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Thrombotic Complications Following Immune Checkpoint Inhibitor Monotherapy: Expanding the Spectrum of Immune-Related Cardiovascular Toxicity: A Narrative Mini-Review

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Abstract

Context: Immune checkpoint inhibitors (ICIs) have transformed cancer treatment but are associated with cardiovascular toxicities, particularly myocarditis. Thrombotic adverse effects remain underrecognized despite increasing reports of venous and arterial complications.

Evidence Acquisition: This narrative mini-review examined the current evidence on the risk of thrombotic events following ICI monotherapy, potential immunothrombosis-related mechanisms, and the clinical implications of these events.

Results: Population-level studies have reported venous thromboembolic event rates of 2% to 4% at 6 months and 4% to 7% at 12 months, whereas chart-reviewed cohorts have reported higher rates of 5% to 15%. Arterial complications, including myocardial infarction and stroke, have also been reported. Thrombosis most commonly occurs within the first 6 months of treatment and may be associated with other immune-mediated adverse effects. *Immunothrombosis* involving T-cell activation, endothelial inflammation, and neutrophil extracellular traps may contribute to these events.

Conclusions: ICI-associated thrombosis may represent part of a broader spectrum of immune-mediated cardiovascular toxicity that differs from conventional cancer-associated thrombosis. Clinicians should maintain a low threshold for diagnostic evaluation, particularly during the first few months of immunotherapy.

Keywords: Thrombosis, Thromboembolism, Immune Checkpoint Inhibitors, Cardiovascular Toxicity, Cancer

1. Context

The advent of immune checkpoint inhibitors (ICIs) has transformed the management of many cancers by improving survival in metastatic disease and becoming an integral component of therapy for early-stage cancers, including potentially curative settings. With their increasing use, understanding the cardiotoxic effects of ICIs has become essential (1, 2).

Although considerable attention has focused on ICI-associated myocarditis because of its early onset and potentially severe outcomes, thrombotic events have been underreported relative to other manifestations (3). This is clinically important because thrombosis is part of the spectrum of cardiovascular adverse effects associated with immunotherapy and may occur at a clinically relevant frequency (4, 5).

Real-world data indicate that venous thromboembolism and other vascular complications, including myocardial infarction and ischemic stroke, may occur more frequently in patients receiving ICIs (4). In a recent cohort analysis, the incidence rates of venous thrombosis, myocardial infarction, and ischemic stroke were substantially higher during ICI treatment than those in the general population (3). Previous systematic analyses have also documented pulmonary embolism and deep vein thrombosis among patients receiving ICIs (6).

From a mechanistic perspective, these events may reflect more than conventional cancer-associated thrombosis. Activated immunity, endothelial

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inflammation, platelet activation, cytokines, and tissue factor pathways have all been proposed as contributors to the distinctive prothrombotic state observed during ICI treatment (5, 7). Cardio-oncology specialists must therefore consider whether thrombosis following ICI monotherapy represents an immune-mediated cardiovascular complication of cancer treatment or a consequence of the malignancy itself.

2. Evidence Acquisition

This narrative mini-review provides a focused overview of the current evidence on thrombotic complications associated with ICI monotherapy. PubMed and Google Scholar were searched for studies examining thromboembolic events during ICI-based treatment.

Search terms included combinations of "immune checkpoint inhibitors," "PD-1," "PD-L1," "CTLA-4," "thrombosis," "venous thromboembolism," "arterial thrombosis," "stroke," "myocardial infarction," "immunothrombosis," and "cardio-oncology." Additional relevant articles were identified by manual review of the reference lists of key publications. Although the primary focus was ICI monotherapy, selected studies involving combination checkpoint blockade were cited to provide mechanistic or contextual background.

3. Results

3.1. Rethinking Cancer-Associated Thrombosis

Cancer-associated thrombosis (CAT) is a well-established clinical phenomenon, but the immunotherapy era raises questions regarding the validity of existing risk-prediction models (8, 9). Algorithms based on tumor site, metastatic burden, chemotherapy exposure, and laboratory parameters were developed largely during the cytotoxic-therapy era and may not capture the thrombotic risk associated with ICI monotherapy (10, 11). Key studies reporting thrombotic events following ICI treatment are summarized in Table 1.

Observational studies, chart reviews, and registries have reported substantial but variable rates of venous thromboembolism (VTE) among patients receiving ICIs. These differences reflect cohort characteristics, follow-up duration, and methods of event ascertainment. Recent syntheses suggest that population-based studies generally report 6-month VTE rates of approximately 2% to 4% and 12-month rates of 4% to 7%, whereas chart-reviewed cohorts have reported rates approaching 5% to 15% (3, 4, 10).

Arterial thrombotic events must also be considered. Myocardial infarction and stroke have been reported during ICI therapy, demonstrating that these complications are not limited to the venous circulation (3, 6). Thrombosis may also occur in patients who would not be classified as high risk by existing CAT models (3, 5, 10, 11).

