META-ANALYSIS

Meta-analysis of Risk Factors for Venous Thromboembolism in Patients with Gynecologic Malignant Tumors

Jiewei Pan, BS; Gang Zhao, BS

ABSTRACT

Objective • This study aims to investigate the risk factors associated with the development of venous thromboembolism (VTE) in patients diagnosed with gynecologic malignant tumors.

Methods • A comprehensive meta-analysis was conducted by searching databases such as The Cochrane Library, PubMed, EMbase, Web of Science, CNKI, etc., covering the period from January 2010 to January 2020. Inclusion and exclusion criteria were applied to identify relevant literature. Two researchers independently conducted literature screening, data extraction, and quality assessment of the included studies. Meta-analysis was performed using RevMan 5.3 software. The analyzed indicators included age, tumor diameter, diabetes, coronary heart disease, tumor staging, body mass index, hypertension, hospitalization time, and surgery time. In this meta-analysis, the inclusion criteria for the studies were as follows: (1) Study type: Case-control studies; (2) Study population: Patients with gynecologic malignant tumors who developed venous thromboembolism; (3) Study focus: Risk factors for venous thromboembolism in patients with gynecologic malignant tumors; (4) Publication type: Journal articles. The exclusion criteria were: (1) Non-journal articles; (2) Non-case-control studies.; (3) Literature published in different forms multiple times; (4) Literature with incomplete information such as abstracts, keywords, conclusions, and study results. To conduct a comprehensive literature search, multiple databases were searched, including The Cochrane Library, PubMed, EMbase, Web of Science, CNKI, etc. The reason for selecting the time frame from January 2010 to January 2020 was to focus on recent research and include the most up-to-date studies available within the specified period. This time frame ensures that the analysis considers the relevant literature published in the past decade, providing a comprehensive understanding of the risk factors for venous thromboembolism in patients with gynecologic malignant tumors.

Results • The meta-analysis incorporated eight studies, comprising a total of 6,436 cases (793 in the study group and 5,643 in the control group). The results revealed that, compared to the control group, the study group exhibited statistically significant older age [OR=1.41, 95% CI (1.00, 1.98), $P = .05$], higher tumor staging [OR=1.37, 95% CI (1.04, 1.81), $P = .03$], elevated body mass index [OR=1.42, 95% CI (1.12, 1.81), $P = .004$], increased prevalence of hypertension [OR=1.72, 95% CI (1.30, 2.28), $P = .0002$], and prolonged surgery time [OR=1.37, 95% CI (1.02, 1.85), $P = .04$]. However, there were no statistically significant differences in tumor diameter [OR=0.52, 95% CI (0.05, 5.32), $P = .58$], diabetes prevalence [OR=1.32, 95% CI (0.42, 4.11), $P = .64$], coronary heart disease incidence [OR=1.16, 95% CI (0.91, 1.47), $P = .23$], and hospitalization time [OR=1.90, 95% CI (0.98, 3.69), $P = .06$] between the study group and the control group.

Regarding the statistical terms used in the results, odds ratio (OR) is a measure of the association between an exposure (in this case, risk factors) and an outcome (venous thromboembolism). It compares the odds of the outcome occurring in the study group (patients with gynecologic malignant tumors who developed VTE) to the odds of the outcome occurring in the control group (patients with gynecologic malignant tumors who did not develop VTE). An OR greater than 1 indicates a higher odds of the outcome in the study group compared to the control group, while an OR less than 1 indicates a lower odds.

Confidence intervals (CIs) provide a range of values within which the true population parameter (in this case, the true OR) is likely to fall. The 95% confidence interval is commonly used, and it represents the range within which we can be 95% confident that the true OR lies. If the CI includes the value 1, it suggests that there is no statistically significant difference between the study and control groups, while if the CI does not include 1, it indicates a statistically significant difference.

Conclusion • Age, tumor staging, body mass index, hypertension, and surgery time emerge as significant risk factors for VTE in gynecologic malignant tumor surgery patients. Monitoring these risk factors can effectively facilitate risk assessment and prevention of VTE.

These findings have important clinical implications. Firstly, they emphasize the importance of considering these risk factors during the assessment of VTE risk in patients with gynecologic malignancies. Healthcare professionals can use this information to identify high-risk patients and implement appropriate preventive measures. For example, older patients, those with advanced tumor staging, elevated body mass index, or hypertension may require closer monitoring and prophylactic strategies to reduce the risk of VTE.

Furthermore, these findings can contribute to the development of targeted prevention strategies. By recognizing the specific risk factors associated with VTE in gynecologic malignancies, healthcare providers can implement interventions tailored to the individual patient's risk profile. This may include optimizing perioperative management, providing prophylactic anticoagulation, promoting early mobilization, and employing compression stockings or intermittent pneumatic compression devices. (*Altern Ther Health Med.* 2024;30(12):416-423).

Jiewei Pan, BS, Department of Obstetrics and Gynecology; Huzhou Maternity & Child Health Care Hospital; Huzhou; China. **Gang Zhao**, BS, Department of Obstetrics and Gynecology; Huzhou Maternity & Child Health Care Hospital; Zhejiang Province; China.

