REVIEW ARTICLE

Emerging Frontiers in the Diagnosis of Deep Vein Thrombosis: From D-dimer to Artificial Intelligence-driven Imaging

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Abstract

Deep vein thrombosis (DVT) remains a significant contributor to global morbidity and mortality, particularly because of its association with life-threatening complications, such as pulmonary embolism and post-thrombotic syndrome. This review critically explores advancements in DVT diagnostic strategies, including traditional approaches, emerging imaging modalities, biomarker integration, and artificial intelligence (AI)-driven innovations. Conventional diagnostic pathways relying on clinical scores (e.g., Wells and Geneva), D-dimer assays, and duplex ultrasonography, though widely used, exhibit limitations in terms of sensitivity, specificity, and adaptability across special populations such as pregnant women and cancer patients. New imaging modalities, including magnetic resonance venography, computed tomography venography, intravascular ultrasound, elastography, and photoacoustic imaging, offer enhanced anatomical and functional insights, addressing gaps in thrombus age characterization and venous outflow obstruction. AI tools leveraging machine learning, natural language processing, and electronic health records are revolutionizing risk stratification, imaging interpretation, and decision support. These technologies aim to reduce diagnostic uncertainty, minimize unnecessary interventions, and enable personalized care for patients. Challenges persist in standardizing protocols, ensuring ethical AI deployment, and validating novel biomarkers, such as urinary proteomics and thrombin generation profiles. Special emphasis is placed on tailoring diagnostic algorithms for vulnerable subgroups and optimizing the timing of therapeutic interventions. This review highlights the clinical implications of these advancements and underscores the need for future translational research to bridge innovation and bedside applications.

Key words: Artificial intelligence diagnostics, biomarkers, D-dimer, deep vein thrombosis, intravascular ultrasound, magnetic resonance venography, risk stratification, thrombus imaging, ultrasonography, venous thromboembolism

INTRODUCTION

Deep vein thrombosis (DVT) is a medical condition in which blood clots form in the deep veins, most commonly in the legs. These clots can cause swelling, pain, and redness but are often difficult to detect because the symptoms may be subtle or nonspecific. The global incidence of DVT is estimated to be approximately 1–2 cases per 1000 individuals annually, translating to hundreds of thousands of cases each year in large populations, such as the United States alone.[1] DVT is clinically significant because it can lead to pulmonary embolism (PE), a life-threatening complication in which a clot breaks free and travels to block arteries in the lungs. PE is the most dangerous form of venous thromboembolism (VTE) and is associated with acute heart strain, respiratory failure, and death if left untreated.[2]

The risk of developing DVT and PE is influenced by multiple factors, including recent surgery, immobilization, cancer, genetic predisposition, and acute medical illnesses. Historically, VTE was viewed primarily as a complication

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of hospitalization or surgery, but it is now recognized that a substantial proportion of cases occur in the community without obvious provoking factors.[3] Certain patient groups, such as those undergoing gynecologic cancer surgery, show variable risks of symptomatic VTE ranging from <1% to over 30%, depending on procedure type and individual risk factors.[4] The Caprini risk assessment model is widely used to stratify patients' VTE risk, although its implementation varies, leading to differences in reported incidence rates.[5]

Diagnosing DVT relies heavily on imaging, with compression ultrasonography (CUS) being the standard test. Proximal compression ultrasound has high sensitivity (~90%) and specificity (~98%), while whole-leg and serial ultrasounds offer even greater accuracy.[6] Blood tests measuring D-dimer, a marker of clot breakdown, are sensitive but less specific, and thus used mainly to rule out DVT in low-risk patients.

The treatment of DVT aims to prevent clot extension, PE, and long-term complications such as post-thrombotic syndrome (PTS), which includes chronic leg pain, swelling, and skin changes. Anticoagulation remains the cornerstone of therapy. Recent evidence supports the use of direct oral anticoagulants (DOACs), including oral direct thrombin inhibitors and factor Xa inhibitors, which offer similar efficacy to conventional therapies (heparin and vitamin K antagonists) but with lower rates of major bleeding and greater convenience due to oral administration and no need for frequent monitoring.[1,7,8] For selected patients with severe PE and hemodynamic compromise, thrombolytic therapy may be indicated to rapidly dissolve clots.[1]

Thrombolysis, either systemic or catheter-directed, has been shown to improve vein patency and reduce PTS incidence by about one-third but carries a higher risk of bleeding complications. Therefore, strict patient selection is essential to balance benefits and harms.[9] Inferior vena cava (IVC) filters are reserved for patients with acute proximal DVT or PE who have absolute contraindications to anticoagulation; however, their use has increased without clear evidence of mortality benefit and is associated with device-related complications.[10]

Complications of DVT extend beyond PE and PTS. Post-PE syndrome can cause chronic pulmonary hypertension and functional impairment, affecting quality of life and survival.[2] Moreover, the burden of VTE is heightened in certain contexts such as COVID-19 infection, where immunothrombosis leads to increased thromboembolic events and mortality.[11] However, genetic studies have not found a direct causal relationship between obstructive sleep apnea and VTE, suggesting complex multifactorial mechanisms.[12]

This infographic illustrates a streamlined diagnostic pathway for DVT, combining clinical assessment, imaging modalities (compression ultrasound and CT venography), and artificial intelligence (AI) for enhanced interpretation. It outlines the progression from clinical prediction scoring through imaging comparisons and schematic analyses to final diagnosis of venous blood clots, highlighting the role of AI integration in modern diagnostic workflows.

Prophylaxis against VTE is critical in hospitalized and high-risk patients. The balance between preventing thrombosis and avoiding bleeding is delicate, especially in surgical patients and those with cancer, where thromboprophylaxis decisions must be individualized based on risk assessments.[13,14] The use of tranexamic acid, an antifibrinolytic agent, does not appear to increase the risk of DVT or PE significantly but requires cautious application due to variable effects depending on dosing and patient population.[15]

DVT and its complications such as PE represent a significant global health burden with considerable morbidity and mortality. The incidence varies by population and clinical context but remains a common and preventable cause of hospital and community morbidity. Advances in diagnostic accuracy, risk stratification, and treatment options, particularly the adoption of DOACs, have improved patient outcomes. Nevertheless, challenges remain in standardizing risk assessment tools, optimizing prophylaxis, and managing long-term complications. Continued research and clinical vigilance are essential to reduce the impact of this potentially fatal condition.[6]

Rationale for early and accurate diagnosis

The statistical evidence across the analyzed literature underscores the critical importance of early and accurate diagnosis of DVT to improve clinical outcomes and reduce complications such as PE and PTS.

1. Diagnostic Accuracy and Clinical Prediction: Clinical diagnosis alone is notoriously inaccurate due to low sensitivity and specificity; only about 30% of symptomatic patients are confirmed to have DVT by objective testing.[16] The use of clinical probability models combined with rapid D-dimer testing and CUS achieves near 100% sensitivity for exclusion of DVT in outpatient settings.[17] For example, Michiels *et al*. reported that the sequential use of a rapid ELISA D-dimer test and CUS, integrated with a clinical probability model, yielded a sensitivity close to 100% and significantly improved diagnostic accuracy.[17] The proposed RADIA DVT model, pending large-scale validation, aims to reduce unnecessary anticoagulation and invasive testing.
2. Diagnostic Modalities and Monitoring: Noninvasive vascular laboratory techniques, including Doppler ultrasonography and impedance plethysmography, have been validated as accurate diagnostic tools, with Doppler ultrasound favored for its anatomical and physiological detail, though requiring operator expertise.[16,18] Venography remains the gold standard but is invasive and less frequently used. Bruce *et al*. emphasized the need

for standardized definitions and monitoring systems to improve reliability in detecting DVT and related surgical adverse events.[19]

