Wells score for venous thromboembolism

Basic diagnostic algorithm for venous thromboembolism

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Venous thromboembolism (VTE) affects 1-2 per 1000 people in the general population each year, usually as deep-vein thrombosis (DVT) of the leg or pulmonary embolism (PE).[1] Venous thromboembolism is a common, yet challenging diagnostic problem among both inpatients and outpatients. Clinical pre-test probability assessment is a cornerstone of the algorithms for the exclusion, or diagnosis of VTE.[2,3] For patients suspected of VTE, the Wells score appears to be the most useful and well-validated clinical pre-test probability assessment.[3] The Wells score, also called Canada score, including Wells DVT score and Wells PE score, has been built by Philip S. Wells in University of Ottawa, Canada on the basis of a series of investigations. In this article, we summarize the derivation, and the recent investigations of the Wells score for VTE.

Wells DVT score. In 1995 Wells et al[4] developed a clinical model to stratify pretest probability for DVT into high, moderate, and low categories. Items included in the clinical model were assembled from information obtained by a literature review, and from the collective experience of the participating investigators. These items were devided into 3 groups: signs and symptoms of DVT, risk factors for DVT, and potential alternative diagnosis. The clinical model was composed of specific items, designated as either major or minor that included proven risk factors, and pertinent symptoms, and physical signs at patient presentation. A probability score was derived, which categorized the patients into low, moderate, or high probability groups. The clinical model was prospectively tested to stratify symptomatic outpatients with suspected DVT, who had symptoms for less than 60 days. Finally, the clinical model predicted prevalence of DVT in 3 categories: 85% in the high, 33% in the moderate, and 5% in the low category. The weighted Kappa value for the assessment of inter-observer reliability, for the clinical model, was 0.85 which represents an excellent level of agreement. However, the clinical model, criticized as being cumbersome, was not convenient for ordinary physicians, so Wells et al[5] simplified it to a score by univariate, and stepwise logistic regression analysis of 529 patients' clinical data. After retrospective analysis, Wells DVT score including 9 significant variables was shown in **Table 1**. According to the score, 529 patients were divided into 3 categories. In the high probability category the prevalence of DVT was 73%, in the moderate probability category the prevalence was 28%, and in the low probability the prevalence was 6%. The original model and score model were compared with respect to the prevalence of DVT in each of the 3 categories, and no significant difference was demonstrated (p=0.694, p=0.419, p=0.086).

Wells et al[6] used prospectively Wells DVT score in combination with ultrasound to guide management of patients with suspected DVT. Five hundred and ninety-three patients with suspected DVT were categorized as being at low, moderate, or high clinical probability for DVT by the Wells score, then all patients underwent deep venous ultrasound imaging of lower limb. Patients at low clinical probability underwent a single ultrasound test. A negative ultrasound excluded the diagnosis of DVT, whereas a positive ultrasound was confirmed by venography. Patients at moderate probability with a positive ultrasound were treated for DVT, whereas patients with an initial negative ultrasound had a single follow-up ultrasound one week later. Patients at high

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Table 1 - Wells DVT Score [5,7]

Clinical characteristic	Score
Active cancer (treatment ongoing or within previous 6 months or palliative)	1
Paralysis, paresis, or recent plaster immobilization of the lower extremities	1
Recently bedridden for more than 3 days or major surgery, within 4 weeks	1
Localized tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling by more than 3 cm when compared with the asymptomatic leg (measured 10 cm below tibial tuberosity)	1
Pitting edema (greater in the symptomatic leg)	1
Collateral superficial veins (non-varicose)	1
Previously documented DVT*	1
Alternative diagnosis at least as likely as DVT	-2
Clinical pretest probability	Total score
Low	<1
Moderate	1-2
High	>2
Clinical pretest probability†	Total score
Unlikely	<2
Likely	≥2