Corresponding author: Gang Zhao, BS
E-mail: zhaogang0572@163.com

INTRODUCTION

Venous thromboembolism (VTE), encompassing deep vein thrombosis (DVT) and pulmonary embolism (PE), is a significant medical condition associated with substantial morbidity, mortality, and healthcare costs worldwide.[1] In the context of gynecologic tumors, the risk of VTE is particularly relevant and has been a subject of research interest.[2] Understanding the epidemiology and impact of VTE in patients with gynecologic tumors is crucial for optimizing patient care and outcomes.

Epidemiology and Impact of VTE in Gynecologic Tumors: Numerous studies have shed light on the heightened risk of VTE in patients with gynecologic tumors.[3,4] For instance, evidencce demonstrated that women with ovarian cancer had a significantly higher risk of VTE compared to women without cancer, with a hazard ratio of 4.8. Similarly, a prior study reported a 2.5-fold increased risk of VTE in women with endometrial cancer. These findings highlight the importance of recognizing and addressing the elevated risk of VTE in this patient population.[5]

The identification of risk factors associated with venous thromboembolism (VTE) in patients with gynecologic tumors is an area that still presents variability and controversy.

Age has been recognized as a potential risk factor for VTE, with older patients generally having a higher risk. Tumor stage, indicating the extent and spread of the malignancy, has also been implicated as a potential risk factor for VTE in gynecologic tumor patients. Advanced stages of cancer may contribute to a higher risk due to increased tumor burden and potential vascular compression.[6] Body mass index (BMI) has emerged as another potential risk factor, with studies suggesting that overweight and obesity may be associated with an increased risk of VTE. The underlying mechanisms may involve chronic inflammation, altered blood coagulability, and impaired venous flow in individuals with higher BMI. Comorbidities, such as hypertension and diabetes, have been suggested as potential risk factors for VTE in gynecologic tumor patients. These conditions may contribute to a prothrombotic state and endothelial dysfunction, thereby increasing the risk of clot formation.[7] Surgical interventions, particularly major procedures, have long been recognized as a significant risk factor for VTE. The trauma caused by surgery, prolonged immobility, and activation of the coagulation cascade can predispose patients to develop blood clots. Additionally, the use of anesthesia and specific surgical techniques may influence the risk of VTE.[8]

However, despite the identification of these potential risk factors, the magnitude and significance of their association with VTE in gynecologic tumor patients remain uncertain. Variability in study designs, patient populations, and conflicting results across studies contribute to the ongoing controversy. Further investigation through well-designed studies and comprehensive meta-analyses is needed to clarify the exact roles and relative importance of these risk factors in this specific patient population.

The objective of this meta-analysis is to investigate the risk factors associated with the development of VTE in patients diagnosed with gynecologic malignant tumors, with a specific focus on gynecologic malignancies. This study aims to address the gap in current research by providing a comprehensive analysis of the existing evidence and identifying the significant risk factors associated with VTE in this specific population. The findings of this study will contribute to the existing body of knowledge by enhancing our understanding of the risk factors for VTE in patients with gynecologic tumors.

Identifying the risk factors for VTE in patients with gynecologic tumors holds significant clinical relevance. This knowledge can potentially influence patient management, treatment decisions, and outcomes. By recognizing high-risk patients, healthcare providers can implement appropriate thromboprophylaxis measures, optimize surgical techniques, and promote early mobilization. Ultimately, applying these findings in clinical practice can improve the prevention, diagnosis, and management of VTE in patients with gynecologic tumors, leading to better patient outcomes and reduced healthcare burdens. To achieve the objectives of this study, a meta-analysis approach was employed. Meta-analysis is a suitable method for investigating the association between risk factors and VTE in gynecologic tumor patients because it allows for the synthesis of data from multiple studies, providing a more comprehensive and reliable assessment of the risk factors.

The findings of this study have the potential to impact clinical practice significantly. By identifying the specific risk factors associated with VTE in patients with gynecologic tumors, healthcare providers can enhance risk assessment, implement targeted preventive strategies, and optimize treatment approaches. This information can guide decision-making, improve patient care, and ultimately reduce the burden of VTE in this patient population. This meta-analysis aims to analyze the risk factors for VTE in patients diagnosed with gynecologic malignant tumors. The study will consider a range of gynecologic malignancies, including ovarian, endometrial, cervical, and vulvar cancers. The analysis will encompass patients across various stages of cancer, including both preoperative and postoperative periods. In the following sections, we will describe the methods employed in this meta-analysis, including the search strategy, study selection criteria, data extraction process, and statistical analyses.

MATERIALS AND METHODS

Inclusion and Exclusion Criteria

Inclusion Criteria. (1) Study type: Case-control studies. (2) Study population: Patients with gynecologic malignant tumors who developed venous thromboembolism. (3) Study focus Risk factors for venous thromboembolism in patients with gynecologic malignant tumors. (4) Publication type: Journal articles.

Exclusion Criteria. (1) Non-journal articles. (2) Non-case-control studies. (3) Literature published in different forms multiple times. (4) Literature with incomplete information such as abstracts, keywords, conclusions, and study results.

The selection of case-control studies for the meta-analysis strictly adhered to predefined criteria to maintain unbiased representation. Each selected study should describe its randomization method (e.g., computer-generated random numbers, randomization tables) to ensure unbiased allocation of participants into study and control groups.

