

Preliminary Validation of Clinical Assessment for Deep Vein Thrombosis in Orthopaedic Outpatients

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The purpose of our study was to determine if a previously published clinical decision rule designed to estimate the probability of proximal deep vein thrombosis in outpatients is valid when applied exclusively to outpatients with musculoskeletal disorders. We also sought to determine whether probability estimates differed for patients with or without trauma, fracture, or recent orthopaedic surgery. Data collected from outpatients with surgical and nonsurgical musculoskeletal disorders (n = 464) were extracted from the datasets of three previously published studies done on heterogeneous groups of patients (n = 3424). Followup for all patients was 3 months. Testing of all patients for thromboembolic disease was done using validated diagnostic procedures. Probability estimates for orthopaedic outpatients were consistent with estimates from published studies. The proportion of patients who had venous thromboembolism was 5.6% (95% confidence interval, 3.5–8.7%) for the low probability group, 14.1% (95% confidence interval, 8.6–22.4%) for the moderate probability group, and 47.4% (95% confidence interval, 35.3–60%) for the high probability group. Validity estimates for patients with and without recent trauma, surgery, or fracture differed, but not dramatically. The validity of the clinical decision rule as applied to outpatients with musculoskeletal disorders was supported.

Level of Evidence: Prognostic study, Level II-1 (retrospective study). See the Guidelines for Authors for a complete description of the levels of evidence.

Lower-extremity deep vein thrombosis (DVT) is classified as being either proximal (popliteal vein and above) or distal (calf veins). Proximal DVT (PDVT) is the less common but more dangerous form of lower extremity DVT because it is more likely than distal DVT to cause a life threatening pulmonary embolism (PE).^{1,11} Orthopaedic surgery and orthopaedic injuries result in substantial risk for PDVT.⁷ Most outpatients who had orthopaedic procedures have PDVT develop after hospital discharge.^{11,26,31,35} Proximal deep vein thrombosis associated with in-hospital care for orthopaedic patients is well recognized, but PDVT associated with outpatient or posthospital care is less frequently discussed and may be under-recognized.¹⁶ If outpatients with PDVT can be identified early, the risk for severe morbidity and mortality can be decreased.^{1,25}

Some clinicians attempt to identify patients suspected of having PDVT by considering the patient's signs, symptoms, and associated risk factors.²⁴ However, 75–84% of patients who are suspected of having DVT do not have DVT when formal diagnostic testing is completed.^{14,34} In response to the high rate of incorrect clinical diagnoses, numerous researchers have more closely examined the utility of the clinical examination for identifying patients with PDVT.^{20,24,26,31,33} More sophisticated methods for combining risk factors and signs and symptoms into a clinical decision rule (CDR), a clinical tool that quantifies the contributions that history and physical examination data make toward diagnosis, have been described.²¹ The CDR that generally has been accepted as being the most reliable and valid for diagnosing patients suspected of having a lower-extremity PDVT^{9,10,13,17,19,23,27,28} is the CDR developed by Wells et al (Table 1).^{2,4}

Numerous investigators have reported on the validity of the CDR proposed by Wells et al,^{31,33,34} however, a het-

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TABLE 1. Clinical Decision Rule Developed by Wells et al^{31,34}

Clinical Finding	Score*
Activity cancer (treatment ongoing, within previous 6 months, or palliative)	1
Paralysis, paresis, or recent plaster immobilization of the lower extremities	1
Recently bedridden for > 3 days or major surgery within 4 weeks	1
Localized tenderness along the distribution of the deep venous system†	1
Entire leg swelling	1
Calf swelling by > 3 cm when compared with the asymptomatic leg‡	1
Pitting edema (greater in the symptomatic leg)	1
Collateral superficial veins (nonvaricose)	1
Alternative diagnosis as likely or greater than that of PDVT§	-2

*A score is obtained by summing all items that are judged to be present; score of ≤ 0 = low probability of PDVT; score of 1 or 2 = moderate probability of PDVT; score of ≥ 3 = high probability of PDVT

†Tenderness along the deep venous system is assessed by firm palpation in the center of the posterior calf, the popliteal space, and along the area of the femoral vein in the anterior thigh and groin.

‡Measured with a tape measure 10 cm below tibial tuberosity

§More common alternative diagnoses are cellulitis, calf strain, Baker's cyst, or postoperative swelling.