DVT - deep vein thrombosis, * added in 2003, † formed in 2003

probability with a positive ultrasound were treated for DVT whereas those with negative ultrasound had venography. All patients with negative ultrasound or venography studies were not treated with anticoagulants and were followed up for 3 months to monitor any development of symptomatic venous thromboembolic complications. Results showed that the total prevalence of DVT was 16%, the prevalence of DVT in low was 3% [95% confidence interval (CI), 1.7-5.9%], moderate 16.6% (95% CI, 12-23%), and high pretest probability categories was 74.6% (95% CI, 63-84%). Only 0.6% (95%CI 0.1-1.8%) of patients diagnosed as not having DVT had events during the 3-month follow-up. Overall, only 5.6% of patients required venography, and serial ultrasound testing was limited to 28% of patients. Thus, management of patients with suspected DVT based on combination of Wells DVT score with deep veins ultrasound, simplified and improved the diagnostic process, and could decrease costs. With the increasing evaluation of the role of D-dimer assay in the recent decade, in 2003, Wells et al[7] modified the score model for the diagnosis of DVT, which categorized patients into high, moderate, and low probability groups, to one that categorizes patients as likely or unlikely to have DVT. The addition to the scoring system of one point for a previous diagnosis of DVT allows the model to be used in patients with previous thrombosis. After categorized as likely or unlikely to have DVT, 1096 outpatients were randomly assigned to undergo ultrasound imaging alone (control group), or to undergo D-dimer testing (D-dimer group), followed by ultrasound imaging, unless the D-dimer test was negative and the patient was considered clinically unlikely to have DVT, in which the case ultrasound imaging was not performed. Results showed that the total prevalence of DVT was 15.7%. Among patients for whom DVT had been ruled out by the diagnostic strategy, there were 2 confirmed venous thromboembolic events in the D-dimer group (0.4%, 95% CI, 0.05-1.5%), and 6 events in the control group (1.4%, 95% CI, 0.5-2.9%) during 3 months of follow-up. The use of D-dimer testing resulted in a significant reduction in the use of ultrasonography, from a mean of 1.34 tests per patient in the control group, to 0.78 in the D-dimer group (p=0.008). Thirty nine percent of patients in the D-dimer group did not require ultrasound imaging. Thus, DVT can be ruled out in a patient who is judged clinically unlikely to have deep-vein thrombosis, and who has a negative D-dimer test. Ultrasound testing can be safely omitted in such patients. Other trials[8-13] also verified that the algorithm using Wells score along with the D-dimer testing to exclude the diagnosis of DVT among suspected patients is efficacious and cost efficient.

Goodacre et al[14] undertook a meta-analysis of diagnostic cohort studies evaluating the value of clinical findings, Wells score, and physicians' empirical judgments in patients with suspected DVT. Likelihood ratios were pooled from 51 studies using a random effect model. In Wells score, the positive likelihood ratio of high risk was 5.2 (95% CI, 4-6), and the negative likelihood ratio of low risk was 0.25 (95% CI,

Table 2 - Wells PE Score [21]

Clinical characteristic	Score
Clinical signs and symptoms of DVT (minimum of leg swelling and pain with palpation of the deep veins)	3.0
PE as or more likely than an alternative diagnosis	3.0
Heart rate greater than 100	1.5
Immobilization or surgery in the previous 4 weeks	1.5
Previous DVT/PE	1.5
Hemoptysis	1.0
Malignancy (on treatment, treated in the last 6 months or palliative)	1.0
Clinical pretest probability	Total score
Low	<2
Moderate	2-6
High	>6
Clinical pretest probability	Total score
Unlikely	≤4
Likely	>4

PE - pulmonary embolism, DVT - deep vein thrombosis;

0.21-0.29). Physicians' empirical assessment performed similarly to the Wells score. Wells et al[15] systematically reviewed 14 prospective studies that determined the prevalence of DVT using the Wells score, either with or without D-dimer for the diagnosis of DVT. The overall prevalence of DVT in 8239 patients was 19% (95% CI, 16-23%). In low-probability patients with negative D-dimer results, diagnosis of DVT can be excluded without ultrasound. However, after evaluating the Wells score in primary care patients, Oudega et al[16] found the conflicting result. In 1295 patients with suspected DVT in primary care units, the prevalence of DVT in the low clinical probability group was 12%, moderate clinical probability group 17%, and high clinical probability groups 37%. Negative likelihood ratio of low risk was 0.48 (95% CI, 0.38-0.6). So, Oudega et al[16] thought that the Wells score was not useful for ruling out DVT in patients with symptoms. Stevens et al[17] explained that the reason of conflicting outcome was the specific training in the application of the Wells score received by the physicians participating in the Oudega et al[16] study, who were outside of the emergency department or specialty thrombosis setting, was not enough to develop adequate skills. In short, patients with leg symptoms compatible with DVT should initially have a determination of pretest probability of DVT using Wells score. It has now been well established, that suspected patients who are found to be on the score of <2 can have DVT were safely excluded on the basis of negative D-dimer result.

