Hormones, cancer, and thrombosis: sex-specific mechanisms at the interface of hemostasis and vascular biology

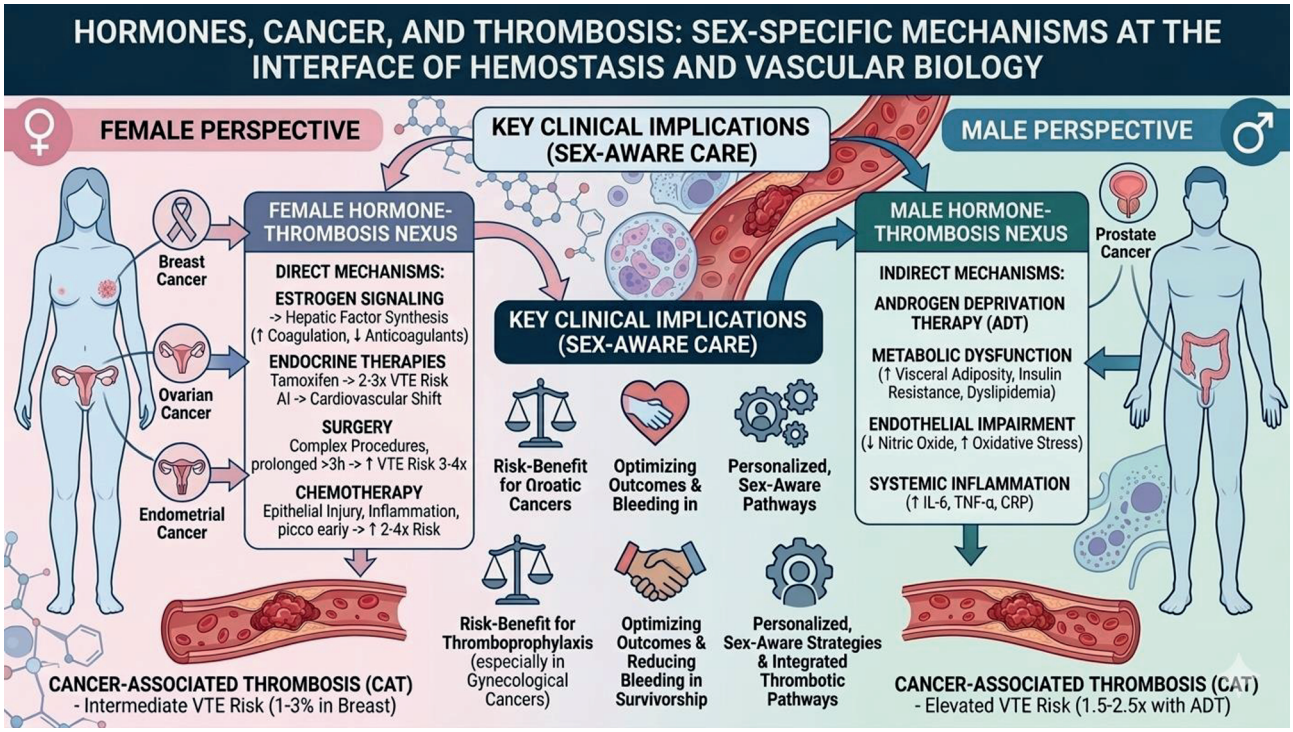
Elvira Grandone,[1] Giovanni Luca Tiscia[2]

[1]Obstetrics and Gynaecology Department, University of Foggia; [2]Thrombosis and Haemostasis Unit, Fondazione IRCCS "Casa Sollievo della Sofferenza", S. Giovanni Rotondo (FG), Italy

ABSTRACT

This review examines the complex relationship between hormonal signaling, cancer biology, and thrombosis, focusing primarily on cancer-associated venous thromboembolism (VTE) in hormone-sensitive malignancies. Hormones regulate key hemostatic processes—including coagulation, platelet activity, endothelial function, and fibrinolysis—and disturbances in these pathways can promote thrombotic complications in patients with cancer. Sex hormones play distinct roles in modulating thrombotic risk. Estrogens tend to promote a prothrombotic state by increasing procoagulant factors and reducing anticoagulant activity, whereas progesterone has minimal direct hemostatic effects. The impact of testosterone remains less clear, although some data suggest a transient increase in VTE risk shortly after initiation of testosterone therapy. In hormone-dependent cancers, endocrine therapies further modify thrombotic risk through their effects on hormonal pathways and tumor-associated inflammation. The magnitude and mechanisms of thrombosis vary across malignancies. In breast cancer, VTE risk is generally moderate but increases with age, obesity, disease stage, chemotherapy, and particularly endocrine therapy such as tamoxifen, which is associated with a two- to three-fold higher VTE risk. Ovarian cancer is among the most thrombogenic solid tumors, driven by tumor biology, inflammatory activation, and intensive treatments such as surgery and platinum-based chemotherapy. Endometrial cancer risk is linked to prolonged estrogen exposure and obesity, while prostate cancer demonstrates increased thrombotic risk primarily related to androgen deprivation therapy, which induces metabolic and vascular changes that favor hypercoagulability. These sex-specific differences highlight the need for risk-adapted strategies for thromboprophylaxis and surveillance. Clinical management should consider tumor type, hormonal environment, treatment modality, and patient-specific risk factors. As survival improves in hormone-sensitive cancers, optimizing prevention of thrombotic complications while minimizing bleeding risk represents an important component of personalized oncologic care.