While randomization is not applicable in case-control studies, the matching process aims to achieve a similar goal

of creating comparable groups. Matching can be done based on factors such as age, sex, socioeconomic status, or other relevant variables depending on the research question. This matching process helps control for potential confounding variables and reduces bias in the estimation of the exposure-outcome association.

Literature Search Strategy

A database search strategy was employed for literature retrieval. The selected databases included The Cochrane Library, PubMed, EMbase, Web of Science, CNKI, etc. The keywords were set as: "Venous Thromboembolism," "VTE," "Gynecologic oncology," and "Gynecological tumors." The publication date was restricted to the period from January 1, 2010, to January 2020.

The search was limited to studies published in English, given the language capabilities of the research team and available resources.

Literature Screening and Data Extraction

Two researchers independently screened the literature and extracted data. Disagreements between the two researchers were resolved by consulting a third party for judgment. Based on the inclusion and exclusion criteria, retrieved literature was categorized and organized. Articles that did not meet the inclusion criteria were excluded through the examination of titles, abstracts, research types, etc. The remaining literature was further assessed through full-text reading to confirm inclusion. Data extraction from the included literature encompassed researchers, publication year, sample size, risk factors, measurement data, and other relevant information.

To manage duplicates across different databases, we used EndNote to import and organize the search results. The software helped identify and removed duplicate records automatically. Additionally, during the screening process, we carefully compared the titles, authors, and publication details of the articles to ensure that duplicate studies are not included in the final analysis.

The screening process had two phases: title/abstract screening and full-text screening. Two independent reviewers screened the titles and abstracts of the retrieved articles based on predefined inclusion and exclusion criteria. The full texts of potentially relevant articles were obtained and assessed for eligibility. Any discrepancies during screening were resolved through discussion and consensus or consultation with a third reviewer if necessary.

For data extraction, a standardized form was developed to collect relevant information from the included studies. The data fields extracted included study characteristics (authors, publication year, study design), participant characteristics (sample size, age, tumor type), risk factors (age, tumor stage, BMI, comorbidities, surgical interventions), outcome measures (incidence of VTE), and statistical analyses used. If necessary, attempts were made to contact the corresponding authors of the included studies to obtain missing or incomplete data.

In cases where data were missing or incomplete in the included studies, efforts were made to contact the corresponding authors to request the missing information. If the data could not be obtained, the impact of missing data on the overall analysis was carefully considered, and any limitations associated with incomplete data were reported in the final publication.

Literature Bias Assessment

Publication bias was evaluated using the Newcastle-Ottawa Scale (NOS).[9] Studies with a score of 6 or higher were considered high-quality research, while those scoring below 6 were excluded from the analysis.

The NOS is a widely accepted tool for evaluating the quality of observational studies. It consists of three domains: selection, comparability, and exposure or outcome assessment. Each domain was assessed using specific criteria, and studies were awarded stars based on their adherence to these criteria. The total number of stars allocated to each study reflected its overall quality, with a higher number indicating better methodology and lower risk of bias. The quality assessment was conducted independently by two reviewers, and any discrepancies were resolved through discussion or consultation with a third reviewer if needed.

Statistical Analysis

In the statistical analysis of this meta-analysis, RevMan 5.3 software was employed, acknowledged for its efficacy in medical research. The effect size was determined using Relative Risk (RR) with a 95% Confidence Interval (CI), a method well-suited for evaluating the strength of association in case-control studies involving binary outcomes.

To assess heterogeneity among the included studies, we calculated the I^2 statistic, which quantified the percentage of total variation across studies that was due to heterogeneity rather than chance. We utilized the following thresholds to interpret the I^2 values: low heterogeneity ($I^2 < 25\%$), moderate heterogeneity ($I^2 = 25\%$ to 50%), and high heterogeneity ($I^2 > 50\%$). When substantial heterogeneity was observed (moderate to high), we explored potential sources of heterogeneity through subgroup analyses and sensitivity analyses.

The choice of the meta-analysis model, either fixed-effect or random-effects, depended on the degree of heterogeneity observed among the included studies. In cases of minimal heterogeneity ($I^2 < 25\%$), suggesting that the true effect sizes were similar across studies, we used a fixed-effect model. This model assumed that all studies estimated the same underlying effect size, and the pooling of results was based on precision. Conversely, when significant heterogeneity was detected ($I^2 \geq 25\%$), indicating substantial variability in effect sizes, we employed a random-effects model. This model considered both within-study and between-study variability and provided a more conservative estimation by incorporating the assumption that true effects may differ across studies.

To assess potential publication bias, we employed various methods. First, we visually inspected funnel plots, which