In cardio-oncology, an emerging question is not only the existence of CAT in ICI-treated patients, but also whether ICI therapy may independently contribute to immune-mediated vascular changes, in addition to the inherent cancer risk (12, 13). Proposed biological mechanisms, derived from preclinical models and translational studies, include endothelial activation by inflammatory processes, neutrophil extracellular traps, and cytokine-mediated activation of coagulation (10, 14-16).

3.2. Immunothrombosis: A Plausible Mechanistic Link

ICIs act by blocking inhibitory immune checkpoints, primarily the programmed cell death protein 1/programmed death-ligand 1 (PD-1/PD-L1) and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) pathways (17, 18). The enhanced antitumor immunity responsible for their therapeutic efficacy may also contribute to a prothrombotic environment within the vessel wall (19). Thus, thrombosis may not occur merely as an incidental consequence of malignancy, but may result from dysregulated immune activity (4).

Immunothrombosis provides a biologically plausible explanation for this association. Under physiological conditions, innate immune activation promotes localized thrombosis that helps contain infection; under pathological conditions, the same process may cause harmful clot formation (20, 21). ICI therapy may activate T cells, monocytes, neutrophils, and platelets, leading to endothelial cell activation, factor X activation, and coagulation (10, 22).

Several mechanisms may contribute. ICI-induced systemic inflammation may increase cytokine release, enhance endothelial permeability, and stimulate the coagulation cascade. Endothelial dysfunction may reduce the antithrombotic capacity of the vessel wall (23, 24). Platelet activation may further promote thrombosis, while neutrophil extracellular traps can provide a structural scaffold for clot formation and amplify local inflammation (10).

This concept is clinically relevant. Chemotherapy-induced thrombosis is usually regarded as a

Table 1. Key Studies Reporting Thrombotic Events Following Immune Checkpoint Inhibitor Treatment [a]

Studies	Population	ICI Agent(s)	Sample Size	Follow-Up	Key Findings
Sussman et al. (2025) (28)	Mixed cancers	PD-1 (76%), PD-L1 (13%), CTLA-4 (4%), CTLA-4/PD-1 combination (7%)	10,638	25.1 months	6-month cumulative VTE: 7.6% (95% CI 7.1 - 8.1%); 12-month: 11.1% (95% CI 10.5 - 11.8%); median time to VTE: 5.4 months; dual CTLA-4/PD-1 increased VTE risk vs. PD-1 (HR 1.43); PD-L1 reduced risk vs. PD-1 (HR 0.79); anticoagulation post-ICI (non-VTE indication) reduced VTE risk by 40% (HR 0.60)
Gong et al. (2021) (19)	Mixed cancers	Anti-PD-1 (75%), anti-PD-L1 (10%), anti-CTLA-4 (8%), combination (7%)	2,854	194 days post-ICI	VTE incidence: 7.4% at 6 months, 13.8% at 1 year; VTE risk > 4-fold higher after ICI vs. pre-ICI (HR 4.98, 95% CI 3.65 - 6.79, $p < 0.001$); risk factors: age < 65, hypertension (HR 1.37), Khorana score ≥ 2 (HR 1.54); melanoma associated with lower VTE risk (HR 0.59)
van Lent et al. (2025) (3)	Mixed cancers	Nivolumab (30%), pembrolizumab (35%), ipilimumab (7%), combination (20%)	663	Variable	Age- and sex-adjusted incidence rate vs. general population: venous thrombosis 22.7-fold higher (95% CI 16.6 - 31.0), MI 3.0-fold higher (95% CI 1.2 - 7.1), ischemic stroke 3.2-fold higher (95% CI 1.6 - 5.7); gynecologic malignancy associated with increased VTE risk (HR 6.7); VTE during follow-up associated with 2.3-fold increased mortality
Khorana et al. (2023) (33)	Advanced NSCLC (stage IV)	ICI-based (monotherapy or combination without chemo)	2,299	9.1 months	VTE incidence rate per 100 person-years: 13.5 (ICI-based), 18.0 (chemo-based), 22.4 (ICI+chemo); 6-month cumulative VTE: 8.1% (ICI-based), 10.9% (chemo-based), 12.8% (ICI+chemo); ICI-based associated with 26% lower VTE risk vs. chemo (HR 0.74, $p = 0.03$); risk factors: prior radiation (HR 1.25) and severe obesity
Connors et al. (2023) (36)	Mixed cancers	Pembrolizumab (49.7%), nivolumab (31.8%), ipilimumab, atezolizumab, durvalumab	10,638	25.1 months	Cumulative VTE incidence: 7.6% at 6 months, 11.1% at 1 year, 13.8% at 2 years; ipilimumab associated with highest VTE risk (HR 1.90 vs. pembrolizumab); durvalumab lowest risk (HR 0.59); anticoagulation post-ICI (non-VTE indication) associated with 41% VTE risk reduction (HR 0.59)
Roopkumar et al. (2021) (14)	Mixed cancers	Nivolumab (52%), pembrolizumab (27%), atezolizumab (10%), nivolumab+ipilimumab (6%)	1,686	14.6 months	VTE incidence: 24% (404/1,686); 6-month cumulative VTE: 7.1%; 12-month: 10.9%; VTE associated with decreased OS (HR 1.22, 95% CI 1.06 - 1.41, $p = 0.008$); patients who developed VTE had higher pre-treatment levels of MDSCs ($p = 0.0045$), IL-8 ($p = 0.016$), and sVCAM-1 ($p = 0.038$)
Vladić et al. (2025) (11)	Mixed cancers	ICI monotherapy (15.4%), ICI+chemo (16.6%), ICI+targeted (1.6%) – 33.6% received ICI	806	11.8 months	6-month cumulative VTE incidence: 11.2% (95% CI 9.0 - 13.3); performance of VTE risk scores: CAT Score best (c-statistic 0.65), Khorana score poor (c-statistic 0.53), COMPASS-CAT worst (c-statistic 0.50); traditional Khorana parameters (Hb, platelets, WBC, BMI) not significantly associated with VTE
Icht et al. (2021) (32)	Advanced NSCLC	Single-agent ICI (nivolumab 67%, pembrolizumab 26%, ipilimumab+nivolumab 2%)	345	6 months	6-month cumulative VTE: 4.5% (ICI) vs. 7.1% (chemotherapy) (HR for chemo 1.6, 95% CI 0.66 - 3.9); Khorana score did not stratify VTE risk in ICI cohort (high-risk HR 0.17, 95% CI 0.02 - 1.36) but showed trend toward risk stratification in chemotherapy cohort (high-risk HR 3.04, 95% CI 0.82 - 11.22)

