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Study of performance of modified well's criteria in assessing the risk of lower limb deep vein thrombosis

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Abstract

Background: Deep vein thrombosis has a very vague clinical presentation. Most of the patients who undergo lower limb colour venous doppler do not show evidence of deep vein thrombosis. The Modified Wells criteria was hence proposed to assess the pretest probability and thereby reduce the number of unnecessary lower limb colour venous doppler scan. However this scoring system is not widely used in India due various reasons including lack of studies proving its effectiveness in Indian population.

Aims and Objectives

To assess the performance of Modified Wells criteria as a clinical tool in risk stratification of patients with lower limb deep vein thrombosis

Methods: This is a cross-sectional study conducted between January 2021 and June 2022 with patients presenting to the outpatient department or the casualty of ESI Hospital, Rajajinagar, with a clinical picture suggestive of lower limb deep vein thrombosis. After appropriate statistical analysis sample size was estimated to be 93. Data was collected prospectively through a prescribed proforma from 93 cases of patients with clinical suspicion of lower limb deep vein thrombosis, who met the inclusion criteria, visiting the outpatient department general surgery at our hospital during the study period. All patients with suspected deep Vein thrombosis were assigned a Modified Wells score and stratified into three pretest probability categories. Then they were followed up by lower limb venous doppler

ultrasound to confirm the diagnosis. Statistical analysis was performed to measure the discriminatory accuracy of the Wells score for risk of deep vein thrombosis identified on lower limb venous doppler scan.

Results: In a study cohort of 93 inpatients, 137 (12.1%) had deep vein thrombosis. Lower limb deep vein thrombosis incidence in low and high pretest probability groups was (0 of 32) and 31.20% (19 of 61), respectively (p-value< .001, CI-95%). The area under the receiver operating characteristics curve for the discriminatory accuracy of the Wells score for risk of proximal DVT identified on lower-extremity venous duplex ultrasound studies was 0.824. The failure rate of the Wells scores to classify patients with a low pretest probability ("Unlikely" group) was 0% (95% CI); the efficiency was 43.25%. Thus, we concluded that the Modified Wells score is an effective method of assessing the probability of the presence of lower limb deep veing thrombosis.

Conclusion: We concluded that the Modified Wells score is an effective method of assessing the probability of the presence of lower limb deep vein thrombosis. However due to limitations of this study such as lack of randomization and bias; further studies must be conducted before reaching a definitive conclusion.

Keywords: DVT, Doppler Scan, Thrombosis

Introduction

Deep vein thrombosis is an illness that presents a clinical challenge to practically all practitioners. In deep vein thrombosis, the regulatory processes responsible for hemostasis are inappropriately activated due to some pathological process(es) leading to clot formation within deep veins. The word thrombus is derived from the Greek word "thrombose", which means a blood clot. It commonly complicates the course of a disease, but it is not rare to find a person without any of the precipitating/risk factors with deep vein thrombosis.[1,2] Thrombosis can occur in any section of the venous system but primarily affects the leg's deep veins. The blood clot usually develops in the deep calf veins and propagates proximally.[1]The complications of deep vein thrombosis of the lower limbs can be dreadful. Quite often, they lead to either morbidity or mortality. Long-term morbidity due to post-thrombotic syndrome is common and can be substantial.[3]However, the primary concern is the embolisation of the thrombus to the lung, which can be fatal [Pulmonary Thromboembolism].[4] Deep vein thrombosis is a highly prevalent disease that significantly burdens the health economy. The disorder and its sequelae are also among the best examples of preventable diseases.[3-6] Patients with deep vein thrombosis of the legs may be asymptomatic or have various symptoms mimicking other diseases.[1,8] Based on the history and clinical examination, diagnosing, or ruling out deep vein thrombosis is impossible. Hence, most clinicians heavily rely on diagnostic modalities such as venous doppler, venography, and D-dimer levels.[9] In Tier 1 and a few Tier 2 cities in India, healthcare is affordable, and many diagnostic centres would perform venous colour doppler.[10] Hence clinicians in India have a low threshold to order a venous doppler to rule out deep vein thrombosis.[11] However, in the west, in many countries, the healthcare cost is insane.[12] Hence, various scoring systems were devised to check for the Pretest probability of deep vein thrombosis to avoid unnecessary doppler scanning. The most well-known and validated score is the Well's score.[13] Based on Pretest probability, it is decided whether to perform a colour venous doppler or not to reduce healthcare costs and the burden on the scarcely available radiology facilities. Although Modified Wells

