-6.00; I^2 = 0.0%; P = .42), those undergoing laparoscopic surgery (RR, 3.72; 95% CI, 2.31-6.00; I^2 = 0.0%; P = .42), and for those with a D-dimer threshold of 0.5 mg/L (RR, 3.72; 95% CI, 2.31-6.00; I^2 = 0.0%; P = .42), indicating that these are likely the main sources of heterogeneity (Figure 6, Supplementary Figure S2, and Supplementary Table S2). No statistically or clinically significant differences were observed in the other subgroup results.

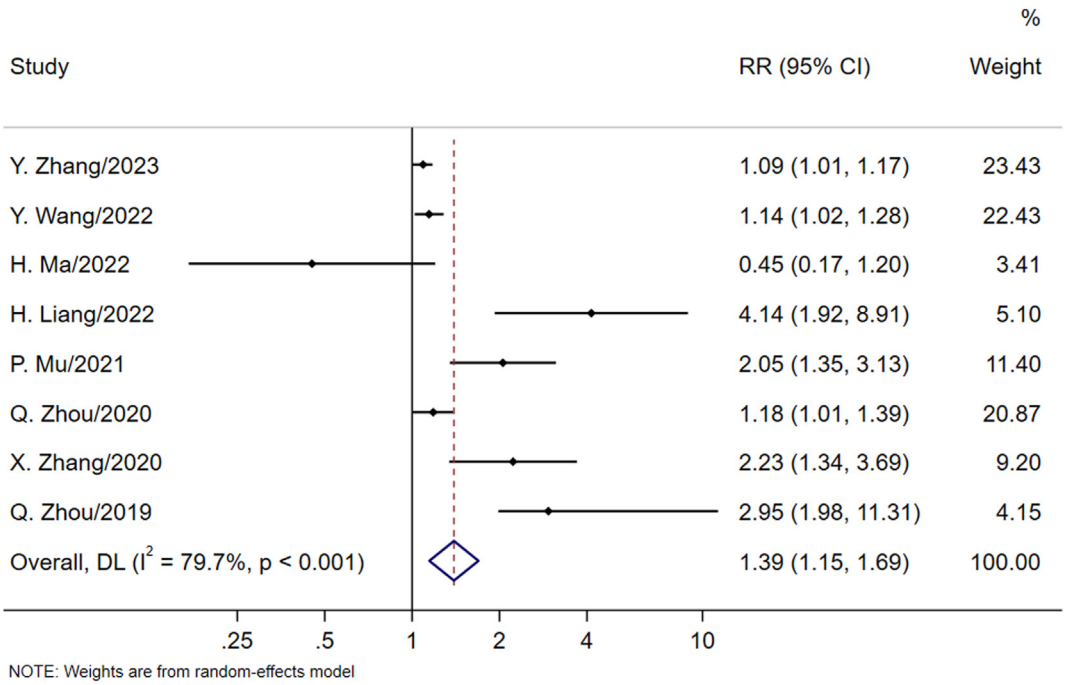

FIGURE 3 Forest plot of the relationship between the continuous variable D-dimer and venous thromboembolism. DL, DerSimonian-Laird; RR, relative risk.

3.5 | Sensitivity analysis and publication bias

The sensitivity analysis indicated that 95% CIs for both continuous and binary variables exceeded unity across all datasets, aligning with the original aggregate study outcomes. However, RR values varied among data groups, indicating a moderate level of result stability (Supplementary Figure S3). The funnel analysis revealed essentially no publication bias in the data for continuous and binary variables (Supplementary Figure S4).

4 | DISCUSSION

In this comprehensive meta-analysis of 15 studies, a comprehensive and quantitative evaluation of the association between preoperative D-dimer and incidence risk of postoperative VTE was first performed in patients with gynecological tumors. Elevated preoperative D-dimer was found to be significantly associated with an increased VTE risk after gynecological tumor surgery. Overall, the VTE risk was increased by 42% per milligram per liter increase in the D-dimer.

