Risk Factors for Postoperative Venous Thromboembolism in Patients With Gynecologic Malignancies

A Meta-analysis

Tingting Zhang, BSc, Zhuoxia Chen, BSc,* and Haina Fu, BSc†*

Abstract: To systematically evaluate the risk factors for postoperative complications of venous thromboembolism in patients with gynecologic malignancies. Cohort studies and case-control studies on the risk factors of postoperative venous thromboembolism in gynecologic malignancy patients were included in the search of China Knowledge, Wanfang, Wipro, China Biomedical Literature Database, PubMed, Cochrane Library, Embase, and Web of Science databases from inception to March 2025, and were analyzed. Studies. Data were statistically analyzed using RevMan 5.2 software. A total of 19 studies involving 123,329 patients with gynecologic malignancies were included. The analysis showed that advanced age (OR = 3.08, 95% CI = 2.85-3.32, $P < 0.00001$), open surgery (OR = 9.18, 95% CI = 2.38-35.34, $P = 0.001$), high surgical complexity (OR = 9.97, 95% CI = 5.80-17.15, $P < 0.00001$), and surgical duration (OR = 3.33, 95% CI = 2.97-3.73, $P < 0.00001$), high BMI (OR = 4.77, 95% CI = 3.47-6.57, $P < 0.00001$), comorbidities (OR = 21.02, 95% CI = 8.72-50.70, $P < 0.00001$), and prolonged bed rest in the postoperative period (OR = 25.16, 95% CI = 10.32-61.32, $P < 0.00001$), high intraoperative bleeding (OR = 107.53, 95% CI = 17.71-652.85, $P < 0.00001$), and high D-dimer level (OR = 5.55, 95% CI = 3.27-9.43, $P < 0.00001$), advanced tumor stage (OR = 7.58, 95% CI = 2.22-25.90, $P = 0.001$), high tumor grade (OR = 27.67, 95% CI = 8.39-91.18, $P < 0.00001$), and occurrence of lymph node metastasis (OR = 31.21, 95% CI = 9.54-102.15, $P < 0.00001$) were all were risk factors for postoperative venous thrombosis in patients with gynecologic malignancies. Clinical staff should take into account the 12 risk factors identified in this study to actively identify gynecologic malignant tumor patients at high risk for venous thromboembolism after surgery and provide targeted measures to prevent or reduce the risk of postoperative DVT.

Key Words: venous thromboembolism, gynecologic malignancy, risk factors, meta-analysis

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The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). As this study involves the summary and analysis of other studies, it does not involve medical ethics approval or patient-informed consent.

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Venous thromboembolism (VTE), including deep venous thrombosis (DVT) and pulmonary thromboembolism (PE), is a common and serious postoperative complication in patients with gynecologic malignancies. Due to the lymphatic drainage involving direct contact between pelvic-growing gynecologic tumors and lower-extremity vessels, women with gynecologic cancers have a significantly higher incidence of VTE compared with other cancers.[1] Relevant studies indicate that the postoperative incidence of DVT in gynecologic malignancy patients is as high as 26%, while postoperative PE reaches up to 9%.[2] Notably, existing research has predominantly focused on independent risk factors for DVT, whereas comprehensive risk assessment studies encompassing both DVT and PE remain relatively insufficient.[3] This research bias may lead to inadequate prevention of PE, a potentially fatal complication, in clinical practice. According to the latest statistics, postoperative PE in gynecologic cancer patients carries a mortality rate as high as 18% to 20%,[4] underscoring the necessity for a thorough evaluation of VTE risk factors.

Recent studies have confirmed that the pathogenesis of postoperative venous thromboembolism (VTE) in patients with gynecologic malignancies has unique characteristics. Tumor cells can directly activate the coagulation system by releasing tissue factors and procoagulant substances, while factors such as surgical trauma, chemotherapy, and hormone therapy further exacerbate the hypercoagulable state.[5] Multiple studies have shown that advanced tumor stage (FIGO III-IV), prolonged surgery (> 3 h), significant intraoperative blood loss (> 500 mL), and persistently elevated postoperative D-dimer levels are independent risk factors for VTE.[6,7] Notably, compared with isolated deep vein thrombosis (DVT), the occurrence of pulmonary embolism (PE) exhibits a stronger correlation with tumor metastasis, cardiovascular comorbidities, and specific genetic polymorphisms.[8] These findings suggest that the risk factor profile for VTE may be more complex than that for DVT alone.

Therefore, this study is the first to systematically evaluate the overall risk factors for postoperative VTE (including DVT and PE) in gynecologic cancer patients through a meta-analysis, aiming to provide clinicians with a more comprehensive VTE risk assessment tool. This will facilitate individualized prevention strategies, ultimately reducing the incidence and mortality of VTE.

METHODS

Inclusion and Exclusion Criteria

Inclusion criteria:

(1) Cohort studies or case-control studies published in Chinese or English only;
(2) Patients with gynecologic malignancies confirmed by histopathologic examination and undergoing gynecologic surgery;
(3) Patients diagnosed with DVT and/or PE after gynecologic surgery via vascular color Doppler ultrasound, CT, or pulmonary CTA;
(4) Studies employing multivariate logistic regression analysis to identify risk factors for postoperative VTE in patients undergoing gynecologic surgery for malignancies, including age, surgical approach, surgical complexity, operative time, BMI, comorbidities, postoperative bed rest duration, intraoperative blood loss, D-dimer levels, tumor stage, tumor grade, and lymph node metastasis, and providing odds ratios (ORs) with 95% CIs for these risk factors, or allowing data conversion and application.

Exclusion criteria:
(1) Studies with insufficient data, duplicate publications, or unavailable full texts;
(2) Reviews, conference abstracts, case reports, or animal studies.

