Prevalence of musculoskeletal disorders in patients referred for suspected deep vein thrombosis: insights from a rheumatologist-led clinic

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Summary

Objective. To assess the frequency of deep vein thrombosis (DVT) and alternative diagnoses in patients with suspected DVT when evaluated by a rheumatologist. Secondly, to describe the distribution of different diagnoses across three Wells score categories (low, moderate, and high).

Methods. This is an observational study of patients evaluated at a DVT clinic for suspected DVT, with a rheumatologist-supervised evaluation, performing ultrasound scans on the affected limbs and assessing their results. The obtained diagnoses were noted along with the initial Wells scores performed by the rheumatologist.

Results. 649 patients were included. DVT was confirmed in 119/649 (18.3%) cases, with musculoskeletal (MSK) disorders, particularly arthritis and knee-related conditions, being the most common alternative diagnoses (166/649, 25.6%). 288/649 (44.4%) patients did not receive a definitive diagnosis. Higher Wells scores were more common in confirmed DVT cases, while patients with MSK disorders generally had lower Wells scores, likely due to clinical assessments that identified alternative diagnoses early.

Conclusions. MSK disorders frequently present with symptoms mimicking DVT, underscoring the value of rheumatologist-led evaluations in suspected DVT cases. Further research is needed to refine diagnostic approaches for patients with DVT-like symptoms, particularly regarding the role of MSK expertise in both physical and ultrasound assessments.

Introduction

Deep vein thrombosis (DVT) is a common vascular condition characterized by the formation of thrombi in the deep veins, primarily in the lower extremities (1). Diagnosing DVT poses a clinical challenge due to its diverse presentations and the risk of pulmonary embolism (2, 3). While clinical suspicion for DVT is common, confirmed diagnoses are relatively rare. Studies suggest that up to 85% of patients presenting with typical DVT symptoms may often have alternative diagnoses; however, a specific diagnosis is rarely established (4-7).

Differential diagnoses for DVT include venous insufficiency, superficial thrombophlebitis, cellulitis, and lymphedema. Additionally, musculoskeletal (MSK) conditions such as muscular strain, tendon injuries, Baker's cysts, osteoarthritis, and synovitis can mimic DVT symptoms (4). Given this broad range of potential diagnoses, clinical presentation alone is often insufficient for accurately diagnosing DVT (2, 4, 5, 7). Ultrasound, recognized as the gold standard for DVT diagnosis, is also helpful in identifying MSK conditions that could explain the symptoms, making it crucial in excluding both DVT and its mimics. Rheumatologists routinely use ultrasound for MSK and vascular assessments and are well-positioned to identify such DVT mimics (8, 9). Assessing pretest likelihood using validated clinical prediction tools to improve diagnostic accuracy when DVT is suspected is essential. The Wells score, the most widely used tool, incorporates clinical factors, including the likelihood of an alternative diagnosis, to assign a score that estimates the probability of DVT (2). Systematic assessment for alternative diagnoses is a key component of the Wells score, as clinicians deduct two points if an alternative diagnosis appears more likely than DVT (10). This study aims to examine the frequency of DVT and alternative diagnoses in patients suspected of having DVT who are evaluated by a rheumatologist and to describe the distribution of final diagnoses across different Wells score categories.

Materials and Methods

Study design

This is an observational study with consecutive enrollment of adult patients suspected of having new onset DVT.

Setting and participants

The study was conducted at the Esbjerg DVT Clinic at Esbjerg University Hospital, established in September 2020 as part of a COVID-19 response strategy to reduce patient flow in the emergency department to lower infection risk. The clinic operated on weekdays from 8:00 AM to 3:00 PM. Referrals were made based

on general practitioners' (GPs) clinical suspicion of DVT without specific requirements for Wells score or D-dimer testing. At the clinic, junior doctors performed initial physical examinations and Wells scoring under the supervision of a rheumatologist, followed by Doppler ultrasound evaluations conducted by the supervising rheumatologist.