[a] Abbreviations: CTLA-4, cytotoxic T-lymphocyte-associated protein 4; CTVPA, computed tomography venography and pulmonary angiography; DVT, deep vein thrombosis; GI, gastrointestinal; GU, genitourinary; HR, hazard ratio; ICI, immune checkpoint inhibitor; IL-8, interleukin-8; irAE, immune-related adverse event; MDSC, myeloid-derived suppressor cell; MI, myocardial infarction; NLR, neutrophil-to-lymphocyte ratio; NSCLC, non-small cell lung cancer; OS, overall survival; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PE, pulmonary embolism; RCC, renal cell carcinoma; sVCAM-1, soluble vascular cell adhesion molecule-1; VTE, venous thromboembolism. Unless otherwise specified, ICI exposure refers to monotherapy or combination therapy without concurrent chemotherapy. Effect sizes represent adjusted hazard ratios or odds ratios from multivariable analyses or cumulative incidence estimates with competing risk adjustment where specified.

consequence of endothelial damage, immobilization, cancer burden, or bone marrow suppression (25). However, thrombosis associated with ICIs may represent an immune-mediated vascular injury that can occur regardless of traditional thrombotic risk factors (26). If these findings are confirmed by further research, ICI-triggered thrombosis may be considered a component of immune-mediated cardiovascular toxicity (27).

3.3. Clinical Implications for Oncologists

ICI-associated thrombosis has important clinical implications. Events often occur within the first months after treatment initiation; several studies report a median time to VTE measured in months, with most events occurring within 6 months (19, 28, 29). This period overlaps with routine monitoring for immune-related toxicity.

Thrombotic events may also occur with other immune-related adverse events (irAEs), supporting the possibility of a shared inflammatory background (29). Systemic immune activation, endothelial dysfunction, and cytokine signaling may contribute to both thrombotic and nonthrombotic irAEs, suggesting that thrombosis may be part of a broader immune-toxicity syndrome rather than an isolated vascular complication (10, 30). The coexistence of thrombosis with rash, colitis, pneumonitis, hepatitis, or endocrinopathy may indicate a more inflammatory phase of treatment toxicity (15).

Conventional methods for estimating thrombotic risk may be inadequate in this setting. Traditional CAT models were developed without accounting for ICI-related immune activation, changes in inflammatory markers, or endothelial dysfunction (10, 31). Consequently, patients with a low baseline risk may still develop clinically important venous or arterial events during treatment (28).

The threshold for diagnostic evaluation should therefore remain low. New or unexplained dyspnea,

Table 2. Clinical Implications of Thrombotic Complications Following Immune Checkpoint Inhibitor Monotherapy [a]