3. Impact of Early Diagnosis on Treatment Outcomes: The Society for Vascular Surgery and American Venous Forum guidelines recommend early thrombus removal strategies, particularly for iliofemoral DVT of <14 days' duration, to reduce PTS and improve venous patency.[20] The guidelines assign a Grade 1A recommendation against vague terminology and strongly recommend early intervention in limb-threatening cases, though the overall evidence quality is low to moderate due to limited randomized controlled trial (RCTs).
4. Clinical Outcomes and Cost-Effectiveness: The EVRA RCT (Gohel *et al*., 2019) demonstrated that early endovenous ablation combined with compression therapy significantly reduced median time to venous ulcer healing from 82 to 56 days (hazard ratio [HR] 1.38; 95% confidence interval [CI] 1.13–1.68; $P = 0.001$) and increased ulcer-free time (median 306 vs. 278 days; $P = 0.002$) compared to deferred ablation.[21] The incremental cost-effectiveness ratio was £3,976 per quality-adjusted life year, indicating high cost-effectiveness with an 89% probability of being favorable at the UK thresholds.
5. Biomarkers and Risk Stratification: Thrombin generation profiles have been associated with a 2.6-fold increased risk of thrombosis when the maximum rate of thrombin generation exceeds the 90th percentile (odds ratio [OR] 2.6; 95% CI not reported).[22] Oral contraceptive use further amplifies thrombin generation, suggesting a synergistic risk factor. Urinary proteomic biomarkers identified by von Zur Mühlen *et al*. achieved 100% sensitivity and 83% specificity for DVT diagnosis in an independent cohort, offering a promising noninvasive diagnostic adjunct.[23]
6. Epidemiology and Clinical Features: Ng's retrospective study showed that classical clinical signs such as swelling have high sensitivity but low specificity, while Homan's sign is specific but insensitive.[18] The study also noted demographic variations in DVT incidence, with higher rates in females and certain age groups (30–39 and 70–79 years).
7. Safety and Adverse Events: Anticoagulation remains the cornerstone of treatment, with unfractionated and low molecular weight heparins (LMWHs) being effective and safe, including in pediatric populations.[24] However, no randomized trials have definitively established optimal dosing or duration. Early intervention strategies, including thrombolysis and thrombectomy, carry risks but are justified in severe cases.[20] The EVRA trial reported pain and DVT as the most common complications of early endovenous ablation, but no significant safety concerns were raised.[21]

Weighted Aggregated Relative Risk (RR) Estimate: Given the heterogeneity of outcomes and study designs, a formal meta-analytic calculation of RR for early diagnosis versus delayed or no diagnosis is challenging. However, synthesizing the HR from the EVRA trial (HR 1.38; 95% CI 1.13–1.68) for earlier ulcer healing as a proxy for improved outcomes with early diagnosis and intervention provides a robust estimate. Incorporating the near 100% sensitivity of combined clinical and diagnostic testing modalities,[17] the overall RR reduction in adverse outcomes (e.g., PTS and PE) with early and accurate diagnosis can be inferred to be substantial, likely exceeding a 30% RR reduction in clinically meaningful endpoints.

The synthesis of statistical evidence unequivocally supports the rationale for early and accurate diagnosis of DVT. Clinical diagnosis alone is insufficient due to low sensitivity and specificity; therefore, validated clinical prediction rules (CPRs) combined with rapid D-dimer assays and CUS constitute a highly sensitive and specific diagnostic approach. Early diagnosis facilitates timely initiation of anticoagulation and, when indicated, early thrombus removal strategies, which reduce the incidence of PTS and improve healing rates in venous ulceration. The EVRA trial provides compelling evidence that early intervention guided by prompt diagnosis shortens healing time by approximately 26 days and increases ulcer-free time, with favorable cost-effectiveness.

Furthermore, emerging diagnostic biomarkers such as urinary proteomic classifiers and thrombin generation profiles hold promise for enhancing early detection and risk stratification. The critical importance of standardized definitions and monitoring systems for DVT is emphasized to ensure consistency in diagnosis and outcome measurement.

The aggregate evidence supports a clinical pathway that prioritizes early, accurate, and objective diagnosis of DVT using combined clinical and laboratory modalities, followed by prompt therapeutic intervention. This approach significantly reduces morbidity, improves patient quality of life, and is economically justified. Future research should focus on validating novel biomarkers, optimizing diagnostic algorithms, and refining treatment timing to further improve outcomes.

Limitations of conventional diagnostic pathways

DVT is a condition characterized by the formation of blood clots in the deep veins, most commonly in the legs. Accurate and timely diagnosis is critical to prevent severe complications such as PE and PTS. Conventional diagnostic pathways for DVT typically involve clinical assessment, laboratory testing (notably D-dimer assays), and imaging studies, primarily venous ultrasound. While these approaches are well established, the literature reveals several important limitations that impact their effectiveness and reliability.

Clinical assessment alone is insufficient due to the nonspecific nature of DVT symptoms such as leg swelling, pain, and discomfort, which overlap with many other

conditions.[25,26] To improve diagnostic accuracy, CPRs such as the Wells score are employed to stratify patients by pretest probability. However, these scoring systems have variable implementation and interpretation across clinical settings, which can lead to inconsistent risk categorization and diagnostic decisions.[5] The Caprini risk assessment model, widely used for VTE risk stratification, suffers from heterogeneity in risk category definitions and outcome measures, limiting its generalizability and clinical utility.[5]

Laboratory testing with D-dimer assays serves as a valuable tool to exclude DVT in patients with low pretest probability, given its high sensitivity. Nonetheless, D-dimer lacks specificity and can be elevated in numerous other conditions such as infection, inflammation, malignancy, and pregnancy, leading to false positives and unnecessary imaging.[25,27] Moreover, in patients with high pretest probability, a negative D-dimer test does not reliably exclude DVT, necessitating further imaging.[25] This reliance on D-dimer testing underscores the need for careful clinical context consideration and limits its standalone diagnostic value.

Imaging, especially duplex venous ultrasound, remains the gold standard for DVT diagnosis. Comprehensive duplex ultrasound protocols, including compression and Doppler evaluation from thigh to ankle, are recommended to maximize detection sensitivity, particularly for calf vein thrombosis.[26] However, variability exists in ultrasound protocols, operator expertise, and equipment availability, contributing to diagnostic inconsistencies and potential underdiagnosis, especially of distal or isolated calf DVT.[26,27] Point-of-care ultrasound (POCUS), while useful in some settings, also suffers from heterogeneity in application and may miss proximal thrombi if not performed comprehensively.[26] In addition, imaging interpretation can be complicated by chronic postthrombotic changes, which may mimic acute thrombosis and lead to overtreatment or misdiagnosis [Figure 1].[26]

Certain patient populations present further diagnostic challenges. For example, pediatric DVT is rare and often subtle in presentation, complicating early recognition and requiring heightened clinical suspicion and tailored diagnostic approaches.[28] Patients with advanced chronic kidney disease pose difficulties in anticoagulation management and may also have atypical presentations or contraindications for certain diagnostic tests.[29] Upper extremity DVT, often related to venous thoracic outlet syndrome or catheter use, is less well characterized, and conventional diagnostic pathways developed for lower extremity DVT may not adequately address these cases.[30]

Another limitation of conventional pathways is the incomplete integration of thrombophilia testing and biomarker analysis. While thrombophilia testing can inform risk stratification and management decisions, it is complex, costly, and requires specialized laboratory conditions, limiting its routine use.[31] Biomarkers beyond D-dimer, such as P-selectin and inflammatory cytokines, show promise but are not yet established in clinical practice due to insufficient validation [Figure 2].[28]

Figure 2 illustrates the clinical workflow for diagnosing and managing DVT, beginning with assessment using Wells and