Figure 1. Literature screening process

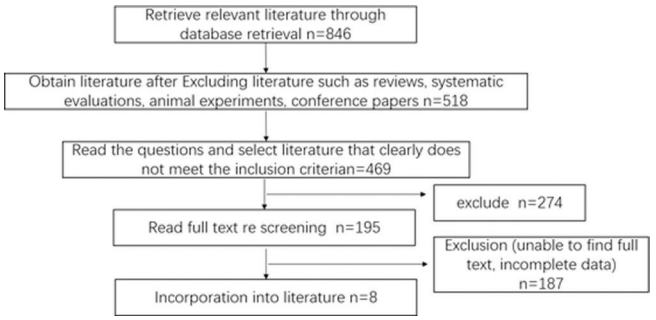


Table 1. Basic Characteristics and Quality Assessment of Included Studies

Included studies	year of publication	Type of Study	NOS score	risk factors
Zhou 2015[10]	2015	controlled study	7 points	①③⑥⑦⑨
Liu 2017[11]	2017	controlled study	8 points	①③⑤⑥⑦⑧⑨
Abraham Peedicayil[12]	2010	controlled study	9 points	①⑤⑥⑨
Masao Okadome[13]	2010	controlled study	9 points	④⑤⑦⑧⑨
Feras Abu Saadeh[14]	2013	controlled study	8 points	⑤⑥
Koji Matsuo[15]	2015	controlled study	8 points	②
Koji Matsuo[16]	2017	controlled study	8 points	②⑤
Qun Li[17]	2019	controlled study	9 points	①④⑤⑦⑨

Note: ① age; ② Tumor diameter; ③ diabetes; ④ Coronary heart disease; ⑤ Tumor staging; ⑥ Body mass index; ⑦ Hypertension; ⑧ Hospitalization time; ⑨ Surgery time.

Figure 2. Forest plot of age in the study group and control group

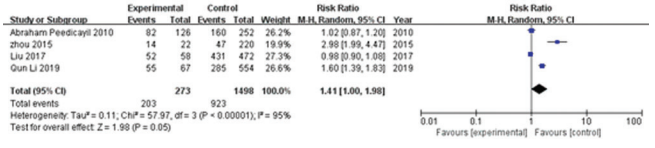
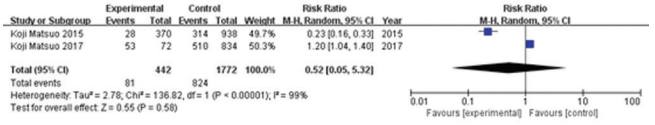


Figure 3. Forest plot of tumor diameters in the study group and control group



plotted the effect size estimates against the standard error or sample size of the studies. Asymmetric funnel plots could indicate publication bias, with small studies reporting larger effect sizes. Additionally, we used statistical tests such as Egger's regression test or Begg's rank correlation test to evaluate the presence of publication bias quantitatively. If publication bias was detected, we considered adjusting the effect sizes using methods like the trim-and-fill method to account for potential missing studies and estimate the impact of publication bias on the overall results.

If there were sufficient studies and data available, we conducted subgroup analyses based on different types of gynecologic tumors. This analysis allowed us to explore potential differences in the association between gynecologic tumors and the risk of venous thromboembolism across various tumor types. The subgroup analyses were performed by comparing effect sizes and heterogeneity estimates between different tumor groups. We conducted sensitivity analyses to assess the robustness of our findings. This involved re-analyzing the data after excluding studies one by one or excluding studies with certain characteristics (e.g., high risk of bias or small sample size) to evaluate the influence of individual studies on the overall results. Sensitivity analyses helped determine if the findings were heavily dependent on any specific study or study characteristic.

RESULTS

Literature Selection

Following the literature search strategy outlined above, a total of 846 articles were initially identified. After applying the inclusion and exclusion criteria, 518 relevant articles were obtained. Upon reviewing abstracts and excluding clearly non-compliant articles, 469 articles remained. After a thorough examination of the full texts, 195 articles were retrieved. Articles lacking complete full texts or presenting incomplete data were excluded, resulting in a final selection of 8 articles for inclusion in this study.[10-17] The total number of cases across these studies was 6436, with 793 in the study group and 5643 in the control group. The literature screening process is illustrated in Figure 1.

Basic Characteristics and Quality Assessment of Included Studies

The essential characteristics of the included studies are detailed in Table 1. All studies incorporated in this analysis were randomized controlled trials. Publication bias in the included studies was assessed using the Newcastle-Ottawa Scale (NOS), with all studies scoring above 6 points, indicating a high quality of literature inclusion. This is conducive to the subsequent formation of results in the meta-analysis.

Meta-Analysis Results

Age. Four studies[10-12,17] provided characteristics of the older age group in both patient sets. The heterogeneity test showed significant heterogeneity among the studies (P < .00001, I^2 = 95%). Meta-analysis was conducted using a random-effects model, as shown in Figure 2. The results revealed that, compared to the control group, patients in the study group were significantly older, with a substantial difference between the two groups [OR=1.41, 95% CI (1.00, 1.98), P = .05].

Tumor Diameter. Two studies[15,16] reported characteristics of the tumor diameter in both groups. The heterogeneity test showed significant heterogeneity among the studies (P < .00001, I^2 = 99%). Meta-analysis was conducted using a random-effects model, as illustrated in Figure 3. The results indicated that there was no statistically significant difference in tumor diameter between the study group and the control group [OR=0.52, 95% CI (0.05, 5.32), P = .58], suggesting that patients in the study group tended to have larger tumor diameters.

Diabetes. Two studies[10,11] reported characteristics of the diabetes population in both groups. The heterogeneity test showed significant heterogeneity among the studies (P = .01,

I^2 = 84%). Meta-analysis was conducted using a random-effects model, as depicted in Figure 4. The results revealed that there was no statistically significant difference in the prevalence of diabetes between the study group and the control group [OR=1.32, 95% CI (0.42, 4.11), P = .64], indicating a higher likelihood of diabetes in the study group patients.