Clinical Domain	Practical Implication	Suggested Clinical Approach
Recognition of Thrombotic Risk	Thrombotic complications during ICI monotherapy may represent a distinct immune-mediated cardiovascular toxicity rather than only conventional cancer-associated thrombosis	Incorporate venous and arterial thrombosis into routine cardio-oncology surveillance during ICI therapy
Timing of Events	Many thrombotic events occur within the first 6 months of treatment	Increase vigilance and clinical monitoring during early treatment cycles
Spectrum of Complications	Both venous and arterial events may occur, including VTE, pulmonary embolism, myocardial infarction, and ischemic stroke	Maintain broad differential diagnosis when new cardiopulmonary or neurologic symptoms arise
Association with irAEs	Thrombosis may overlap with other immune-related adverse events (e.g., pneumonitis, colitis, rash, hepatitis)	Consider thrombotic evaluation in patients entering a more inflammatory phase of treatment toxicity
Risk Assessment Limitations	Conventional CAT models may underestimate risk in patients receiving ICIs	Supplement standard risk tools with individualized clinical judgment and inflammatory assessment
Baseline Evaluation	Preexisting cardiovascular and thrombotic risk factors remain important	Assess prior thrombosis, cardiovascular disease, obesity, metastatic burden, platelet count, and cancer type before ICI initiation
Role of Biomarkers	Biomarkers such as CRP and neutrophil-to-lymphocyte ratio may reflect immune-driven thrombotic risk	Consider serial inflammatory marker monitoring in selected high-risk patients, while recognizing current lack of validation
Diagnostic Vigilance	Symptoms may be misattributed to cancer progression or general treatment effects	Promptly investigate unexplained dyspnea, chest pain, syncope, neurologic deficits, tachycardia, or unilateral swelling
Multidisciplinary Management	Optimal care often requires collaboration across specialties	Coordinate management between oncology, cardiology, hematology, thrombosis, and emergency medicine teams
Anticoagulation Strategy	Evidence for universal prophylactic anticoagulation remains insufficient	Use individualized anticoagulation decisions based on thrombotic and bleeding risks
Immunotherapy Continuation	Stopping ICIs after thrombosis may not always be necessary	Make treatment continuation decisions through multidisciplinary discussion balancing oncologic benefit and vascular risk
Research Implications	Current evidence is largely retrospective and heterogeneous	Support development of prospective registries, biomarker-guided stratification, and randomized prophylaxis trials
Cardio-oncology Framework	ICI-associated thrombosis may warrant inclusion within irCVT definitions	Expand institutional cardio-oncology protocols to include thrombotic surveillance and management pathways

[a] Abbreviations: ICI, immune checkpoint inhibitor; VTE, venous thromboembolism; irAEs, immune-related adverse events; CAT, cancer-associated thrombosis; CRP, C-reactive protein; irCVT, immune-related cardiovascular toxicity.

pleuritic chest pain, neurologic deficits, syncope, tachycardia, unilateral limb edema, or functional decline during ICI therapy should prompt evaluation for VTE, pulmonary embolism, acute coronary syndrome, stroke, or another vascular disorder (32). These findings should not be attributed automatically to disease progression, anemia, deconditioning, or other treatment effects (10, 15). Practical implications for clinicians managing patients receiving ICI monotherapy are summarized in Table 2.

From a cardio-oncology perspective, ICI-associated thromboembolism requires timely management. Early diagnosis, prompt imaging, and collaboration among oncologists, cardiologists, hematologists, and thrombosis specialists may improve outcomes, particularly when thrombosis coincides with inflammatory toxicity or occurs in patients without traditional risk factors.

3.4. Toward a Practical Risk-Adapted Strategy

In the absence of randomized trial evidence, several authorities have proposed practical, risk-adapted strategies for thrombosis during ICI therapy, although none has been validated. Available data suggest that ICI treatment may independently increase VTE risk, that anticoagulation initiated after ICI treatment for non-VTE indications may be associated with a lower VTE hazard in retrospective analyses, and that existing CAT models do not fully capture this risk (4, 15, 28, 33). A proposed risk-adapted approach is shown in Figure 1.

Baseline assessment should be performed before ICI administration and should include a history of thrombosis, cardiovascular risk factors, and cancer-related factors such as metastatic burden, tumor type, obesity, and platelet count (34). Inflammatory biomarkers, including C-reactive protein (CRP) and the neutrophil-to-lymphocyte ratio (NLR), are being investigated as predictors of thrombotic risk, although they are not validated for clinical decision-making (10). Nevertheless, they may help identify patients in whom inflammation and thrombotic risk overlap (4).

Dynamic monitoring is also important because events may occur early and may overlap with other irAEs (30). Reassessment may be particularly relevant during

