

Original Article**CLINICAL PROBABILITY ASSESSMENT USING MODIFIED WELLS CRITERIA AND D-DIMER FOR DIAGNOSIS OF LOWER LIMB DVT*****Santosh Shah, Rajesh Poudel, Sabir Miya***Department of Surgery, Universal College of Medical Sciences and Teaching Hospital, Bhairahawa, Nepal***Submitted: 27th -September-2024, Revised: 14th -November-2024, Accepted: 2nd -December-2024****ABSTRACT****Background**

Deep vein thrombosis (DVT) is a frequent problem in ambulatory and hospitalized patients. It is linked to considerable illness and death related to post-thrombotic syndrome, pulmonary embolism (PE), and pulmonary hypertension secondary to chronic PE. The comparatively low prevalence of DVT leads to a significant number of negative initial ultrasound (US) examinations. A combination of clinical pretest probability assessment using Modified Wells Score (MWS) and D-Dimer testing and subsequent venous US is a good diagnostic approach.

Methods

This study is a descriptive cross-sectional analysis on patients attending UCMS hospital with suspected DVT from September 2021 to March 2023 in order to evaluate the reliability of a combined approach of clinical assessment score (Modified Wells Score) followed by D-dimer test to exclude deep vein thrombosis. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of Modified Wells Score and D-Dimer individually and in combination were noted as outcomes.


Results

The study was undertaken in 79 patients. Among the patients, 31 out of 79 (39.24%) were confirmed to have DVT (group one), while 48 patients (60.76%) were ruled out for DVT (group two). In individual Modified Wells Score both the sensitivity and PPV were found to be 77.4%, and both the specificity and NPV were found to be 85.4%. The individual D-dimer test sensitivity was 93.5% with a specificity of 87.5%, while PPV and NPV were 82.9% and 95.5%, respectively. In combined strategy the sensitivity, specificity, PPV and NPV for the likely group combined with D-dimer test results were 100%, 42.9%, 85.7% and 100% respectively. The sensitivity, specificity, PPV and NPV for unlikely group combined with D-dimer test results were 71.4%, 95.1%, 71.4% and 95.1% respectively.

Conclusion

Combination of Modified Well's Criteria along with D-dimer level increases the sensitivity and Negative Predictive Value in DVT diagnosis in suspected cases.

Keywords: Deep vein thrombosis, Modified Wells Score, Pulmonary embolism

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INTRODUCTION

Deep vein thrombosis (DVT) is a prevalent condition affecting both ambulatory and hospitalized individuals. Untreated DVT may lead to substantial morbidity and mortality, mainly attributed to complications such as post-thrombotic syndrome, pulmonary embolism (PE), and pulmonary hypertension resulting from chronic Pulmonary Embolism.^{1,2} Conversely, administering anticoagulation therapy without proper justification poses a risk for bleeding. Thus, accurate diagnosis and timely treatment are of utmost importance.²

Presently, non-invasive diagnostic strategies employed to rule out suspected DVT encompass pretest probability estimation, D-dimer testing (cut-off; 0.50 mg/L), and ultrasonography. Numerous clinical prediction models and guidelines have been developed and validated across diverse populations to streamline and enhance the diagnostic process for patients presenting with suspected DVT.^{2,3}

The scoring method is both practical and safe for utilization, encompassing considerations of efficacy, treatment effectiveness, and cost efficiency. Among the established evaluation scales are the Wells Score, Caprini Score, Padua Score, and various other scoring methodologies.³ The Wells score is the most extensively authenticated prediction rule, and it has been subsequently modified.

D-dimer is distinctive cross-linked fibrin degradation products, formed in consequence of the breakdown of fibrin by the enzyme plasmin. As a result, levels of D-dimers become elevated in individuals who are afflicted with venous thrombosis. Several additional factors can lead to heightened D-dimer levels, including advanced age, cancer, infections, inflammation, ischemic heart disease, stroke, peripheral artery disease, ruptured aneurysm or aortic dissection, pregnancy, and recent instances of trauma or surgery.^{4,5}

This study aims to assess the diagnostic accuracy of the Modified Wells Score and D-dimer level in diagnosing suspected cases of DVT (Table 1).

