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ENDOMETRIOSIS AND VTE: A REVIEW OF THE EVIDENCE AND PATHOPHYSIOLOGICAL MECHANISMS

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ABSTRACT

Introduction and objective: Endometriosis is a chronic inflammatory condition affecting approximately 10% of women of reproductive age. Venous thromboembolism (VTE) is a major cause of mortality worldwide. Because the relationship between endometriosis and VTE is not well-defined, we conducted a review of studies that assessed the occurrence of VTE in women with endometriosis.

Review methods: A structured PubMed search was conducted to identify studies published between January 2015 and April 2025 assessing the risk of VTE in patients with endometriosis. Seven studies met the inclusion criteria after screening for relevance and exclusion of case reports.

Abbreviated description of the state of knowledge: Some large-scale studies suggest an elevated VTE risk in women with endometriosis, particularly in younger individuals, during pregnancy, or when using hormonal therapy. However, results vary due to differences in study design, diagnostic definitions, and confounder adjustment. Pathophysiologically, endometriosis-related inflammation, hormonal influences, and endothelial dysfunction may contribute to a prothrombotic state.

Summary: The association between endometriosis and VTE remains unclear; biologically plausible mechanisms and clinical patterns suggest it may be relevant in certain populations. Future research should focus on well-characterized, prospective studies. Clinicians should remain alert to thrombotic risk in women with endometriosis, especially when additional risk factors are present.

KEYWORDS

Deep Vein Thrombosis, Endometriosis, Venous Thromboembolism

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Introduction.

Endometriosis is a chronic, estrogen-dependent inflammatory condition characterized by the presence of endometrial-like tissue outside the uterus (Giudice & Kao, 2004). It affects around 10% of women of reproductive age and key risk factors include an early onset of menarche, shorter menstrual cycle length, and lower body mass index (Shafir et al., 2018). The most common symptoms encompass dysmenorrhea, chronic pelvic pain, dyspareunia, and infertility (Sinai et al, 2008). This condition is increasingly recognized as a systemic disorder due to its association with chronic inflammation and oxidative stress (Taylor et al., 2021).

Venous thromboembolism (VTE) is a clinical condition that includes deep vein thrombosis (DVT) and pulmonary embolism (PE). DVT involves the formation of thrombi within the deep venous system, most commonly in the lower limbs. PE occurs when part of a thrombus detaches and travels to the pulmonary arteries, causing an obstruction of blood flow in the lungs. The incidence of VTE is between 1 and 1.6 cases per 1000 person-years (Naess et al., 2007; Braekkan & Hansen, 2023; Waheed et al., 2025). DVT presents with unilateral leg swelling, pain and redness, though many cases remain asymptomatic. PE commonly presents with symptoms such as dyspnea, pleuritic chest pain, cough, and occasionally hemoptysis (Braekkan & Hansen, 2023). The pathology of VTE is connected to Virchow's triad—venous stasis, endothelial injury, and a hypercoagulable state (Kumar et al., 2010). Known risk factors include advanced age, surgery, obesity, pregnancy, trauma, malignancy, prolonged immobility, hormonal therapy, systemic inflammation and thrombophilias (Zhang et al., 2018; Mammen, 1992; Li et al., 2024).

Given that both conditions involve inflammation and dysregulated coagulation, a pathophysiological intersection is plausible. This review aims to examine current literature on the relationship between endometriosis and VTE, focusing on whether endometriosis may increase the risk of thrombotic events and what biological mechanisms may explain this association. Identifying and understanding the full spectrum of VTE risk factors is essential for refining prevention strategies and improving patient outcomes (Beckman et al., 2010).

Methodology

We conducted a literature search using the PubMed database to identify studies examining the association between endometriosis and DVT. The search was limited to English articles published between January 2015 and April 2025. The keywords used were “endometriosis” AND “deep vein thrombosis” OR “venous thromboembolism”. This search resulted in a total of 53 articles, from which one duplicate was removed. All remaining titles and abstracts were screened for relevance. Studies were included if they involved human subjects, assessed the risk or incidence of VTE in patients with diagnosed endometriosis, and provided original data. Case reports were excluded as they did not provide enough data to support broader conclusions. In total, seven studies were included in the final review.

Results

I. Association Between Endometriosis and Deep Vein Thrombosis

A pooled analysis of data from three international prospective cohort studies: INAS-VIPOS, INAS-FOCUS, and INAS-SCORE was conducted by De Corte et al. (2025). It encompassed a total of 113,128 women who were newly initiated on oral contraceptive therapy. Individuals with a prior history of DVT were excluded from the analysis to reduce potential bias. The findings revealed a 1.79-fold higher likelihood of developing VTE among women diagnosed with endometriosis, controlling for age, body mass index, smoking, education, age at menarche, and family history of VTE. Additionally, the endometriosis cohort had distinct baseline characteristics: a higher mean age (32.6 vs. 27.5 years), reduced prevalence of prior oral contraceptive use (25.8% vs. 59.0%), greater incidence of a familial history of VTE (7.8% vs. 2.6%), and a substantially higher frequency of prior surgical interventions, including gynecological procedures (81.9% vs. 26.3%). These factors may collectively contribute to the elevated VTE risk observed in this population.

