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Acute Pulmonary Embolism in the Cardiometabolic Patient

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Abstract

Background: Acute pulmonary embolism (PE) remains one of the most clinically relevant manifestations of venous thromboembolism and continues to pose important diagnostic and prognostic challenges. In routine practice, however, PE is still often considered separately from the broader framework of cardiometabolic disease.

Methods & Scope: This mini-review discusses acute PE in the cardiometabolic patient, focusing on the intersection between obesity, visceral adiposity, type 2 diabetes, and metabolic dysfunction-associated steatotic liver disease (MASLD).

Results: Current evidence suggests that obesity, particularly central and visceral adiposity, represents the most consistent cardiometabolic determinant of venous thromboembolic risk, through mechanisms involving chronic low-grade inflammation, endothelial dysfunction, impaired fibrinolysis, and procoagulant imbalance. Type 2 diabetes appears to play a more nuanced role, acting less as an isolated driver and more as a marker of clustered metabolic vulnerability, especially in the presence of poor glycemic control, renal impairment, and long disease duration. MASLD may further amplify thrombo-inflammatory susceptibility through the liver's central role in coagulation and fibrinolytic pathways.

Conclusion: In this setting, PE may be more difficult to recognize because symptoms frequently overlap with those of obesity, heart failure, respiratory disease, and general functional limitation. A more integrated cardiometabolic perspective may improve diagnostic vigilance, risk interpretation, and post-event clinical management.

Introduction

Acute pulmonary embolism (PE) remains the most severe clinical presentation of venous thromboembolism (VTE) and one of the most time-sensitive cardiovascular diagnoses in daily practice. Contemporary European guidance emphasizes that PE must be approached through integrated clinical probability assessment, judicious D-dimer testing, and prompt imaging because symptoms and signs are frequently nonspecific[1,2]. Yet, despite the centrality of PE in acute medicine, VTE is still often considered separately from the broader universe of cardiometabolic risk. This separation is increasingly artificial.

Patients with type 2 diabetes (T2D), obesity, visceral adiposity, hypertension, dyslipidemia, chronic kidney disease, obstructive sleep apnea, and metabolic dysfunction-associated steatotic liver disease (MASLD) are immediately recognized as "high-risk" for atherosclerotic and heart failure outcomes. Less routinely, they are recognized as living in a biologic and clinical environment that may also facilitate venous thrombosis. Chronic low-grade inflammation,

endothelial dysfunction, impaired fibrinolysis, physical deconditioning, recurrent hospitalization, and polypharmacy often coexist in these patients, creating a terrain in which thrombotic vulnerability may be amplified rather than isolated[2,3,4].

The key argument of this mini-review is therefore not that PE is simply another manifestation of arterial disease, nor that diabetes alone is a powerful independent cause of VTE in every context. Rather, acute PE in the cardiometabolic patient should be viewed as a clinical expression of broader metabolic, inflammatory, and prothrombotic vulnerability. Within this framework, obesity and visceral adiposity appear to represent the most consistent risk signals; T2D is a more complex and partly confounded contributor; and MASLD may act as a clinically relevant amplifier of systemic thrombotic risk[3,5,6,7,8,9,10,11,12,13,14,15,16].

The cardiometabolic prothrombotic milieu

The modern "cardiometabolic patient" is not defined by a single diagnosis but by clustering. Obesity, insulin resistance, T2D, dyslipidemia, hypertension, renal dysfunction, fatty liver disease, reduced exercise capacity, and overt cardiovascular disease often overlap. From a venous thrombosis perspective, this overlap matters because the classic components of Virchow's triad can all be reinforced: blood becomes more thrombogenic, the endothelium more dysfunctional, and venous stasis more likely through immobility, venous insufficiency, hospitalization, and cardiorespiratory compromise[2,3].