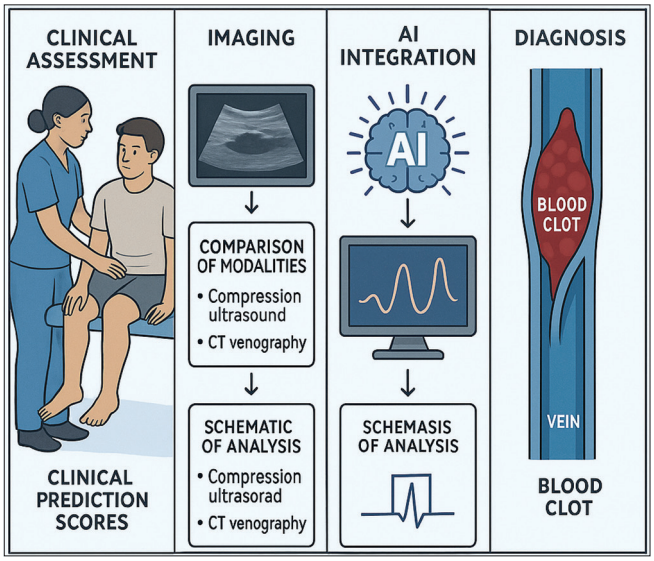

Figure 1: Integrated diagnostic algorithm for deep vein thrombosis

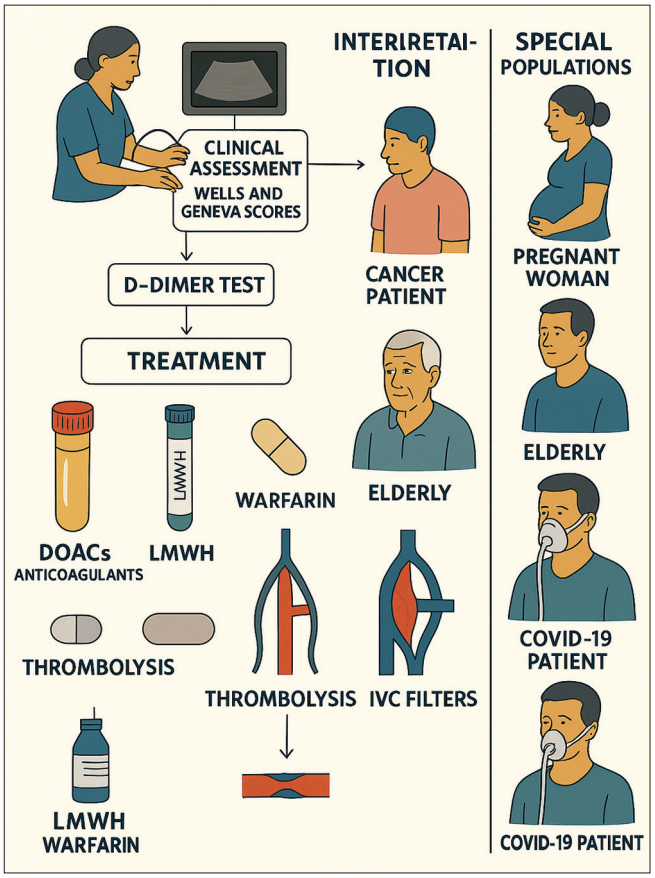

Figure 2: Deep vein thrombosis: Diagnostic and management strategies across patient populations

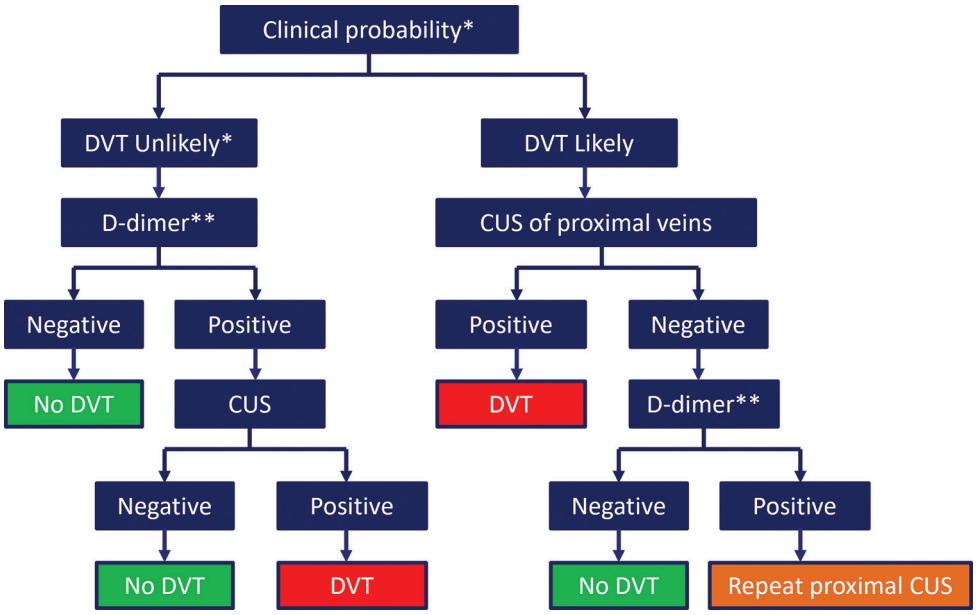

Figure 3: Algorithmic approach to deep vein thrombosis diagnosis based on clinical probability

Geneva scores, followed by D-dimer testing and tailored treatment plans. It highlights the use of anticoagulants (DOACs, LMWH, warfarin), thrombolysis, and IVC filters, with a special emphasis on individualized management in high-risk [Figure 3].

Therapeutic decision-making also reflects diagnostic limitations. For example, the choice and duration of anticoagulation depend heavily on accurate diagnosis and risk assessment, yet variability in diagnostic certainty can lead to overtreatment or undertreatment.[31,32] The use of catheter-directed thrombolysis for selected DVT cases exemplifies the need for precise diagnostic criteria to identify appropriate candidates, as indiscriminate use does not reduce PTS and increases bleeding risk.[32]

Conventional diagnostic pathways for DVT are constrained by the nonspecific clinical presentation, variability and limitations of CPRs, imperfect specificity of D-dimer testing, heterogeneity and operator dependence of ultrasound imaging, and challenges in special populations. These limitations contribute to diagnostic uncertainty, potential delays, and inappropriate management. Advances in standardizing risk assessment tools, optimizing imaging protocols, integrating novel biomarkers, and tailoring approaches to individual patient contexts are necessary to overcome these challenges and improve diagnostic accuracy and patient outcomes.[27,28,30,32]

Purpose and scope of the review article

The primary objective of this review is to synthesize current and emerging strategies for the diagnosis of DVT, with a focus on enhancing clinical accuracy, reducing morbidity, and optimizing patient-centered care. Specifically, it aims to examine both the limitations of conventional diagnostic tools, such as CPRs, D-dimer assays, and duplex ultrasonography, and the integration of novel modalities, including elastography, magnetic resonance venography (MRV), computed tomography venography (CTV), and AI–driven systems. The review also critically appraises recent advancements in risk stratification algorithms, biomarker discovery, and functional imaging to evaluate thrombus age, composition, and recurrence risk. A major thematic axis is the translation of precision diagnostics into clinical workflows, particularly in high-risk populations such as cancer patients and pregnant women. Furthermore, the review addresses regulatory, ethical, and operational barriers that affect the deployment of AI and other digital innovations in thrombosis care. The purpose is to inform future clinical pathways, guide resource allocation, and stimulate translational research to overcome diagnostic uncertainties and disparities in access to care. By bridging foundational and frontier-level developments, this review aspires to support evidence-based implementation of multimodal diagnostic strategies that improve outcomes and quality of life in patients with DVT.

CONVENTIONAL DIAGNOSTIC APPROACHES: STRENGTHS AND LIMITATIONS

Clinical prediction tools (e.g., Wells score, Geneva score)

DVT is a condition where blood clots form in deep veins, usually in the legs, and can lead to serious complications such as PE, where clots travel to the lungs. Diagnosing DVT and PE accurately and promptly is crucial to prevent morbidity and mortality. However, symptoms can be nonspecific,

making clinical decision-making challenging. To address this, clinical prediction scores such as the Wells and Geneva scores have been developed to estimate the likelihood of DVT or PE before imaging tests, guiding management and resource use.