score is a validated score, many reliable studies question the validity of the Modified WELL's score.[13,14,15] Even if the accuracy of the Pretest probability score in ruling out deep vein thrombosis is 99%, there would be a lingering concern that the one missed patient with DVT might end up with pulmonary embolism or post-thrombotic limb will remain. Therefore, In India, a clinician would like to get a doppler scan (which is not as expensive as in the west) to effectively rule out deep vein thrombosis.[11]In India, radiology facilities at government hospitals are scarce, and the entire system is overburdened.[16] If clinicians start applying validated scoring. Systems, such as the Wells, unnecessary radiological scanning can be avoided, and already scarce radiology facilities can tend to more needy patients.[13] In this study, we present our experience using the Modified Wells score [not for decision-making during management, all suspected cases of DVT will undergo a colour doppler scan] while managing patients with lower limb deep vein thrombosis. Materials and Methods

Materials and Methods

This is a cross-sectional study conducted between January 2021 and June 2022 with patients presenting to the outpatient department or the casualty of ESI hospital, Rajajinagar, with a clinical picture suggestive of lower limb deep vein thrombosis.

Methods of collection of data:

Study design: Cross-sectional study

Study period: March 2021 to august 2022

Place of study: Dept. of General Surgery, ESICMC & PGIMSR, Rajajinagar, Bangalore

Sample size: The sample size was calculated based on a previous study by Patricia. C et al. In which it was found that the area under the receiver operating characteristics curve for discriminatory accuracy of wells score for risk of deep vein thrombosis was 0.60. In the present study, a minimal sample size was estimated, considering an 8% margin of error and a confidence interval of 95%. The total sample size was estimated to be 93**.**

Inclusion criteria

- Those consenting to the study (**annexure i**)
- Patients presenting to the outpatient department or casualty with a clinical picture suggestive of lower limb deep vein thrombosis.
- Age greater than 18 years
- The onset of symptoms within seven days

Exclusion criteria

- Patients not consenting to the study.
- Patients less than 18 years old
- Critically ill patients with multiple comorbidities
- Patients with bleeding diathesis

Methodology

After obtaining approval and clearance from the institutional ethics committee, the patients fulfilling the inclusion criteria were enrolled for the study after obtaining informed consent. (**Annexure – i**)

A detailed clinical assessment of the patients was performed and recorded using a standard proforma (**Annexure-III**)

All patients with suspected deep Vein thrombosis were assigned a Modified Wells score and then stratified into three Pretest probability categories (**Annexure- II**).

Then they were followed up by lower limb venous doppler ultrasound to confirm the diagnosis.

Statistical analysis was performed to measure the discriminatory accuracy of the Wells score for risk of

deep vein thrombosis identified on lower limb venous doppler scan.

Basic blood investigations, such as complete blood counts, urea, blood sugar, serum creatinine and electrolytes, and a chest x-ray and ECG, were sent.

Assessment Tools: Modified Wells criteria for deep vein thrombosis

Outcome Measures: Performance of the Modified Wells score for risk stratification among patients with suspected deep vein thrombosis will be measured by,

- The difference in the incidence of lower limb deep vein thrombosis among the modified Wells score Pretest groups
- The failure rate of Modified Wells score prediction
- The efficiency of the Modified Wells scores to exclude deep vein thrombosis

Results

The prospective cross-sectional study was done on ninety-three consecutive patients with clinical suspicion of lower limb deep vein thrombosis who had presented to the outpatient department/casualty of ESICMC & PGIMSR during the study period from March 2021 to august 2022.