Table 1: Clinical Model for Predicting the Pretest Probability of Deep-Vein Thrombosis.^{2,4,6}

Clinical variable	Score
Active cancer (treatment on -going or within previous 6 months or palliative)	1
Paralysis, paresis, or recent plaster immobilization of the lower extremities	1
Recently bedridden for 3 days or more, or major surgery within the previous 12 weeks requiring general or regional anesthesia	1
Localized tenderness along the distribution of the deep venous system	1
Entire leg swelling	1
Calf swelling at least 3 cm larger than that on the asymptomatic leg (measured 10 cm below the tibial tuberosity)	1
Pitting oedema confined to the symptomatic leg	1
Collateral superficial veins (non-varicose)	1
Previously documented DVT	1
Alternative diagnosis at least as likely as DVT	-2

A score of ≥ 2 , indicates that the probability of deep-vein thrombosis is likely; a score of < 2 indicates that the probability of deep-vein thrombosis is unlikely. In patients with symptoms in both legs, the more symptomatic leg is used.

OR

Alternatively, Pretest probability scores may be categorized as follows: “high”: ≥ 3 ; “moderate”: 1–2; “low”: ≤ 0 .

METHODS

This study is a descriptive cross-sectional analysis in patients presenting with clinical features suspicion of Deep Vein Thrombosis in OPD and Emergency department of Universal College of Medical Sciences, Bhairahawa. This study was conducted with ethical clearance from Institutional review committee of UCMS-TH with reference number UCMS/IRC/101/21.

Pretest clinical probability by Modified Wells Criteria (Likely ≥ 2) and Unlikely < 2) and laboratory test D-dimer level were evaluated. Venous Doppler ultrasonography was used as the standard test to confirm the presence of DVT. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of Modified Wells Score and D-Dimer individually and in combination were noted as outcomes.

All Individuals suspected of having deep vein thrombosis (DVT) were included. Excluded patients are Age < 18 years, Patient not willing to participate in the study, Patients which are already diagnosed with DVT, Patient who are on anticoagulant for any comorbidities and Pregnancy.

Detailed history of the patients were taken and clinical examination of all patients were done. Laboratory findings evaluated and Modified Wells scoring was done for each patient. D-dimer level of all patients analyzed. Venous Doppler ultrasonography was used as the standard reference test to confirm the presence of DVT. Informed written consent was obtained from the patients prior to their enrollment in the study, following their fulfillment of the inclusion criteria. Patients were managed according to standardized practice.

RESULTS

A total of 79 A total of seventy-nine patients presenting with symptoms suggestive of Deep Vein Thrombosis (DVT) were enrolled in the study. patients presenting with symptoms suggestive of Deep Vein Thrombosis (DVT) were enrolled in the study. Among the patients, 31 out of 79 (39.24%) were confirmed to have DVT (group one), while 48 patients (60.76%) were ruled out for DVT (group two).

The average age of patients in group one was 47.90 years, with an age range of 23 to 77 years. And for

patients in group two, it was 50.08 years (range 22 – 88 years). Among the patients diagnosed with DVT, 16 (51.61%) were males, and 15 (48.39%) were females, as shown in Figure 1.