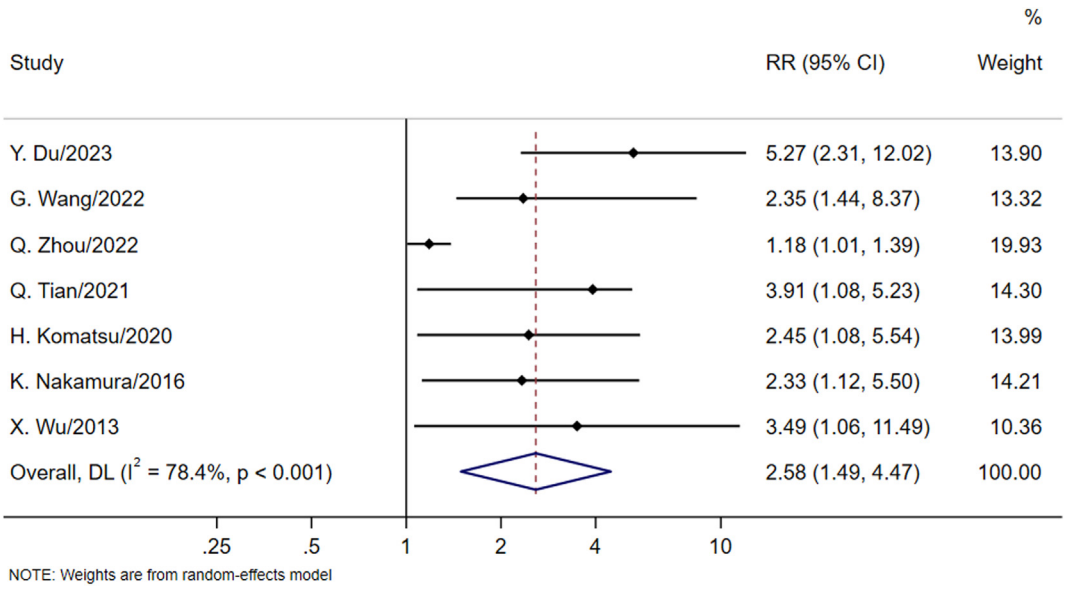

FIGURE 4 Forest plot of the relationship between D-dimer as a binary variable and venous thromboembolism. DL, DerSimonian-Laird; RR, relative risk.