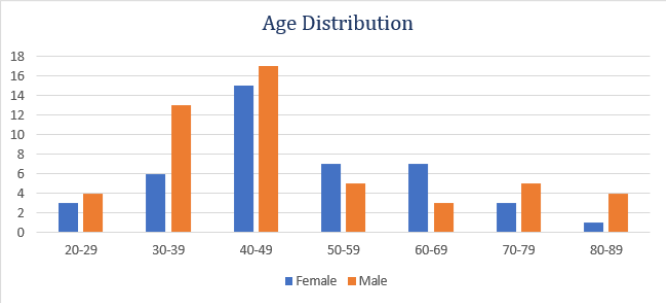
Baseline characteristics of the patients

Age distribution

Table 1: age distribution

Age (In Years)	Female	Male	Total	Percentage
20-29	3	4	7	7.52
30-39	6	13	19	20.43
40-49	15	17	32	34.40
50-59	7	5	12	12.90
60-69	7	3	10	10.75
70-79	3	5	9	9.67
80-89	1	4	5	5.37
Total	42	51	93	100

Graph 1 : Age Distribution



The mean age of the patients included in our study was 48.78 ± 1.62 years. The range of age variation was 65, with the youngest subject being 20 years old and the oldest one being 85 years old. Most of the patients included in this study (n=54, 58.7%) belonged to the age group of 30 to 50 years. There was no statistically significant correlation between increasing age and the probability of having a modified Wells score of more than 2 (p-value-0.104, CI=95%) or testing positive for deep vein thrombosis on a lower limb colour doppler (p-value-0.151, CI=95%). [p-value of less than 0.05 at 95% CI was considered statistically significant]

Sex Distribution

In our study, males (n=51, 54.8%) were slightly more numerous than females (n=42, 45.2%). However, no statistically significant relation was found between gender and the likelihood of having lower limb deep vein thrombosis (p-value- 0.83, CI-95%) or a higher Wells score (p-value-0.673, CI=95%). There was no statistically significant association between gender and the likelihood of falling under either of the pretest probability groups (p-value=0.287, CI=95%).[Statistical significance was calculated using the 2-tailed test, a p-value of less than 0.05 would be considered statistically significant]

Graph 2: Sex Distribution

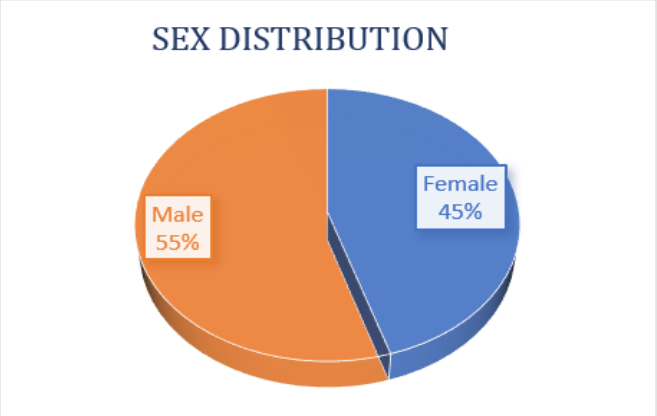


Table 2

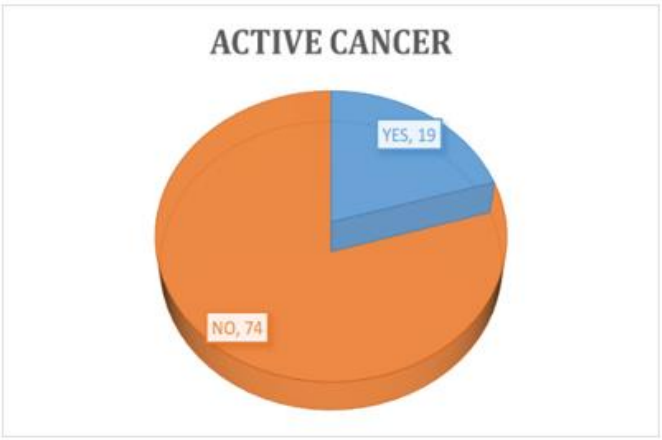
Sex	No. of Cases	Percentage
Female	42	45.16%
Male	51	54.84%

Individual Parameters Used to Ascertain the Modified Wells Score:

a. Active cancer (ongoing treatment/treatment within the last six months or palliative)

In our study group, out of the 93 patients, twenty-three patients had active cancer (n=23, 24.7%).