Among these determinants, obesity is the most robustly supported. Recent reviews continue to describe obesity as an independent VTE risk factor, with risk increasing across BMI categories and appearing particularly relevant for abdominal adiposity[3,7]. A dose-response meta-analysis further showed a significant linear relationship between BMI and the risk of both VTE and PE, supporting the idea that excess adiposity is not just an associated feature but a clinically relevant contributor to venous thrombotic disease[5].

This association is biologically plausible. Expanded adipose tissue, particularly when dysfunctional, is associated with altered adipokine secretion, chronic activation of inflammatory pathways, increased plasminogen activator inhibitor-1, thrombin generation, and endothelial activation. Obesity also increases the frequency of surgery, temporary immobility, respiratory impairment, and comorbid disease. In practice, therefore, obesity acts both as a direct biologic driver and as a multiplier of thrombogenic exposures[3,17].

Visceral adiposity: beyond BMI

If obesity is the strongest epidemiologic signal, visceral adiposity may be the most conceptually interesting one. BMI is simple and useful, but it cannot distinguish between metabolically "quiet" excess weight and ectopic or centrally distributed fat. This matters because visceral fat reflects a more inflammatory and insulin-resistant phenotype and may therefore be more tightly coupled to thrombosis than body weight alone[6,7].

Mechanistic work in severe obesity has shown that visceral adiposity is independently associated with a hypercoagulable thrombin generation profile, suggesting that fat distribution, not only total fat mass, contributes to the prothrombotic state[6]. More recently, imaging-based evidence reported that visceral adipose tissue (VAT) volume demonstrated a stronger association with VTE risk than BMI, supporting the idea that central adiposity may better capture clinically meaningful thrombotic vulnerability[7].

Adipokine studies reinforce this view. In the Multi-Ethnic Study of Atherosclerosis, lower adiponectin and higher leptin levels were associated with incident VTE, indicating that the endocrine behavior of adipose tissue may be relevant to venous thrombosis risk and not merely to metabolic risk scoring[17]. For a cardiometabolic commentary, this is an important point: the conversation should move from "obesity" in the generic sense to "adipokine tissue dysfunction," which is closer to the real biology of these patients.

Type 2 diabetes: independent culprit or marker of clustered risk?

Compared with obesity, the relationship between T2D and VTE is more nuanced. Some meta-analyses have suggested an increased risk of VTE in people with diabetes[8,9,10], whereas others concluded that the association becomes weak or even non-significant after adjustment for confounders, especially obesity[8]. A prudent interpretation is therefore necessary: diabetes may contribute to thrombotic risk, but it probably does so less as a solitary culprit and more as one element of a high-risk cardiometabolic phenotype.

This nuanced position is also biologically coherent. Chronic hyperglycemia, oxidative stress, protein glycation, endothelial injury, increased tissue factor activity, and impaired fibrinolysis all provide plausible pathways through which diabetes could promote venous thrombosis[11]. At the same time, many patients with T2D who develop VTE also have obesity, chronic kidney disease, reduced mobility, systemic inflammation, or cardiovascular disease. In real-world practice, these elements are difficult to disentangle and may be more informative as a cluster than as isolated variables. Rather than being viewed as a simple dichotomous variable, type 2 diabetes should probably be interpreted as a graded modifier of thrombotic vulnerability, with poor glycemic control, longer disease duration, and the presence of microvascular complications—particularly diabetic kidney disease—likely contributing to a more unfavorable

prothrombotic profile, even if the epidemiologic signal remains inconsistent across studies[4,10,18].

This distinction matters because overclaiming the role of diabetes alone weakens the argument. A stronger and more credible interpretation is that T2D identifies a patient in whom the threshold for thrombotic vulnerability may be lower, the symptom burden more confusing, and the consequences of PE more severe. In other words, diabetes is clinically meaningful even when it is not the dominant independent epidemiologic signal[4,8,11].