Search Strategy

Computerized searches were conducted in the following databases: China National Knowledge Infrastructure (CNKI), Wanfang, VIP, China Biology Medicine (CBM), PubMed, Cochrane Library, Embase, and Web of Science. The search period spanned from inception to March 2025. The search terms included "Thrombosis" OR "Venous thrombus" OR "Deep vein thrombosis" OR "Pulmonary thromboembolism," "Gynecological malignancies" OR "Gynecological oncology" OR "Cervical carcinoma" OR "Endometrial carcinoma" OR "Oophoroma." A combination of Medical Subject Headings (MeSH) terms and free-text keywords was employed. In addition, the references of included studies were manually screened. The English search strategy for PubMed is as follows: ((((Thrombosis[MeSH Terms]) OR (venous thrombus[Title/Abstract])) OR (Deep vein thrombosis[Title/Abstract])) OR (pulmonary thromboembolism[Title/Abstract])) AND (((((((Cervical tumor [Title/Abstract]) OR (Endometrial tumor[Title/Abstract])) OR (ovarian tumor[Title/Abstract])) OR (Gynecologic malignancies[Title/Abstract])) OR (gynecologic oncology [Title/Abstract])) OR (cervical carcinoma[Title/Abstract])) OR (endometrial carcinoma[Title/Abstract])) OR (oophoroma[Title/Abstract])).

Literature Screening and Data Extraction

The literature screening process began with automatic deduplication using the NoteExpress computerized literature management system. After deduplication, preliminary screening was conducted by reviewing titles and abstracts. Subsequently, full texts were examined to exclude studies that did not meet the inclusion criteria. Data extraction was performed independently by 2 researchers based on the inclusion and exclusion criteria, with discrepancies resolved by a third researcher. Extracted data included authors, publication year, country, study type, number of cases in the venous thrombosis and nonvenous thrombosis groups, and risk factors, among others.

Literature Quality Assessment

Two researchers independently and impartially conducted literature retrieval, selection, and data extraction according to predefined inclusion and exclusion criteria. A data extraction template was designed to facilitate the pre-extraction process, ensuring the integrity of the raw data. The 2 researchers independently assessed the quality of the included cohort or case-control studies using the Newcastle-Ottawa Scale (NOS).[9] Discrepancies in quality assessment were resolved through consultation with an internal evidence-based research team. The NOS framework is designed to evaluate the quality of nonrandomized studies in meta-analyses, comprising 2 sections for assessing cohort and case-control studies. It includes 3 domains: selection of study groups, comparability of groups, and ascertainment of exposure or outcome, culminating in a composite score out of 9. If the 2 researchers disagreed in their evaluations, a third researcher was consulted to reach a final decision.

Statistical Methods

The analysis was performed using RevMan 5.2 statistical software, with clinical heterogeneity assessed by the I^2 test. When $P \geq 0.05$ and $I^2 < 50\%$, it indicated no statistical heterogeneity among the studies, and a fixed-effects model was applied for the meta-analysis. Conversely, if statistical heterogeneity was present, the source of heterogeneity was first analyzed. If no significant clinical differences were identified and no definitive statistical source of heterogeneity could be determined, a random-effects model was employed for the meta-analysis. The outcome measures included in this study were all dichotomous variables; thus, the odds ratio (OR) with its 95% CI was used as the effect size. A P-value < 0.05 was considered statistically significant.

RESULTS

Basic Characteristics and Quality Assessment of Included Studies

A total of 2755 articles were retrieved from the databases, of which 19 studies[3,10–27] were ultimately included. The literature screening process is illustrated in Figure 1.

Basic Characteristics and Methodological Quality Assessment of Included Studies

A total of 19 studies[3,10–27] were included, comprising 4 English-language articles and 15 Chinese-language articles. These studies involved 123,329 gynecologic cancer patients, including 1,598 with venous thrombosis and 121,731 without venous thrombosis. The basic characteristics of the included studies are presented in Table 1. Quality assessment of the included studies yielded the following scores: 6 studies scored 9 points, 5 scored 8 points, 5 scored 7 points, 2 scored 6 points, and 1 scored 5 points (Table 2). A total of 38 risk factors were identified, among which 12 underwent data pooling for meta-analysis.

Meta-Analysis Results

Age

Twelve studies[3,12,13,15,17–20,24–27] reported the impact of age on postoperative VTE in patients with gynecologic malignancies. Significant heterogeneity was observed among the studies ($P < 0.00001$, $I^2 = 88\%$), and a random-effects

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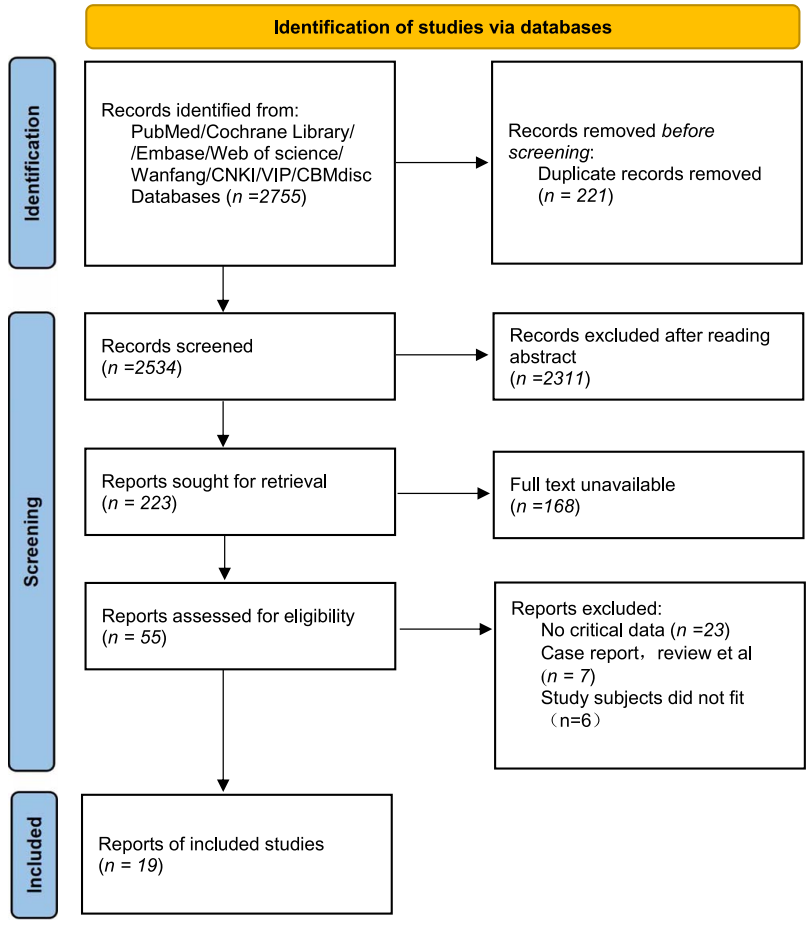