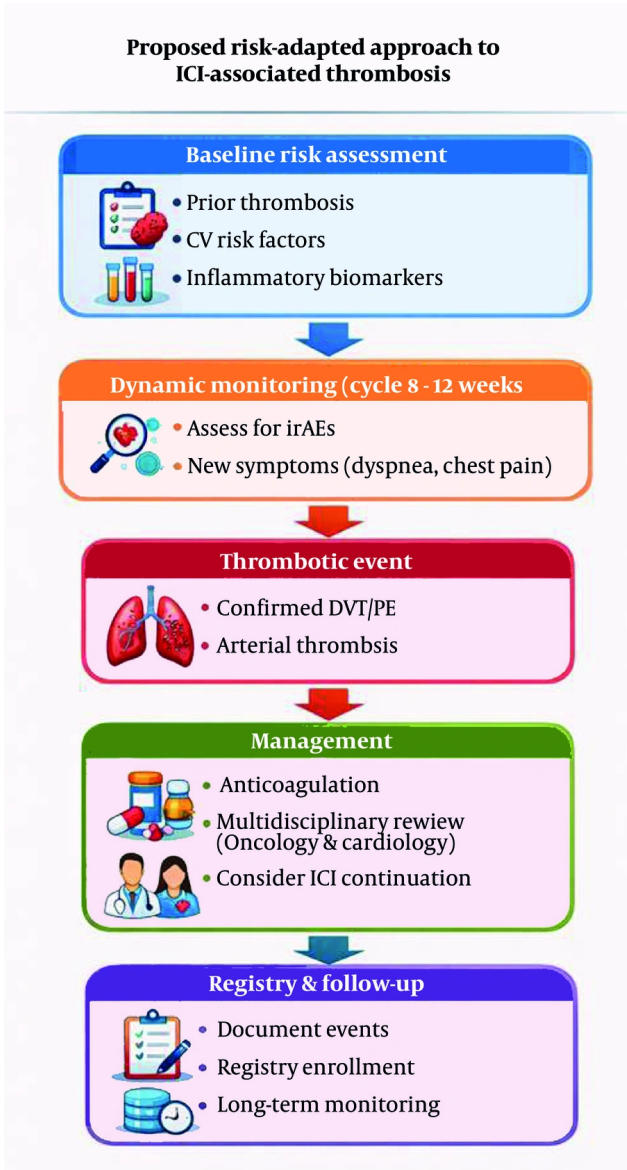

Figure 1. Proposed risk-adapted approach to ICI-associated thrombosis. The framework integrates four components: (1) baseline risk assessment (prior thrombosis, cardiovascular risk factors, inflammatory biomarkers); (2) dynamic monitoring at 8- to 12-week intervals (assessment for new irAEs and thrombotic symptoms); (3) management of confirmed thrombotic events (anticoagulation, multidisciplinary cardio-oncology review, individualized ICI continuation); and (4) long-term follow-up with registry documentation. Abbreviations: ICI, immune checkpoint inhibitor; irAE, immune-related adverse event; DVT, deep vein thrombosis; PE, pulmonary embolism.

the early treatment period and when pneumonitis, colitis, hepatitis, or skin eruptions develop, as these findings may indicate heightened immune activation. Current evidence does not support universal primary anticoagulant prophylaxis for all patients receiving ICI therapy (15, 28).

Confirmed VTE can generally be managed according to current cancer-associated thrombosis guidelines, with individualized assessment of bleeding risk. Decisions to withhold, restart, or continue immunotherapy after a vascular event are complex because the oncologic benefits may outweigh the

vascular risks (10, 35), particularly in patients with limited treatment options.

Current evidence does not support universal primary anticoagulant prophylaxis for all patients receiving ICI therapy. Retrospective observations suggest that anticoagulation may reduce VTE risk in selected patients, but this possibility requires further study (36, 37).

3.5. The Need for Prospective Data and Registries

A major evidence gap is the absence of adequately powered prospective trials focused on thrombosis during ICI monotherapy (38, 39). Most available data are derived from retrospective analyses and registries and are therefore vulnerable to ascertainment bias (10, 28).

Prospective registries of venous and arterial thrombotic events, biomarker-based risk stratification using CRP, NLR, or novel endothelial markers, translational studies of immunothrombosis, and trials of targeted interventions in high-risk populations are needed.

International collaboration through cardio-oncology networks is essential to generate sufficiently large data sets and support evidence-based recommendations.

3.6. Expanding the Definition of Immune-Related Cardiovascular Toxicity

As immunotherapy becomes a central component of oncology, the phenotype of immune-related cardiovascular toxicity (irCVT) may need to expand beyond myocarditis and pericarditis to include thrombosis. Current literature suggests that ICI-associated thrombotic events arise in a prothrombotic milieu characterized by endothelial inflammation, T-cell activation, and neutrophil extracellular traps (4, 40).

This expanded framework would classify VTE, myocardial infarction, and stroke as immune-mediated vascular disorders that often develop within 6 months and may coexist with irAEs such as pneumonitis or colitis. *Immunothrombosis provides* a mechanistic link and underscores the importance of monitoring and managing vascular risk without unnecessarily discontinuing effective treatment (40, 41).

These observations support consideration of ICI-associated thrombosis as a potential component of irCVT. Recognizing thrombosis within this framework may improve patient safety and risk assessment while preserving oncologic efficacy.

3.7. Limitations

This narrative mini-review has several limitations. First, it was not conducted as a systematic review, and relevant studies may therefore have been missed. Second, most evidence on ICI-associated thrombosis comes from observational studies and registries that are susceptible to bias. Third, studies vary substantially in their definitions of thrombosis, follow-up duration, and participant characteristics.

4. Conclusions

Increasing evidence suggests that thrombosis during ICI monotherapy may be more complex than conventional cancer-associated thrombosis. Venous and arterial events may result, at least in part, from immune-mediated vascular inflammation and immunothrombosis. Clinicians should remain particularly vigilant during the first months of ICI treatment and recognize the potential overlap with other immune-related toxicities. Existing risk-prediction models do not adequately account for these mechanisms. Prospective studies, biomarker-based risk stratification, and cardio-oncology registries are therefore needed. Until stronger evidence becomes available, prompt diagnosis and multidisciplinary decision-making may reduce the risk of serious complications without compromising oncologic outcomes.