Metabolic syndrome and MASLD as amplifiers of thrombotic vulnerability

The concept of metabolic syndrome offers a useful bridge between arterial and venous thinking. Earlier studies suggested that metabolic syndrome may be linked to idiopathic venous thrombosis and perhaps act as a conceptual interface between venous disease and atherosclerosis[12,13,19]. Later work refined this picture: abdominal adiposity appears to be the strongest single component, but the clustering of metabolic abnormalities still seems relevant, particularly when recurrence is considered[14,15,20,21].

This is where MASLD becomes especially attractive for a commentary focused on cardiometabolic medicine. MASLD is not simply a liver diagnosis appended to obesity or diabetes; it is a marker of multisystem metabolic dysfunction. Increasing evidence indicates that patients with steatotic liver disease exhibit altered primary and secondary hemostasis, reduced fibrinolytic balance, and a broader procoagulant profile[14,15,16]. Recent work has specifically reviewed the link between MASLD and VTE, while experimental and translational data in metabolic dysfunction-associated steatohepatitis (MASH) support enhanced venous thrombosis and hypercoagulability[15,16].

Beyond serving as a clinical marker of metabolic dysfunction, MASLD may actively participate in thrombo-inflammatory imbalance because the liver is central to the synthesis of coagulation factors, anticoagulant proteins, and regulators of fibrinolysis. In this context, increased hepatic production of procoagulant mediators and impaired fibrinolysis, including pathways involving plasminogen activator inhibitor-1 (PAI-1), provide a biologically plausible explanation for why MASLD may amplify venous thrombotic vulnerability rather than merely accompany it[14,15,16].

MASLD therefore helps sharpen the central thesis. It anchors the discussion in a clinically familiar condition that diabetologists and cardiometabolic physicians increasingly see every day, while also extending the argument beyond BMI and glucose alone. In this context, the steatotic liver can be viewed as both a marker and a participant in systemic thromboinflammatory dysregulation[14,15,16].

Why PE is harder to recognize in the cardiometabolic patient

PE is difficult precisely because it so often presents with symptoms that are common and nonspecific: dyspnea, chest discomfort, tachycardia, exercise intolerance, presyncope, or hypoxemia[1,2]. In the cardiometabolic patient, these symptoms are even more likely to be misattributed. Obesity itself may cause exertional breathlessness; heart failure, chronic coronary disease, obstructive sleep apnea, anemia, chronic lung disease, and deconditioning are all frequent alternative explanations. The result is not simply diagnostic complexity, but diagnostic delay.

A patient with T2D, obesity, MASLD, and mild chronic dyspnea may not appear acutely thrombotic at first glance, even when PE is present. Thus, awareness of the cardiometabolic setting should not lead to reflex overtesting, but to a more disciplined and less complacent use of structured PE assessment[1,22].

An additional challenge is the interpretation of diagnostic biomarkers. In patients with obesity, chronic low-grade inflammation, or multimorbidity, D-dimer concentrations may be less specific, potentially increasing the likelihood of false-positive results and downstream imaging. At the same time, prospective data suggest that age-adjusted D-dimer strategies remain safe in obese patients with suspected PE and may improve efficiency compared with a fixed conventional cutoff[22].

From a diagnostic perspective, computed tomography pulmonary angiography (CTPA) remains the reference imaging modality in most patients with suspected PE, but its use may be more challenging in individuals with severe obesity because of technical, logistic, and image-quality issues, including body habitus limitations and suboptimal contrast enhancement. In selected cases, when CTPA is not feasible or remains inconclusive, alternative or complementary strategies such as ventilation/perfusion imaging and compression ultrasonography of the lower limbs may still contribute to the diagnostic work-up within a structured clinical probability-based approach.

Prognostic and therapeutic implications

Prognostic stratification also remains essential in this setting. Validated tools such as the Pulmonary Embolism Severity Index (PESI) and simplified PESI (sPESI) continue to provide useful support for early risk assessment in acute PE. However, in cardiometabolic patients, multimorbidity, impaired functional reserve, chronic kidney disease, heart failure, and obesity-related respiratory limitation may complicate the overall clinical picture, reinforcing the need to interpret formal risk scores within a broader integrated clinical assessment.