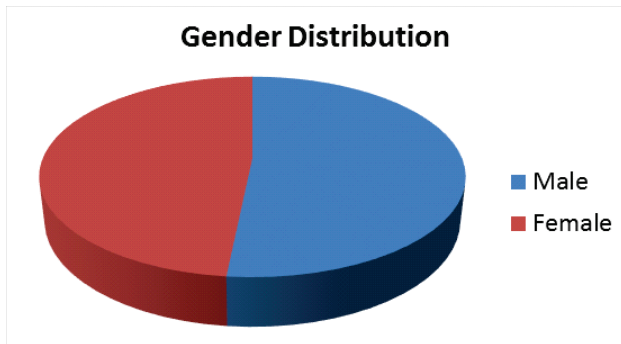


Figure 1: Gender Distribution of DVT Cases

The age distribution histogram, depicted in Figure 4, displays an increased incidence of DVT cases in the age range of 35 to 45 years, with a second peak observed in the age range of 60 to 65 years.

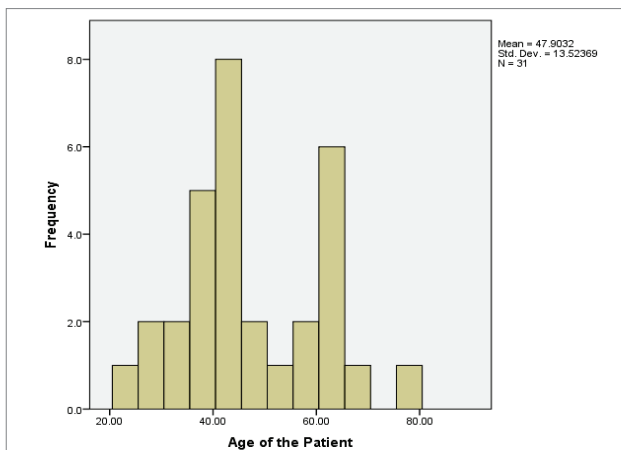


Figure 2: Age Histogram of DVT Cases

Patients were categorized into two groups based on DVT risk assessment by Modified Wells criteria: 31 patients in likely group, and 48 patients in unlikely groups. Of the 31 patients in the likely group, 24(77.41%) had DVT according to the standard reference test, while in the unlikely groups, 7(22.58%) had DVT. Based on the above findings, the Modified Wells Score have both the sensitivity and PPV were 77.4% , and both the specificity and NPV were 85.4 %(Table 2).

Table 2: Sensitivity, Specificity, PPV and NPV of D-Dimer and Modified Wells Score individually.

	Sensitivity	Specificity	Positive Predictive Value (PPV)	Negative Predictive Value (NPV)
Modified Wells Score	77.4%	85.4%	77.4%	85.4%
D-Dimer	93.5%	87.5%	82.9%	95.5%

of the 31 patients diagnosed with DVT, 29 patients had positive results for D-dimer test, while among the 48 patients in whom DVT diagnosis was not confirmed, 6 patients had positive results for D- dimer test (Table 5). Overall, the D-dimer test sensitivity in diagnosing DVT was calculated as 93.5% with a specificity of 87.5%, while PPV and NPV were 82.9% and 95.5%, respectively. The results are shown in Table 2.

Table 3: Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of D-dimer (cut-off value: 500 ng mL⁻¹) for the diagnosis of deep vein thrombosis according to Modified Wells Score.

	Sensitivity	Specificity	Positive Predictive Value (PPV)	Negative Predictive Value(NPV)
Likely	100.0%	42.9%	85.7%	100.0%
Unlikely	71.4%	95.1%	71.4%	95.1%

The sensitivity, specificity, NPV, and PPV of Modified Wells criteria were calculated in combination with D-dimer results for each group with presence of DVT. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for the likely group combined with D-dimer test results were 100%, 42.9%, 85.7%, and 100%, respectively. The sensitivity, specificity, PPV and NPV for unlikely group combined with D-dimer test results were 71.4%, 95.1%, 71.4% and 95.1% respectively. The positive predictive value (PPV) for the likely group with positive D-dimer test results increased to 85.7%, while the negative predictive value (NPV) for the unlikely group with negative D-dimer test results was 95.1%. These results are presented in Table 3. D-dimer outcomes were assessed separately in both groups, based on the Modified Wells risk assessment, which is Statically meaningful using Chi-square test with p-value of <0.001. The results are presented in Table 4.