Footnotes

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References

1. Becker RC. Immune checkpoint inhibitors and cardiovascular toxicity: immunology, pathophysiology, diagnosis, and management. *Journal of thrombosis and thrombolysis*. 2025;**58**(8):1021-44. [PubMed ID: 40673965]. [PubMed Central ID: PMC12740968]. https://doi.org/10.1007/s11239-025-03146-7.
2. Ball S, Ghosh RK, Wongsaengsak S, Bandyopadhyay D, Ghosh GC, Aronow WS, et al. Cardiovascular Toxicities of Immune Checkpoint Inhibitors. *JACC*. 2019;**74**(13):1714-27. [PubMed ID: 31558256]. https://doi.org/10.1016/j.jacc.2019.07.079.
3. van Lent A, Puscasu R, Kaasjager KAH, Haitjema S, Suelmann BBM, Verhaar MC, et al. Venous and arterial thrombosis in patients receiving immune checkpoint inhibitors. *PloS one*. 2025;**20**(4). e0321112. [PubMed ID: 40168398]. [PubMed Central ID: PMC11960909]. https://doi.org/10.1371/journal.pone.0321112.
4. Wang TF, Carrier M. Immune Checkpoint Inhibitors-Associated Thrombosis: Incidence, Risk Factors and Management. *Current oncology (Toronto, Ont)*. 2023;**30**(3):3032-46. [PubMed ID: 36975443]. [PubMed Central ID: PMC10047296]. https://doi.org/10.3390/curroncol30030230.
5. Thuny F, Naidoo J, Neilan TG. Cardiovascular complications of immune checkpoint inhibitors for cancer European Heart Journal. *European Heart Journal*. 2022;**43**(42):4458-68. [PubMed ID: 36040835]. [PubMed Central ID: PMC10263267]. https://doi.org/10.1093/eurheartj/ehac456.
6. Solinas C, Saba L, Sganzerla P, Petrelli F. Venous and arterial thromboembolic events with immune checkpoint inhibitors: A systematic review. *Thrombosis research*. 2020;**196**:444-53. [PubMed ID: 33065409]. https://doi.org/10.1016/j.thromres.2020.09.038.
7. Raschi E, Rossi S, De Giglio A, Fusaroli M, Burgazzi F, Rinaldi R, et al. Cardiovascular Toxicity of Immune Checkpoint Inhibitors: A Guide for Clinicians. *Drug safety*. 2023;**46**(9):819-33. [PubMed ID: 37341925]. [PubMed Central ID: PMC10442274]. https://doi.org/10.1007/s40264-023-01320-5.
8. Chen K, Zhang Y, Zhang L, Zhang W, Chen Y. Machine learning models for risk prediction of cancer-associated thrombosis: a systematic review and meta-analysis. *Journal of thrombosis and haemostasis: JTH*. 2025;**23**(2):610-26. [PubMed ID: 39549838]. https://doi.org/10.1016/j.jtha.2024.11.001.
9. Moik F, Riedl JM, Englisch C, Ay C. Update on Thrombosis Risk in Patients with Cancer: Focus on Novel Anticancer Immunotherapies. *Hamostaseologie*. 2024;**44**(1):40-8. [PubMed ID: 38190985]. https://doi.org/10.1055/a-2215-9909.
10. Ilari A, Abbate MI, Verso M, Graziani M, Cafaro P, Sala L, et al. Cancer-Associated Thrombosis in Patients Treated with Immune Checkpoint Inhibitors. *Int J Mol Sci*. 2026;**27**(4):1874. [PubMed ID: 41752012]. [PubMed Central ID: PMC12941293]. https://doi.org/10.3390/ijms27041874.
11. Vladić N, Englisch C, Berger JM, Moik F, Berghoff AS, Preusser M, et al. Validation of risk assessment models for venous thromboembolism in patients with cancer receiving systemic therapies. *Blood Advances*. 2025;**9**(13):3340-9. [PubMed ID: 40117478]. [PubMed Central ID: PMC12268659]. https://doi.org/10.1182/bloodadvances.2025016044.
12. Michel L, Rassaf T, Totzeck M. Cardiotoxicity from immune checkpoint inhibitors. *International journal of cardiology Heart & vasculature*. 2019;**25**. 100420. [PubMed ID: 31517036]. [PubMed Central ID: PMC6736791]. https://doi.org/10.1016/j.ijcha.2019.100420.
13. Khunger A, Battel L, Wadhawan A, More A, Kapoor A, Agrawal N. New Insights into Mechanisms of Immune Checkpoint Inhibitor-Induced Cardiovascular Toxicity. *Current oncology reports*. 2020;**22**(7). 65. [PubMed ID: 32514647]. https://doi.org/10.1007/s11912-020-00925-8.