Acute PE also carries a potentially different meaning

in the cardiometabolic patient. Even when the embolic burden is not massive, the event often occurs in a host with reduced cardiopulmonary reserve, stiffer vasculature, renal dysfunction, chronic inflammation, and multiple competing morbidities. This may translate into greater hemodynamic fragility, more difficult recovery, and more complicated long-term follow-up. Importantly, recurrence data suggest that metabolic syndrome may increase the risk of recurrent VTE after both PE and DVT, reinforcing the concept that the metabolic terrain remains relevant even after the index event[14,15].

Management should not be reduced to anticoagulant selection, but anticoagulant issues cannot be ignored. Obesity raises longstanding pharmacokinetic and pharmacodynamic concerns, especially at higher body weights. Recent reviews and meta-analyses, however, are generally reassuring: DOACs appear to have efficacy and safety profiles at least comparable to warfarin in obese and morbidly obese patients, although high-quality randomized evidence remains limited[23,24,25]. Current practice is therefore increasingly pragmatic, favoring standard-dose apixaban or rivaroxaban in many obese patients while recognizing the evidence gaps that persist at extremes of body weight[23,24].

Renal function also deserves explicit attention in this cluster. Because diabetic kidney disease is common in cardiometabolic patients with acute PE, periodic reassessment of kidney function is essential when selecting and dosing direct oral anticoagulants, particularly in older adults and in patients with fluctuating renal function, polypharmacy, or multiple competing risks for both thrombosis and bleeding[23,24,26].

More broadly, a PE diagnosis in a cardiometabolic patient should trigger a wider reassessment. Weight trajectory, central adiposity, glycemic control, renal function, sleep apnea, mobility, heart failure status, and liver phenotype all matter. The event should be treated not only as a clot to be anticoagulated, but also as a warning signal of systemic vulnerability.

What should change in practice

Three practical implications follow from this framework. First, VTE risk should become more visible within cardiometabolic medicine. In patients with obesity, T2D, visceral adiposity, and MASLD, clinicians should think not only about myocardial infarction, stroke, and kidney disease, but also about venous events. Second, new or disproportionate dyspnea in such patients should not be too quickly attributed to "baseline obesity," deconditioning, or heart failure without structured consideration of PE. Third, the follow-up after acute PE should include a deliberate review of cardiometabolic drivers rather than ending with a prescription for anticoagulation duration.

This does not mean that every cardiometabolic patient warrants a VTE-centered mindset at all times, nor that venous and arterial thrombosis should be collapsed into a single pathophysiologic entity. It means, more modestly and more usefully, that cardiometabolic medicine should enlarge its field of view. PE is not peripheral to these patients' biology; it is often a downstream expression of it.

Conclusion

Acute PE remains one of the most dangerous manifestations of venous thromboembolism, but in contemporary practice it should increasingly be interpreted through a cardiometabolic lens. Obesity and visceral adiposity provide the strongest epidemiologic and mechanistic signal, diabetes contributes within a clustered-