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erogeneous mix of outpatients was examined in their studies (Table 2).^{3,8,10–12,16,18,22,27,30} We found no studies that validated the CDR on a homogeneous sample of outpatients with musculoskeletal disorders. If the CDR developed by Wells et al^{31,33,34} is valid for estimating the probability of PDVT in outpatients with musculoskeletal dis-

orders, we think orthopaedic surgeons should consider routine use of the CDR for outpatients who are suspected of having PDVT.

The primary aim of our study was to determine whether the CDR developed by Wells et al^{31,33,34} is valid for use with outpatients with musculoskeletal disorders. Validity was judged using two methods. First, if the probability of PDVT in outpatients judged as having either a low, moderate, or high risk from an orthopaedic surgical procedure approximated probability estimates reported in the literature for heterogeneous groups of patients, then validity was supported.^{19,31,33,34} Second, if the point estimates for low, moderate, and high probabilities were significantly different from each other, as measured by nonoverlap of confidence intervals, the validity of the CDR was supported. We hypothesized that the CDR proposed by Wells et al would be valid when applied to outpatients with musculoskeletal disorders.

Our second purpose was to determine if the PDVT probability estimates obtained with the CDR differed for patients with traumatic injuries, fractures, or orthopaedic surgical procedures as compared with patients with orthopaedic, nontraumatic disorders or chronic diseases. We suspected that the point estimates for these two groups of patients would differ because patients with fractures or orthopaedic surgical procedures are among those at highest risk for having PDVT develop.^{7,14,17,35}

MATERIALS AND METHODS

Data from the institutions of three of our authors (PSW, RAK, MRH) were provided. The subgroup of outpatients in our study

TABLE 2. PDVT Probability Estimates from Literature Examining the Validity of the CDR of Wells et al^{31,34}

Study†	Sample Size	Prevalence of VTE (%)	Percentage of Patients with VTE for Each Probability Estimate*		
			Low Risk (95% CI)	Moderate Risk (95% CI)	High Risk (95% CI)
Current study	464	12.7	5.6 (3.5–8.7)	14.1 (8.6–22.4)	47.4 (35.3–60.0)
Wells et al (1997) ³¹	593	16.0	3.0 (1.7–5.9)	16.6 (1.0–23.0)	74.6 (63.0–84.0)
Anderson et al (2003) ³	1075	18.1	4.5 (2.7–6.8)	18.8 (15.2–22.8)	47.3 (40.2–54.4)
Kraaijenhagen et al (2002) ¹⁹	1756	22.0	8.0 (7.0–10.0)	27.0 (23.0–31.0)	66.0 (61.0–71.0)
Anderson et al (1999) ⁴	344	13.1	3.2 (1.2–6.7)	14.3 (8.3–22.4)	49.0 (34.55–63.6)
Shields et al (2002) ²⁸	102	17.0	2.0 (0.1–11.0)	14.0 (4.0–24.0)	59.0 (35.0–82.0)
Miron et al (2000) ²³	270	21.0	3.2 (0.9–7.9)	19.4 (12.1–28.6)	73.9 (58.9–85.7)
Constans et al (2003) ⁹	282	25.2	6.0	20.0	69.0
Cornuz et al (2002) ¹⁰	278	29.0	13 (7.0–9.0)	30.0 (22.0–38.0)	67.0 (54.0–70.0)
Kearon et al (2001) ¹²	445	14.4	2.0	13.0	69.0
Dryjski et al (2001) ¹²	114	5.3	0	0	16.7
Funfsinn et al (2001) ¹³	92	32.6	0	13.3	68.4

*Some studies did not provide 95% confidence intervals for each of the probability estimates.

†All studies with the exception of the current study included a heterogeneous sample of patients with a broad mix of diagnoses.

VTE = venous thromboembolism

was derived from the samples examined in three previously reported studies^{3,19,31} and includes only outpatients with musculoskeletal disorders. In the study by Kraaijenhagen et al,¹⁹ 1756 consecutive outpatients with clinically suspected DVT were referred by family physicians to one of five vascular medicine centers for workup. The patients' mean age was 60 years, and the mean time to onset of symptoms of possible DVT was 7 days. Thirteen percent of the patients had a malignancy, 15% had a recent surgical procedure, and 15% had recent trauma. Of the 1756 patients, 180 (10.2%) were diagnosed by the referring physician as having a musculoskeletal problem in addition to possible DVT.

Wells et al³¹ admitted 593 consecutive outpatients referred by various physicians to one of two vascular medicine departments for clinical suspicion of DVT. The mean age of the patients was 57 years, and DVT-related symptoms were present an average of 9 days before referral. Thirteen percent had a malignancy, and 6.5% had a recent surgical procedure. Of the 593 outpatients in the study by Wells et al,³¹ 168 (28.3%) were diagnosed by the referring physician with a musculoskeletal disorder and possible DVT.