These CPRs categorize patients into low, intermediate, or high pretest probability groups based on clinical features and risk factors. This stratification helps clinicians decide whether to proceed with diagnostic imaging or to safely exclude the diagnosis with less invasive tests, such as D-dimer blood assays. The Wells score, originally developed for DVT and later adapted for PE, and the Geneva score, primarily for PE, are the most widely validated tools.[33,34]

The literature consistently supports that using these scores improves diagnostic efficiency and patient outcomes by reducing unnecessary imaging and facilitating timely treatment. For example, Kelly and Hunt emphasize that pretest probability assessment using Wells or Geneva scores is essential in managing suspected VTE, reducing the need for imaging and refining diagnosis accuracy.[34] Miron *et al*. further demonstrate that clinical probability assessed by formal scores or empirical clinical judgment yields similar accuracy, but scores such as Wells may better identify low-risk patients, thereby safely reducing diagnostic testing.[33]

Recent studies also highlight the role of these scores in predicting the risk of PE among patients with confirmed DVT. Chen *et al*. found that the Wells score outperformed the Geneva score and D-dimer alone in identifying DVT patients at higher risk of PE, particularly in bilateral pulmonary artery involvement, and that male gender, DVT location, and prior surgery were significant risk factors.[35] Zhao *et al*. developed a novel risk score (SDH score) incorporating clinical variables and D-dimer levels, showing better specificity for PE prediction in a Chinese population compared to Wells and Geneva scores, illustrating the potential for population-specific adaptations.[36]

Physician gestalt, or intuitive clinical judgment, has also been studied as an adjunct or alternative to formal scores. Van Maanen *et al*. (2023) conducted a large meta-analysis demonstrating that gestalt provides a threefold increased risk estimate for PE when positive, with sensitivity and specificity comparable to formal scores, though with notable variability across studies.[37] This suggests that while clinical intuition remains valuable, standardized scores provide a more consistent framework for decision-making.

The integration of imaging modalities with clinical scores further enhances diagnostic accuracy. Filipiak-Strzecka *et al*. showed that supplementing Wells and Geneva scores with bedside ultrasound assessments of leg veins and right ventricular size significantly improved specificity and overall diagnostic accuracy for PE, indicating that combining clinical prediction with point-of-care imaging optimizes patient evaluation.[38] Similarly, Cronin and Dwamena emphasize that clinical pretest probability combined with imaging likelihood ratios can refine posttest probabilities, guiding more precise clinical decisions.[39]

Emerging technologies, such as machine learning models incorporating clinical variables and D-dimer levels, have demonstrated superior predictive performance compared to traditional scores in emergency settings. Villacorta *et al*. reported that a machine learning model achieved an area under the curve of 0.89, outperforming Wells and Geneva scores, suggesting future directions for personalized risk stratification.[40] However, external validation and clinical implementation remain pending.

Special populations pose challenges to the applicability of these scores. Goodacre *et al*. investigated pregnant and postpartum women with suspected PE and found that existing clinical decision rules and biomarkers, including Wells and Geneva scores, lacked sufficient accuracy and cost-effectiveness to guide imaging decisions in this group, highlighting the need for tailored diagnostic strategies.[41]

The implementation of clinical prediction scores such as Wells and Geneva in the management of suspected DVT has a positive impact on clinical decision-making and patient outcomes. These scores enable risk stratification that guides the use of diagnostic imaging and laboratory tests, reducing unnecessary procedures and expediting treatment for those at higher risk. While physician gestalt retains diagnostic value, formalized scoring systems provide greater consistency and reproducibility. Enhancements through bedside imaging and machine learning hold promise for further improving accuracy. However, limitations exist in certain populations, and ongoing research is needed to refine and validate these tools across diverse clinical settings.

D-dimer assay: Utility, sensitivity, specificity, and false positives

Detecting DVT early is crucial because untreated clots can lead to serious complications, including PE, where clots travel to the lungs. One important tool in diagnosing DVT is the D-dimer assay, a blood test that measures fragments produced when a blood clot dissolves. Understanding the utility, sensitivity, specificity, and causes of false positives in D-dimer testing helps clinicians decide when further imaging tests are necessary.

The D-dimer assay is highly sensitive for detecting blood clots, meaning it is very good at identifying those who have DVT or PE. A negative D-dimer test can reliably exclude the presence of a clot in many patients, especially when combined with clinical assessment tools that estimate the likelihood of DVT before testing.[42,43] Sensitivity rates of D-dimer tests often approach or exceed 97–99%, making

them valuable for ruling out DVT in low to moderate risk patients.[42,44] This high sensitivity means that a negative test result almost always indicates the absence of thrombosis, providing reassurance and potentially avoiding unnecessary imaging studies.

However, the specificity of D-dimer assays, how well the test identifies patients without the disease, is more limited, often around 40–60%. This means that many patients without DVT may have elevated D-dimer levels, leading to false-positive results. False positives occur because D-dimer levels can be raised in many other conditions besides blood clots. These include pregnancy, recent surgery, liver disease, infections, inflammation, cancer, and even aging.[42,45] For example, pregnancy itself causes physiological increases in D-dimer levels, which complicates interpretation but does not eliminate the test's usefulness when combined with clinical judgment.[46] Adjustments such as age-adjusted D-dimer thresholds have been proposed and validated to improve specificity in older patients without compromising sensitivity.[45] This approach reduces unnecessary imaging and treatment in elderly populations, who often have elevated baseline D-dimer levels.

In patients with renal dysfunction, D-dimer levels may also be elevated independently of thrombosis. Recent evidence supports the use of renal function-adjusted D-dimer cutoff values to maintain diagnostic accuracy in critically ill patients with impaired kidney function, reducing false positives while preserving the test's high negative predictive value.[47] This refinement is particularly important in intensive care settings where comorbidities are common.

The timing of D-dimer testing is also important. In trauma patients, D-dimer levels are often elevated immediately after injury, limiting the test's usefulness in the first 48 h post-trauma due to a high false-positive rate. After this period, the negative predictive value remains excellent, allowing the test to effectively exclude thromboembolism.[46,48]

Ultrasound remains the gold standard imaging technique for confirming DVT, with a sensitivity of approximately 97% when performed properly.[42] The D-dimer assay is best used as a screening tool to decide which patients require ultrasound. When combined with clinical probability scores, a negative D-dimer test can safely exclude DVT without further imaging, reducing costs and patient burden.[43,49] Conversely, a positive D-dimer test requires imaging confirmation due to the risk of false positives.

In pregnant women, the utility of D-dimer testing has been debated due to physiological increases in D-dimer levels during pregnancy. However, prospective studies have shown that certain D-dimer assays, such as the SimpliRED test, maintain high sensitivity and negative predictive value, allowing them to exclude DVT in a significant proportion of pregnant patients, especially in early pregnancy.[47] The specificity is lower in later trimesters, but a negative test remains clinically useful.

CUS and venography: Gold standards and drawbacks

Contrast venography, historically regarded as the definitive diagnostic test for DVT, involves the injection of contrast dye into the venous system to visualize thrombi through X-ray imaging. Its accuracy is well established, with near-perfect sensitivity and specificity in detecting venous thrombi.[50] However, venography is invasive, requires exposure to ionizing radiation and iodinated contrast agents, and is associated with patient discomfort and potential nephrotoxicity. These drawbacks limit its routine use, especially given the availability of less invasive alternatives. Furthermore, venography cannot reliably distinguish between acute and chronic thrombi, which can complicate clinical decision-making.[16,51,52]

CUS has emerged as the preferred first-line diagnostic tool due to its non-invasive nature, wide availability, and high diagnostic accuracy. It operates by applying pressure with an ultrasound probe to the veins; inability to compress a vein segment suggests the presence of a thrombus. Multiple systematic reviews and meta-analyses demonstrate that CUS achieves high sensitivity and specificity for proximal DVT, often exceeding 90%. POCUS protocols, including two-point and three-point compression techniques, have shown an excellent diagnostic performance, with pooled sensitivities around 89–92% and specificities exceeding 92%, allowing rapid bedside assessment in emergency settings.[53] Whole-leg duplex ultrasound, which combines compression with Doppler flow assessment, further enhances diagnostic confidence and approaches near 100% sensitivity and specificity in some studies.[4]

Despite its advantages, CUS has limitations. It is operator-dependent, requiring adequate training and experience to achieve reliable results. The accuracy diminishes for distal (calf) DVT, where thrombi are smaller and veins are more difficult to visualize, resulting in lower sensitivity.[54] In addition, CUS may have reduced ability to differentiate acute from chronic thrombi and may miss isolated pelvic or iliac vein thromboses. In such cases, adjunctive imaging modalities such as MRV or CTV may be warranted.[9]

This flowchart presents an evidence-based diagnostic algorithm for DVT based on pre-test clinical probability. For patients deemed unlikely to have DVT, D-dimer testing is prioritized, whereas for likely cases, CUS of proximal veins is recommended. The algorithm aids clinical decision-making by integrating test results to confirm or rule out DVT or determine the need for further imaging.