FIGURE 1. Literature screening flowchart. full color online

model was applied following sensitivity analysis. The results indicated that advanced age was a risk factor for postoperative VTE in gynecologic malignancy patients (OR = 3.08, 95% CI = 2.85-3.32, $P < 0.00001$), as shown in Figure 2. Funnel plot analysis of the included studies revealed an asymmetric distribution of scatter points on both sides of the weighted mean SD, suggesting a high publication bias (Fig. 3).

Surgical Approach

Five studies[3,10,11,24,25] examined the influence of surgical approach on postoperative VTE in gynecologic malignancy patients. Significant heterogeneity was observed among the studies ($P < 0.00001$, $I^2 = 97\%$), and a random-effects model was employed after sensitivity analysis. The results demonstrated that open abdominal surgery was a risk factor for postoperative VTE (OR = 9.18, 95% CI = 2.38-35.34, $P = 0.001$), as shown in Figure 4.

Surgical Complexity

Four studies[3,10,12,26] reported the impact of surgical complexity on postoperative VTE in gynecologic malignancy patients. The heterogeneity among studies was low ($P = 0.25$, $I^2 = 27\%$), so a fixed-effects model was adopted. The results indicated that high surgical complexity was a risk factor for postoperative VTE in gynecologic malignancy patients (OR = 9.97, 95% CI = 5.80-17.15, $P < 0.00001$), as shown in Figure 5.

Operative Time

Eight studies[3,12–14,17,23,24,26] examined the effect of operative time on postoperative VTE in gynecologic malignancy patients. Significant heterogeneity was observed among studies ($P < 0.00001$, $I^2 = 91\%$), and a random-effects model was applied after sensitivity analysis. The results demonstrated that prolonged operative time was a risk factor for postoperative VTE in gynecologic malignancy patients (OR = 3.33, 95% CI = 2.97-3.73, $P < 0.00001$), as shown in Figure 6.

BMI

Seven studies[10,13,16,23–25,27] evaluated the influence of BMI on postoperative VTE in gynecologic malignancy patients. Considerable heterogeneity was present among studies ($P < 0.00001$, $I^2 = 84\%$), and a random-effects model was employed following sensitivity analysis. The findings revealed that high BMI was a risk factor for postoperative VTE in gynecologic malignancy patients (OR = 4.77, 95% CI = 3.47-6.57, $P < 0.00001$), as shown in Figure 7.

Comorbidities

Eight studies[3,14,18,19,22,23,25,26] reported the impact of comorbidities on postoperative VTE in gynecologic

TABLE 1. Basic Characteristics of Included Literature

Author and year	Sample size		Thrombosis type	Risk factors
	Venous thrombosis	Nonvenous thrombosis		
Kahr2019[10]	103	51,235	VTE	Surgical approach, surgical complexity, BMI
Wagner2023[11]	16	938	VTE	Surgical approach, tumor stage, tumor grade
Peedicayil2011[12]	126	4032	VTE	Age, surgical complexity, operative time, tumor stage
Swift2022[3]	781	62417	DVT, PE, DVT +PE	Age, surgical approach, surgical complexity, operative time, comorbidities
Liu2024[13]	32	48	VTE	Age, operative time, BMI, postoperative bed rest duration
Song2024[14]	38	304	LEDVT	Operative time, comorbidities, intraoperative blood loss, tumor grade, lymph node metastasis
Cui2023[15]	35	211	LEDVT	Age, D-dimer
Zhu2023[16]	26	130	LEDVT	BMI, D-dimer
Wang2021[17]	47	341	LEDVT	Age, operative time, intraoperative blood loss, tumor stage, tumor grade, lymph node metastasis
Zhen2021[18]	84	119	LEDVT	Age, D-dimer
Li2021[19]	21	275	LEDVT	Age, comorbidities, postoperative bed rest duration
Qin2021[20]	28	92	LEDVT	Age, comorbidities
Zhang2020[21]	17	34	DVT, PE	D-dimer
Chen2020[22]	20	40	DVT	Comorbidities, D-dimer, lymph node metastasis
Du2019[23]	41	41	DVT	Operative time, BMI, comorbidities, Intraoperative blood loss, tumor stage, tumor grade, lymph node metastasis
Liu2017[24]	58	472	DVT, PE, DVT +PE	Age, surgical approach, operative time, BMI, tumor stage
Lv2015[25]	32	612	VTE	Age, surgical approach, BMI, comorbidities, intraoperative blood loss, tumor stage
Zou2015[26]	22	220	LEDVT	Age, surgical complexity, operative time, comorbidities
Huang2011[27]	16	65	LEDVT	Age, BMI, postoperative bed rest duration

BMI indicates body mass index; DVT, deep vein thrombosis; LEDVT, deep vein thrombosis of lower extremity; PE, pulmonary embolism; VTE, venous thromboembolism

malignancy patients. Significant heterogeneity was observed among the studies ($P < 0.00001$, $I^2 = 88\%$). After sensitivity analysis excluding the Swift 2022 study,[3] heterogeneity was reduced ($P = 0.17$, $I^2 = 34\%$), and a fixed-effects model was adopted. The results demonstrated that comorbidities were a risk factor for postoperative VTE in gynecologic malignancy patients (OR = 21.02, 95% CI = 8.72-50.70, $P < 0.00001$), as shown in Figure 8.