In the third study, 1075 patients were seen in one of four emergency departments.³ The mean age of the patients was 56.6 years; 10.5% reported recent surgery, and 5.1% reported having cancer. One hundred sixteen (9.3%) had a musculoskeletal disorder as a primary diagnosis in addition to the suspected DVT. The methods used to collect the data were well described by Kraaijenhagen et al,¹⁹ Wells et al,³¹ and Anderson et al.³

Patients were included in the studies if they were referred by a physician, had clinically suspected PDVT, no history of venous thromboembolism in the same lower extremity, and no anticoagulant therapy at least 24 hours before testing. All patients then had a clinical examination, and the CDR was used to place the patient into a low, moderate, or high risk category (Table 1). Items in the CDR are summed to create a total score.

The reference diagnostic method used by Kraaijenhagen et al¹⁹ for patients with suspected DVT (either at referral or during the 3 months followup), was compression ultrasonography, or venography if the ultrasound of the legs was inconclusive. B-mode grey-scale compression ultrasonography of the legs was done from the common femoral vein in the groin and the popliteal vein from the midpopliteal fossa until the trifurcation of the calf veins.⁶ The calf veins were not investigated. Ultrasound findings were scored as normal if both vein segments were fully compressible and as abnormal when at least one of the veins contained a noncompressible segment. The same criteria were applied by Wells et al³¹ and Anderson et al,³ except the deep veins from groin to the calf trifurcation were evaluated for compressibility at 1–3-cm intervals.

To ensure the initial assessment did not miss PDVT that could lead to pulmonary embolism, patients in all three studies were followed up for 3 months to rule out the development of a pulmonary embolism. The reference diagnostic method in the studies, for patients with suspected pulmonary embolism (during the 3 months followup), was ventilation-perfusion lung scanning or angiography. The results were classified as normal, nondiagnostic, or high probability, according to the criteria described by

Hull et al.¹⁵ Pulmonary angiography was done to prove or exclude pulmonary embolisms in patients in whom a nondiagnostic lung scan result was obtained.²⁹ The angiography was done and interpreted according to the method described by van Beek et al.³⁰ Pulmonary embolism was considered to be present if the ventilation-perfusion scan was high probability or if the angiogram was abnormal, whereas the disease was refuted by a normal lung scan or normal angiogram result.

Four hundred sixty-four patients with various musculoskeletal disorders were included in our study. The mean age of the patients was 55.4 years (median, 55.0 years; SD, 17.8 years; minimum, 19 years; maximum, 95 years), and 60.3% of the patients were women. The patients had either lower-extremity surgery, traumatic injury, or fracture, or they were diagnosed with one or more of various chronic diseases or soft tissue disorders of the spine or lower extremities. Among the more common diagnostic categories represented in our sample were postorthopaedic trauma, postorthopaedic surgery, and ruptured Baker's cyst (Table 3).

Fifty-nine patients (12.7%) were found to have a PDVT on initial compression ultrasonography or were found, based on ultrasonography or ventilation perfusion scans or autopsy, to have either a PDVT or a pulmonary embolism at some point during the 3-month followup testing. Most (85%) of the 59 patients were diagnosed with PDVT at admission whereas the remaining 15% were diagnosed during the 3-month followup. The remaining 405 patients (87.3%) were not found to have a PDVT on initial testing and did not have a PDVT or a pulmonary embolism during the followup period (Table 4).

The proportion of patients who were found to have a PDVT on initial testing, or a PDVT or pulmonary embolism during followup testing based on the gold standard assessments, was

TABLE 3. Patient Characteristics

Variable	Patients with DVT n = 59	Patients without DVT n = 405
Gender (% female)	54.2%	61.2%
Age (years)	53.7 (17.4%)	55.7 (17.9%)
19–30	4 (6.7%)	31 (7.7%)
31–40	13 (22.0%)	67 (16.4%)
41–50	13 (22.0%)	61 (15.1%)
51–60	9 (15.4%)	83 (20.5%)
61–70	7 (11.9%)	63 (15.6%)
> 70	13 (22.0%)	100 (24.7%)
Diagnosis		
Posttrauma	20 (33.9%)	91 (22.5%)
Ruptured Baker's cyst	2 (3.4%)	27 (6.7%)
Nonruptured Baker's cyst	0	18 (4.4%)
Arthritis	0	26 (6.4%)
Postsurgery	21 (35.6%)	67 (16.5%)
Postfracture	5 (8.5%)	14 (3.5%)
Hematoma/contusion	1 (1.7%)	15 (3.7%)
Gout	0	5 (1.2%)
Other diagnoses*	10 (16.9%)	142 (35.1%)