GRAPHICAL ABSTRACT



Key words: hormones; cancer; sex; thrombosis.

Introduction

Hormones are fundamental regulators of human physiology, exerting pleiotropic effects on growth, metabolism, reproduction, immune function, and vascular homeostasis. Through their systemic and tissue-specific actions, hormones influence endothelial function, platelet activity, inflammatory signaling, and the balance between procoagulant, anticoagulant, and fibrinolytic pathways.[1] Perturbations of these finely regulated mechanisms may predispose to thrombosis or bleeding, conditions that represent major sources of morbidity and mortality in patients with cancer.

Beyond their physiological roles, hormonal pathways critically shape cancer initiation, progression, and response to therapy. Increasing evidence indicates that these same pathways contribute to cancer-associated thrombosis (CAT) through both direct effects on hemostatic factors and indirect effects mediated by tumor biology, vascular injury, and inflammation.[2] The interplay between hormonal signaling, malignancy, and thrombosis is complex and multifactorial, reflecting dynamic interactions between tumor cells, the coagulation system, and the vascular endothelium.

Hormone-sensitive malignancies, particularly breast cancer and prostate cancer- the most common non-cutaneous cancers in women and men worldwide- provide paradigmatic models to understand how endocrine pathways drive tumor behavior and how therapeutic hormonal manipulation modifies hemostatic risk over time. The hormonal therapies that are cornerstone for treatment of both cancers improve survival but increase cardiovascular morbidity and mortality.[3] While these therapies and the underlying malignancy also influence the risk of arterial thromboembolism (ATE), including myocardial infarction and stroke, the clinical data regarding ATE in this context remain relatively scarce and inconsistent compared to venous events. Consequently, this review focuses primarily on venous thromboembolism (VTE), which represents the most well-characterized and prevalent thrombotic complication in these patients.

The primary aim of this review is to provide a comprehensive analysis of how hormonal pathways and their therapeutic manipulation influence the risk of cancer associated VTE. Specifically, we aim to delineate the distinct pathophysiological mechanisms in breast, gynecological, and prostate cancers, and to offer evidence-based insights into risk stratification and thromboprophylaxis tailored to the hormonal profile and sex of the patient.

Sex-specific hormonal effects on thrombosis

Hormones play a crucial role in modulating hemostasis by directly affecting coagulation factor synthesis, natural anticoagulant pathways, platelet function, endothelial activation, and fibrinolysis. Sex-related differences in thrombotic risk arise mainly from distinct hormonal types, synthetic pathways, and exposure patterns in women and men, including hormonal fluctuations across different life stages in women, sustained androgen exposure in men, and the use of exogenous hormones in endocrine therapies.[4] The hormones most extensively studied in this context are estrogens, progesterone, and androgens.

Estrogens exert pleiotropic effects through nuclear estrogen receptors (ERα and ERβ) and membrane-bound G protein–coupled receptors, influencing not only reproductive tissues but also cardiovascular and vascular biology, including vasodilation, vascular remodeling, myocardial hypertrophy, and coagulation.[3] From a hemostatic perspective, estrogens promote a pro-thrombotic state by increasing hepatic synthesis of pro-coagulant factors and reducing anticoagulant activity, thereby shifting the hemostatic balance toward hypercoagulability.[5] These effects are consistently observed in high-estrogen states such as pregnancy, oral contraceptive use, and postmenopausal hormone replacement therapy.[5]

In hormone-sensitive cancers, estrogen-related thrombotic risk is further modified by endocrine therapies (Table 1). In estrogen receptor–positive (ER+) tumors, selective estrogen receptor modulators (SERMs) and aromatase inhibitors either interfere with estrogen receptor signaling or reduce systemic estrogen levels. Tamoxifen- a selective estrogen receptor modulator -despite favorable effects on lipid profiles and cardiovascular parameters, increases venous thromboembolic risk due to its partial estrogen-agonistic effects on hepatic coagulation pathways, whereas aromatase inhibitors may shift risk toward adverse cardiovascular outcomes.[3] These therapy-related effects interact with cancer-associated hypercoagulability, which is driven by tumor cell expression of tissue factor and cancer procoagulant, as well as by pro-inflammatory cytokines such as Interleukin-6 (IL-6) and Tumor Necrosis Factor α (TNF-α) released by both tumor and immune cells, leading to amplification of coagulation cascade activation.[6,7] Prolonged cancer treatments, including hormonal therapies, may further enhance thrombotic risk through endothelial injury and venous stasis.[6,7]

Progesterone appears to have minimal direct effects on coagulation pathways.[5] In contrast, the thrombotic impact of

Corresponding author: Elvira Grandone, Obstetrics and Gynaecology Department, University of Foggia, Viale Pinto, Foggia, Italy.
E-mail: elvira.grandone@unifg.it

Funding: this research is funded by the European Union under the Horizon Europe Innovation Action ThrombUS (Grant Agreement No. 101137227). The views and opinions expressed are solely those of the authors and do not necessarily represent those of the European Union or HADEA, the granting authority. Neither the European Union nor HADEA can be held responsible for these views.