Postoperative Bed Rest Duration

Three studies[13,19,27] examined the effect of postoperative bed rest duration on VTE in gynecologic malignancy patients, with significant heterogeneity among studies ($P = 0.001$, $I^2 = 86\%$). After sensitivity analysis excluding the Liu 2024 study,[13] heterogeneity decreased ($P = 0.18$, $I^2 = 43\%$), and a fixed-effects model was applied. The results indicated that prolonged postoperative bed rest was a risk factor for VTE (OR = 25.16, 95% CI = 10.32-61.32, $P < 0.00001$), as shown in Figure 9.

Intraoperative Blood Loss

Four studies[14,17,23,25] investigated the influence of intraoperative blood loss on postoperative VTE in gynecologic malignancy patients, showing substantial heterogeneity ($P < 0.00001$, $I^2 = 93\%$). After sensitivity analysis excluding the Du 2019 study,[23] heterogeneity was minimized ($P = 0.14$, $I^2 = 49\%$), and a fixed-effects model was used. The analysis revealed that high intraoperative blood loss was a significant risk factor for postoperative VTE (OR = 107.53, 95% CI = 17.71-652.85, $P < 0.00001$), as shown in Figure 10.

D-Dimer

Five studies[15,16,18,21,22] reported the impact of D-dimer on postoperative VTE in gynecologic malignancy patients, with significant heterogeneity among studies ($P < 0.00001$, $I^2 = 89\%$). A random-effects model was applied after sensitivity analysis. The results indicated that elevated D-dimer levels were a risk factor for postoperative VTE in gynecologic malignancy patients (OR = 5.55, 95% CI = 3.27-9.43, $P < 0.00001$), as shown in Figure 11.

Tumor Stage

Six studies[11,12,17,23–25] reported the impact of tumor stage on postoperative VTE in gynecologic malignancy patients, with significant heterogeneity among studies ($P < 0.00001$, $I^2 = 94\%$). A random-effects model was applied after sensitivity analysis. The results indicated that advanced tumor stage was a risk factor for postoperative VTE in gynecologic malignancy patients (OR = 7.58, 95% CI = 2.22-25.90, $P = 0.001$), as shown in Figure 12.

Tumor Grade

Four studies[11,14,17,23] reported the impact of tumor grade on postoperative VTE in gynecologic malignancy patients, with significant heterogeneity among studies ($P = 0.005$, $I^2 = 77\%$). After sensitivity analysis excluding the study by Wang,[17] heterogeneity was reduced ($P = 0.14$, $I^2 = 49\%$), and a fixed-effects model was adopted. The results indicated that high tumor grade was a risk factor for postoperative VTE in gynecologic malignancy patients (OR = 27.67, 95% CI = 8.39-91.18, $P < 0.00001$), as shown in Figure 13.

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TABLE 2. Quality Assessment of Included Literature

	Study population selection				Comparability between groups	Outcome measurement			
	1. Representativeness of cases	2. Case definition	3. Control selection	4. Baseline comparability	5. Control of Confounding Factors	6. Outcome assessment method	7. Follow-up completeness	8. Follow-up duration	
Author and year	Was the source and selection method of the study population clearly described?	Were the cases (patients undergoing gynecologic malignant tumor surgery) clearly defined?	Were the controls selected from the same population and comparable to the cases?	Were the key baseline characteristics reported for both case and control groups?	Were major confounding factors (eg, age, BMI, surgical approach) adequately controlled?	Were objective criteria (eg, ultrasound examination, laboratory indicators) used to assess VTE?	Did all patients complete follow-up?	Was the follow-up duration sufficient ($\geq$90 d)?	Total Score
Kahr2019[10]	1	1	1	1	2	1	1	1	9
Wagner2023[11]	1	1	1	1	2	1	1	1	9
Peedicayil2011[12]	1	1	1	1	2	1	1	1	9
Swift2022[3]	1	1	1	1	1	1	1	1	8
Liu2024[13]	1	1	1	0	1	1	0	0	5
Song2024[14]	1	1	0	1	1	1	1	0	6
Cui2023[15]	1	1	1	1	1	1	0	0	7
Zhu2023[16]	1	1	1	1	2	1	1	1	7
Wang2021[17]	1	1	1	1	2	1	1	1	9
Zhen2021[18]	1	1	1	1	2	1	1	0	8
Li2021[19]	1	1	0	1	1	1	0	0	6
Qin2021[20]	1	1	1	1	2	1	1	1	9
Zhang2020[21]	1	1	1	1	1	1	0	0	7
Chen2020[22]	1	1	1	1	2	1	0	0	8
Du2019[23]	1	1	1	0	2	1	1	0	8
Liu2017[24]	1	1	1	1	2	1	1	1	9
Lv2015[25]	1	1	1	0	1	1	1	1	8
Zou2015[26]	1	1	0	1	1	1	1	0	7
Huang2011[27]	1	1	1	1	1	1	0	1	7