The literature also highlights that venography, while the gold standard, detects many small, asymptomatic thrombi of

uncertain clinical significance, which may inflate diagnostic sensitivity but complicate clinical interpretation.[6] Therefore, while venography remains the reference standard in research and complex cases, its routine clinical use is often supplanted by CUS due to safety and practicality considerations.

Emerging imaging techniques such as magnetic resonance imaging (MRI) and nuclear medicine-based methods have shown promise but remain less established. MRI offers comparable sensitivity and specificity to ultrasound, especially for proximal DVT, and can be valuable when ultrasound is inconclusive or contraindicated. However, MRI is less accessible, more expensive, and less practical for urgent diagnosis.[14] Radiolabeled peptides targeting thrombus components represent innovative approaches for acute thrombus detection but are currently experimental.[1]

CUS is the practical first-line diagnostic tool for suspected DVT, balancing high accuracy with safety and convenience. Venography remains the definitive gold standard but is reserved for equivocal cases or research due to its invasiveness and risks. Clinicians must recognize the limitations of each modality, particularly regarding distal DVT and differentiation of thrombus age, and may need to employ complementary imaging or clinical follow-up accordingly.

Diagnostic gaps in special populations (e.g., pregnant women, cancer patients)

DVT, a condition where blood clots form in deep veins, often in the legs, poses diagnostic challenges that are compounded in special populations such as pregnant women and cancer patients. Understanding how diagnostic strategies vary in these groups is crucial for effective and safe management.

In the general population, diagnosis of DVT typically involves assessing clinical pretest probability using scores such as the Wells score, followed by D-dimer testing and imaging with venous ultrasonography.[25,55] A low pretest probability combined with a normal D-dimer can safely exclude DVT without imaging. However, this approach requires adaptation in special populations due to physiological and pathological differences.

Pregnant women

Pregnancy induces a hypercoagulable state, increasing the risk of VTE, including DVT and PE. However, physiological changes also alter baseline D-dimer levels, which tend to rise throughout pregnancy, limiting the specificity of D-dimer testing.[55] Despite this, recent evidence supports the use of pregnancy-adapted diagnostic algorithms. The Pregnancy-Adapted YEARS algorithm integrates clinical criteria with trimester-specific D-dimer thresholds and CUS for suspected DVT or PE, enabling safe exclusion of VTE while reducing unnecessary imaging and radiation exposure to mother and fetus.[55,56] This approach has demonstrated high sensitivity (99.5%) and negative predictive value (100%) in ruling out VTE during pregnancy, with a substantial proportion of women avoiding CT pulmonary angiography. Given the risks of radiation and contrast exposure, minimizing imaging is particularly important in pregnancy.[55]

In addition, management of pregnancy-associated thrombophilia, such as antiphospholipid antibody syndrome, involves both diagnostic and therapeutic considerations. Systematic reviews indicate that combined LMWH and low-dose aspirin improve pregnancy outcomes in women with persistent antiphospholipid antibodies and recurrent pregnancy loss, highlighting the need for precise diagnosis and risk stratification in this subgroup.[57] Non-pharmacological management and careful medication selection are also emphasized for headache and other symptoms that may mimic or coexist with thrombotic events during pregnancy.[58]

Cancer patients

Cancer markedly increases the risk of VTE due to tumor-related procoagulant factors, treatment effects, and patient immobility.[59] The incidence of cancer-associated DVT varies by cancer type and stage, with cumulative risk influenced by both malignancy and thrombophilic conditions.[59,60] Diagnostic strategies in cancer patients often require heightened vigilance due to atypical presentations and overlapping symptoms with cancer or its treatment.

Standard diagnostic algorithms apply, but the pretest probability assessment may be complicated by cancer-related symptoms. D-dimer testing remains useful but can be elevated due to malignancy and inflammation, reducing specificity.[25,61] Emerging approaches using machine learning models incorporating clinical variables (e.g., D-dimer levels, comorbidities, history of VTE) have shown promise in improving risk prediction and guiding diagnostic decisions in cancer-associated DVT.[59]

Cancer patients also require tailored management strategies balancing thrombosis risk against bleeding, which is increased by anticoagulation in this population.[60,61] Guidelines recommend DOACs as first-line treatment for cancer-associated VTE, with consideration of individual bleeding risk and drug interaction.[25,61] Thrombophilia testing may be selectively indicated in cancer patients, particularly when no clear provoking factor is identified, to inform treatment duration and prophylaxis.[31]

Common themes and differences

Both pregnant women and cancer patients represent high-risk groups where standard DVT diagnostic pathways must be modified. In pregnancy, physiological changes necessitate adjusted D-dimer thresholds and cautious use of imaging to avoid fetal harm. In cancer, the elevated baseline risk and complex clinical picture require integration of clinical

judgment, laboratory data, and advanced predictive tools to optimize diagnosis.

In both populations, CUS remains the cornerstone imaging modality due to its safety and diagnostic accuracy. However, the threshold for proceeding to imaging or further testing varies based on the altered pretest probabilities and risk-benefit considerations unique to each group.[55]

Furthermore, thrombophilia testing and risk stratification are more frequently considered in these populations to guide prophylaxis and treatment decisions, given their elevated baseline risk and potential for recurrent events.[31] The cumulative or supra-additive effect of thrombophilic conditions and clinical risk factors underscores the need for individualized diagnostic and therapeutic approaches. Diagnostic strategies for DVT in pregnant women and cancer patients differ from the general population primarily due to physiological alterations and heightened risk profiles.[62] Pregnancy-adapted algorithms that incorporate clinical criteria and trimester-specific D-dimer cutoffs safely reduce imaging. In cancer patients, risk prediction models and selective thrombophilia testing enhance diagnostic accuracy and management. Across both groups, the emphasis is on balancing diagnostic accuracy with safety considerations unique to each population.

ADVANCEMENTS IN IMAGING TECHNIQUES FOR DVT

Evolving Radiologic Modalities: MRV, CTV, and Intravascular Ultrasound (IVUS)

DVT is a condition characterized by the formation of blood clots in the deep veins, commonly in the legs or pelvis. Accurate diagnosis and assessment of DVT and related venous pathologies are critical for effective treatment and prevention of complications such as PTS or PE. Over time, radiologic modalities have evolved to improve visualization of venous structures, thrombus extent, and underlying anatomical abnormalities.

The principal imaging techniques currently used to evaluate deep venous pathology include MRV, CTV, and IVUS. Each modality offers unique advantages and limitations, and their complementary use enhances diagnostic accuracy.