Received: 2 January 2026.
Accepted: 15 March 2026.

Licensee PAGEPress, Italy
Bleeding, Thrombosis and Vascular Biology 2026; 5(s1):435
doi:10.4081/btvb.2026.435

testosterone remains uncertain. Overall, testosterone therapy is generally associated with a low thrombotic risk: a systematic review and meta-analysis reported no statistically significant association between testosterone therapy and VTE (odds ratio [OR] 1.41, 95% confidence interval [CI] 0.96–2.07), although heterogeneity was high and risk of bias was moderate.[8] However, a large case-crossover study including 39,622 men with VTE demonstrated an approximately two-fold increased risk associated with testosterone exposure during the six-month hazard period, independent of hypogonadism status.[9] These findings suggest a potential short-term increase in thrombotic risk following initiation of testosterone therapy, supporting the need for close clinical monitoring during early treatment phases.

The translation of these sex-specific hormonal effects into clinical thrombotic phenotypes varies substantially across hormone-sensitive malignancies, as summarized in a comparative framework (Table 2).

Breast cancer: hormone dependence and thrombotic risk

Breast cancer is the most frequently diagnosed malignancy worldwide, accounting for approximately one in eight new cancer diagnoses, with over two million women affected annually.[3] Around 70% of tumors express estrogen and/or progesterone receptors, reflecting a strong dependence on estrogen-driven proliferative signaling and underpinning the effectiveness of endocrine therapy.[15] Despite a relatively favorable prognosis compared with other solid tumors, breast cancer represents the most common cause of CAT in women, largely due to its high incidence and prolonged exposure to systemic treatments.

From an epidemiological perspective, the intrinsic risk of VTE in breast cancer is lower than that observed in highly thrombogenic malignancies such as pancreatic or lung cancer.

Table 1. Hormones and thrombotic risk in hormone-sensitive cancers.

Category	Hormone/therapy	Main cancers	Core mechanism	VTE risk	Key clinical notes
Estrogens/ progestins	Estrogens ± progesterone	Breast, endometrium, ovary	↑ Hepatic synthesis of coagulation factors; ↓ natural anticoagulant proteins	↑↑	Strongest hormonal driver of VTE; risk increases with dose and oral route
Androgens	Testosterone/DHT	Prostate	AR-mediated metabolic and endothelial effects	↔/↑	Replacement therapy usually low risk; deprivation increases cardiometabolic burden
Endocrine cancer therapy	Tamoxifen	ER+ breast	ER modulation with hepatic procoagulant shift	↑↑	Highest VTE risk among endocrine agents
	Aromatase inhibitors	ER+ breast	Estrogen depletion	↔/↓	Lower VTE risk than tamoxifen
	Androgen deprivation therapy	Prostate	Hormonal suppression → metabolic dysfunction	↑	Risk may be duration-dependent
Exogenous hormones	HRT, GAHT	Breast	Systemic hormone exposure	↑	Route (oral > transdermal) matters

ADT, androgen deprivation therapy; AR, androgen receptor; DHT, dihydrotestosterone; ER, estrogen receptor; ER+, estrogen receptor–positive; GAHT, gender-affirming hormone therapy; HRT, hormone replacement therapy; VTE, venous thromboembolism.

Table 2. Comparative framework: hormone-sensitive cancers and venous thromboembolism.

Cancer	Hormone driver	Hormone dependence	Baseline VTE	Key risk factors / treatments	Prophylaxis notes
Breast	Estrogens ± progesterone	High (~70% ER/PR+)	Low-moderate	Estrogen effects, inflammation; chemotherapy, tamoxifen, catheters	Individualized; integrate RAMs (*e.g.*, Khorana) during chemo balance VTE risk vs bleeding
Endometrial	Unopposed estrogens	High	Moderate-high	Obesity, chemotherapy, surgery, radiotherapy	Extended postoperative thromboprophylaxis; use RAMs for ambulatory chemotherapy
Ovarian	Indirect	Low-moderate	High	Aggressive tumor, inflammation; chemotherapy, cytoreductive surgery	Extended postoperative thromboprophylaxis; use RAMs for ambulatory chemotherapy
Prostate	Androgens	High	Moderate	Androgen deprivation → metabolic/endothelial dysfunction	Monitor during prolonged ADT; perioperative prophylaxis

ER/PR+, estrogen/progesterone receptor–positive; VTE, venous thromboembolism; ADT, androgen deprivation therapy.