Table 4: Frequency of DVT Cases Based on Groups and D-dimer Test Results.

Groups	Total patient's No.	Confirmed DVT D-Dimer positive	Ruled out DVT D-Dimer negative	p-value
Likely	31	24	7	<0.001
Unlikely	48	7	41	<0.001

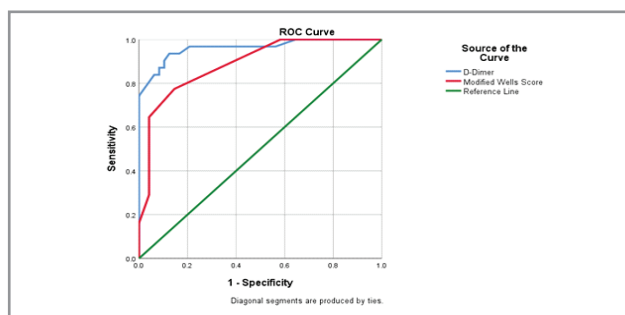


Figure 3: Receiver operating characteristic curve (ROC) analysis for accuracies of D-dimer and Modified Wells Score for the presence Deep Vein Thrombosis.

The ROC curve for the Modified Wells Score and D-dimer test is shown in Fig. 3. The area under the curve (AUC) for the Modified Wells Score was 0.88 (95% CI: 0.81–0.96), while the AUC for the D-dimer test was 0.96 (95% CI: 0.91–1.00), indicating a higher sensitivity of the D-dimer test in diagnosing suspected Deep Vein Thrombosis.

DISCUSSION

Ultrasonography (US) is widely considered the preferred diagnostic method for lower-extremity DVT due to its noninvasive nature, easy accessibility, and lack of side effects. Additionally, US can detect other conditions that can mimic DVT, such as Baker's cyst, thrombophlebitis, lymphadenopathy, subcutaneous edema, chronic DVT, fluid collection, hematoma, and muscle tears.^{7,8}

However, the relatively low prevalence of DVT may lead to a substantial number of negative initial ultrasound examinations, resulting in inefficient utilization of this resource. A contemporary diagnostic approach for patients with suspected DVT involves a multi-step strategy that includes clinical pretest probability assessment using the Modified Wells Score (MWS), D-dimer testing, and subsequent venous ultrasound.^{9,10}

Initially, patients were classified into low, moderate, or high-risk categories and further dichotomized into Likely (Wells Score ≥ 2) and Unlikely (Wells Score < 2) groups. A total of seventy-nine patients were included in our study, with 31 patients confirmed to have DVT in group one, and 48 patients without DVT, categorized as group two.

The mean age of patients in group one, those diagnosed with confirmed DVT, was... 47.90 years (range 23 – 77 years), and for patients in group two without DVT, it was 50.08 years (range 22 – 88 years). There was an increased incidence of DVT cases in the age range of 35 to 45 years, with a second peak observed in the age range of 60 to 65 years. In the study of Mozafar et al. The mean age for patients in the group confirmed with DVT and not having DVT were 53.23 years (49 ± 3.07) and 50.32 years (50 ± 4.2), respectively. This study has almost similar findings compared to our study. The few younger patients in our study with

confirmed DVT compared to other studies may be due the sample size variation.^{1,11}