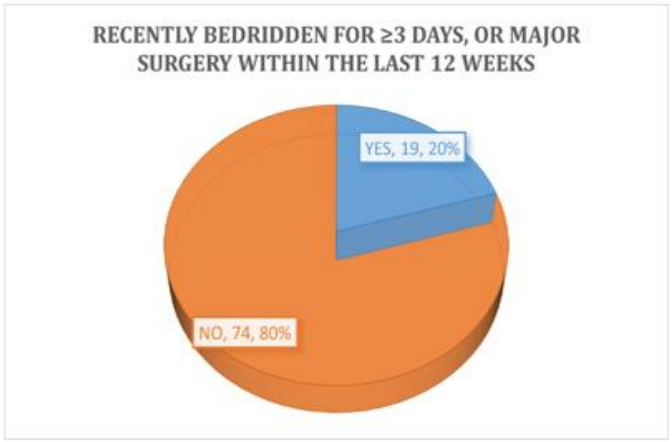
Graph 3: Proportion of patients with an active cancer



b. Recently bedridden for ≥3 days, or major surgery within the last 12 weeks requiring general or local anaesthetics.

Nineteen patients (n=19, 20.4%) were recently immobilized for more than three days or had undergone major surgery within the last 12 weeks.

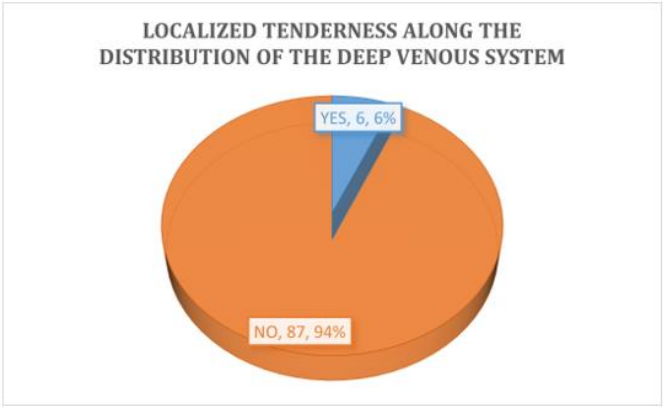
Graph 4: Proportion of patients with a recent history of immobilization



c. **Localized tenderness along the distribution of the deep venous system**

Six patients (n=6, 6.5%) had localized tenderness along the distribution of the deep venous systems.

Graph 5: Proportion of patients with localized tenderness all the distribution of deep venous system

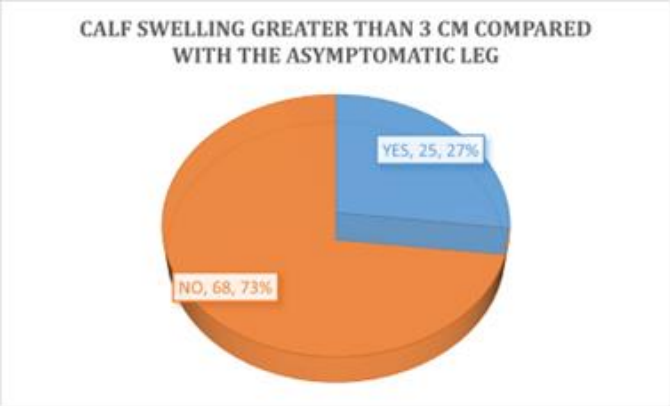


D. Calf swelling >3 cm compared with the asymptomatic leg (measured at 10 cm below the tibial tuberosity

More than a quarter of the 93 patients (n=25, 26.9%) had a significant calf swelling measuring greater than 3 cm

compared with the asymptomatic leg (measured at 10 cm below the tibial tuberosity