Coronary Heart Disease. Two studies[13,17] reported characteristics of the coronary heart disease population in both groups. The heterogeneity test showed no significant heterogeneity among the studies (P = 0.99, I^2 = 0%). Meta-analysis was conducted using a fixed-effects model, as presented in Figure 5. The results indicated that there was no statistically significant difference in the incidence of coronary heart disease between the study group and the control group [OR=1.16, 95% CI (0.91, 1.47), P=0.23], suggesting a higher occurrence of coronary heart disease in the study group patients.

Tumor Staging. Six studies[11-14,16-17] reported characteristics of the tumor staging population in both groups. The heterogeneity test showed significant heterogeneity among the studies (P < .00001, I^2 = 92%). Meta-analysis was conducted using a random-effects model, as shown in Figure 6. The results indicated that there was a statistically significant difference in tumor staging between the study group and the control group [OR=1.37, 95% CI (1.04, 1.81), P = .03], suggesting a higher tumor staging level in the study group patients.

Body Mass Index. Four studies[10-12,14] reported characteristics of the body mass index (BMI) population in both groups. The heterogeneity test showed significant heterogeneity among the studies (P = .09, I^2 = 53%). Meta-analysis was conducted using a random-effects model, as illustrated in Figure 7. The results indicated that there was a statistically significant difference in BMI between the study group and the control group [OR=1.42, 95% CI (1.12, 1.81), P = .004], suggesting a higher BMI in the study group patients.

Hypertension. Four studies[10-11,13,17] reported characteristics of the hypertension population in both groups. The heterogeneity test showed significant heterogeneity among the studies (P = .04, I^2 = 64%). Meta-analysis was conducted using a random-effects model, as presented in Figure 8. The results indicated that there was a statistically significant difference in the prevalence of hypertension between the study group and the control group [OR=1.72, 95% CI (1.30, 2.28), P = .0002], suggesting a higher incidence of hypertension in the study group patients.

Hospitalization Time. Two studies[11,13] reported characteristics of the hospitalization time population in both groups. The heterogeneity test showed significant heterogeneity among the studies (P = .02, I^2 = 81%). Meta-analysis was conducted using a random-effects model, as depicted in Figure 9. The results indicated that there was no statistically significant difference in hospitalization time between the study group and the control group [OR=1.90, 95% CI (0.98, 3.69), P = .06], suggesting a tendency for longer hospitalization time in the study group patients.

Figure 4. Forest plot of diabetes in the study group and control group

Figure 5. Forest plot of coronary heart disease in the study group and control group

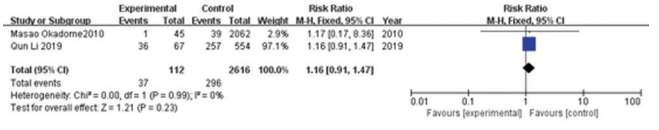


Figure 6. Forest plot of tumor stages in the study group and control group

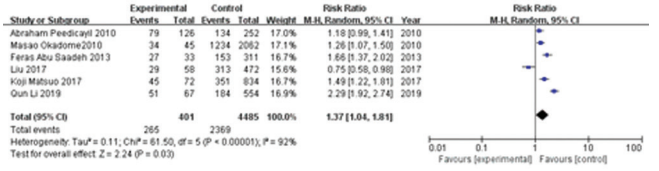


Figure 7. Forest plot of body mass index of the study group and control group

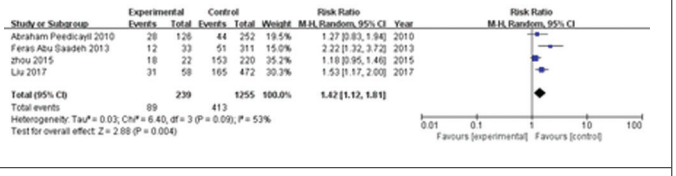


Figure 8. Forest plot of hypertension in the study group and control group

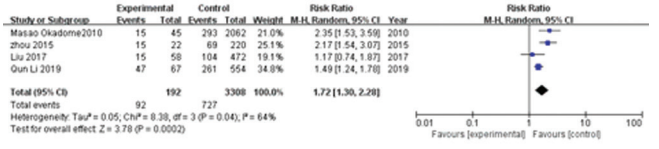
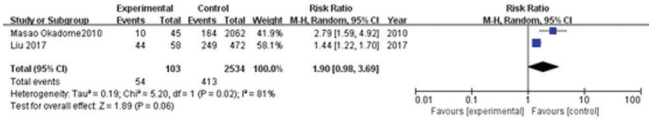


Figure 9. Forest plot of hospitalization time between the study group and the control group



Surgery Time. Five studies[10-13,17] reported characteristics of the surgery time population in both groups. The heterogeneity test showed significant heterogeneity among the studies (P < .00001, I^2 = 91%). Meta-analysis was conducted using a random-effects model, as shown in Figure 10. The results indicated that there was a statistically significant difference in surgery time between the study group and the control group [OR=1.37, 95% CI (1.02, 1.85), P = .04], suggesting a tendency for longer surgery time in the study group patients.