Cumulative VTE incidence is generally reported in the range of 1-3% for breast cancer, compared with approximately 5-10% for lung cancer and 10-20% for pancreatic cancer, underscoring marked heterogeneity in tumor-associated thrombotic risk.[16]

Nevertheless, thrombotic risk in breast cancer is dynamic and multifactorial, increasing with age, obesity, comorbidity burden, and advancing disease stage. Older age is a consistent and independent predictor of VTE, with women aged ≥70 years experiencing approximately a 2- to 3-fold higher risk compared with younger patients, reflecting age-related changes in coagulation activation, endothelial dysfunction, and reduced mobility.[17] Obesity further amplifies thrombotic risk through chronic inflammation and increased pro-coagulant factor levels, while cardiovascular comorbidities and diabetes contribute additional vascular vulnerability.[18]

Treatment-related factors also play a major role. Chemotherapy exposure is associated with a 2- to 4-fold increase in VTE risk, particularly during the first months of treatment, whereas endocrine therapies and targeted agents contribute to a more sustained, lower-grade prothrombotic state over time.[1] Regional nodal involvement approximately doubles VTE risk, while metastatic disease is associated with up to a 6-fold increase, reflecting progressive systemic activation of coagulation pathways and tumor burden-driven inflammation.[20]

Treatment-related modifiers of thrombosis in women

Surgical management is undertaken in the vast majority of patients with non-metastatic breast cancer and introduces a transient period of increased thrombotic vulnerability. While the absolute 30-day VTE incidence for surgery is relatively low (ranging from 0.2% to 1.2%), this risk can increase significantly - up to 3- to 4-fold - in patients undergoing complex autologous reconstruction or prolonged procedures exceeding 3 hours.[21] Although breast surgery is generally less invasive than procedures for other solid tumors, the combination of malignancy, anesthesia, and postoperative immobility contributes to VTE risk.[22] Importantly, this risk must be carefully balanced against bleeding complications, which can adversely affect cosmetic outcomes and delay adjuvant therapy -considerations that are particularly relevant in women with otherwise excellent long-term survival.[23]

Chemotherapy further amplifies thrombotic risk through endothelial injury, inflammatory activation, and frequent use of central venous catheters. Large population-based studies demonstrate a marked increase in VTE incidence during chemotherapy, with reported rates of 2% to 5% within the first year of treatment, representing a 4- to 7-fold increase compared to the general population.[24] This risk persists for several months after treatment completion.[25] With regard to the ambulatory setting during chemotherapy, it is useful to integrate available risk assessment models (RAMs) into clinical decision-making. Although models such as the Khorana score have recognized limitations in sensitivity—particularly within specific cohorts like breast cancer[26]—their use is supported by current international guidelines to identify high-risk patients who may benefit from primary thromboprophylaxis. These tools should complement, rather than replace, individualized clinical judgment in assessing the multifactorial thrombotic risk profile of the oncologic patient.[19,27,28]

Endocrine therapy represents the most distinctive and sex-specific contributor to thrombosis risk. As previously mentioned, tamoxifen is consistently associated with a two- to threefold increase in VTE risk compared to age-matched controls, with absolute annual incidences reaching approximately 0.5% to 1% in postmenopausal women.[29] Mechanistic studies demonstrate enhanced thrombin generation and reduced sensitivity to endogenous anticoagulant pathways, consistent with its partial estrogen agonist effects in hepatic tissue. In contrast, aromatase inhibitors suppress systemic estrogen levels and do not appear to induce pro-thrombotic changes in hemostatic biomarkers, maintaining a VTE profile comparable to placebo in most large-scale trials.[14] These divergent effects highlight how distinct endocrine strategies differentially influence coagulation biology in women.

The integration of endocrine therapy with novel targeted agents has added further complexity. CDK4/6 inhibitors (e.g., palbociclib, ribociclib, abemaciclib), when combined with endocrine therapy, have been associated with VTE rates of 2% to 5% in clinical trials and up to 8% in real-world observational studies.[30] This suggests a potential underestimation of thrombotic risk in controlled settings. Conversely, HER2-targeted therapies and immune checkpoint inhibitors have not demonstrated a clear increase in VTE risk in breast cancer, although underreporting remains a concern.[31] Specifically, the use of trastuzumab emtansine in the anti-HER2 landscape serves as a critical example of the need to balance thrombotic and hemorrhagic risks, given its association with clinically significant bleeding and treatment-induced thrombocytopenia.[32] This highlights the necessity of a nuanced approach to anticoagulation that accounts for the specific toxicity profiles of modern targeted agents.