14. Roopkumar J, Swaidani S, Kim AS, Thapa B, Gervaso L, Hobbs BP, et al. Increased Incidence of Venous Thromboembolism with Cancer Immunotherapy. *Med (New York, NY)*. 2021;**2**(4):423-34. [PubMed ID: 34036293]. [PubMed Central ID: PMC8143033]. https://doi.org/10.1016/j.medj.2021.02.002.
15. Fawaz H, Numan H, El Charif MH, Charbel N, El Khoury S, Rizkallah J, et al. Exploring the Emerging Association Between Immune Checkpoint Inhibitors and Thrombosis. *J Clin Med*. 2025;**14**(10):3451. [PubMed ID: 40429445]. [PubMed Central ID: PMC12112099]. https://doi.org/10.3390/jcm14103451.
16. Nichetti F, Ligorio F, Zattarin E, Signorelli D, Prelaj A, Proto C, et al. Is There an Interplay between Immune Checkpoint Inhibitors, Thromboprophylactic Treatments and Thromboembolic Events? Mechanisms and Impact in Non-Small Cell Lung Cancer Patients. *Cancers (Basel)*. 2019;**12**(1):67. [PubMed ID: 31881699]. [PubMed Central ID: PMC7016680]. https://doi.org/10.3390/cancers12010067.
17. Wojtukiewicz MZ, Rek MM, Karpowicz K, Górska M, Polityńska B, Wojtukiewicz AM, et al. Inhibitors of immune checkpoints-PD-1, PD-L1, CTLA-4-new opportunities for cancer patients and a new challenge for internists and general practitioners. *Cancer metastasis reviews*. 2021;**40**(3):949-82. [PubMed ID: 34236546]. [PubMed Central ID: PMC8556173]. https://doi.org/10.1007/s10555-021-09976-0.
18. Gu L, Khadaroo PA, Su H, Kong L, Chen L, Wang X, et al. The safety and tolerability of combined immune checkpoint inhibitors (anti-PD-1/PD-L1 plus anti-CTLA-4): a systematic review and meta-analysis. *BMC cancer*. 2019;**19**(1). 559. [PubMed ID: 31182049]. [PubMed Central ID: PMC6558837]. https://doi.org/10.1186/s12885-019-5785-z.
19. Gong J, Drobni ZD, Alvi RM, Murphy SP, Sullivan RJ, Hartmann SE, et al. Immune checkpoint inhibitors for cancer and venous thromboembolic events. *Eur J Cancer*. 2021;**158**:99-110. [PubMed ID: 34662835]. [PubMed Central ID: PMC9010482]. https://doi.org/10.1016/j.ejca.2021.09.010.
20. Schulz C, Engelmann B, Massberg S. Crossroads of coagulation and innate immunity: the case of deep vein thrombosis. *Journal of thrombosis and haemostasis: JTH*. 2013;**11**:233-241. [PubMed ID: 23809127]. https://doi.org/10.1111/jth.12261.
21. Poels K, van Leent MMT, Boutros C, Tissot H, Roy S, Meerwaldt AE, et al. Immune Checkpoint Inhibitor Therapy Aggravates T Cell-Driven Plaque Inflammation in Atherosclerosis. *JACC CardioOncology*. 2020;**2**(4):599-610. [PubMed ID: 34396271]. [PubMed Central ID: PMC8352210]. https://doi.org/10.1016/j.jaccao.2020.08.007.
22. Joseph JJ, Rajan A, Gulley JL, Ito S, Kessler CM. Acquired Coagulopathy With Immune Checkpoint Inhibitors: An Underrecognized Association Between Inflammation and Coagulation. *JTO clinical and research reports*. 2020;**1**(3). 100049. [PubMed ID: 34589945]. [PubMed Central ID: PMC8474288]. https://doi.org/10.1016/j.jtocrr.2020.100049.
23. Poredos P, Jezovnik MK. Endothelial Dysfunction and Venous Thrombosis. *Angiology*. 2018;**69**(7):564-7. [PubMed ID: 28954526]. https://doi.org/10.1177/0003319717732238.
24. Undas A, Zabczyk M. Antithrombotic medications and their impact on fibrin clot structure and function. J Physiol Pharmacol. 2018;69(4). 10. *26402/jpp*. 2018;**69**(4). [PubMed ID: 30415236]. https://doi.org/10.26402/jpp.2018.4.02.
25. Haddad TC, Greeno EW. Chemotherapy-induced thrombosis. *Thrombosis research*. 2006;**118**(5):555-68. [PubMed ID: 16388837]. https://doi.org/10.1016/j.thromres.2005.10.015.
26. Hou J, Mu G, Zhang Z, Xiang Q, Cui Y. Hematological toxicities and thrombosis risk associated with immune checkpoint inhibitors: a pharmacovigilance study from 2014 to 2024. *Cancer immunology, immunotherapy: CII*. 2026;**75**(5). 147. [PubMed ID: 41984243]. [PubMed