Figure 10. Forest plot of operation time in the study group and control group

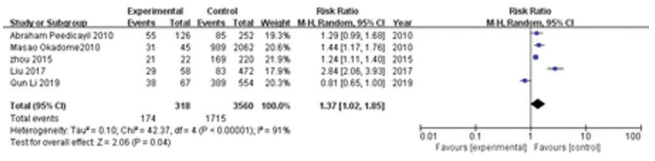
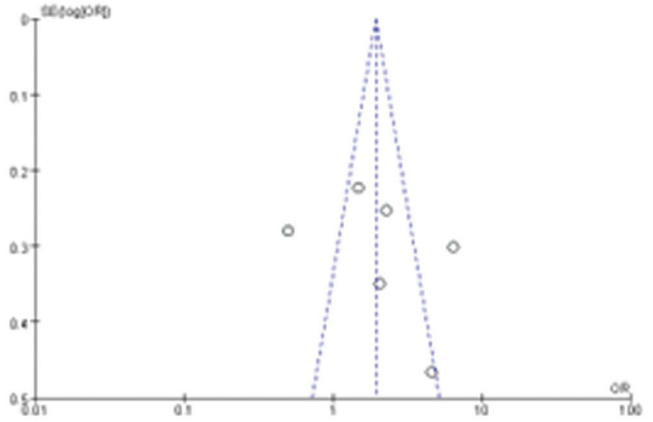


Figure 11. Funnel chart



Publication Bias

An analysis of publication bias for the included studies revealed a funnel-shaped distribution, indicating a small publication bias in the selected literature. See Figure 11 for details.

The funnel chart provides a visual representation of the relationship between the effect size estimates and their precision for each study included in the meta-analysis. In an unbiased scenario, the funnel plot should resemble an inverted funnel shape, with smaller studies scattered around the bottom due to their larger standard errors and larger studies concentrated near the top due to their smaller standard errors. Any asymmetry in the funnel plot may suggest the presence of publication bias. If there is publication bias, smaller studies with non-significant results may be missing, causing the funnel plot to appear asymmetrical. We used statistical tests to quantify publication bias, such as Egger's test to assess the funnel plot's asymmetry by regressing the standard error against the effect size estimate. A significant *P* value in Egger's test suggests the presence of publication bias.

DISCUSSIONS

Venous thromboembolism (VTE) stands as a critical complication in gynecological oncology, profoundly influencing patient outcomes and quality of life. The heightened risk—nearly quintupling in tumor patients compared to non-tumor patients[18]—underscores the urgent need for vigilant VTE risk assessment in the perioperative care of gynecological malignancy patients. This study's findings contribute substantially to our clinical understanding by identifying specific risk factors (age, tumor staging, body mass index, hypertension, and surgery duration) that clinicians can monitor closely. By doing so, healthcare providers can tailor their strategies for VTE prevention and management, thus directly enhancing patient safety, reducing the likelihood of postoperative complications, and improving overall patient care outcomes.

The results of this meta-analysis show that, compared with the control group, the study group had a statistically significant older age [OR=1.41, 95% CI (1.00, 1.98), *P* = .05], higher tumor staging [OR=1.37, 95% CI (1.04, 1.81), *P* = .03], higher body mass index [OR=1.42, 95% CI (1.12, 1.81), *P* = .004], higher prevalence of hypertension [OR=1.72, 95% CI (1.30, 2.28), *P* = .0002], and longer surgery duration [OR=1.37, 95% CI (1.02, 1.85), *P* = .04]. However, there were no statistically significant differences in tumor diameter [OR=0.52, 95% CI (0.05, 5.32), *P* = .58], diabetes prevalence [OR=1.32, 95% CI (0.42, 4.11), *P* = .64], coronary heart disease incidence [OR=1.16, 95% CI (0.91, 1.47), *P* = .23], and length of hospital stay [OR=1.90, 95% CI (0.98, 3.69), *P* = .06] between the study group and the control group, indicating no statistically significant differences.

For the risk factor of age is considered a significant influencing factor for the development of venous thromboembolism (VTE) in gynecological tumor patients. Various studies have different definitions of age in relation to gynecological tumor patients. Still, they generally lean towards the understanding that the older the age, the higher the probability of VTE complications in these patients. The variations in research lie mainly in the definition of the age range at higher risk. Some studies define the high-risk age as being over 50 years old,[19] while others point out that patients over 60 years old are more prone to venous thromboembolism.[20]

Furthermore, research also indicates that postoperative venous thromboembolism risk is higher in obese patients.[21] This heightened risk is primarily attributed to factors such as activation of the endogenous coagulation system, platelet adhesion, and aggregation. Therefore, both age and body mass index are considered risk factors for the occurrence of VTE in gynecological malignancy patients during the perioperative period, a conclusion supported by the findings of this study.

Additionally, some studies suggest that tumor staging is also one of the risk factors influencing the development of venous thromboembolism (VTE) in cancer patients. It is generally believed that the higher the tumor stage, the greater the probability of VTE complications.[22] This may be attributed to the increased severity of tumor cell deterioration with higher staging, making the relevant tissues more susceptible to invasion. This increased vulnerability of tissue-associated vessels facilitates damage, promoting the interference of relevant invasive factors. Consequently, the blood becomes abnormally viscous, making clot formation more likely.