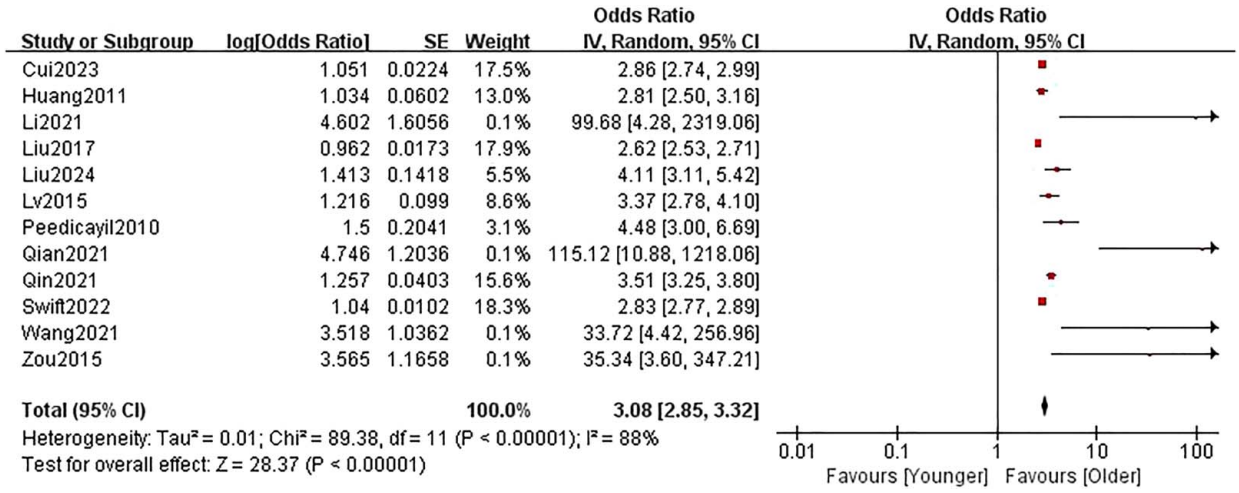

FIGURE 2. Forest plot of the association between age and postoperative VTE in gynecologic malignancy patients. full color online

Lymph Node Metastasis

Four studies[14,17,22,23] reported the impact of lymph node metastasis on postoperative VTE in gynecologic malignancy patients, with significant heterogeneity among studies ($P = 0.06$, $I^2 = 59\%$). After sensitivity analysis excluding the study by Du,[23] heterogeneity was reduced ($P = 0.17$, $I^2 = 44\%$), and a fixed-effects model was adopted. The results indicated that lymph node metastasis was a risk factor for postoperative VTE in gynecologic malignancy patients (OR = 31.21, 95% CI = 9.54-102.15, $P < 0.00001$), as shown in Figure 14.

DISCUSSION

This meta-analysis systematically evaluated the association between 12 risk factors and postoperative venous thromboembolism (VTE) in patients with gynecologic malignancies. The results demonstrated that age, surgical approach, surgical complexity, operative duration, BMI, comorbidities, postoperative bed rest duration, intraoperative blood loss, D-dimer levels, tumor stage, tumor grade, and lymph node metastasis were all significantly correlated with VTE occurrence. These findings provide critical evidence for VTE risk assessment and the formulation of preventive strategies in clinical practice.

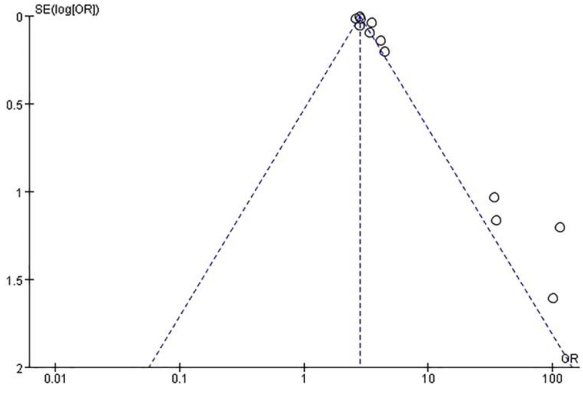

FIGURE 3. Funnel plot of the association between age and postoperative VTE in gynecologic malignancy patients. full color online

Regarding patient characteristics, this study identified advanced age, high BMI, comorbidities, and prolonged postoperative bed rest as independent risk factors for VTE in gynecologic cancer patients, which aligns with recent research findings.[27] From a pathophysiological perspective, the increased VTE risk in elderly patients may stem from multiple factors: age-related reductions in venous wall elasticity, endothelial dysfunction, and imbalances in the coagulation-fibrinolysis system.[28] In Addition, elderly cancer patients exhibit significantly elevated levels of pro-inflammatory cytokines (eg, IL-6, TNF-α) in circulation. These inflammatory mediators can induce tissue factor expression in endothelial cells while downregulating thrombomodulin, collectively promoting a hypercoagulable state.[29] The strong association between obesity (BMI ≥ 30 kg/m²) and VTE may be mediated through the following mechanisms: excessive secretion of adipokines such as leptin and resistin by adipose tissue, which activate platelets and enhance their aggregability, as well as increased intra-abdominal pressure due to visceral fat accumulation, impairing lower-extremity venous return.[30] Comorbidities—particularly hypertension and diabetes—demonstrated the strongest predictive value for VTE risk, a finding with significant clinical implications. Hypertension may promote vascular endothelial injury and platelet activation via renin-angiotensin system activation, while diabetes increases thrombotic risk through multiple pathways: hyperglycemia-induced advanced glycation end products impair endothelial anticoagulant function, insulin resistance leads to overexpression of plasminogen activator inhibitor-1 (PAI-1), and diabetic microangiopathy causes localized blood stasis.[31] Notably, prolonged postoperative bed rest contributes to venous stasis and reduced venous return due to diminished lower-limb muscle pump function. The interplay of these patient-specific risk factors exacerbates systemic prothrombotic states, underscoring the need for healthcare providers to adopt more aggressive preventive strategies in high-risk patients, such as early mobilization, extended postoperative low-molecular-weight heparin administration, or combined mechanical prophylaxis.