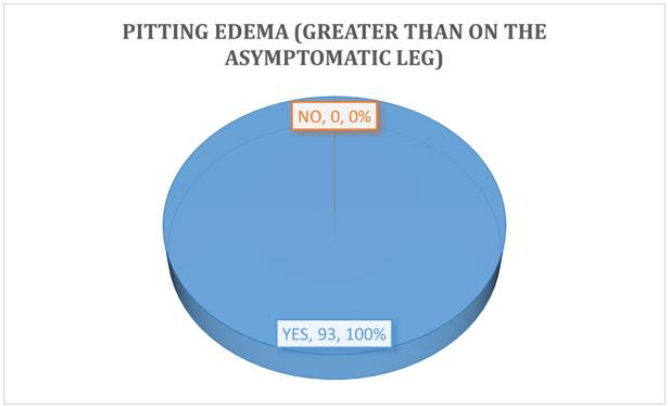
Graph 6: Proportion of patients with calf swelling greater than 3 cm as compared to the asymptomatic side.



E. Pitting oedema (greater than on the asymptomatic leg)

All patients in our study group had pitting pedal oedema greater on the symptomatic side than on the symptomatic leg (n=93, 100%)

Graph 7: Proportion of patients with pitting edema (greater than on the asymptomatic side)



F. Previously documented DVT

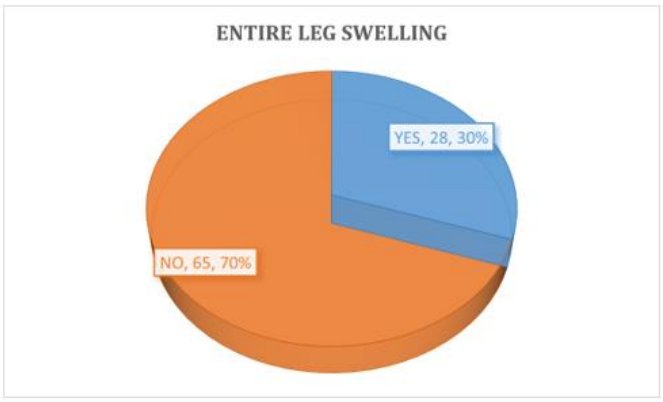
Forty-two out of the 93 patients (n=42, 45.2%) had a previous history of deep vein thrombosis.

Graph 8: Proportion of patients with previously documented deep vein thrombosis

g. Entire leg swelling

Twenty-eight patients had (n=28, 30.1%) an entire limb swelling.

Graph 9 : Proportion of patients with an entire leg swelling



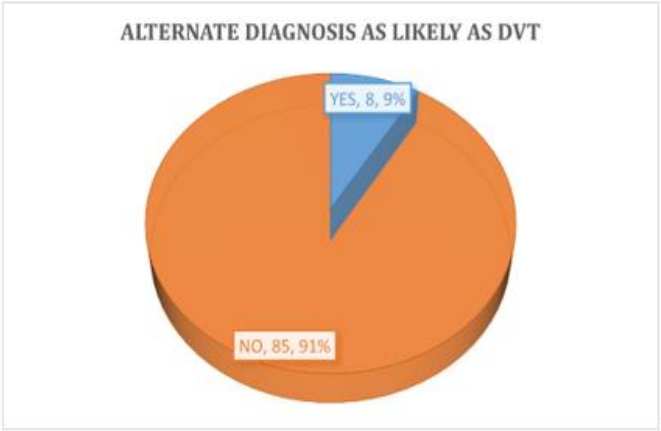
h. Intravenous drug abuse

None of the patients had a previous history of intravenous drug abuse

i. Intravenous drug abuse an alternative diagnosis is more likely than DVT (e.g., Muscular tear, cellulitis, etc.)