The Wells criteria were used to calculate the Wells score for the risk of DVT. The Wells scoring system used the following criteria: i) active cancer; ii) paralysis, paresis or recent immobilization of the extremity; iii) recent bedridden status longer than 3 days or major surgery within the last 12 weeks; iv) previous DVT; v) pain along the deep veins; vi) unilateral swelling of the entire limb; vii) unilateral calf enlargement with circumference more than 3 cm bigger than the healthy side, measured 10cm below the tibial tuberosity; viii) pitting edema in the affected extremity; ix) dilatation of the superficial venous network of the affected extremity (not varicose veins); x) alternative diagnosis more likely than DVT. All the criteria give +1 points when present, apart from criterion number 10 "alternative diagnosis more likely than DVT", which, in case it is present, gives minus 2 points. The total Wells score is calculated and divided into the following risk groups: if the Wells score is ≥3, then the patient is at high risk for DVT. If the Wells score is 1-2, the patient is at moderate risk for DVT. If the Wells score is ≤0, the patient is at low risk for DVT (11).

For suspected lower-extremity DVT cases, a 3-point ultrasound scan of the femoral and popliteal veins was performed; upper-extremity cases involved scanning the subclavian and axillary veins. A Doppler ultrasound scan was considered positive for DVT if a non-compressible vein segment or intraluminal thrombus was observed. Standard practice included 3-point Doppler scanning of the femoral, popliteal, and tibialis posterior veins. Distal vein scans were not routinely performed without specific clinical indications, and this limitation has been acknowledged. In cases where DVT was not confirmed by ultrasound, a thorough MSK ultrasound examination of the affected limb was conducted. This included evaluation of relevant joints, tendons, and bursae at key sites such as the shoulder, elbow, wrist-hand, hip, knee, and ankle. Additionally, the surrounding muscles were assessed to identify alternative causes of the patient's symptoms. For patients diagnosed with arthritis, additional procedures, including arthrocentesis, microscopy, and local corticosteroid injections, were performed as indicated.

Patients diagnosed with DVT were referred to the local Thrombosis Center for further evaluation and follow-up. In cases of diagnostic uncertainty, the DVT clinic was consulted. Patients without a confirmed diagnosis were advised to contact their GP if symptoms persisted beyond 1 week.

Five rheumatologists from the department, each with extensive experience in MSK ultrasound (over 3000 scans) and in vessel vasculitis ultrasound (over 100 scans), received further training in Doppler ultrasound, specifically focused on DVT evaluation. When diagnostic uncertainty arose, patients were referred to the radiology department for further vascular ultrasound assessment, typically arranged within 24 hours.

The training program in Doppler ultrasound consisted of: i) a theoretical component covering the principles of Doppler ultrasound and imaging characteristics of DVT; ii) a practical training supervised by radiologists experienced in vascular ultrasound, during which the rheumatologists performed scans on patients with confirmed DVT; iii) a 2-month supervision period led by SC, a rheumatologist with extensive experience in DVT ultrasound, to ensure proficiency among the participating rheumatologists.

To ensure continuous diagnostic coverage, GPs referred patients presenting after hours or on weekends directly to the emergency department for further evaluation. These patients were managed in the emergency department or scheduled for follow-up at the DVT clinic on the next working day. For confirmed DVT cases, treatment initiation took place promptly in the emergency department as needed.

If DVT remained a clinical suspicion despite a normal initial ultrasound, patients were scheduled for a follow-up clinical evaluation and repeat ultrasound examination at the DVT clinic 1 week later.

Variables, data sources, and measurements

Patient data included age, anticoagulation status, Wells score, repeat ultrasound evaluations, D-dimer levels (abnormal ≥0.7 mg/L, measured initially at the general practice or the DVT clinic), and final diagnosis. Final diagnoses were categorized into four groups: i) DVT; ii) MSK disorders (including arthritis, Baker's cyst, muscle injuries, and Achilles tendon abnormalities); iii) other conditions (including superficial thrombophlebitis, erysipelas, and hematoma); iv) no specific diagnosis.

Statistics

Descriptive statistical analyses and multinomial regression analyses were conducted in STATA SE 13.

Ethics

The administrative and authorization committee of Esbjerg University Hospital approved this study according to Danish regulations (Authorization Number: 23/57419).

Results

Patient characteristics

As depicted in Figure 1, during the 14-month observation period, 649 patients were referred to the DVT clinic, 636 with suspicion of lower limb DVT and 13 with suspicion of upper limb DVT.