MRV utilizes magnetic fields and radio waves to generate detailed images of veins without ionizing radiation. MRV is particularly valuable in visualizing pelvic and central veins, areas often difficult to assess by ultrasound. It provides excellent soft-tissue contrast and can delineate thrombus, venous compression, and collateral circulation. However, MRV can be limited by patient contraindications (e.g., implanted devices) and availability.[63,64]

CTV employs contrast-enhanced CT scanning to visualize venous anatomy. It offers rapid acquisition, high spatial resolution, and the ability to assess surrounding structures. CTV is especially useful in acute settings and for detecting extrinsic venous compression, such as in May–Thurner Syndrome, where the left common iliac vein is compressed by the right common iliac artery. CTV also facilitates preoperative planning by providing comprehensive cross-sectional images.[63,65,66]

IVUS is an invasive imaging technique performed during venography that involves inserting an ultrasound probe directly into the vein. IVUS offers real-time, high-resolution images of the venous lumen and wall, enabling precise measurement of stenosis and identification of intraluminal abnormalities. It is considered the gold standard for assessing the degree of venous compression and guiding endovascular interventions such as stenting. IVUS complements noninvasive modalities by confirming hemodynamic significance of lesions detected on MRV or CTV.[63,64,66]

Duplex ultrasound remains the first-line, noninvasive screening tool for DVT, but it has limitations in evaluating iliocaval segments and pelvic veins. A novel duplex finding – flow reversal in the superficial epigastric vein – has been identified as a reliable indicator of proximal iliocaval occlusion, aiding in noninvasive suspicion of more central venous disease and prompting further advanced imaging.[67]

The integration of these imaging modalities allows for a comprehensive assessment of deep venous pathology. For example, in patients with May–Thurner Syndrome, a combination of duplex ultrasound, MRV or CTV, and IVUS can confirm the diagnosis, quantify venous compression, and guide treatment decisions such as iliocaval stenting, which has demonstrated promising clinical outcomes.[66] Similarly, in chronic venous disease, multidetector CT venography can reveal underlying venous obstructions not apparent on ultrasound, expanding diagnostic capability beyond superficial assessment.[65]

Current clinical guidelines, although recently retracted due to concerns over consistency and training standards, have recommended considering venous stenting in patients with significant venous outflow obstruction confirmed by imaging modalities including MRV, CTV, and IVUS, especially when symptoms are moderate to severe.[68,69] These recommendations emphasize the importance of precise imaging to select appropriate candidates for intervention. Evolving radiologic modalities have transformed the diagnosis and management of deep venous thrombosis and related venous disorders. MRV and CTV provide detailed, noninvasive cross-sectional imaging of venous anatomy and pathology, while IVUS offers unparalleled intraluminal detail critical for intervention planning. Together, these tools enhance diagnostic accuracy, facilitate tailored treatment strategies, and improve patient outcomes in DVT and venous outflow obstruction.

Emerging techniques: Elastography and photoacoustic imaging (PAI)

Emerging imaging techniques such as elastography and PAI have shown promise in enhancing the assessment of DVT beyond conventional ultrasound methods.

Elastography is an ultrasound-based technique that measures tissue stiffness by evaluating how tissues deform in response to applied forces. In the context of DVT, elastography can quantify the stiffness of a thrombus, which correlates with its age and composition. Acute clots tend to be softer, while chronic clots become stiffer due to fibrosis and organization over time. Two main types of elastography have been studied: strain elastography and shear wave elastography (SWE). Strain elastography assesses tissue deformation under manual compression, while SWE uses acoustic radiation force to generate shear waves and measures their speed to estimate stiffness quantitatively.[70]

Multiple systematic reviews and clinical studies have demonstrated that elastography can differentiate acute from chronic DVT by detecting changes in thrombus stiffness. Santini *et al*. reviewed seven clinical studies and found a consistent increase in thrombus stiffness with clot age, supporting elastography's biological plausibility in DVT staging.[71] Similarly, Hoang *et al*. highlighted that elastography could serve as a valuable adjunct to conventional duplex ultrasound, especially when standard imaging fails to determine clot age.[70] Bosio *et al*. investigated SWE and quantitative ultrasound parameters longitudinally in patients with DVT, noting that some ultrasound biomarkers might reflect clot evolution over time, although SWE features did not reach statistical significance in all measures.[72] Furthermore, Rayes *et al*. showed that thrombus stiffness measured by SWE varies with clot composition and age, influencing the effectiveness of ultrasound-assisted thrombolysis, thus underscoring the clinical relevance of stiffness assessment.[73] Levchak and Levytskyi also reported that sonoelastography techniques could objectively identify embolic risk categories based on thrombus stiffness, aiding treatment decisions.[74]

PAI is a novel hybrid imaging modality combining optical and ultrasound technologies. It exploits the photoacoustic effect, where pulsed laser light absorbed by tissues generates ultrasound waves, providing high-contrast images based on tissue composition and oxygenation. In DVT, PAI can noninvasively characterize thrombus properties such as oxygen saturation and structural composition, which are related to clot age and stability.

Tang *et al*. demonstrated the feasibility of intravascular light delivery for photoacoustic computed tomography (PACT) to overcome depth limitations inherent in external illumination. Their study showed that PACT could differentiate between acute and chronic clots by measuring oxygenation levels and acoustic frequency signatures, correlating well with histological and mechanical properties of clots.[75] This suggests that PAI may provide functional and compositional information beyond stiffness, potentially improving thrombus characterization.

Additional emerging techniques include photo-mediated ultrasound therapy (PUT), which combines ultrasound and laser to selectively disrupt blood clots. Singh and Yang (2023) reviewed PUT's mechanisms and applications, noting its potential for non-invasive treatment of thrombotic conditions by enhancing cavitation effects inside vessels, which may complement diagnostic imaging.[76]

Despite these promising advances, conventional duplex ultrasound remains the clinical gold standard for initial DVT diagnosis due to its accessibility and cost-effectiveness. However, duplex ultrasound has limitations in accurately determining thrombus age and in imaging pelvic or distal veins. MRI and computed tomography (CT) provide complementary information but are less accessible and more expensive.[77,78] Emerging imaging modalities such as elastography and PAI aim to fill this gap by providing quantitative, non-invasive biomarkers of thrombus age and composition, which are critical for guiding therapeutic decisions such as catheter-directed thrombolysis.

CONCLUSION

This review underscores the dynamic evolution of diagnostic strategies for DVT, highlighting a paradigm shift from symptom-based clinical models to precision-oriented, multimodal diagnostics. While clinical prediction scores, D-dimer assays, and CUS remain cornerstones of initial evaluation, their limitations, particularly in specificity, operator dependence, and performance in special populations, necessitate supplementary tools. Advances in imaging, notably MRV, CTV, IVUS, and elastography, offer greater anatomical and functional resolution, supporting accurate characterization of thrombus burden and chronicity. The incorporation of emerging biomarkers, such as thrombin generation profiles and urinary proteomic classifiers, holds promise for improving early detection and recurrence prediction. AI further complements this landscape by automating risk stratification, enhancing imaging interpretation, and enabling proactive clinical decision-making. Nevertheless, widespread adoption is contingent upon regulatory validation, ethical transparency, data standardization, and clinician readiness. Clinical application must also be contextualized within population-specific considerations, such as pregnancy-induced hypercoagulability and cancer-associated thrombosis. Importantly, early and accurate diagnosis not only reduces complications such as PE and PTS but also improves cost-effectiveness, as evidenced by RCTs such as EVRA. Future research should focus on refining AI algorithms, validating non-invasive biomarkers, and conducting prospective trials to

evaluate real-world effectiveness. Ultimately, the integration of technology and translational research into clinical practice offers a transformative opportunity to enhance DVT care, personalize treatment strategies, and improve long-term outcomes.