In our study, eight out of the ninety-three patients (n=8, 8.6%) were more likely to have a diagnosis other than deep vein thrombosis.

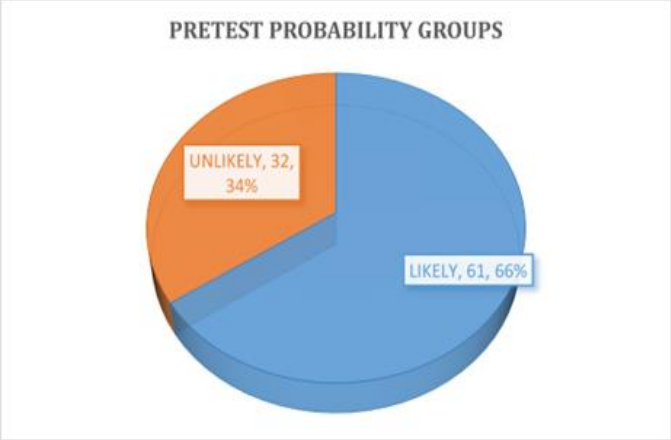
Graph 10: Proportion of patients having an alternate diagnosis as likely as deep vein thrombosis



The Modified Wells score and the pretest probability of having lower limb deep vein thrombosis

In our study, based on the modified wells score, the patients were stratified into two groups, namely, “LIKELY” (if the score was greater than or equal to two) and “UNLIKELY” (if the score was less than two). Thirty-two patients (n=32, 34.5%) had a score of less than two, and the remaining sixty-one patients (n=61, 65.6%) had a score of equal or greater than two, and hence they were grouped as “UNLIKELY” and “LIKELY" respectively.

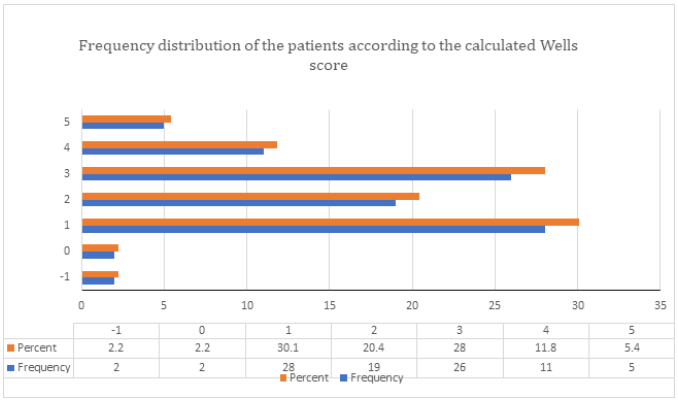
Graph 11: Proportion of patients belonging to each of the Pretest probability groups



Frequency distribution of the patients according to the Wells score

Table 3: Frequency distribution of the patients according to the Wells score

Wells score	Frequency	Percent	Pretest Probability
-1	2	2.2	UNLIKELY
0	2	2.2	
1	28	30.1	
2	19	20.4	LIKELY
3	26	28.0	
4	11	11.8	
5	5	5.4	
Total	93	100.0	---------