The analysis of surgery-related factors yields significant clinical implications. This meta-analysis demonstrates that surgical approach, complexity of the procedure, operative

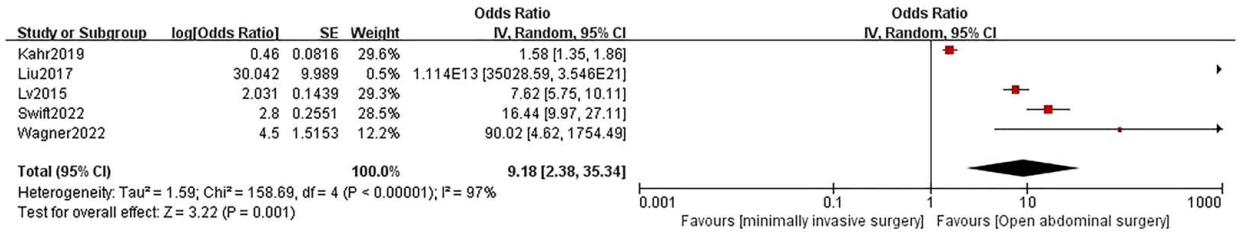

FIGURE 4. Forest plot of the relationship between surgical approach and postoperative VTE in gynecologic malignancy patients. full color online

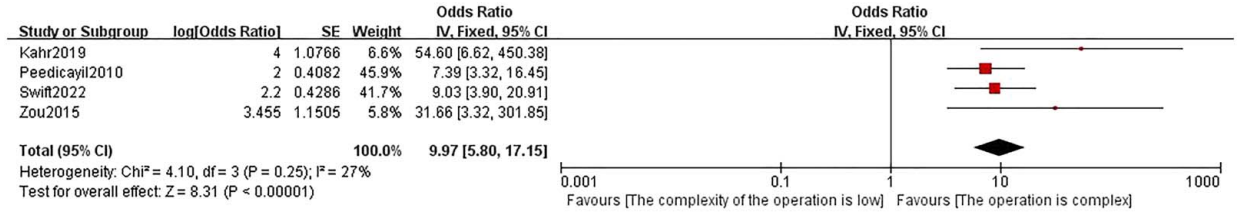

FIGURE 5. Forest plot of the relationship between surgical complexity and postoperative VTE in gynecologic malignancy patients. full color online

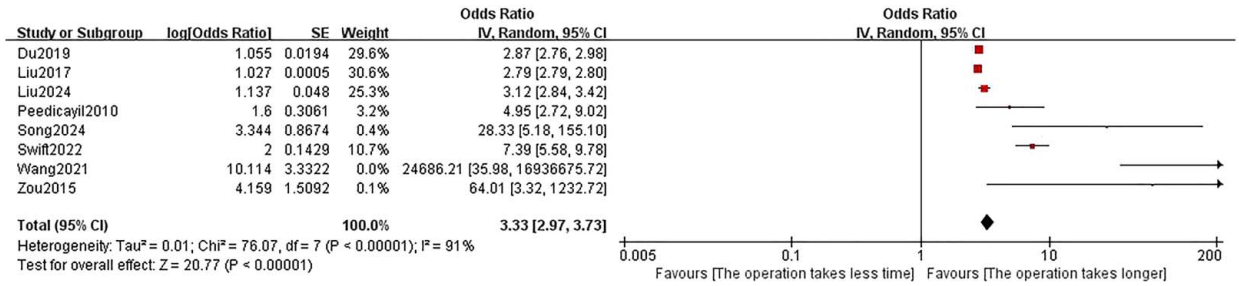

FIGURE 6. Forest plot of the relationship between operative time and postoperative VTE in gynecologic malignancy patients. full color online

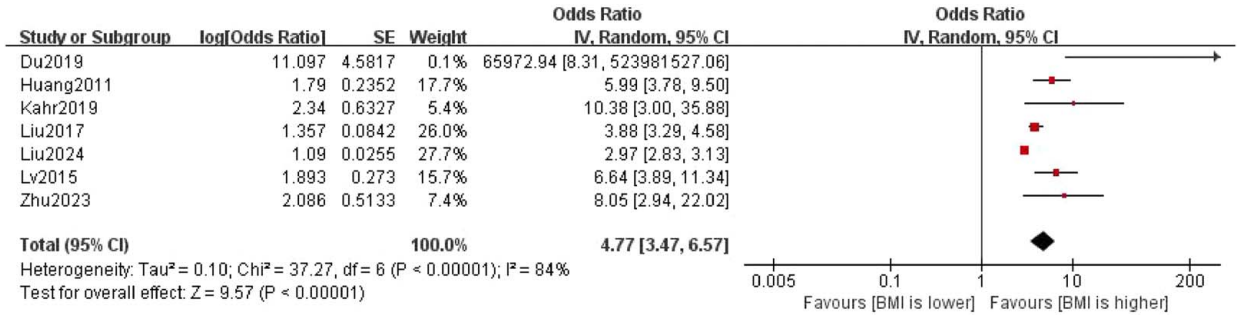

FIGURE 7. Forest plot of the relationship between BMI and postoperative VTE in gynecologic malignancy patients. full color online

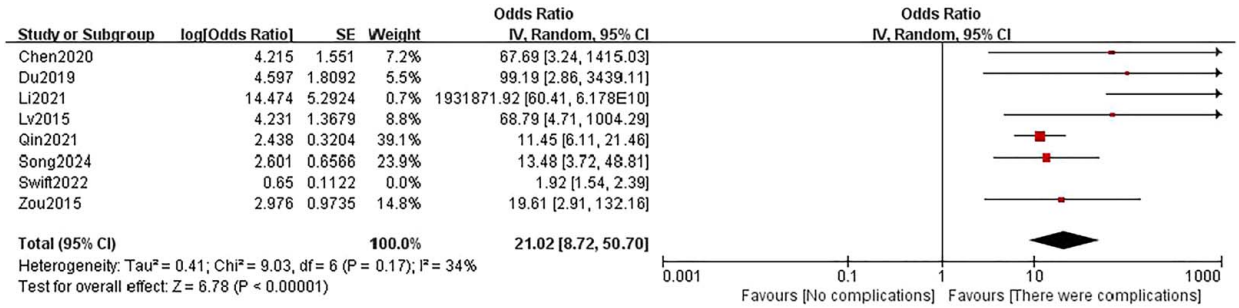

FIGURE 8. Forest plot of the relationship between comorbidities and postoperative VTE in gynecologic malignancy patients. full color online