In this study, an analysis was conducted on patients with tumor staging classified as stages III and IV. The findings revealed a significantly higher number of patients in these two stages in the study group compared to the control group, indicating that tumor staging is indeed a risk factor for the occurrence of VTE in patients with gynecological malignancies during the perioperative period. The likelihood of VTE

occurrence is also notable in patients with hypertension. Typically, hypertensive patients are more susceptible to vascular wall damage, leading to platelet aggregation. Additionally, the increased fibrosis of smooth muscle cells in the vascular wall reduces elasticity, further contributing to thrombus formation and exacerbating the degree of embolism.[23]

Moreover, research by Moulder and colleagues[24] on patients undergoing hysterectomy indicates that surgery duration is another important risk factor for VTE in cancer patients. The study results demonstrate that for each additional hour of surgery, the probability of VTE occurrence increases by 35%. The risk of VTE occurrence accumulates continuously with prolonged surgery duration. The findings of this study align with this conclusion, affirming that hypertension and surgery duration are risk factors for the development of VTE in patients with gynecological malignancies.

Moreover, some studies have indicated that tumor diameter,[25] diabetes,[10] coronary heart disease,[13] and length of hospital stay[11] also increase the risk of postoperative venous thromboembolism (VTE) in malignant tumor patients. However, the results of this meta-analysis show that, compared with the control group, there were no statistically significant differences in tumor diameter, diabetes prevalence, coronary heart disease incidence, and length of hospital stay in the study group. This finding is not entirely consistent with the conclusions of the aforementioned studies, and the author believes that this discrepancy may be related to the limited sample size included in this meta-analysis.

The identification of the significant risk factors for venous thromboembolism (VTE) in gynecologic oncology patients has important clinical implications. By recognizing these risk factors, clinicians can develop targeted strategies for VTE prevention, leading to improved patient outcomes. The findings of our study provide valuable insights that can inform personalized medicine approaches, where risk factor assessment is used to tailor prophylactic treatments for individual patients. For example, knowing that advanced age, tumor staging, higher BMI, hypertension, and prolonged surgery duration are associated with an increased risk of VTE allows clinicians to prioritize preventive measures in patients with these risk factors. This may include implementing pharmacological prophylaxis, such as low molecular weight heparin, in high-risk patients, ensuring early mobilization post-surgery, and closely monitoring patients during the perioperative period. Additionally, these findings underscore the importance of risk factor modification, such as blood pressure control and weight management, to mitigate the risk of VTE in gynecologic oncology patients.

We acknowledge several limitations of our study, including the small number of studies available for inclusion and the potential for implementation bias. These limitations highlight the need for further research to strengthen our understanding of VTE in gynecologic oncology patients.

Future studies should aim to include larger sample sizes to enhance statistical power and provide more robust evidence regarding the association between risk factors and VTE. Additionally, investigations into additional potential risk factors, such as genetic predispositions or specific tumor biomarkers, could further refine risk stratification and guide personalized preventive strategies. Prospective studies that incorporate standardized data collection methods and rigorous study designs will help overcome the limitations of existing research and provide more reliable evidence.

Our findings contribute to the broader context of VTE management in oncology, specifically in gynecologic malignant tumors. By identifying the specific risk factors associated with VTE in this patient population, our study adds to the existing body of knowledge on the pathophysiology and prevention of VTE.

These results have implications for the overall management of gynecologic malignant tumors, as VTE is a significant complication that can impact treatment outcomes and patient survival. The findings underscore the importance of comprehensive VTE risk assessment and tailored preventive measures in gynecologic oncology practice. Integrating VTE risk assessment into the clinical decision-making process can help clinicians optimize patient care and improve patient safety.

In conclusion, age, tumor staging, body mass index, hypertension, and surgery duration are risk factors for the development of postoperative VTE in gynecological malignant tumor patients. By paying attention to these risk factors, the risk of VTE occurrence can be effectively assessed and prevented.