Endometrial and ovarian cancer: hormonal dependence and thrombotic vulnerability

Endometrial and ovarian cancers exemplify the complex interplay between sex hormones, malignancy, and hemostasis. Although both arise from hormonally responsive tissues, they differ substantially in their intrinsic thrombotic risk.[33] Ovarian cancer is among the most thrombogenic solid tumors, with a VTE incidence approximately 3-4 times higher than that observed in endometrial cancer and up to 10 times higher than in breast cancer.[33] Recent real-world data from the RIETE registry further highlight this disparity: 55% of patients with ovarian cancer develop VTE within the first three months after diagnosis, compared with only 19% of breast cancer patients. Moreover, patients with ovarian cancer exhibit the highest rate of VTE recurrence during anticoagulant therapy, reaching 7.29 per 100 patient-years.[34]

This pronounced thrombogenicity, affecting 11-27% of patients,[35] reflects a combination of biological, anatomical, and treatment-related factors. Among histological subtypes, clear cell carcinoma carries a 2.5–4-fold higher risk than other ovarian cancer subtypes, largely driven by increased expression of tissue factor (TF), cancer-derived inflammatory cytokines, and neutrophil extracellular traps (NETs).[36] In addition, advanced stage, high tumor grade, and the presence of ascites—reflecting peritoneal carcinomatosis—are important predictors of a heightened

thrombotic phenotype. Anatomical factors, such as external compression from the primary tumor or lymphadenopathy, further increase the risk of unusual-site thrombosis, including splanchnic vein thrombosis.[37]

Unlike breast cancer, in which endocrine therapy represents a major long-term determinant of thrombotic risk, the thrombotic burden in ovarian cancer is primarily driven by disease extent and treatment intensity, leaving limited opportunity for risk attenuation through endocrine modulation.[37, 38] Chemotherapy also contributes substantially to thrombotic risk, as platinum-based regimens are associated with an almost sevenfold increase in VTE risk.[39] In addition, major surgical interventions—particularly extensive cytoreductive surgery and Hyperthermic Intraperitoneal Chemotherapy (HIPEC)—can induce systemic inflammatory responses, with CAT occurring in approximately 5.6% of patients after HIPEC. Lastly, while targeted therapies such as anti-VEGF agents and PARP inhibitors have significantly improved outcomes, they are also associated with a mild to moderate increase in thrombotic risk.[40]

Thrombotic risk in endometrial cancer is largely related to prolonged exposure to unopposed estrogen and is further amplified by obesity, which increases baseline VTE risk by two- to threefold through chronic inflammation and elevated PAI-1 levels.[37,41] The absolute risk of VTE following surgery for endometrial cancer ranges from 2% to 4% in the absence of thromboprophylaxis—substantially higher than the <1% reported after breast surgery[27,28,42] Consequently, extended postoperative thromboprophylaxis for up to 28 days is recommended, particularly given the extensive pelvic procedures and lymphadenectomy often required.

Prostate cancer: androgen deprivation and thrombosis in men

Prostate cancer represents the archetypal androgen-dependent malignancy, with tumor growth driven by testosterone and dihydrotestosterone signaling. Androgen deprivation therapy (ADT) remains the cornerstone of treatment in advanced disease and is associated with a clinically meaningful increase in VTE risk. Large population-based studies and meta-analyses consistently demonstrate a 1.5- to 2.5-fold higher risk of VTE in men receiving ADT compared with those not exposed.[37,43]

The biological mechanisms underlying this association are multifactorial and distinct from those observed in women. Profound androgen suppression induces a constellation of physiopathological changes that converge toward a pro-thrombotic phenotype. ADT promotes metabolic derangements, including increased visceral adiposity, insulin resistance, dyslipidemia, and sarcopenia, which are themselves established contributors to VTE.[44] In parallel, hypogonadism is associated with endothelial dysfunction, characterized by reduced nitric oxide bioavailability, increased oxidative stress, and up-regulation of endothelial adhesion molecules, facilitating platelet–endothelium interactions and leukocyte recruitment. ADT also induces a pro-inflammatory milieu, with increased circulating levels of IL-6, TNF-α, and C-reactive protein, which may amplify tissue factor expression and thrombin generation.[45] Alterations in hemostatic balance, including increased fibrinogen levels and impaired fibrinolysis, further contribute to a state of hypercoagulability.[46]

From a clinical perspective, the magnitude of thrombotic risk appears to vary according to ADT modality and treatment duration. Observational studies and population-based cohorts have consistently reported a 1.5- to 2-fold increase in VTE risk among men receiving ADT compared with non-exposed patients with prostate cancer modifiers, with higher rates observed in those undergoing combined androgen blockade or prolonged therapy exceeding 6-12 months. Observational studies and large population-based cohorts have consistently demonstrated a 1.5- to 2-fold increased risk of VTE among men receiving ADT compared with non-exposed patients with prostate cancer, with the highest rates observed in those undergoing combined androgen blockade or prolonged treatment exceeding 6-12 months.[47] In a large population-based study conducted between 1997 and 2013, 11,242 men received anti-androgen monotherapy, were treated with gonadotropin-releasing hormone (GnRH) agonists, 1,091 underwent combined androgen blockade, and 3,789 underwent orchiectomy. The excess thromboembolic risk increased over time, rising from 2.52 (95% CI 1.54-4.12) during the first year of therapy to 4.05 (95% CI 2.51-6.55) in the second year. The incidence of VTE increased with treatment duration and was highest among men who switched ADT regimens, suggesting that both disease progression and cumulative hormonal manipulation contribute to thrombotic risk. Notably, the excess risk was already evident within the first year of treatment, supporting a synergistic interaction between acute hormonal withdrawal, cancer-related pro-thrombotic factors, and ADT-induced metabolic alterations.[48]