Wells pulmonary embolism (PE) score. In 1998 Wells et al[18] used criteria from the published literature[19,20] to establish a PE pretest probability model. This model consisted of consideration, of whether the patients clinical presentation based on symptoms, signs and risk factors was typical for PE, and whether there was an alternative diagnosis at least as likely as PE, to account for their symptoms. Patients with suspected PE could be classified as having a low, moderate, or high clinical probability of PE by using this model. One thousand and two hundred thirty-nine consecutive inpatients and outpatients with suspected PE in 5 Canadian medical centers were evaluated prospectively by physicians to determine the clinical probability of PE using this model. The prevalence of PE in the low clinical probability group was 3.4% (95% CI, 2.2-5%), moderate clinical probability group 27.8% (95% CI, 23.4-32.2%), and high clinical probability groups 78.4% (95% CI, 69.2-86.0%). However, this model was rather complex. Thus, Wells et al[21] simplified this model and determined a scoring system, namely, Wells PE score (**Table 2**). At first, an univariate regression analysis was performed to identify the variables in the original clinical model (40 variables) to include in a stepwise logistic regression. Secondly, for each significant variable ($p<0.05$) a regression coefficient was obtained. Finally, points for the clinical prediction model were assigned by doubling the value of regression coefficient from the stepwise logistic regression, and rounding to the nearest 0.5. The Wells PE score including 2 judgment criteria was shown

in **Table 2**. In the first criterion, patients were classified as having low, moderate, and high probability of PE. The second criterion, so-called dichotomized Wells score, was designed to create 2 categories, PE likely and unlikely. The prevalence of PE was 7.8% in PE unlikely group, 40.7% in PE likely group. In patients designated PE unlikely, only 2.2% of patients with a negative D-dimer had PE. Therefore, application of the Wells PE score should result in a safe, effective, and largely noninvasive means to manage patients with suspected PE. Righini et al[22] thought that the dichotomized Wells score could increase the proportion of patients at lower risk of PE, who could require a less extensive diagnostic workup; the score also could increase the proportion of patients at higher risk of PE, who should receive anticoagulant while awaiting the outcome of diagnostic tests according to the American College of Chest Physicians seventh (ACCP) consensus conference on antithrombotic and thrombolytic therapy.[23] Siragusa et al[24] evaluated a simplified algorithm using Wells score and D-dimer for safely postponing diagnostic imaging for PE. At the index visit, 336 outpatients with suspected PE, who were stable hemodynamically, were assessed clinical probability using Wells score, then were categorized into 2 groups: high risk group (patients with a moderate probability and a positive D-dimer test, or patients with a high probability) and low risk group (patients with a low clinical probability, or moderate probability with a negative D-dimer test). The high risk group received full dosage low molecular weight heparin, while the low risk group was left untreated until the performance of diagnostic imaging (maximum 72 hours). During this period, no thromboembolic events occurred in low-risk patients, only one event occurred in those at high-risk (0.8%). Siragusa et al[24] demonstrated that diagnostic imaging for PE could be safely deferred for up to 3 days on the basis of Wells score and D-dimer test.