The patients who were classified as low risk (with scores < 1) based on The Wells scoring system, it effectively excluded the likelihood of DVT, displaying both a sensitivity and negative predictive value (NPV) of 100%. On the other hand, among patients categorized as having moderate to high risk (with scores ≥ 2), the Wells scoring system displayed the capability to anticipate DVT occurrence with a specificity of 90%. The calculated area under the Receiver Operating Characteristic (ROC) curve amounted to 0.859 ($p < 0.0001$), affirming the precision of the Wells scoring system in effectively stratifying DVT risk within the population of post-trauma patients.¹² The negative predictive value (NPV) for low scores (regardless of the D-dimer) was 93.3% and the positive predictive value (PPV) was 27.3%. In our study Seven patients in unlikely group were found to have DVT and seven patients in likely group found not having DVT. Both the sensitivity and PPV was found to be 77.4%, and both the specificity and negative predictive value was found to be 85.4 % and AUC was 0.88 (95% CI 0.81–0.96) for Modified Wells Score. Comparing to this study, our study shows lower sensitivity and lower NPV in diagnosing DVT in suspected cases.¹³ The lower sensitivity and negative predictive value of Modified Wells score alone could be due to lower sample size and dichotomized form of scoring, In the trichotomized scoring system score of “1 – 2” is categorized as moderate risk and the score “1” doesn't exist in “Low” score but in dichotomized scoring score of “1” is categorized as unlikely.

The D-dimer test demonstrated a sensitivity of 88.05% and a specificity of 84.54% in diagnosing DVT. Furthermore, the positive predictive value (PPV) and negative predictive value (NPV) were calculated at 77.63% and 92.07%, respectively.¹¹ While in our study , the D-dimer test sensitivity in diagnosing DVT was calculated as 93.5% with a specificity of 87.5%, while PPV and NPV were 82.9% and 95.5%, respectively. And AUC was 0.96 (95% CI 0.91 – 1.00) for D-Dimer. The reason behind the higher sensitivity in our study might be due to use of high sensitive fluorescence immunoassay (Fineware™) rapid quantitative D-dimer test compared to the agglutination test used in the their study.¹¹ The D-dimer test demonstrated a negative predictive value (NPV) of 97.7% (95% CI, 94.7% to 99.2%). The sensitivity of the D-dimer test was 98.4% (95% CI, 96.4% to 99.5%), with 312 out of 317 patients testing positive and specificity was 42.4% (95% CI, 38.1% to 46.8%). Which also shows higher sensitivity because they also used the D-dimer assay of high sensitivity and high negative predictive value.¹⁴

The patients classified as low risk based on PCP (Pretest Clinical Probability), the D-dimer testing exhibited a sensitivity of 100%, along with a specificity of 46%. The positive predictive value (PPV) for this group was 4.8%, while the negative predictive value (NPV) reached 100% in the diagnosis of DVT. Similarly, in the moderate risk PCP group, the D-dimer testing demonstrated a sensitivity of 100% and a specificity of 45%, with a positive predictive value (PPV) of 49% and a negative predictive value (NPV) of 100%. In the high-risk PCP group, the D-dimer testing achieved a sensitivity of 100%, alongside a specificity of 57%. The positive predictive value (PPV) for this group was 80%, and the negative predictive value (NPV) remained at 100% in the diagnosis of DVT.¹⁵ The PPV for the high-risk group with positive D-dimer test results was 85.71%, and the NPV for the low-risk group with negative D-dimer test results was 96%. While in our study the sensitivity, specificity, PPV, NPV for the likely group with D-dimer test results was 100%, 42.9%, 85.7%, and 100% respectively and the sensitivity, specificity, PPV and NPV for unlikely group with D-dimer test results was 71.4, 95.1%, 71.4% and 95.1% respectively. There is

statistically significant (p value < 0.01) results for Modified Wells Score in combination with D-dimer for diagnosis of DVT in both likely and unlikely group. These combined approach The results of the D-dimer and pretest clinical probability tests are similar, showing increased sensitivity and negative predictive value for diagnosing and excluding DVT in suspected cases.¹¹

CONCLUSION

This study concludes that Modified Wells Score is an effective pretest probability score and when used alongside with D-dimer level there is an increased sensitivity and negative predictive value. As a result, the diagnostic accuracy for ruling out Deep Vein Thrombosis in suspected DVT cases is significantly improved.

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Conflict of interest: None

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