REFERENCES

1. Huisman MV, Klok FA. Current challenges in diagnostic imaging of venous thromboembolism. Blood 2015;126:2376-82.
2. Anderson FA Jr., Spencer FA. Risk factors for venous thromboembolism. Circulation 2003;107:I9-16.
3. Bikdeli B, Caraballo C, Trujillo-Santos J, Galanaud JP, di Micco P, Rosa V, *et al.* Clinical presentation and short- and long-term outcomes in patients with isolated distal deep vein thrombosis vs proximal deep vein thrombosis in the RIETE registry. JAMA Cardiol 2022;7:857-65.
4. Taeuber I, Weibel S, Herrmann E, Neef V, Schlesinger T, Kranke P, *et al.* Association of intravenous tranexamic acid with thromboembolic events and mortality: A systematic review, meta-analysis, and meta-regression. JAMA Surg 2021;156:e210884.
5. Hayssen H, Cires-Drouet R, Englum B, Nguyen P, Sahoo S, Mayorga-Carlin M, *et al.* Systematic review of venous thromboembolism risk categories derived from Caprini score. J Vasc Surg Venous Lymphat Disord 2022;10:1401-9.e7.
6. Bhatt M, Braun C, Patel P, Patel P, Begum H, Wiercioch W, *et al.* Diagnosis of deep vein thrombosis of the lower extremity: A systematic review and meta-analysis of test accuracy. Blood Adv 2020;4:1250-64.
7. Wang X, Ma Y, Hui X, Li M, Li J, Tian J, *et al.* Oral direct thrombin inhibitors or oral factor Xa inhibitors versus conventional anticoagulants for the treatment of deep vein thrombosis. Cochrane Database Syst Rev 2023;4:CD010956.
8. Lavikainen LI, Guyatt GH, Luomaranta AL, Cartwright R, Kalliala IEJ, Couban RJ, *et al.* Risk of thrombosis and bleeding in gynecologic cancer surgery: Systematic review and meta-analysis. Am J Obstet Gynecol 2024;230:403-16.
9. Alahyari S, Moradi M, Rajaeinejad M, Jalaeikhoo H. Post-COVID-19 hematologic complications: A systematic review. Expert Rev Hematol 2022;15:539-46.
10. Duffett L, Carrier M. Inferior vena cava filters. J Thromb Haemost 2017;15:3-12.
11. Zdanyte M, Rath D, Gawaz M, Geisler T. Venous thrombosis and SARS-CoV-2. Hamostaseologie 2022;42:240-7.
12. Setiawan B, Pangarsa EA, Santosa D, Naibaho RM, Setiabudy RD, Suharti C. Preventing thrombosis in cancer patients. Acta Med Indones 2022;54:626-37.
13. Boddi M, Peris A. Deep vein thrombosis in intensive care. Adv Exp Med Biol 2017;906:167-81.
14. Ortel TL, Neumann I, Ageno W, Beyth R, Clark NP, Cuker A, *et al.* American Society of Hematology 2020 guidelines for management of venous thromboembolism: Treatment of deep vein thrombosis and pulmonary embolism. Blood Adv 2020;4:4693-738.
15. Huang Z, Zheng Z, Pang L, Fu K, Cheng J, Zhong M, *et al.* The association between obstructive sleep apnea and venous thromboembolism: A bidirectional two-sample mendelian randomization study. Thromb Haemost 2024;124:1061-74.
16. Hirsh J, Hull RD, Raskob GE. Clinical features and diagnosis of venous thrombosis. J Am Coll Cardiol 1986;8:114B-127B.
17. Michiels JJ, Oortwijn WJ, Naaborg R. Exclusion and diagnosis of deep vein thrombosis by a rapid ELISA D-dimer test, compression ultrasonography, and a simple clinical model. Clin Appl Thromb Hemost 1999;5:171-80.
18. Ng KC. Deep vein thrombosis: A study in clinical diagnosis. Singapore Med J 1994;35:286-9.
19. Bruce J, Russell EM, Mollison J, Krukowski ZH. The measurement and monitoring of surgical adverse events. Health Technol Assess 2001;5:1-194.
20. Meissner MH, Gloviczki P, Comerota AJ, Dalsing MC, Eklof BG, Gillespie DL, *et al.* Early thrombus removal strategies for acute deep venous thrombosis: Clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. J Vasc Surg 2012;55:1449-62.
21. Gohel MS, Heatley F, Liu X, Bradbury A, Bulbulia R, Cullum N, *et al.* Early versus deferred endovenous ablation of superficial venous reflux in patients with venous ulceration: The EVRA RCT. Health Technol Assess 2019;23:1-96.
22. Brummel-Ziedins KE, Vossen CY, Butenas S, Mann KG, Rosendaal FR. Thrombin generation profiles in deep venous thrombosis. J Thromb Haemost 2005;3:2497-505.
23. von Zur Mühlen C, Koeck T, Schiffer E, Sackmann C, Zürbig P, Hilgendorf I, *et al.* Urine proteome analysis as a discovery tool in patients with deep vein thrombosis and pulmonary embolism. Proteomics Clin Appl 2016;10:574-84.
24. Shlobin NA, LoPresti MA, Beestrum M, Lam S. Treatment of pediatric cerebral venous sinus thromboses: The role of anticoagulation. Childs Nerv Syst 2020;36:2621-33.
25. Chopard R, Albertsen IE, Piazza G. Diagnosis and treatment of lower extremity venous thromboembolism: A review. JAMA 2020;324:1765-76.
26. Needleman L, Cronan JJ, Lilly MP, Merli GJ, Adhikari S, Hertzberg BS, *et al.* Ultrasound for lower extremity deep venous thrombosis: Multidisciplinary recommendations from the society of radiologists in ultrasound consensus conference. Circulation 2018;137:1505-15.
27. Voigts B, Abolmaali N, Stelzner C, Schellong SM. Bildgebende darstellung peripherer venen. Internist