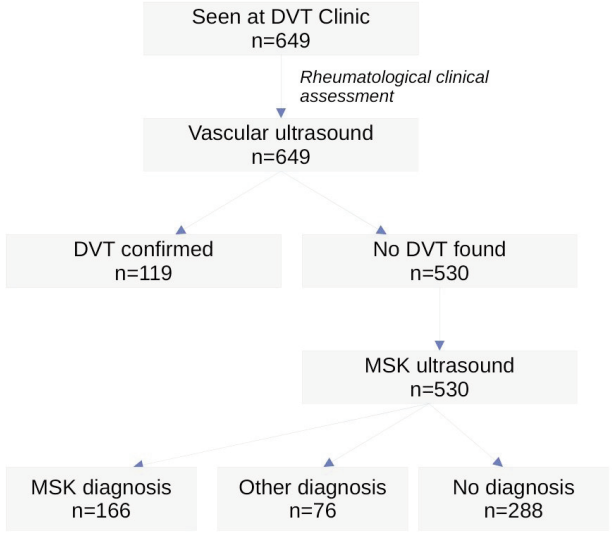

Figure 1. Flowchart of the study population. DVT, deep vein thrombosis; MSK, musculoskeletal.

The mean age of participants was 63.97±15.13 years. Nearly one-fourth were receiving anticoagulation therapy upon referral (168/649). Wells scores were available in 312/649 (48%) patients, while D-dimer levels were available for 306/649 (47%). Among referrals, DVT was confirmed in 119/649 (18.34%). MSK disorders represented the most common findings (166/649 or 25.57%). 288/649 (44.37%) had no definitive diagnosis (Table 1).

D-dimer levels were measured in 306/649 patients. Elevated D-dimer was found in all DVT cases, 73/75 (97%) of the MSK instances, 24/26 (92%) of the cases that received other diagnoses, and 66/99 (67%) of the cases with no specific diagnosis.

Among referred patients, 168/649 (26%) were receiving anticoagulation therapy. Only six of these patients were confirmed to have a thrombus on ultrasound, with four cases determined to be chronic and not classified as new DVT. In all four chronic cases, D-dimer levels were normal. Patients on anticoagulants more commonly received no specific diagnosis than those not on anticoagulants (Table 1).

Wells score

The Wells score was available for 312/649 patients, with those in the DVT group scoring higher than those in the MSK and other diagnosis groups (Table 1 and Figure 2). The lower Wells score can be explained by the deduction of 2 points because of an alternative diagnosis being considered more likely.

Among the 166 patients in the MSK group, arthritis was diagnosed in 46.9% (72/153 at the lower limb and 6/13 at the upper limb). Among the 636 patients with lower extremity DVT suspicion, Baker's cysts were identified in 82 (12.8%), with 40 cases associated with arthritis and 42 cases linked to degenerative knee pathologies. The most frequently identified etiology of arthritis was calcium pyrophosphate dihydrate crystal deposition disease. In most cases, the location was the knee, while unilateral, bilateral ankle arthritis or tenosynovitis was found in seven patients. Additionally, seven patients with swelling, pain and warmth at the distal part of the leg were diagnosed with complete or partial ruptures of the Achilles tendon. In 69/636 (10.7%) of the patients, non-arthritis

Table 1. Patient characteristics grouped by final diagnosis.

	All patients (n=649)	DVT diagnosis (n=119)	MSK diagnosis (n=166)	Other diagnoses (n=76)	No specific diagnosis (n=288)
Age (years)	63.9±15.1	66.4±11.1	61.9±13.5	65.3±16.6	63.7±16.8
On anticoagulants	168 (25.8)	16 (13.4)	35 (21)	24 (31.5)	93 (32.2)
Repeat scan	80 (12.3)	8 (6.7)	14 (8.4)	0 (0)	58 (20.1)
Elevated D-dimer	269/306 (87.9)	106/106 (100)	73/75 (97.3)	24/26 (92.3)	66/99 (66.6)
Wells score	(n=312)	(n=80)	(n=74)	(n=25)	(n=133)
-2	12 (3.8)	0 (0)	3 (4)	0 (0)	9 (6.7)
-1	20 (6.4)	0 (0)	9 (12.1)	2 (8)	9 (6.7)
0	84 (26.9)	2 (2.5)	43 (58.1)	3 (12)	36 (27)
1	77 (24.6)	13 (16.2)	12 (16.2)	7 (28)	45 (33.8)
2	52 (16.6)	17 (21.2)	7 (9.4)	8 (32)	20 (15)
3	28 (8.9)	14 (17.5)	0 (0)	3 (12)	11 (8.2)
4	20 (6.4)	16 (20)	0 (0)	2 (8)	2 (1.5)
5	19 (6)	18 (22)	0 (0)	0 (0)	1 (0.7)

All values presented as mean±standard deviation or n(%) or n/total n(%). DVT, deep vein thrombosis; MSK, musculoskeletal.