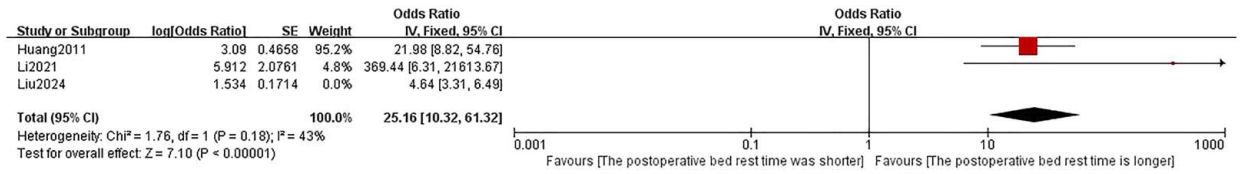

FIGURE 9. Forest plot of the relationship between postoperative bed rest duration and VTE in gynecologic malignancy patients. full color online

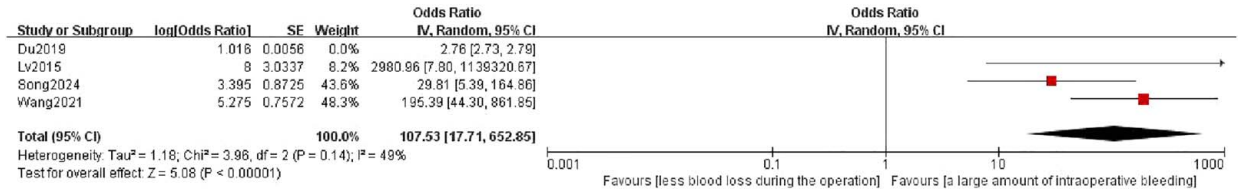

FIGURE 10. Forest plot of the relationship between intraoperative blood loss and postoperative VTE in gynecologic malignancy patients. full color online

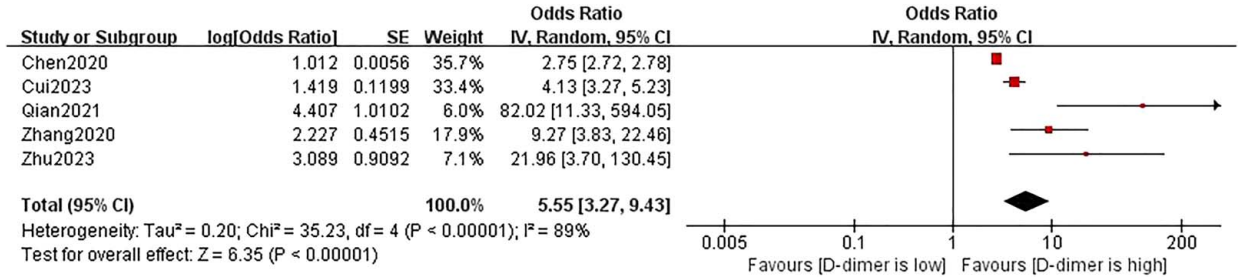

FIGURE 11. Forest plot of the relationship between D-dimer and postoperative VTE in gynecologic malignancy patients. full color online

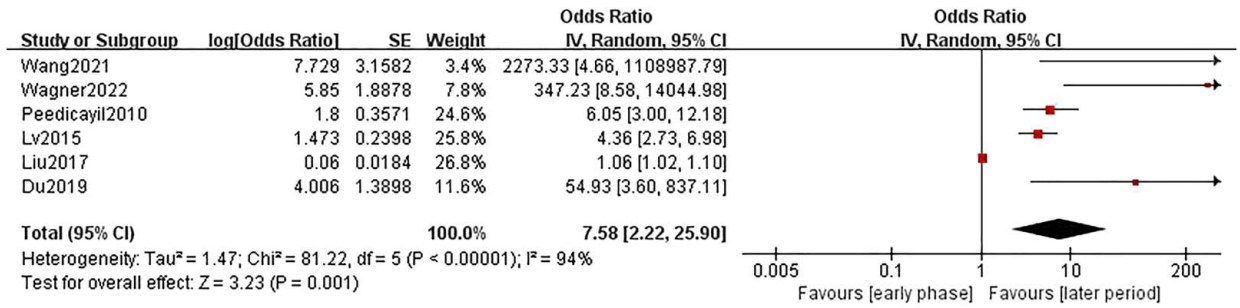

FIGURE 12. Forest plot of the relationship between tumor stage and postoperative VTE in gynecologic malignancy patients. full color online

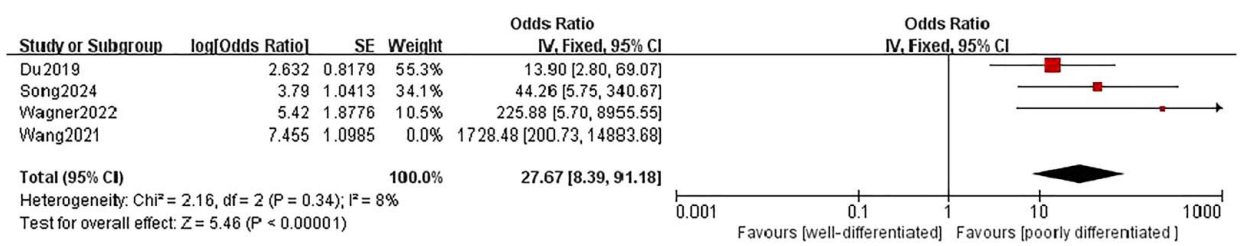

FIGURE 13. Forest plot of the relationship between tumor grade and postoperative VTE in gynecologic malignancy patients. full color online