Kigloo et al. (2025) aimed to evaluate the connection between PCOS, endometriosis, DVT and PE. The study included 12,814,970 hospitalized women aged 18 to 49 years, using data from the Healthcare Cost and Utilization Project between 2007 and 2014. The results showed a significant link between endometriosis and VTE, with age as a modifying factor. Women aged 18–24 with endometriosis had a higher risk of VTE, while women aged 35 and older exhibited a lower risk. These findings suggest that age plays an important role in the risk of blood clots in women with endometriosis.

II. Association Between Endometriosis and Deep Vein Thrombosis During Pregnancy

Epelboin et al. (2021) conducted a population-based cohort study in France to assess maternal and perinatal morbidity among three groups of single pregnancies between 2013 and 2018: spontaneous pregnancies without endometriosis, spontaneous pregnancies with endometriosis, and pregnancies conceived via assisted reproductive technology in women with endometriosis. When comparing spontaneous pregnancies in women with endometriosis to those without the condition, the study found that endometriosis was independently associated with an increased risk of venous thrombosis (adjusted odds ratio [aOR] 1.51, $P < 0.001$), along with a higher incidence of additional obstetric complications. These findings underscore the role of endometriosis as an independent risk factor for thrombotic and perinatal morbidity, warranting careful monitoring and potential prophylactic interventions in this population.

A nationwide birth cohort study conducted in Japan by Sugiura-Ogasawara et al. (2019) investigated VTE risk factors during pregnancy and the postpartum period. The study analyzed data from 103,070 pregnancies enrolled in the Japan Environment and Children's Study between 2011 and 2014. The frequency of VTE was found to be 7.5 per 10,000 pregnancies. After adjusting for multiple covariates, endometriosis emerged as a novel independent risk factor for VTE, with an aOR of 2.70 (95% confidence interval [CI], 1.21 – 6.00). This indicates that pregnant women with endometriosis have a significantly higher risk of developing VTE compared to those without the condition. However, the diagnosis of endometriosis was based on self-reported medical history obtained through questionnaires, which may lead to misclassification bias.

III. Lack of Association Between Endometriosis and Deep Vein Thrombosis

Stewart et al. (2022) conducted a retrospective cohort study using data from the American College of Surgeons National Surgical Quality Improvement Program, a database that tracks surgical outcomes. The study included 29,742 women aged 18 to 55 who underwent total hysterectomy for benign conditions between January 2018 and December 2019. Out of these, 3,596 (12.1%) had surgery for endometriosis. Covariates included in the adjusted models were age, race, ethnicity, and surgical route. The analysis found no difference

in the rate of VTE between women with and without endometriosis. However, patients with endometriosis had a slightly higher rate of major complications (3.8% vs. 3.4%) and were more likely to experience deep or organ-space infections (2.3% vs. 1.6%). They were less likely to require a blood transfusion (1.8% vs. 3.0%). No significant differences were found in minor complications, overall morbidity, superficial infections, sepsis, or 30-day mortality. These findings suggest that while endometriosis may be associated with certain surgical risks, it does not increase the risk of VTE following a hysterectomy. A potential issue is that patients with endometriosis had fewer comorbidities, possibly impacting the accuracy of outcome comparisons.

The THROMBOGYN study, conducted by Mottais-Cosnefroy et al. (2022), involved 125 women aged 18 to 50 years who were hospitalized for a VTE event at Saint Joseph Hospital in Paris between 2016 and 2020. Eleven women (9%) had endometriosis. The study found that the prevalence of polycystic ovary syndrome and endometriosis among participants was similar to that in the general French population. However, the results were limited by the small number of participants and the fact that the study was restricted to one hospital.

Wiegers et al. (2022) carried out a retrospective cohort study including 533 women with histologically and surgically confirmed severe endometriosis who underwent laparoscopic surgery between January 2015 and December 2019. Eleven patients with a prior history of VTE were excluded. During follow-up, only one postoperative VTE event was observed, corresponding to an incidence rate of 0.3 per 1,000 person-years. These results indicate a low incidence of VTE in this population, suggesting that severe endometriosis alone may not independently elevate postoperative VTE risk. The study is limited by its monocentric design and the low event rate.