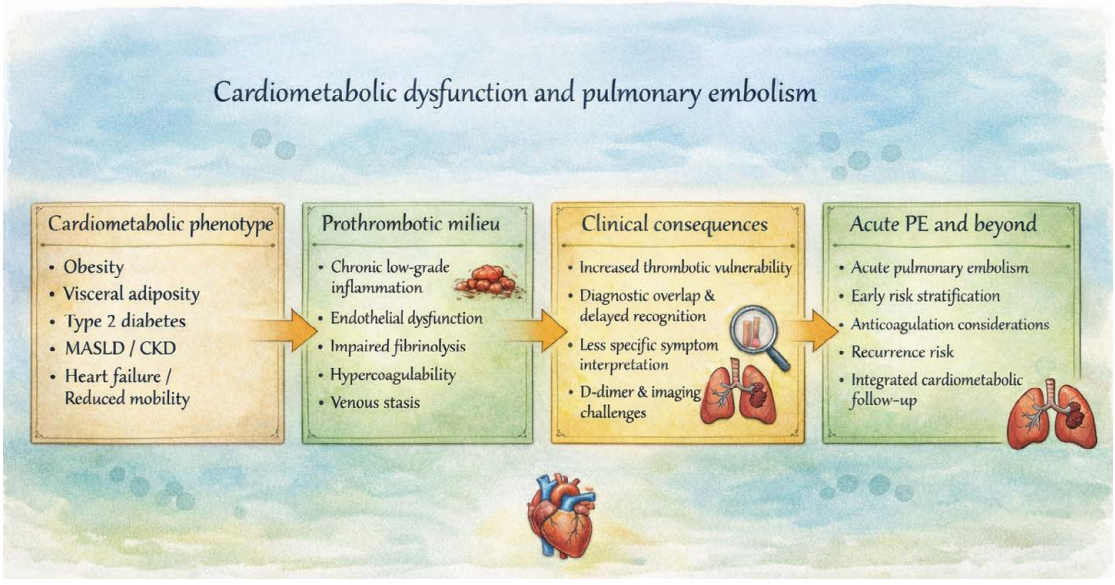

Figure 1. Cardiometabolic dysfunction and pulmonary embolism: from prothrombotic milieu to clinical complexity.

risk phenotype rather than as a universally dominant independent factor, and MASLD offers a compelling model of systemic thromboinflammatory amplification. The practical consequence is straightforward: in the cardiometabolic patient, PE should be considered earlier, interpreted more broadly, and followed by a more integrated reassessment than is often done today. In an era increasingly shaped by cardiometabolic medicine, VTE—and particularly acute PE—should no longer remain outside the main clinical narrative[1,2,3,16,23,24,25]. The main conceptual links discussed in this review are summarized in Figure 1.

Conflict of Interest

The authors declare no conflict of interest.