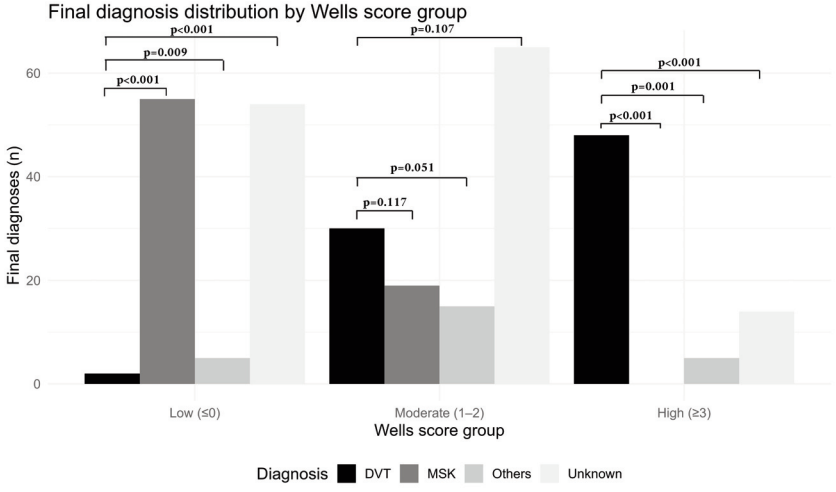

Figure 2. Final diagnosis distribution by Wells score group (low≤0, moderate 1-2, high≥3). Diagnoses are grouped into four categories: DVT (deep vein thrombosis), MSK (musculoskeletal disorders), others and unknown (no specific diagnosis). The p-values shown result from multinomial regression analysis with DVT as the base outcome.

knee pathologies were diagnosed, the majority in combination with a Baker's cyst. Among the group with other pathologies, erysipelas and superficial thrombophlebitis were the most common findings (Table 2). In 29/649 patients, other related pathologies were found, with lymphedema, venous insufficiency, and post-operative conditions being the most common findings (Table 2).

Finally, in 288/649 patients, no specific diagnosis was made. In 58/288 or 20% of cases who received a no diagnosis, a reevaluation in the DVT clinic 1 week after the initial referral was necessary due to the high suspicion of having DVT despite the normal ultrasound at baseline (Table 1). 21/649 cases (3.2%) were referred to radiology for further evaluation. These referrals were prompted by inconclusive ultrasound findings or the need for a complete lower-leg Doppler ultrasound. No diagnostic uncertainties were reported at the thrombosis center follow-up. However, eight patients were referred again to the DVT clinic by their GPs, with no DVT diagnosis confirmed upon reevaluation. In most patients with MSK pathologies, the cause of symptoms was readily identifiable, with differential diagnoses established through physical examination and confirmed *via* MSK ultrasound. In 14/166 or 8% of patients with an MSK condition as the final diagnosis, a repeat evaluation in the DVT clinic was necessary; all these patients' initial assessments were performed in the emergency department.

Discussion

This is the first study that describes a rheumatologist-led DVT clinic. Interestingly, we found that MSK disorders are common diagnoses in patients suspected of having DVT. MSK conditions, especially arthritis and knee pathologies, frequently mimic DVT symptoms, complicating clinical assessment.

Baker's cyst emerged as one of the most prevalent differential diagnoses for DVT. This condition is frequently linked with underlying knee conditions (12, 13). To our knowledge, this is the first study to evaluate Baker's cysts in the context of DVT differential diagnosis, using clinical and ultrasound assessments by a rheumatologist, thus providing valuable insights into their role in the differential diagnosis of DVT.

Our findings align with prior studies, where classical DVT signs and symptoms, such as pain, swelling, warmth, and erythema, have shown low specificity for DVT (14, 15), underscoring the challenge of clinical diagnosis. Moreover, our DVT confirmation rate of approximately 20% mirrors the figure reported in similar studies (16).

The Wells score, a validated tool for DVT assessment, is heavily influenced by the presence of MSK disorders. It allows a reduction of 2 points if an alternative diagnosis is more likely. However, the score's reliability can vary depending on the assessor's expertise (17). Our findings suggest that patients with MSK conditions generally score lower on the Wells scale when evaluated by a rheumatologist with MSK expertise, which is more commonly seen in those receiving a non-DVT diagnosis. This underscores the importance of MSK knowledge in accurate DVT assessment. Unfortunately, we do not have data on the Wells score performed by the referring doctor, whereas it would be interesting to compare the Wells score measured by the GPs *vs.* the one measured by the rheumatologists. In our cohort, 14 patients were initially evaluated in the emergency department by a non-rheumatologist. These patients were later found to have MSK causes for DVT-like symptoms at the DVT clinic 1 week later.