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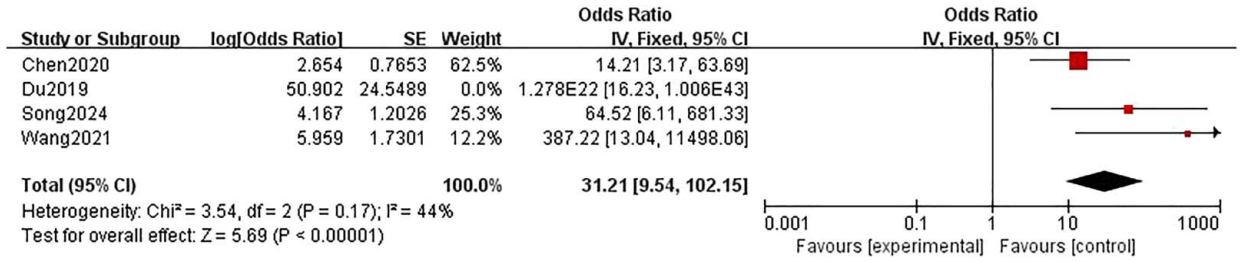

FIGURE 14. Forest plot of the relationship between lymph node metastasis and postoperative VTE in gynecologic malignancy patients. full color online

duration, and intraoperative blood loss are all significantly associated with postoperative VTE occurrence in gynecologic malignancy patients. A clear dose-response relationship exists between the degree of surgical trauma and VTE risk, with open surgeries carrying higher VTE risks compared with minimally invasive approaches, attributable to more extensive tissue damage during the procedure. Surgical trauma can trigger substantial tissue factor release into circulation, activating the extrinsic coagulation pathway. Moreover, complex procedures (eg, tumor debulking surgery) often involve extensive peritoneal dissection and lymphadenectomy, which not only amplify tissue factor release but also cause lymphatic vessel injury, allowing lymph fluid rich in procoagulant substances to enter the circulatory system.[32] Prolonged operative time contributes to venous stasis, while surgical stress induces sustained sympathetic activation, enhancing platelet reactivity and aggregation. In addition, lengthy procedures often coincide with hypothermia, which suppresses thrombin inhibitor activity and impairs fibrinolysis.[33] Intraoperative blood loss exhibits the most pronounced impact on VTE risk, a finding of particular clinical relevance. Hemorrhage leads to hemoconcentration and coagulation factor concentration effects, followed by compensatory thrombocytosis and hyperactivation of platelets. Relevant studies[34] indicate a nonlinear relationship between blood loss and VTE risk, with a sharp increase in VTE incidence when blood loss exceeds 800 mL, suggesting that patients surpassing this threshold may require intensified thromboprophylaxis. Therefore, minimally invasive approaches should be prioritized when oncologically feasible. For complex surgeries, meticulous techniques should be employed to minimize tissue trauma and bleeding. Operative duration should be strictly controlled, with consideration of staged procedures when necessary.

Advanced tumor stage, high-grade tumors, and lymph node metastasis are independent risk factors for postoperative venous thromboembolism (VTE) in patients with gynecologic malignancies, with high-grade tumors and lymph node metastasis demonstrating strong predictive value. This finding reveals the intrinsic link between tumor aggressiveness and activation of the coagulation system. From a molecular mechanism perspective, tumor-associated VTE primarily involves 3 pathologic processes: first, malignant cells directly activate the extrinsic coagulation pathway through overexpression of tissue factor (TF) and cancer procoagulant (CP); second, inflammatory mediators (eg, IL-6, TNF-α) in the tumor microenvironment induce endothelial cell phenotypic transformation, disrupting physiological anticoagulant mechanisms; and third, mechanical compression and hemodynamic changes caused by tumor metastasis create favorable conditions for thrombus formation.[35] Therefore, tumor biological characteristics should serve as key indicators for VTE risk assessment, particularly for patients with lymph node metastasis or poorly differentiated tumors, who may require more aggressive prophylactic anticoagulation strategies. Future research should focus on exploring the relationship between tumor molecular features (eg, HRD status, BRCA mutations) and coagulation function, as well as novel VTE prevention approaches in the era of targeted therapies.

Regarding laboratory markers, the predictive value of elevated D-dimer levels aligns with recent studies,[36] supporting its use as a critical indicator for postoperative VTE monitoring. This result underscores the central role of coagulation-fibrinolysis system activation in tumor-associated VTE pathogenesis. From a pathophysiological standpoint, tumor cells activate the coagulation cascade by secreting procoagulant substances (eg, tissue factor), while tumor-associated inflammatory responses contribute to a hypercoagulable state by suppressing the fibrinolytic system (eg, through upregulation of PAI-1).[37] Notably, as a fibrin degradation product, the degree of D-dimer elevation positively correlates with tumor burden and malignancy, reflecting the dynamic balance between tumor procoagulant activity and systemic fibrinolytic response. Thus, for high-risk patients with abnormal laboratory markers, dynamic monitoring and individualized prophylaxis based on clinical manifestations should be considered. Future research should aim to develop predictive models integrating laboratory indicators and clinical features to enhance the accuracy of VTE risk assessment.

However, this study also has several limitations. First, there was substantial heterogeneity among the included studies, which, despite adjustments through sensitivity analysis, may still affect the stability of the results. Second, the number of studies investigating certain risk factors was insufficient, preventing their inclusion in the analysis. Third, most studies did not differentiate between the risk factors for DVT and PE. Future research should focus on addressing these limitations, particularly in exploring specific risk factors for different types of VTE.

In summary, the results of this meta-analysis indicate that advanced age, open abdominal surgery, high surgical complexity, prolonged operative time, elevated BMI, comorbidities, extended postoperative bed rest, significant intraoperative blood loss, high D-dimer levels, advanced tumor stage, high tumor grade, and lymph node metastasis collectively constitute a multifaceted risk profile for VTE occurrence. These findings provide evidence-based support for clinical practice, emphasizing the need for individualized and stratified VTE prevention strategies in patients with

multiple risk factors. Future research should prioritize the development of precision prediction models integrating clinical characteristics and molecular biomarkers, as well as explore novel preventive measures targeting tumor-specific procoagulant pathways.

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