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References

1. Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J. 2020;41(4):543-603. doi:10.1093/eurheartj/ehz405
2. Pastori D, Ferro D, Loffredo L, et al. A comprehensive review of risk factors for venous thromboembolism. Semin Thromb Hemost. 2023;49(6):635-650
3. Zawadzka PS, Zawieja M, Banach M, et al. The interplay between obesity and venous thromboembolism. Int J Mol Sci. 2025;26(21):10292. doi:10.3390/ijms262110292
4. Marx N, Federici M, Schütt K, et al. 2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes. Eur Heart J. 2023;44(39):4043-4140. doi:10.1093/eurheartj/ehad192
5. Rahmani J, Haghighian HK, Shab-Bidar S, et al. Relationship between body mass index, risk of venous thromboembolism and pulmonary embolism: a systematic review and dose-response meta-analysis of cohort studies among four million participants. Thromb Res. 2020;192:64-72
6. Chitongo PB, Roberts LN, Arya R. Visceral adiposity is an independent determinant of hypercoagulability as measured by thrombin generation in morbid obesity. TH Open. 2019;3(2):e146-e154
7. Xiang R, Huang A, Stevens H, et al. Visceral adipose tissue demonstrates a stronger association with venous thromboembolism than body mass index. J Thromb Haemost. 2025;23(9):2883-2889. doi:10.1016/j.jtha.2025.05.020
8. Bell EJ, Folsom AR, Lutsey PL, et al. Diabetes mellitus and venous thromboembolism: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2016;111:10-18
9. Bai J, Ding X, Du X, Zhao X, Wang Z, Ma Z. Diabetes is associated with increased risk of venous thromboembolism: a systematic review and meta-analysis. Thromb Res. 2015;135(1):90-95
10. Ding C, Wang Y, Wang C, et al. Association between diabetes and venous thromboembolism: a systematic review and meta-analysis. Front Endocrinol (Lausanne). 2023;14:1215232
11. Panchagnula N, Lee LH, White RH. Hyperglycemia and venous thromboembolism. Res Pract Thromb Haemost. 2024;8:e70036
12. Ageno W, Prandoni P, Romualdi E, et al. The metabolic syndrome and the risk of venous thrombosis: a case-control study. J Thromb Haemost. 2006;4(9):1914-1918
13. Ageno W, Dentali F, Squizzato A, et al. Association between the metabolic syndrome, its individual components, and unprovoked venous thromboembolism: results of a patient-level meta-analysis. Arterioscler Thromb Vasc Biol. 2014;34(11):2478-2485
14. Spinosa M, Hebbard L, Lucchi C, et al. Nonalcoholic fatty liver disease—evidence for a thrombophilic state? J Thromb Haemost. 2020;18(7):1550-1560
15. Pandey N, Kasikara C, Noels H, et al. Enhanced venous thrombosis and hypercoagulability in murine and human metabolic dysfunction-associated steatohepatitis. J Thromb Haemost. 2024;22(11):3084-3097
16. González-Mendoza DE, Fernández-Nogueira F, Uribe M, Chávez-Tapia NC, Nuño-Lámbarri N. Hemostatic alterations in metabolic dysfunction-associated steatotic liver disease (MASLD) and their link to venous thromboembolism (VTE). Thromb Res. 2025;253:109395. doi:10.1016/j.thromres.2025.109395
17. Broni EK, Ogunmoroti O, Michos ED, et al. Adipokines and incident venous thromboembolism: the Multi-Ethnic Study of Atherosclerosis. J Thromb Haemost. 2023;21(2):303-310
18. Charlier SHR, Meier C, Jick SS, Meier CR, Becker C. Association between glycemic control and risk of venous thromboembolism in diabetic patients: a nested case-control study. Cardiovasc Diabetol. 2022;21(1):2. doi:10.1186/s12933-021-01432-1
19. Di Minno MN, Tufano A, Guida A, et al. Abnormally high prevalence of major components of the metabolic syndrome in patients with idiopathic venous thromboembolism. Thromb Res. 2011;127(6):e214-e219
20. Stewart LK, Kline JA. Metabolic syndrome increases risk of venous thromboembolism recurrence after acute pulmonary embolism. Ann Am Thorac Soc. 2020;17(7):821-828. doi:10.1513/AnnalsATS.201907-518OC
21. Stewart LK, Kline JA. Metabolic syndrome increases risk of venous thromboembolism recurrence in patients with deep vein thrombosis. Blood Adv. 2020;4(1):127-135. doi:10.1182/bloodadvances.2019000561
22. Gaugler JO, Righini M, Robert-Ebadi H, et al. Obesity as a predictor for pulmonary embolism and performance of the age-adjusted D-dimer strategy in obese patients with suspected pulmonary embolism. Thromb Haemost. 2024;124(2):159-167. doi:10.1055/s-0043-57018
23. Sorodoc V, Bontas E, Tuta S, et al. Anticoagulation approach in morbid obesity: a comprehensive review on venous thromboembolism management. Front Pharmacol. 2024;15:1457280
24. Talerico R, D'Eugenio C, Li Puma M, et al. Direct-acting oral anticoagulants in patients at extremes of body weight: a review of pharmacological considerations and clinical implications. TH Open. 2024;8(1):e31-e41. doi:10.1055/s-0043-1776989
25. Karakasis P, Siafis S, Mantas C, et al. Efficacy and safety of direct oral anticoagulants versus warfarin in obese patients: a systematic review and meta-analysis. J Clin Med. 2024;13(13):3784. doi:10.3390/jcm13133784
26. Elenjickal EJ, Mavrakanas T, Brodsky S, Bansal N. Anticoagulation in patients with chronic kidney disease. Semin Nephrol. 2024;44(1):151443