Discussion

The relationship between endometriosis and VTE remains incompletely defined, but data suggest that the risk may be elevated in specific subgroups. Among the strongest evidence is the pooled analysis by De Corte et al. (2025), which found a 1.79-fold increase in VTE risk in women with endometriosis. This study is particularly valuable because it compares two groups initiating oral contraceptive use. Combined hormonal contraception is a well-established risk factor for VTE, with multiple studies demonstrating an elevated risk of thrombotic events among users (Lidegaard et al., 2009; Lidegaard et al., 2012; van Hylckama Vlieg et al., 2009). Given that hormonal contraceptives are also a common therapeutic option for managing endometriosis symptoms (Dunselman et al., 2014), their use may confound the relationship between endometriosis and VTE. Studies that do not adequately adjust for hormonal contraceptive use may overestimate or underestimate the true association between endometriosis and thrombotic risk. Moreover, the absence of consistent adjustment for other known VTE risk factors, such as obesity, malignancy, surgery, infection, smoking and prolonged immobility (Zhang et al., 2018; Mammen, 1992; Li et al., 2024) further limits the interpretability of existing evidence. These gaps underscore the importance of rigorous confounder control in future research aiming to clarify this relationship. Kigloo et al.'s (2025) large administrative dataset identified a potential age-modified effect, with younger women with endometriosis facing a higher thrombotic risk. Endometriosis has been recognized as an independent risk factor for VTE in women during pregnancy and the postpartum period by Epelboin et al. (2021) and Sugiura-Ogasawara et al. (2019). Studies such as Stewart et al. (2022) and Wiegers et al. (2022), conducted in surgical populations, reported no increased incidence. However, both were limited by low event rates and healthier baseline populations. Additionally, studies that are limited to surgical populations may obscure the thrombotic contribution of endometriosis as operations themselves are associated with an increased risk of VTE (Meknas et al., 2023; Smeets et al., 2023).

A key source of heterogeneity lies in diagnostic definition. Studies relying on histological or surgical confirmation provide more specific, but narrower, case definitions; population-based studies using administrative codes capture broader phenotypes but risk misclassification.

A biologically plausible link between endometriosis and thrombosis is supported by emerging evidence. Chronic systemic inflammation in endometriosis can upregulate procoagulant factors, downregulate natural anticoagulants and inhibit fibrinolysis (Esmon, 2003). In a study by Rana et al. (1996), levels of cytokines Tumor Necrosis Factor-alpha and Interleukin 8 were significantly elevated in women with endometriosis. Both have been associated with prothrombotic activity (Pircher et al., 2012; van Aken et al., 2002). While some cytokines are being investigated as a marker for endometriosis, there isn't a single, definitive biomarker currently used in clinical practice for diagnosis (May et al., 2010; Nisenblat et al., 2016). Endothelial dysfunction, a key component of Virchow's triad, has also been associated with endometriosis (Smyk et al., 2024). Additionally, some studies have reported shortened activated partial thromboplastin time in patients with endometriosis, suggesting a hypercoagulable state (Ottolina et al., 2020; Viganò et al., 2018).

The convergence of epidemiological and mechanistic data suggests that women with endometriosis may benefit from individualized VTE risk assessment. However, routine thromboprophylaxis in this population is not currently supported by evidence.

Conclusions

The current evidence raises the possibility that endometriosis may be associated with an elevated risk of VTE in certain clinical contexts, particularly among younger women, those exposed to hormonal therapy and pregnant patients. While findings across studies are inconsistent, the pattern warrants further investigation. Mechanistic links such as chronic inflammation, estrogen-mediated procoagulant shifts, and endothelial dysfunction offer a biologically plausible explanation. The lack of standardized diagnostic criteria, inconsistent adjustment for confounders, and heterogeneous study designs continue to obscure the strength and scope of the association. Moving forward, large, multicenter prospective studies with rigorous confounder adjustment and validated outcome measures are essential. Until such data is available, clinicians may consider endometriosis as a potential modifier of thrombotic risk, particularly when multiple risk factors are present, and incorporate this awareness into individualized decision-making.

Declarations

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Author Contributions:

Conceptualization: J.D. and A.N.; Methodology: P.K.; Software: S.C.; Validation: M.G., Z.T., and A.Pr.; Formal Analysis: J.C.; Investigation: A.Pe. and A.Z.; Resources: Z.T.; Data Curation: A.Z. and J.D.; Writing – Original Draft Preparation: J.C. and S.C.; Writing – Review & Editing: A.N., M.G., and P.K.; Visualization: A.Pr.; Supervision: P.K. and A.Pe.; Project Administration: J.D.

Conflicts of Interest: No conflicts of interest to declare.

Data Availability Statement: All data generated or analyzed during this study are included in this published article

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