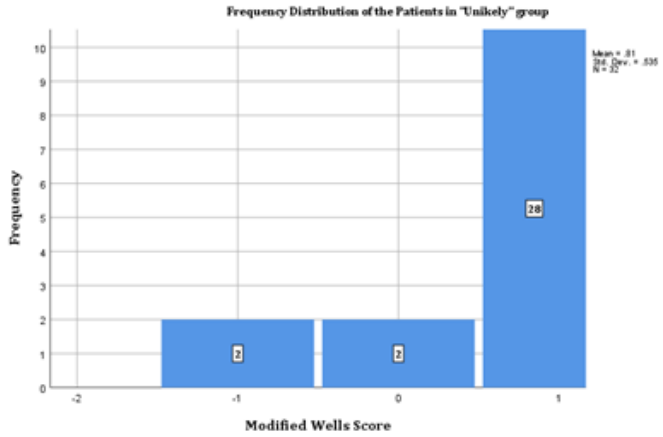


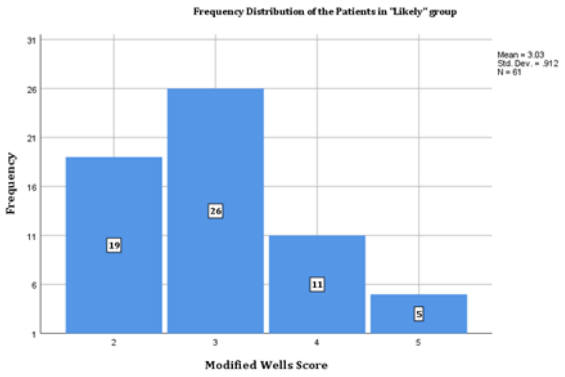
Graph 12: Frequency distribution of the patients according to the calculated Wells score

“Unlikely” group

Of the 93 patients in our study, 32 (n=32, 34.5%) were unlikely to have lower limb deep vein thrombosis according to the Modified Wells Criteria. In this group, 28 patients scored 1, and two scored -1 and 0. The mean Modified Wells score in this group was 0.81, with a standard deviation of 0.54. The minimum score recorded in this group was -1; by definition, the highest score was 1 (patients with a score greater than one are included in the “Likely” group). None of these 32 patients tested positive for lower limb deep vein thrombosis on colour venous doppler.

Graph 13: Frequency distribution of Wells score in each of the Pretest probability groups

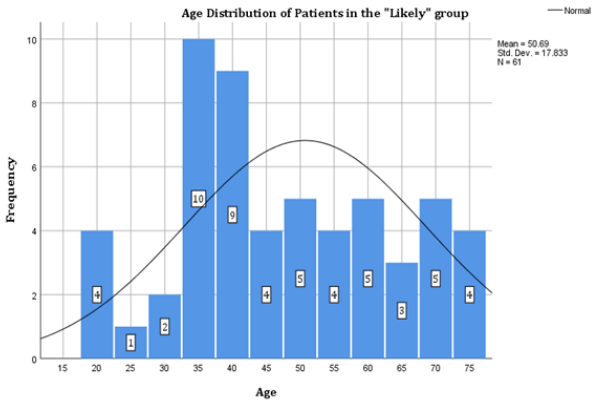




"Likely" group

A total of sixty-one patients (n=61, 65.6%) belonged to the "likely" group. The mean modified wells score in this group was 3.03, with a standard deviation of 0.92. Nineteen patients scored 2, twenty-six patients scored 3, eleven patients scored 4, and five scored 5. None of the patients scored more than 5. Of these sixty-one patients, thirty-one were male, and thirty were female. Of these 61 patients, nineteen (n=19, 31.1%) were diagnosed with lower limb deep vein thrombosis on doppler scanning, and forty-two (n=42, 68.9%) did not show evidence of lower limb deep vein thrombosis on doppler scan.

Graph 14 : Frequency distribution of Wells score in "Likely" group



Determination of the effectiveness of the Modified Wells criteria in risk stratification of patients with suspected lower limb deep vein thrombosis

Table 4: Contingency Table

Pretest Probability \ Venous doppler	DVT present	DVT absent	Total
Likely	19 (a)	42 (b)	61 (a+b)
Unlikely	0 (c)	32 (d)	32(c+d)
Total	19 (a+c)	74 (b+d)	93 (a+b+c+d)

A=True Positives, b= False Negatives,

C= False Negatives, d= True Negatives

The above table was prepared by analysing the data collected for our study; Then, the Chi-Square test was performed to check for the association between the Modified Wells Score pretest probability groups and the lower limb deep vein thrombosis.

$$Sensitivity = \frac{True\ Positive}{(True\ Positive + False\ Negative)}$$

$$Specificity = \frac{True\ Negative}{(True\ Negative + False\ Positive)}$$

$$Positive\ Predictive\ Value = \frac{True\ Positives}{(True\ Positives + False\ Positives)}$$

$$Negative\ Predictive\ Value = \frac{True\ Negative}{(True\ Negative + False\ Negative)}$$