REFERENCES

1. Hirsh J. Venous thromboembolism[J]. *Chest*, 1986, 556(none):378-385.doi:10.1378/chest.89.5_Supplement.369S.
2. Heit JA. The epidemiology of venous thromboembolism in the community: implications for prevention and management. [J]. *J Thromb Thrombolysis*. 2006;21(1):23-29. doi:10.1007/s11239-006-5572-y
3. Chopra V, Kaatz S, Grant P, et al. Risk of Venous Thromboembolism Following Peripherally Inserted Central Catheter Exchange: An Analysis of 23,000 Hospitalized Patients. [J]. *Am J Med*. 2018;131(6):651-660. doi:10.1016/j.amjmed.2018.01.017
4. Bannow BT, et al. *Laboratory biomarkers for venous thromboembolism risk in patients with hematologic malignancies: A review.* [J] Thrombosis Research An International Journal on Vascular Obstruction Hemorrhage & Hemostasis; 2018.
5. Brandão GMS, Malgor RD, Vieceli T, et al. A network meta-analysis of direct factor Xa inhibitors for the treatment of cancer-associated venous thromboembolism. [J]. *Vascular*. 2022;30(1):130-145. doi:10.1177/17085381211002726
6. Zhang Y J, Li Z H, Shen D, et al.Association of Combined Lifestyle and Polygenetic Risk with Incidence of Venous Thromboembolism: A Large Population-Based Cohort Study[J].Thrombosis and Haemostasis: Journal of the International Society on Thrombosis and Haemostasis, 2022.
7. Sirisena PLA, Samarakkody SN, Subhani B, et al. A Study on Risk Factors for Venous Thromboembolism and the Requirement of Thromboprophylaxis in Pregnancy and Postpartum Period in a Tertiary Care Centre in South Asian Country: A Cross Sectional Study [J]. *J Obstet Gynaecol*. 2023;13(3):403-413.
8. Takeda C, Yamashita Y, Takeuchi M, et al. Incidence, clinical characteristics and long-term prognosis of postoperative symptomatic venous thromboembolism: a retrospective cohort study. [J]. *BMJ Open*. 2022;12(2):e055090. doi:10.1136/bmjopen-2021-055090
9. Wells G. The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Non-Randomised Studies in Meta-Analyses[C]//Symposium on Systematic Reviews: Beyond the Basics.2014. doi:10.1006/bioe.2002.0137.
10. Luofang Z, Hongbei HU. *Risk factors associated with developing lower extremity deep venous thrombosis after laparoscopic operation of gynecology malignant tumor.* [J] Lingnan Modern Clinics in Surgery; 2015.
11. Liu SN, Lu SL, Gu ZY, et al. Risk factors analysis of venous thromboembolism in post-operative patients with gynecological malignant tumor and application of related risk assessment table [J]. *Academic Journal of Second Military Medical University*. 2017;38(10):1244-1249. doi:10.16781/j.0258-879x.2017.10.1244
12. Peedicayil A, Weaver A, Li X, Carey E, Cliby W, Mariani A. Incidence and timing of venous thromboembolism after surgery for gynecological cancer. [J]. *Gynecol Oncol*. 2011;121(1):64-69. doi:10.1016/j.ygyno.2010.11.038
13. Okadome M, Saito T, Miyahara D, Yamanaka T, Kuroiwa T, Kurihara Y. Postoperative pulmonary embolism including asymptomatic cases in gynecologic oncology. [J]. *Int J Gynecol Cancer*. 2010;20(4):655-663. doi:10.1111/IGC.0b013e3181bdbeb5
14. Abu Saadeh F, Norris L, O'Toole S, Gleeson N. Venous thromboembolism in ovarian cancer: incidence, risk factors and impact on survival. [J]. *Eur J Obstet Gynecol Reprod Biol*. 2013;170(1):214-218. doi:10.1016/j.ejogrb.2013.06.004

15. Matsuo K, Hasegawa K, Yoshino K, et al. Venous thromboembolism, interleukin-6 and survival outcomes in patients with advanced ovarian clear cell carcinoma. [J]. *Eur J Cancer*. 2015;51(14):1978-1988. doi:10.1016/j.ejca.2015.07.012
16. Significance of venous thromboembolism in women with uterine carcinosarcoma[J].Gynecologic Oncology An International Journal, 2018.
17. Li Q, Xue Y, Peng Y, Li L. Analysis of risk factors for deep venous thrombosis in patients with gynecological malignant tumor: A clinical study. [J]. *Pak J Med Sci*. 2019;35(1):195-199. doi:10.12669/pjms.35.1.365
18. Khorana AA, Francis CW, Culakova E, Fisher RI, Kuderer NM, Lyman GH. Thromboembolism in hospitalized neutropenic cancer patients. [J]. *J Clin Oncol*. 2006;24(3):484-490. doi:10.1200/JCO.2005.03.8877
19. Stein PD, Hull RD, Kayali F, Ghali WA, Alshab AK, Olson RE. Venous thromboembolism according to age: the impact of an aging population. [J]. *Arch Intern Med*. 2004;164(20):2260-2265. doi:10.1001/archinte.164.20.2260
20. Hokenstad ED, Habermann EB, Glasgow AE, Occhino JA. Risk of venous thromboembolism in patients undergoing surgery for pelvic organ prolapse. [J]. *Int Urogynecol J*. 2016;27(10):1525-1528. doi:10.1007/s00192-016-2990-z
21. Bakirhan K, Strakhan M. Pharmacologic prevention of venous thromboembolism in obese patients. [J]. *J Thromb Thrombolysis*. 2013;36(3):247-257. doi:10.1007/s11239-012-0844-1
22. Chew HK, Wun T, Harvey D, Zhou H, White RH. Incidence of venous thromboembolism and its effect on survival among patients with common cancers. [J]. *Arch Intern Med*. 2006;166(4):458-464. doi:10.1001/archinte.166.4.458
23. Chew HK, Wun T, Harvey DJ, Zhou H, White RH. Incidence of venous thromboembolism and the impact on survival in breast cancer patients. [J]. *J Clin Oncol*. 2007;25(1):70-76. doi:10.1200/JCO.2006.07.4393
24. Moulder JK, Moore KJ, Strassle PD, Louie M. Effect of length of surgery on the incidence of venous thromboembolism after benign hysterectomy. [J]. *Am J Obstet Gynecol*. 2021;224(4)(suppl 2):364.e1-364.e7. doi:10.1016/j.ajog.2020.10.007
25. Suzuki N, Yoshioka N, Ohara T, et al. Risk factors for perioperative venous thromboembolism: A retrospective study in Japanese women with gynecologic diseases. [J]. *Thromb J*. 2010;8(1):17-17. doi:10.1186/1477-9560-8-17