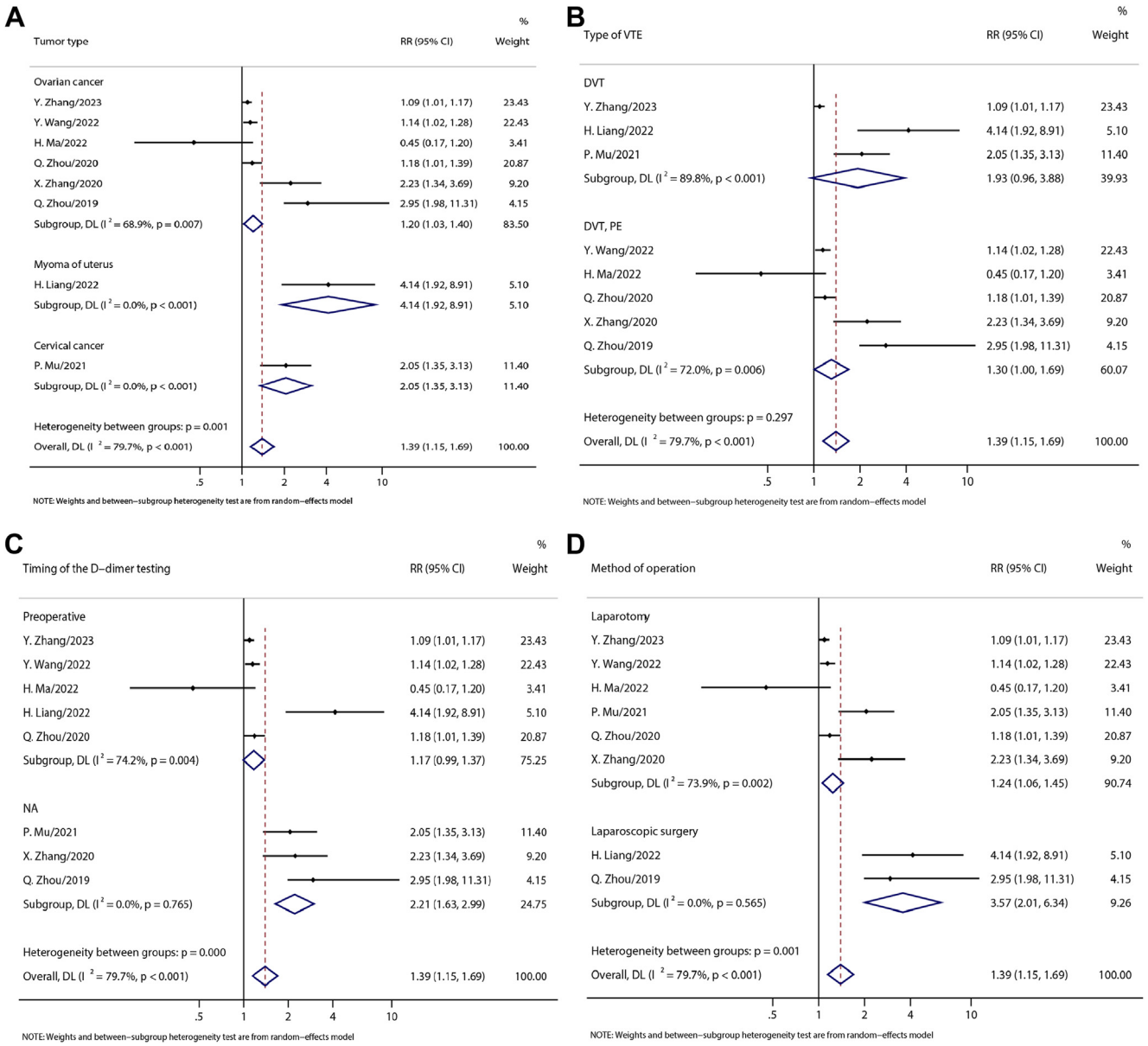

FIGURE 5 Subgroup analysis of continuous variables. DVT, deep vein thrombosis; DL, DerSimonian-Laird; PE, pulmonary embolism; RR, relative risk; VTE, venous thromboembolism.

Our study findings are robust and rigorous. A total of 4401 patients with gynecologic tumors were evaluated, significantly enhancing the statistical power to detect potential correlations. To our knowledge, this is the first meta-analysis on the predictive role of preoperative D-dimer in patients with gynecological tumors after surgery. Furthermore, the quality of studies was assessed using NOS, with the majority of studies included in this meta-analysis (15 studies) being of high quality (score, ≥6; full score, 9), ensuring precise and reliable results. Moreover, a high degree of consistency was observed between continuous and categorical analyses. Finally, by thoroughly analyzing multiple dimensions such as types of VTE and gynecological tumors, diagnostic criteria of VTE, measurement method of D-dimer, operation method, and cutoff thresholds of D-dimer, the study extensively explores how these factors impact the potential value of D-dimer in predicting postoperative VTE risk, marking its significance in assessing the clinical prognosis of patients.