In contrast, newer androgen receptor pathway inhibitors used for treatment intensification, such as abiraterone acetate or enzalutamide, have not consistently emerged as major independent drivers of VTE risk in clinical trials and real-world analyses.[49] This may reflect differences in their mechanisms of action, partial preservation of androgen signaling in non-target tissues, or more selective receptor blockade. However, given the relatively limited duration of follow-up in pivotal trials and the frequent coexistence of other pro-thrombotic risk factors in advanced disease, continued surveillance and longer-term data are warranted to fully delineate their vascular safety profile.

Sex differences and clinical implications

Breast and prostate cancers exemplify how sex-specific endocrine environments shape both tumor biology and thrombotic risk. In women, estrogenic signaling and its pharmacologic modulation exert direct and measurable effects on hemostasis, with endocrine therapy representing a dominant driver of long-term thrombosis risk,[14,50] whereas in men, androgen deprivation produces a distinct prothrombotic phenotype mediated largely through metabolic and vascular pathways rather than direct hepatic effects on coagulation factor synthesis.[3]

These differences have important clinical implications. Risk assessment, thromboprophylaxis, and long-term survivorship care must account for sex-specific hormonal exposures, treatment duration, and cumulative vascular effects.[30,51] As survival continues to improve in hormone-sensitive cancers, optimizing strategies to mitigate thrombotic risk without increasing bleeding complications represents a critical component of personalized, sex-aware oncologic care.

Clinical implications and risk stratification strategies

The transition from understanding the biological interplay of hormones and hemostasis to implementing effective clinical care requires a shift toward risk-adapted management. Rather than a "one-size-fits-all" approach, clinicians should prioritize intensified surveillance and preventive strategies for specific high-risk subgroups defined by their sex, tumor type, and therapeutic regimen.

For patients undergoing surgical intervention, the risk profile varies significantly by anatomical site and procedure complexity. In the context of pelvic oncologic surgery—specifically for ovarian and endometrial cancers—there is substantial agreement across international guidelines supporting the use of extended postoperative thromboprophylaxis (typically up to 28 days).[27,28] This consistent approach reflects the high intrinsic VTE risk associated with major pelvic dissections and the more favorable benefit-to-risk ratio regarding bleeding. In contrast, for breast cancer surgery, which is generally less invasive, pharmacologic prophylaxis should be more selective, focusing on patients with additive risk factors such as advanced age (≥70 years), obesity, or procedures exceeding three hours.

In the ambulatory setting, the initiation of systemic chemotherapy marks a period of higher thrombotic vulnerability. It is increasingly recognized that clinical decision-making during this phase should be guided by validated Risk Assessment Models (RAMs), such as the Khorana score. While these models have known limitations in sensitivity, particularly in breast cancer, their integration into routine care helps identify high-risk individuals (Khorana score ≥2) who may benefit from primary thromboprophylaxis. This is especially pertinent for patients with ovarian cancer or those with metastatic disease, where the pro-inflammatory state of the malignancy synergizes with the endothelial toxicity of chemotherapy.[26-28]

Furthermore, the choice of endocrine therapy necessitates tailored monitoring. Women treated with tamoxifen require vigilance for VTE symptoms, particularly during the first two years of therapy or when the drug is combined with other pro-thrombotic modifiers like surgery or CDK4/6 inhibitors.[29,30] Conversely, for men on ADT, the thrombotic risk is often inextricably linked to metabolic and vascular health. In this cohort, a comprehensive "cardio-metabolic" surveillance strategy—managing obesity, hypertension, and insulin resistance—may serve as an indirect yet vital component of VTE risk mitigation. Ultimately, by aligning thromboprophylaxis with the specific hormonal and treatment-related profile of the patient, clinicians can better balance the prevention of life-threatening VTE with the preservation of long-term oncologic and cardiovascular health.

Conclusions

Hormones exert profound effects on cancer biology, hemostasis, and vascular function, resulting in sex-specific patterns of cancer-associated thrombosis. Integrating hormonal and sex-specific factors into thrombosis and vascular biology research is essential to refine risk stratification, guide strategies of thromboprophylaxis, and improve long-term outcomes in patients with cancer.