Central ID: PMC13083658]. https://doi.org/10.1007/s00262-026-04380-5.

27. Fowler C, Pastores SM. Venous Thromboembolic Events in Cancer Immunotherapy: A Narrative Review. *Journal of clinical medicine*. 2025;**14**(14):4926. [PubMed ID: 40725619]. [PubMed Central ID: PMC12294976]. https://doi.org/10.3390/jcm14144926.
28. Sussman TA, Giobbie-Hurder A, Dryg ID, Manos M, Weirather JL, LeBoeuf NR, et al. Immune checkpoint inhibitor-associated risk for venous thromboembolism: a comprehensive analysis. *Journal for ImmunoTherapy of Cancer*. 2025;**13**(5). e010761. [PubMed ID: 40341027]. [PubMed Central ID: PMC12067813]. https://doi.org/10.1136/jitc-2024-010761.
29. Durbin SM, Zubiri L, Perlman K, Wu CY, Lim T, Grealish K, et al. Late-Onset Immune-Related Adverse Events After Immune Checkpoint Inhibitor Therapy. *JAMA Network Open*. 2025;**8**(3):e252668-e. [PubMed ID: 40146104]. [PubMed Central ID: PMC11950896]. https://doi.org/10.1001/jamanetworkopen.2025.2668.
30. Hsiehchen D, Naqash AR, Espinoza M, Von Itzstein MS, Cortellini A, Ricciuti B, et al. Association between immune-related adverse event timing and treatment outcomes. *Oncoimmunology*. 2022;**11**(1). 2017162. [PubMed ID: 35003896]. [PubMed Central ID: PMC8741287]. https://doi.org/10.1080/2162402X.2021.2017162.
31. Raisi-Estabragh Z, Murphy AC, Ramalingam S, Scherrer-Crosbie M, Lopez-Fernandez T, Reynolds KL, et al. Cardiovascular Considerations Before Cancer Therapy. *JACC: CardioOncology*. 2024;**6**(5):631-54. [PubMed ID: 39479317]. [PubMed Central ID: PMC11520216]. https://doi.org/10.1016/j.jaccao.2024.07.017.
32. Icht O, Darzi N, Shimony S, Jacobi O, Reinhorn D, Landman Y, et al. Venous thromboembolism incidence and risk assessment in lung cancer patients treated with immune checkpoint inhibitors. *Journal of thrombosis and haemostasis: JTH*. 2021;**19**(5):1250-8. [PubMed ID: 33605020]. https://doi.org/10.1111/jth.15272.
33. Khorana AA, Palaia J, Rosenblatt L, Pisupati R, Huang N, Nguyen C, et al. Venous thromboembolism incidence and risk factors associated with immune checkpoint inhibitors among patients with advanced non-small cell lung cancer. *J Immunother Cancer*. 2023;**11**(1):e006072. [PubMed ID: 36657815]. [PubMed Central ID: PMC9853260]. https://doi.org/10.1136/jitc-2022-006072.
34. Zhang J, Xie Y, Yang L, Yang M, Xu R, Liu D. Validation of risk assessment scores in predicting venous thromboembolism in patients with lung cancer receiving immune checkpoint inhibitors. *BMC pulmonary medicine*. 2024;**24**(1). 507. [PubMed ID: 39390440]. [PubMed Central ID: PMC11468413]. https://doi.org/10.1186/s12890-024-03323-z.
35. Chiang CH, Osataphan S, Chang YC, Chi KY, Chiang CH, Chang Y, et al. Anticoagulation for the treatment of immune checkpoint inhibitor-associated venous thromboembolism. *Blood Adv*. 2024;**8**(18):4803-6. [PubMed ID: 38985330]. [PubMed Central ID: PMC11415846]. https://doi.org/10.1182/bloodadvances.2024013869.
36. Connors JM, Sussman TA, Dryg ID, Giobbe-Hurder A, Manos MP, Weirather JL, et al. Risks for venous thromboembolism with immune checkpoint inhibitor therapy. *Blood*. 2023;**142**(Supplement 1):2640-2640. https://doi.org/10.1182/blood-2023-187867.
37. Kartolo A, Yeung C, Moffat GT, Hanna L, Hopman W, Baetz T. Venous thromboembolism events in patients with advanced cancer on immune checkpoint inhibitors. *Immunotherapy*. 2022;**14**(1):23-30. [PubMed ID: 34758641]. https://doi.org/10.2217/imt-2021-0151.
38. Bjørnhart B, Kristiansen C, Asmussen J, Hansen KH, Wedervang K, Jørgensen TL, et al. Clinical impact of venous thromboembolism in non-small cell lung cancer patients receiving immunotherapy. *Thrombosis research*. 2023;**221**:164-72. [PubMed ID: 36396518]. https://doi.org/10.1016/j.thromres.2022.10.020.
39. Goel A, Khorana A, Kartika T, Gowda S, Tao DL, Thawani R, et al. Assessing the risk of thromboembolism in cancer patients receiving immunotherapy. *European journal of haematology*. 2022;**108**(4):271-7. [PubMed ID: 34905252]. [PubMed Central ID: PMC9009190]. https://doi.org/10.1111/ejh.13734.
40. Xiao L, Liu W, Ji Y, Li Q, Pan J, Xie R. Immunotherapy-related cardiovascular toxicity: from mechanisms to management. *Frontiers in Pharmacology*. 2026;**Volume**. 1762011. [PubMed ID: 41716314]. [PubMed Central ID: PMC12913522]. https://doi.org/10.3389/fphar.2026.1762011.
41. Herrmann J, Barac A, Carver J, Cheng RK, Daniele A, Dent S, et al. Immune Checkpoint Inhibitor-Associated Cardiovascular Toxic Effects: International Cardio-Oncology Society Position Statement. *JAMA Oncology*. 2026;**12**(1):90-9. [PubMed ID: 41231466]. https://doi.org/10.1001/jamaoncol.2025.4543.