*Includes patients with various soft tissue disorders including sciatica, torn gastrocnemius muscle, shin splints, and torn meniscus

TABLE 4. Percentage of Patients with Venous Thromboembolism for Each Probability Risk Group

Probability Level	PDVT or PE Present	PDVT or PE Absent	Total Sample	Proportion with PDVT or PE (95% CI)
Low	17	289	306	5.6% (3.5–8.7%)
Moderate	14	85	99	14.1% (8.6–22.4%)
High	28	31	59	47.4% (35.3–60%)
Total sample	59	405	464	

calculated for each CDR probability risk group (ie, low, moderate, and high), along with 95% confidence intervals for each risk group. Probability estimates were calculated for the entire sample (n = 464), for the patients with traumatic injuries, fracture, or surgery (n = 218), and for patients with chronic disorders or nontraumatic soft tissue injuries (n = 246). Statistical analysis was done using the Statistical Package for the Social Sciences (version 11.0.1; SPSS, Chicago, IL).

RESULTS

For the entire sample (n = 464), the likelihood of having a venous thromboembolism develop in patients in the low probability group was 5.6% (95% CI, 3.5–8.7%). For patients in the moderate probability group, the likelihood of having a venous thromboembolism develop was 14.1% (95% CI, 8.6–22.4%). The probability of having a venous thromboembolism develop for patients in the high probability group was 47.4% (95% CI, 35.3–60%). For each of the three groups, 95% confidence intervals indicate that the point estimates were significantly different (Table 4).

Point estimates of the probability for DVT for each of the three categories of low, moderate, and high were higher, although marginally, for the subgroup with fracture, postsurgery, or trauma (Table 5) as compared with the subgroup with only chronic or soft tissue musculoskeletal disorders (Table 6). For patients who had surgery, a fracture, or a traumatic injury, 21.1% had a thromboem-

TABLE 5. Percentage of Patients with Fractures, Surgery, or Traumatic Injuries Who Had Venous Thromboembolism

Probability Level	PDVT or PE Present	PDVT or PE Absent	Total Sample	Proportion with PDVT or PE (95% CI)
Low	12	95	107	11.2% (6.5–18.6%)
Moderate	10	53	63	15.9% (8.9–26.8%)
High	24	24	48	50% (36.4–63.6%)
Total sample	46	172	218	

TABLE 6. Percentage of Patients with Chronic Diseases or Soft Tissue Injuries Who Had Venous Thromboembolism

Probability Level	PDVT or PE Present	PDVT or PE Absent	Total Sample	Proportion with PDVT or PE (95% CI)
Low	5	194	199	2.5% (1.1–5.7%)
Moderate	4	32	36	11.1% (4.4–25.3%)
High	4	7	11	36.4% (15.2–64.6%)
Total sample	13	233	246	

bolic event, whereas 5.3% of patients with chronic disease or nontraumatic soft tissue disorders had a PDVT or pulmonary embolism develop. A Pearson chi square was calculated to compare the distributions for the two samples, and a value of 26.05 was found (p < 0.0001), indicating that the two distributions are significantly different.

DISCUSSION

We found no published evidence to indicate that estimates of DVT probability are valid when applied strictly to outpatients with musculoskeletal problems. Our analysis of data derived from three large studies suggests that the CDR described by Wells et al³¹ is valid when applied to patients with musculoskeletal disorders. The proportion of patients in our study with a low probability of having PDVT develop and who were found to have a thromboembolic event initially or at some point during the 3-month followup was 5.6% (95% CI, 3.5–8.7%). This proportion is comparable to the 3% (95% CI, 1.7–5.9%) reported by Wells et al,³¹ and 8% (95% CI, 7–10%) reported by Kraaijenhagen et al¹⁹ and others.^{4,28} One advantage of using the CDR described by Wells et al is that when a patient with a low probability is identified, the clinician can use a D-dimer test to rule out DVT. Research suggests that the D-dimer test combined with low probability rules out DVT as effectively as compression ultrasound, which is a much more expensive alternative.^{4,5,17,18,19,22} Use of the D-dimer test in postsurgical outpatients receiving anticoagulants is controversial because of a potential decrease in sensitivity of the test. Because patients with a low probability have only a 5% chance, on average, of having DVT, it is unlikely that a small decrease in sensitivity of the D-dimer test would adversely affect outcome.¹⁸

For the moderate probability group, we found that 14.1% (95% CI, 8.6–22.4%) of the patients had a thromboembolic event. This also is comparable to the three parent studies.^{3,19,31} Other studies on different patient populations have had similar estimates for patients with moderate probability of having DVT develop (Table 2).