References

1. Muralikrishnan AS, Biasin V, Zabini D, Osto E. Immune and vascular function in cardiometabolic disorders: interplay with sex differences and impact on incretin therapy. Acta Physiol (Oxf) 2025;241:e70091.
2. Sharma BK, Flick MJ, Palumbo JS. Cancer-associated thrombosis: a two-way street. Semin Thromb Hemost 2019; 45:559-568.
3. Okwuosa TM, Morgans A, Rhee JW, et al. Impact of hormonal therapies for treatment of hormone-dependent cancers (breast and prostate) on the cardiovascular system: effects and modifications: a scientific statement from the American Heart Association. Circ Genom Precis Med 2021;14:e000082.
4. Nordstrom SM, Weiss EJ. Sex differences in thrombosis. Expert Rev Hematol 2008;1:3-8.
5. Barcellona D, Grandone E, Marongiu F. Hormones and thrombosis: the dark side of the moon. Blood Transfus 2024;22:46-54.
6. Hansda S, Das H. Insights into cancer-associated thrombosis leading towards ischemic stroke. Biology (Basel) 2025;14:50.
7. Nadir Y, Brenner B. Cancer and thrombosis-New insights. Rambam Maimonides Med J 2018;9:1-7.
8. Houghton DE, Alsawas M, Barrioneuvo P, et al. Testosterone therapy and venous thromboembolism: A systematic review and meta-analysis. Thromb Res 2018;172: 94-103.
9. Walker RF, Zakai NA, MacLehose RF, et al. Association of testosterone therapy with risk of venous thromboembolism among men with and without hypogonadism. JAMA Intern Med 2020;180:190–197.
10. Miziak P, Baran M, Błaszczak E, et al. Estrogen receptor signaling in breast cancer. Cancers (Basel) 2023;15:4689.
11. Saatci O, Huynh-Dam KT, Sahin O. Endocrine resistance in breast cancer: from molecular mechanisms to therapeutic strategies. J Mol Med (Berl) 2021;99:1691-1710.
12. Quistini A, Chierigo F, Fallara G, et al. Androgen Receptor Signalling in Prostate Cancer: Mechanisms of Resistance to Endocrine Therapies. Res Rep Urol 2025;17:211-223.
13. Abou-Ismail MY, Citla Sridhar D, Nayak L. Estrogen and thrombosis: A bench to bedside review. Thromb Res 2020;192:40-51.
14. Blondon M, Bodmer A, Thouvenin L, et al. Differential impact of tamoxifen and aromatase inhibitors on thrombin generation: the prospective HEMOBREAST cohort. Blood Adv 2022;6:2884-2892.
15. Łukasiewicz S, Czeczelewski M, Forma A, et al. Breast cancer-epidemiology, risk factors, classification, prognostic markers, and current treatment strategies-An updated review. Cancers (Basel) 2021;13:4287.
16. Horsted F, West J, Grainge MJ. Risk of venous thromboembolism in patients with cancer: a systematic review and meta-analysis. PLoS Med 2012;9:e1001275.
17. Razouki ZA, Ali NT, Nguyen VQ, Escalante CP. Risk fac-