Furthermore, as noted in previous studies, we observed that inflammation from MSK conditions can elevate D-dimer levels, potentially leading to false positives in DVT screenings (18, 19).

In our study, 288/649 or 44.3% of patients did not reach a definitive diagnosis, a rate slightly higher than that reported in previous studies (4, 5). This may be due to the high proportion of patients on anticoagulation therapy, comprising 93/288 or 32% of this group (Table 1), which can obscure diagnostic clarity. Additionally, 58/288 or 20% of patients without a confirmed diagnosis underwent a second ultrasound examination (Table 1), underscoring a comprehensive diagnostic approach that ensures thorough exclusion of DVT in this population.

This study has several strengths, including a real-world setting, a comprehensive diagnostic approach conducted by clinicians with expertise in both vascular and MSK ultrasound, and secondary ultrasound with follow-up evaluations. Additionally, the study features a large number of patients, enhancing the reliability and generalizability of its findings. It also aligns with challenges posed by the pandemic, showcasing adaptability and relevance to current healthcare needs.

This study also has several limitations. The monocentric design does not allow strict general liability. There was no follow-up period after the completion of the diagnostic investigation, nor a systematic third-party validation (*e.g.*, by the radiology department) to confirm the accuracy of the ultrasound scan results. In future studies, a good reference standard should be defined, preferably with a follow-up period. Secondly, the study lacks standardized pre-referral requirements, including the Wells score. This is necessary to fully evaluate the prognostic ability of this clinical scoring system. A lack of standardization in the Wells score assessment reflects the real-world nature of this study, as scores were not always calculated in cases where alternative diagnoses were apparent or during busy clinic periods. Finally, the amount of missing data might lead to biases.

Future studies should focus on the performance of pretest probability scores across different observers, particularly regarding MSK experience. Additionally, the utility of MSK ultrasound in populations with suspected DVT requires further investigation in more extensive, well-designed studies.

Table 2. Distribution of final diagnoses.

Final diagnosis n (%)	All patients (n=655)
Deep vein thrombosis	119 (18.3)
Superficial thrombophlebitis	33 (5)
Arthritis	78 (12)
Baker's cyst*	40 (6.1)
Knee pathologies	69 (10.6)
Baker's cyst*	42 (6.4)
Erysipela	9 (1.3)
Achilles tendon lesion	7 (1)
Hematoma	5 (0.7)
Muscle injury	13 (2)
No specific diagnosis	288 (44.3)
Other	23 (3.5)
Other rheumatological conditions	5 (0.7)

All values presented as n (%). *Baker's cysts were found in both the arthritis (40 cases) and knee pathologies (42 cases) groups. Each instance was categorized based on the primary underlying issue. "Other" includes cutaneous infection, subcutaneous edema, lymphangitis, erythema migrans/cutaneous manifestation of Lyme borreliosis, infection of the tibia, varicophlebitis, and calcium pyrophosphate dihydrate crystal deposition. "Other rheumatological conditions" include overexertion of the biceps tendon, overexertion of the hip joint, joint manifestation of Lyme borreliosis and Löfgren syndrome.

Conclusions

This study demonstrates that MSK disorders are diagnosed more frequently than DVT in patients referred for evaluation of suspected DVT when assessed by a rheumatologist with expertise in MSK conditions. These findings underscore the critical importance of integrating MSK expertise into the diagnostic pathway for suspected DVT. This approach facilitates a comprehensive evaluation, ensuring timely identification and management of alternative conditions that may mimic DVT. Future research should focus on refining diagnostic guidelines to incorporate MSK assessments and evaluating their impact in broader, multicentric settings.

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Conflict of interest: the authors have no competing interests with regard to this study.

Ethics approval and consent to participate: the administrative and authorization committee of Esbjerg University Hospital approved this study according to Danish regulations (Authorization Number: 23/57419).

Informed consent: the authors have received formal permission to access the patients' journals and collect and analyze data from the Local Committee of Esbjerg Hospital, and under the circumstances of the study, patient consent has not been deemed necessary by the Committee. The formal permission from the Local Committee of Esbjerg Hospital extends to the publication of the analyzed data.

Patient consent for publication: not applicable due to Paragraph 10 of Danish Data Protection Law.

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