Although no meta-analysis evaluated the association between D-dimer and VTE risk in patients with gynecological tumors, several studies have assessed the predictive value of D-dimer in cancer prognosis. Li et al. [31] pooled 19 eligible cohort studies showing that elevated circulating blood D-dimer was associated with an increased risk of death in patients with lung cancer (hazard ratio, 1.62; 95% CI, 1.39-1.88). Another meta-analysis [11] further observed gynecological cancer patients with high D-dimer and demonstrated a much lower 5-year survival rate than those with low D-dimer (RR, 4.12; 95% CI, 3.04-5.58; $P < .00001$). VTE is an important predictive factor of postoperative death in patients with tumors; thus, several studies have explored its association with VTE. Yang et al. [32] pooled 10

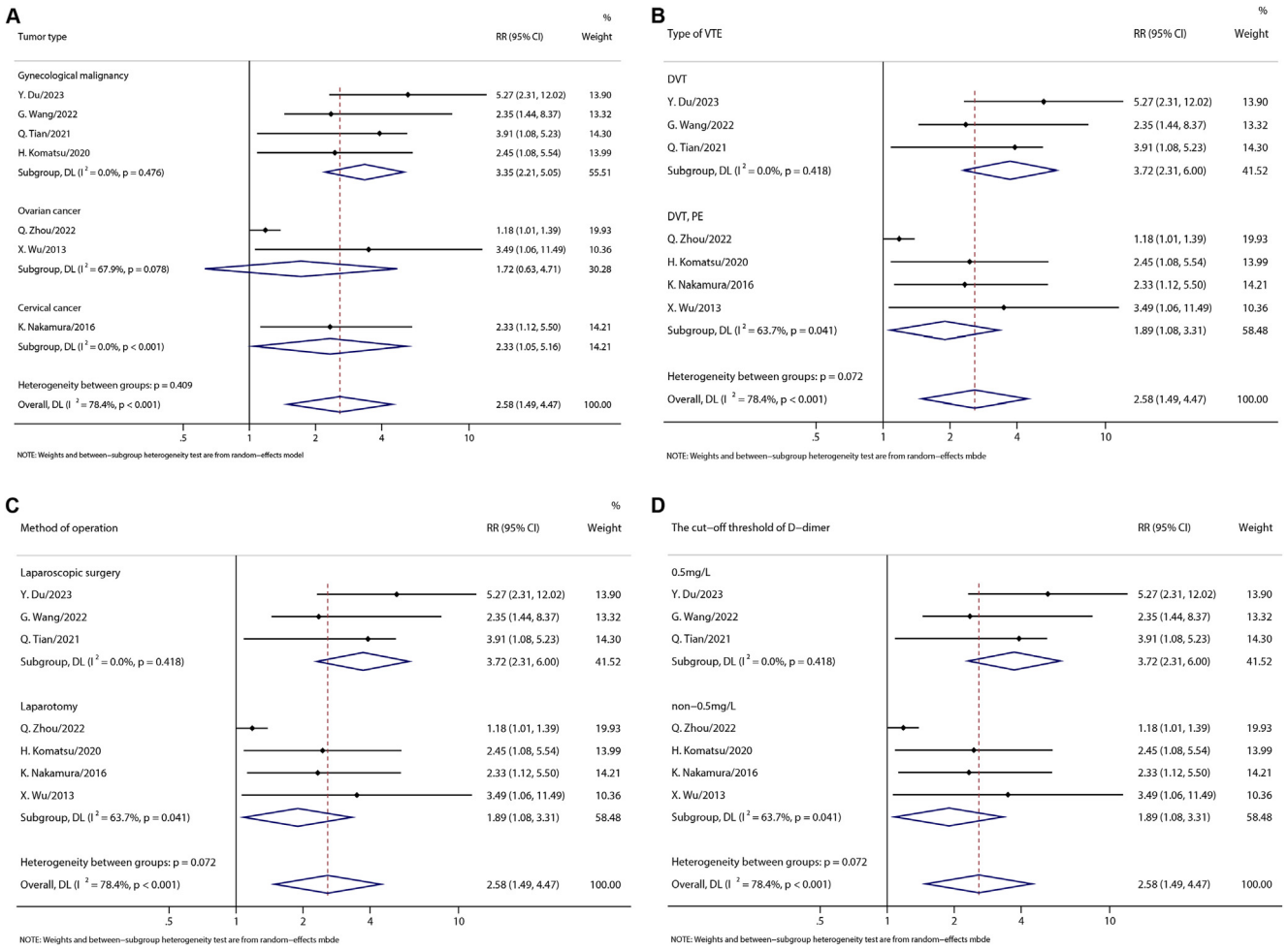

FIGURE 6 Subgroup analysis of binary variables. DVT, deep vein thrombosis; DL, DerSimonian-Laird; PE, pulmonary embolism; RR, relative risk; VTE, venous thromboembolism.