Rodger et al[25] explored the safety of using combinations of 3 bedside tests (dichotomized Wells score, D-dimer test, and alveolar dead-space fraction) to exclude PE before diagnostic imaging by a double-blind, randomized, controlled equivalency trial. Three hundred and ninety-eight patients with suspected PE were randomized to initial bedside tests, or to initial ventilation-perfusion (V/Q) scan without bedside tests. One hundred and ninety-nine patients assigned to the bedside test group had a sham V/Q scan performed, if at least 2 of 3 bedside test results were negative (dichotomized Wells score ≤4, negative D-dimer assay, and alveolar dead-space fraction ≤0.15). Otherwise, they underwent an actual V/Q scan. One hundred and ninety-nine patients assigned to V/Q scan group had an actual V/Q scan directly. Further, diagnostic management was determined by a blinded physician after the V/Q scan. During the 3 months, patients who were not taking anticoagulant agents, the recurrent venous thromboembolic event rate was 2.4% in the bedside test group, and 3% in the V/Q scan group. Pulmonary embolism was excluded in 34% of the bedside test group patients with at least 2 negative results on 3 bedside tests. Rodger et al[25] demonstrated that the diagnostic strategy using at least 2 negative results on 3 bedside tests to exclude PE, is as safe as using initial V/Q scan among patients with suspected PE, the strategy eliminates the need for diagnostic imaging at least in 34% of suspected patients.

Christopher study[26] assessed the clinical effectiveness of a simplified algorithm using dichotomized Wells score, D-dimer testing, and computed tomography (CT) in patients with suspected PE. Three thousand and three hundred six patients (82% outpatients) with suspected PE were categorized as PE unlikely, or PE likely. Two thousand and two hundred six patients classified as unlikely had D-dimer testing, and PE was considered excluded if the D-dimer test result was normal. Other patients underwent CT (88% multi-detector row CT), and PE was considered present or excluded, based on CT results. The prevalence of PE was 12.1% (95% CI, 10.7-13.5%) in unlikely group, and 37.1% (95% CI, 34.2-40%) in likely group. During the 3 months, patients who were not taking anticoagulant agents, the recurrent venous thromboembolic event rate was 0.5% (95% CI, 0.2-1.1%) in "PE unlikely" patients who had a normal D-dimer test result, and 1.3% (95%CI, 0.7-2.0%) in the patients who were excluded PE by CT. The algorithm was completed, and allowed a management decision in 97.9% of patients. So, the diagnostic management strategy using dichotomized Wells score, D-dimer testing, and CT is effective in the evaluation, and management of patients with clinically suspected PE.

Many investigations have certified that patients with suspected PE with a score of <2 points or <4 points using Wells PE score, can have a PE can safely excluded on the basis of negative D-dimer result. There are many other clinical pretest probability assessment rules for PE, such as, Geneva score[27], revised Geneva score[28], Pisa rule,[29] Claudia rule,[30] and so on. Each of the clinical prediction rules has the advantages and disadvantages. Chagnon et al[31] compared Wells score, Geneva score, and implicit assessment among patients with suspected PE. The results showed that Wells score, and Geneva score had a fair and similar prediction accuracy for PE among emergency department patients. Moores et al[32] compared Wells score, and Geneva score by a retrospective analysis of 295 inpatients and

outpatients who were evaluated for suspected PE. This research showed that Wells score was easily applied, and meaningfully stratifies patients with suspected PE, and Geneva score was less useful. After applying the data from the multi-centered Prospective Investigation of Pulmonary Embolism Diagnosis study, Wells score, and Geneva score was evaluated using the area under a fitted receiver operating characteristic curve.[33] Two score rules yielded different diagnostic performances depending in the patient location. Two clinical prediction rules performed best in outpatient. The performance of 2 prediction rules decreased significantly, when applied to inpatients. In particular, 2 rules performed least well, when applied to patients referred from surgical wards, suggesting 2 rules should not be used in this patient group.

Tamariz et al[34] summarized the evidence on the predictive value of clinical prediction rules for the diagnosis of VTE by a systematic review. The results were that the most frequently evaluated prediction rule for DVT was the Wells DVT score, the Wells PE score was the most commonly studied for PE. So, the American academies of family physicians and the American college of physicians recommended that Wells DVT score and Wells PE score have been validated and are used to estimate the probability of VTE before performing more definitive testing on patients.[3]

In conclusion, VTE is an extremely serious and challenging diagnostic problem. The Wells score rules for the diagnosis of DVT and PE are the most useful, well-validated, and should be accepted by more and more physicians.

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