The probability for the low and moderate probability groups was, in our opinion, not substantially different from that reported by other investigators (Table 2). The differences are only on the order of a few percentage points, suggesting the CDR is valid for use in outpatients with musculoskeletal disorders.

The difference between our study and two of the parent studies^{19,31} for the high probability group is somewhat larger, on the order of 25 percentage points. We suspect that this disparity is attributable to the alternative diagnosis item in the CDR (Table 1). For many patients after having lower extremity surgery or trauma, signs suggestive of PDVT such as leg edema or pain may be attributable to the surgical procedure or injury and not to a PDVT. We suspect that the clinicians did not mark the alternative diagnosis item as frequently as they should have, especially in the high probability group, and this would have decreased the probability estimate relative to those reported in earlier research. Other investigators have reported estimates for patients with high probability that were similar to ours, suggesting there is more variability in the high probability category as compared with low or moderate probability (Table 2).

We think that differences in the high probability estimate between our study and those of Wells et al³¹ and Kraaijenhagen et al¹⁹ do not impact the utility of the CDR. Musculoskeletal outpatients in our high probability group still had thromboembolic events almost 50% of the time, which is an important clinical finding. In addition, there is no overlap in the confidence intervals for the moderate and high probability groups in our study, suggesting that patients in these two groups have measurable differences in PDVT risk.

We also found differences in probability estimates for outpatients with a history of orthopaedic surgery, fracture, or trauma and patients with various soft tissue disorders (Tables 5, 6). Given the relatively small sample sizes (and wider confidence intervals) for the two subgroups summarized in Tables 5 and 6, we recommend using probability estimates from the entire sample when applying our data to clinical practice.

Our study has several limitations. Our research does not show the validity of the CDR as used by orthopaedic surgeons. However, we do not suspect that this is a major limitation because the CDR is simple to use, includes only routinely collected patient data, and has been shown to be reliable when used by physicians and nurses.³¹ In addition, our study was retrospective in that we relied on published data. We did this because we found no previous reports regarding use of CDRs for patients with musculoskeletal disorders, and it was unclear to us if data collected using a CDR were generalizable when applied exclusively to outpatients after an orthopaedic procedure. Given that or-

thopaedic surgeons have a different skill set than other types of physicians, this work needs to be replicated prospectively using orthopaedic surgeons as examiners.

The three parent studies from which the sample for this study was drawn seem to have had substantially different types of patients. For example, one study was done in an emergency room,³ whereas the other two studies were done in hospital radiology departments. In addition, the studies were done in different countries with differing healthcare systems. Even with these differences, the probability estimates for the musculoskeletal outpatients were similar to published estimates (Table 2). Finally, the sample size for the two subgroups examined (Tables 5, 6) was small, which limits generalizability. Larger numbers of outpatients need to be examined in these various categories.

The CDR developed by Wells et al is designed for use for outpatients in whom DVT cannot be confidently ruled out in the differential diagnosis.^{31,33,34} Outpatients who have had a recent knee replacement, for example, may have postoperative knee swelling and edema, and the surgeon may be confident that these findings are a routine consequence of the surgery and not indicative of a possible PDVT. In this case, the CDR should not be used. In other cases, the surgeon may be less sure about the causes of a patient's postoperative findings because the signs or symptoms may seem to be out of proportion to what is expected. It is in these cases that the CDR has potential utility. Once an outpatient's PDVT probability is determined by use of the CDR, evidence indicates that radiologic and diagnostic testing can be linked to the probability (low, moderate, or high) to confidently determine the presence of a PDVT with a very high degree of efficiency.^{5,17,18,22,32} Application of the CDR by Wells et al,^{31,34} along with evidence-based diagnostic testing, also has potential for reducing morbidity and mortality in outpatients with lower-extremity PDVT.

Results of our study suggest that orthopaedic surgeons and their staff potentially could improve their ability to identify patients with DVT by using the CDR described by Wells et al. Given the lack of support in the literature for other methods, use of the CDR and evidence-based diagnostic tests on outpatients at risk for DVT should be considered.

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