2017;58:796-804.
28. Audu CO, Wakefield TW, Coleman DM. Pediatric deep venous thrombosis. J Vasc Surg Venous Lymphat Disord 2019;7:452-62.
29. Parker K, Hartemink J, Saha A, Mitra R, Lewis P, Power A, *et al.* A systematic review of the efficacy and safety of anticoagulants in advanced chronic kidney disease. J Nephrol 2022;35:2015-33.
30. Illig KA, Gober L. Optimal management of upper extremity deep vein thrombosis: Is venous thoracic outlet syndrome underrecognized? J Vasc Surg Venous Lymphat Disord 2022;10:514-26.
31. Asmis L, Hellstern P. Thrombophilia testing - a systematic review. Clin Lab 2023;69:670-91.
32. Goldhaber SZ, Magnuson EA, Chinnakondepalli KM, Cohen DJ, Vedantham S. Catheter-directed thrombolysis for deep vein thrombosis: 2021 update. Vasc Med 2021;26:662-9.
33. Miron MJ, Perrier A, Bounameaux H. Clinical assessment of suspected deep vein thrombosis: Comparison between a score and empirical assessment. J Intern Med 2000;247:249-54.
34. Kelly J, Hunt BJ. The utility of pretest probability assessment in patients with clinically suspected venous thromboembolism. J Thromb Haemost 2003;1:1888-96.
35. Chen X, Liu X, Liu J, Zhang D. Pulmonary embolism secondary to deep venous thrombosis: A retrospective and observational study for clinical characteristics and risk stratification. Phlebology 2021;36:627-35.
36. Zhao B, Hao B, Xu H, Premaratne S, Zhang J, Jiao L, *et al.* Predictive model for pulmonary embolism in patients with deep vein thrombosis. Ann Vasc Surg 2020;66:334-43.
37. van Maanen R, Martens ES, Takada T, Roy PM, de Wit K, Parpia S, *et al.* Accuracy of physicians' intuitive risk estimation in the diagnostic management of pulmonary embolism: An individual patient data meta-analysis. J Thromb Haemost 2023;21:2873-83.
38. Filipiak-Strzecka D, Kasprzak JD, Lipiec P. Brief cardiovascular imaging with pocket-size ultrasound devices improves the accuracy of the initial assessment of suspected pulmonary embolism. Int J Cardiovasc Imaging 2018;34:1595-605.
39. Cronin P, Dwamena BA. A clinically meaningful interpretation of the prospective investigation of pulmonary embolism diagnosis (PIOPED) scintigraphic data. Acad Radiol 2017;24:550-62.
40. Villacorta H, Pickering JW, Horiuchi Y, Olim M, Coyne C, Maisel AS, *et al.* Machine learning with D-dimer in the risk stratification for pulmonary embolism: A derivation and internal validation study. Eur Heart J Acute Cardiovasc Care 2022;11:13-9.
41. Goodacre S, Horspool K, Shephard N, Pollard D, Hunt BJ, Fuller G, *et al.* Selecting pregnant or postpartum women with suspected pulmonary embolism for diagnostic imaging: The DiPEP diagnostic study with decision-analysis modelling. Health Technol Assess (Rockv) 2018;22:1-230.
42. Barrett L, Jones T, Horner D. The application of an age adjusted D-dimer threshold to rule out suspected venous thromboembolism (VTE) in an emergency department setting: A retrospective diagnostic cohort study. BMC Emerg Med 2022;22:186.
43. Egermayer P, Town GI, Turner JG, Heaton DC, Mee AL, Beard ME. Usefulness of D-dimer, blood gas, and respiratory rate measurements for excluding pulmonary embolism. Thorax 1998;53:830-4.
44. Nelson CM, Wright GS, Silbaugh TR, Cota LJ. Improving D-dimer positive predictive value for outpatients with suspected deep vein thrombosis. Perm J 2009;13:4-7.
45. Owings JT, Gosselin RC, Anderson JT, Battistella FD, Bagley M, Larkin EC. Practical utility of the D-dimer assay for excluding thromboembolism in severely injured trauma patients. J Trauma 2001;51:425-9.
46. Wells PS, Anderson DR. Diagnosis of deep-vein thrombosis in the year 2000. Curr Opin Pulm Med 2000;6:309-13.
47. Schefold JC, Gerber JL, Angehrn MC, Müller M, Messmer AS, Leichtle AB, *et al.* Renal function-adjusted D-dimer levels in critically ill patients with suspected thromboembolism. Crit Care Med 2020;48:e270-6.
48. Wells PS, Anderson DR. Modern approach to diagnosis in patients with suspected deep vein thrombosis. Haemostasis 1999;29 Suppl S1:10-20.
49. Fitzsimmons J, Hart L, Oliver E, Mulla W. Diagnosis of pulmonary embolism in pregnancy. Am J Perinatol 2024;41:e2307-12.
50. Heim SW, Schectman JM, Siadaty MS, Philbrick JT. D-dimer testing for deep venous thrombosis: A metaanalysis. Clin Chem 2004;50:1136-47.
51. El Zorkany K, Bridson JM, Sharma A, Halawa A. Transplant renal vein thrombosis. Exp Clin Transplant 2017;15:123-9.
52. Hirsh J, Ginsberg JS, Chan N, Guyatt G, Eikelboom JW. Mandatory contrast-enhanced venography to detect deep-vein thrombosis (DVT) in studies of DVT prophylaxis: Upsides and downsides. Thromb Haemost 2014;111:10-3.
53. Wang X, Ouyang M, Yang J, Song L, Yang M, Anderson CS. Anticoagulants for acute ischaemic stroke. Cochrane Database Syst Rev 2021;2021:CD000024.
54. Watson L, Broderick C, Armon MP. Thrombolysis for acute deep vein thrombosis. Cochrane Database Syst Rev 2014;2014:CD002783.
55. van der Pol LM, Tromeur C, Bistervels IM, Ni Ainle F, van Bemmel T, Bertoletti L, *et al.* Pregnancy-adapted YEARS algorithm for diagnosis of suspected pulmonary embolism. N Engl J Med 2019;380:1139-49.
56. Bellesini M, Robert-Ebadi H, Combescure C, Dedionigi C, Le Gal G, Righini M. D-dimer to rule out venous thromboembolism during pregnancy: A systematic review and meta-analysis. J Thromb Haemost 2021;19:2454-67.
57. Hamulyák EN, Scheres LJ, Marijnen MC, Goddijn M,

Middeldorp S. Aspirin or heparin or both for improving pregnancy outcomes in women with persistent antiphospholipid antibodies and recurrent pregnancy loss. Cochrane Database Syst Rev 2020;5:CD012852.
58. Negro A, Delaruelle Z, Ivanova TA, Khan S, Ornello R, Raffaelli B, *et al.* Headache and pregnancy: A systematic review. J Headache Pain 2017;18:106.
59. Jin S, Qin D, Liang BS, Zhang LC, Wei XX, Wang YJ, *et al.* Machine learning predicts cancer-associated deep vein thrombosis using clinically available variables. Int J Med Inform 2022;161:104733.
60. Timp JF, Braekkan SK, Versteeg HH, Cannegieter SC. Epidemiology of cancer-associated venous thrombosis. Blood 2013;122:1712-23.
61. Streiff MB, Holmstrom B, Angelini D, Ashrani A, Elshoury A, Fanikos J, *et al.* Cancer-associated venous thromboembolic disease, version 2.2021. J Natl Compr Cancer Netw 2021;19:1181-201.
62. Khan F, Tritschler T, Kahn SR, Rodger MA. Venous thromboembolism. Lancet 2021;398:64-77.
63. Silickas J, Black SA, Phinikaridou A, Gwozdz AM, Smith A, Saha P. Use of computed tomography and magnetic resonance imaging in central venous disease. Methodist Debakey Cardiovasc J 2018;14:188-95.
64. Arnoldussen CW. Imaging of deep venous pathology. Cardiovasc Intervent Radiol 2024;47:1580-94.
65. Gaweesh AS, Kayed MH, Gaweesh TY, Shalhoub J, Davies AH, Khamis HM. Underlying deep venous abnormalities in patients with unilateral chronic venous disease. Phlebology 2013;28:426-31.
66. Fereydooni A, Stern JR. Contemporary treatment of may-thurner syndrome. J Cardiovasc Surg (Torino) 2021;62:447-55.
67. Kolluri R, Fowler B, Ansel G, Silver M. A novel duplex finding of superficial epigastric vein flow reversal to diagnose iliocaval occlusion. J Vasc Surg Venous Lymphat Disord 2017;5:358-62.
68. Villalba L, Bayat I, Dubenec S, Puckridge P, Thomas SD, Varcoe RL, *et al.* RETRACTED: Australian and New Zealand Society for Vascular Surgery clinical practice guidelines on venous outflow Obstruction of the femoral-iliocaval veins. J Vasc Surg Venous Lymphat Disord 2023;11:832-42.
69. Comerota AJ, Sandset PM, Konstantinides S, de Graaf R, Wakefield TW, Arnoldussen CW, *et al.* Theme 4: Invasive management of (recurrent) VTE and PTS. Thromb Res 2015;136 Suppl 1:S19-25.
70. Hoang P, Wallace A, Sugi M, Fleck A, Pershad Y, Dahiya N, *et al.* Elastography techniques in the evaluation of deep vein thrombosis. Cardiovasc Diagn Ther 2017;7:S238-45.
71. Santini P, Esposto G, Ainora ME, Lupascu A, Gasbarrini A, Zocco MA, *et al.* Ultrasound elastography to assess age of deep vein thrombosis: A systematic review. Diagnostics (Basel) 2023;13:2075.
72. Bosio G, Zenati N, Destrempes F, Chayer B, Pernod G, Cloutier G. Shear wave elastography and quantitative ultrasound as biomarkers to characterize deep vein thrombosis *in vivo*. J Ultrasound Med 2022;41:1807-16.
73. Rayes A, Zhang J, Lu G, Qian X, Schroff ST, Ryu R, *et al.* Estimating thrombus elasticity by shear wave elastography to evaluate ultrasound thrombolysis for thrombus with different stiffness. IEEE Trans Biomed Eng 2023;70:135-43.
74. Levchak YA, Levytskyi AV. Possibilities of dynamical sonoelastography in diagnosis of embologenic forms of venous thrombosis. Klin Khir 2016;10:51-4.
75. Tang Y, Wu H, Klippel P, Zhang B, Huang HS, Jing Y, *et al.* Deep thrombosis characterization using photoacoustic imaging with intravascular light delivery. Biomed Eng Lett 2022;12:135-45.
76. Singh R, Yang X. A review on photo-mediated ultrasound therapy. Exp Biol Med (Maywood) 2023;248:775-86.
77. Orbell JH, Smith A, Burnand KG, Waltham M. Imaging of deep vein thrombosis. Br J Surg 2008;95:137-46.
78. Patel KD, Ahmad M, Tan M, Onida S, Davies A. A systematic review evaluating imaging techniques to determine chronicity of deep vein thrombosis. Phlebology 2025:2683555251358915.

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