tors associated with venous thromboembolism in breast cancer: a narrative review. Support Care Cancer 2022;30: 8589-8597.
18. Donnellan E, Khorana AA. Cancer and venous thromboembolic disease: a review. Oncologist 2017;22:199-207.
19. Lyman GH, Carrier M, Ay C, et al. American Society of Hematology 2021 guidelines for management of venous thromboembolism: prevention and treatment in patients with cancer. Blood Adv 2021;5:927-974.
20. Dickmann B, Ahlbrecht J, Ay C, et al. Regional lymph node metastases are a strong risk factor for venous thromboembolism: results from the Vienna Cancer and Thrombosis Study. Haematologica 2013;98:1309-14.
21. Maesaka JY, Reis YN, Elias LM, et al. Venous thromboembolism incidence in postoperative breast cancer patients. Clinics (Sao Paulo) 2023;78:100229.
22. https://associationofbreastsurgery.org.uk/media/1dygs4yn/z-vte_statement.pdf
23. Dhannoon A, Balasubramanian I, Dhannoon AA, et al. The Risk of Haematoma and Venous Thrombosis Associated With Thromboprophylaxis Use in Breast Cancer Surgery: A Meta-Analysis and Systematic Review. Breast J 2025;2025: 9898596.
24. Gervaso L, Dave H, Khorana AA. Venous and arterial thromboembolism in patients with cancer: JACC: CardioOncology state-of-the-art review. JACC CardioOncol 2021;3:173-190.
25. van Hylckama Vlieg MAM, Nasserinejad K, Visser C, et al. The risk of recurrent venous thromboembolism after discontinuation of anticoagulant therapy in patients with cancer-associated thrombosis: a systematic review and meta-analysis. EClinicalMedicine 2023;64:102194.
26. Vladić N, Englisch C, Berger JM, et al. Validation of risk assessment models for venous thromboembolism in patients with cancer receiving systemic therapies. Blood Adv 2025;9:3340-3349.
27. Key NS, Khorana AA, Kuderer NM, et al. Venous thromboembolism prophylaxis and treatment in patients with cancer: ASCO Guideline Update. J Clin Oncol 2023;41:3063-71.
28. Falanga A, Ay C, Di Nisio M, et al. Venous thromboembolism in cancer patients: ESMO Clinical Practice Guideline. Ann Oncol 2023;34:452-67.
29. Decensi A, Maisonneuve P, Rotmensz N, et al. Effect of tamoxifen on venous thromboembolic events in a breast cancer prevention trial. Circulation 2005; 111:650-6.
30. Sánchez Cánovas M, López Robles J, Adoamnei E, et al. Thrombosis in breast cancer patients on cyclin-dependent kinase inhibitors: Survival impact and predictive factors - A study by the cancer and thrombosis group of the Spanish society of medical oncology (SEOM). Eur J Intern Med 2024;130:98-105.
31. Verso M, Moik F, Graziani M, Cohen AT. Targeted anti-cancer agents and risk of venous thromboembolism. Haematologica 2024;109:3868-78.
32. Kowalczyk L, Bartsch R, Singer CF, et al. Adverse Events of trastuzumab emtansine (T-DM1) in the treatment of HER2-positive breast cancer patients. Breast Care (Basel) 2017;12:401-8.
33. Kubo-Kaneda M, Hirota H, Kotaka S, et al. Symptomatic and asymptomatic venous thromboembolism after minimally invasive surgery for gynecological cancers. J Obstet Gynaecol Res 2025;51:e70054.
34. Sebastián OG, Trujillo-Santos J, Díaz-Pedroche MDC, et al. Venous thromboembolism in patients with breast, ovarian, and uterine cancer. A comparative analysis from the Registro Informatizado Enfermedad TromboEmbólica registry. Res Pract Thromb Haemost 2025;10:103301.
35. Wun T, White RH. Epidemiology of cancer-related venous thromboembolism. Best Pract Res Clin Haematol 2009;22: 9-23.
36. Bakhru A. Effect of ovarian tumor characteristics on venous thromboembolic risk. J Gynecol Oncol 2013;24:52-8.
37. Streiff MB. Thrombosis in the setting of cancer. Hematology Am Soc Hematol Educ Program 2016;2016:196-205.
38. Walker AJ, Card TR, West J, Crooks C, Grainge MJ. Incidence of venous thromboembolism in patients with cancer - a cohort study using linked United Kingdom databases. Eur J Cancer 2013;49:1404-13.
39. Kröger K, Weiland D, Ose C, et al. Risk factors for venous thromboembolic events in cancer patients. Ann Oncol 2006;17:297-303.
40. Poenou G, Corbaux P, Accassat S, et al. Venous thromboembolism in women with breast and gynaecological cancers: what do we know and what should we do? Clin Appl Thromb Hemost 2026;32:10760296251415374.
41. Obeagu EI. Venous thromboembolism in ovarian cancer: pathophysiology, risk, and management. Ann Med Surg (Lond) 2025;87:8587-8596.
42. Falanga A, Lorusso D, Colombo N, et al. Gynecological cancer and venous thromboembolism: a narrative review to increase awareness and improve risk assessment and prevention. Cancers (Basel) 2024;16:1769.
43. Guo Z, Huang Y, Gong L, et al. Association of androgen deprivation therapy with thromboembolic events in patients with prostate cancer: a systematic review and meta-analysis. Prostate Cancer Prostatic Dis 2018; 21:451-60.
44. Quagliariello V, Berretta M, Bisceglia I, et al. In the era of cardiovascular-kidney-metabolic syndrome in cardio-oncology: from pathogenesis to prevention and therapy. Cancers (Basel) 2025;17:1169.
45. Młynarska E, Bojdo K, Frankenstein H, et al. Endothelial dysfunction as the common pathway linking obesity, hypertension and atherosclerosis. Int J Mol Sci 2025;26:10096.
46. Lip GY, Chin BS, Blann AD. Cancer and the prothrombotic state. Lancet Oncol 2002;3:27-34.
47. Blondon M, Righini M. Excess risk of venous thromboembolism associated with androgen deprivation therapy. Eur Urol 2016; 70:62-3.
48. O'Farrell S, Sandström K, Garmo H, et al. Risk of thromboembolic disease in men with prostate cancer undergoing androgen deprivation therapy. BJU Int 2016;118:391-8.
49. Kulkarni AA, Rubin N, Tholkes A, et al. Risk for stroke and myocardial infarction with abiraterone versus enzalutamide in metastatic prostate cancer patients. ESMO Open 2021;6: 100261.
50. Hernandez RK, Sørensen HT, Pedersen L, et al. Tamoxifen treatment and risk of deep venous thrombosis and pulmonary embolism: a Danish population-based cohort study. Cancer 2009;115:4442-9.
51. Key NS, Khorana AA, Kuderer NM, et al. Venous thromboembolism prophylaxis and treatment in patients with cancer: ASCO Guideline Update. J Clin Oncol 2023;41: 3063-71.