studies and found that an elevated D-dimer was a predictive risk of cancer-associated VTE (hazard ratio, 1.85; 95% CI, 1.44-2.39). Our findings are consistent with those results and demonstrate that D-dimer might serve as a reliable predictor of VTE in patients with gynecological tumors postoperatively. Previous studies were inconsistent, maybe due to the type of tumor, time of D-dimer detection, and the type of VTE. Our meta-analysis indicated that preoperative D-dimer increased the risk of postoperative VTE, which may be associated with a worse prognosis and an increased risk of death. Prediction models have been proposed to establish the recurrence risk of idiopathic or unprovoked VTE in patients who have completed anticoagulant therapy. It was reported that sex, age, type, and D-dimer were included in 47% (8/17) of VTE prediction models [33]. Therefore, taking appropriate measures to reduce D-dimer not only reduces VTE risk but also helps improve the prognostic outcomes of gynecological tumors. In clinical practice, the measurement of serum preoperative D-dimer may often be performed as a simple screening test for postoperative VTE.

D-dimer is a small protein fragment produced during the fibrinolysis process. Normally, the coagulation and dissolution of blood within the human body are in balance. Elevated D-dimer generally reflects the activation of the blood coagulation system, typically indicating an increase in thrombus formation and fibrinolytic activity. The blood coagulation process, including platelet aggregation and fibrin formation, is a critical step in thrombogenesis. Fibrin, as a major component of thrombi, accumulates within blood vessels to form clots, sometimes leading to vascular obstruction. Following thrombus formation within the body, the fibrinolytic system is activated to break down these clots. As a product of fibrinolysis, increased D-dimer signifies fibrin degradation, indicating ongoing thrombus formation and dissolution processes. Consequently, an elevated D-dimer is a significant indicator of increased VTE risk, signifying active blood coagulation and fibrinolysis within the body [9]. Hence, specific biological mechanisms by which D-dimer contributes to VTE occurrence require further exploration through more in-depth studies and larger sample sizes, which are crucial for enhancing scientific depth and improving patient prognosis [11,34].

Some limitations are inevitable in this meta-analysis. First, this study included substantially heterogeneous results of continuous variables. Subgroup analysis indicated that the source of this

heterogeneity may be related to gynecologic tumor types, operation methods, and diagnostic criteria for VTE. Second, due to the inability to extract data from certain studies, not all study items were included, potentially increasing the risk of bias. In addition, the studies included in this meta-analysis were from China and Japan; thus, the generalizability to other areas was limited. Lastly, due to limited information, factors such as other coagulation, nonmalignant, type of chemotherapy, and tumor staging were not assessed.

5 | CONCLUSIONS

High D-dimer increases the VTE risk after gynecological tumor surgeries. Therefore, D-dimer can be considered a potential indicator for incidence risk of postoperative VTE in patients with gynecological tumors, which will not only help to screen high risk of postoperative VTE but also streamline patient management strategies, thereby potentially improving clinical outcomes.

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AUTHOR CONTRIBUTIONS

Z.M. and X.Y. contributed to the conception and design of the study; L.L. critically revised the manuscript; Y.X. and Q.Y. contributed to data collection; Z.M. and X.H. analyzed and interpreted the data; Z.M. drafted the article; Y.L. revised the manuscript critically for important intellectual content; and J.L. and D.W. designed the study, conducted the study, and reviewed the manuscript. All authors participated in data interpretation, review, and approval of the final manuscript.

RELATIONSHIP DISCLOSURE

There are no competing interests to disclose.

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SUPPLEMENTARY MATERIAL

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