Using the above formulae, the sensitivity, specificity, positive predictive value (PPV) and Negative Predictive Value (NPV) were calculated. Sensitivity and negative predictive values were 100% due to our study's absence of false negatives. The Specificity was 43.24%, and the positive predictive valve (PPN) was 31.15%. These values concurred with the values obtained on data analysis using IBM SPSS Statistics version 25. The validity of the data in the contingency table (Table) was established using Fischer's test (Fischer-Irwing test). The p-value obtained by Fischer's test was 0.000, indicating that the findings of our study are statistically significant (a p-value <0.05 at a 95% confidence interval

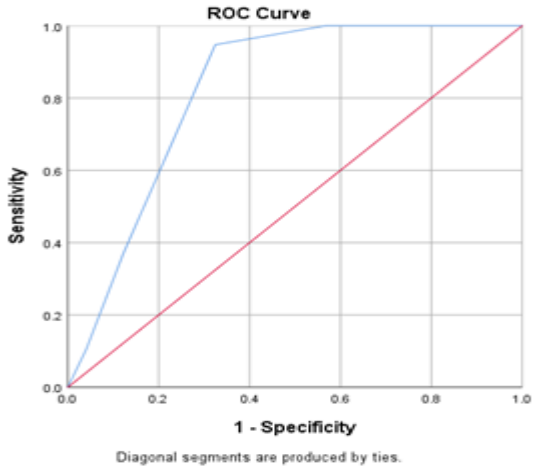
is considered statistically significant). Although the Pearson Chi-Square test yielded an asymptotic significance (p-value) of <0.05, it was not considered to validate the statistical analysis as one of the values in the contingency table was less than five (zero false negatives in our study), and the sample size of our study was relatively small.

Table 4: Test of significance

	Value	Degree of Freedom (df)	Asymptotic Significance (2-sided)	Exact Significance (2-sided)	Exact Significance (1-sided)
Pearson Chi-Square	12.526	1	.000		
Continuity Correction	10.684	1	.001		
Likelihood Ratio	18.500	1	.000		
Fisher's Exact Test				.000	.000

Discriminatory accuracy of the Modified Wells score

The area under the receiver operating characteristics curve (AUC), in which the true positive rate (Sensitivity) is plotted against the false positive rate (1-Specificity), was used to determine the discriminatory accuracy of the Modified Wells score for lower limb deep vein thrombosis diagnosed on lower limb colour venous doppler. An ideal scoring system would have an AUC of 1. A scoring system with an AUC between 0.7 and 0.8 is acceptable, and this kind of scoring system would be considered for adoption in clinical practice. In our study, we found that the area under the curve for the receiver operating curve (AUC) was 0.824 (S.E.- 0.43). The upper and lower bounds were 0.741 and 0.907, respectively (p-value<0.05, 95% CI). Coordinates of the ROC were obtained. In our study, the Modified Wells score of 1.5 (Wells score doesn't have decimals, this is only a hypothetical score used for statistical analysis) had a sensitivity of 100% and specificity of about 43.20% {(1-specificity) at 2.5= 0.568 x 100}. A score of 2.5 had a sensitivity of approximately 94.7% and specificity of roughly 67.6% {(1-specificity) at **2.5**= 0.324 x 100}. This suggests that the trade-off between Sensitivity and specificity begins somewhere between a modified Wells score of 1.5 and 2.5.



Graph15: Receiver Operating Characteristics (ROC) curve

- Sensitivity- True Positive Rate
- 1-Specificity- False Positive Rate

Table 5: Area under the receiver operating characteristics curve

Area Under the Curve				
Area	Standard Error	Asymptotic Sig.[a]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.824	.043	.000	.741	.907

a. Asymptotic Significance is the same as the "p-value."
Null hypothesis: true area = 0.5

Coordinates of the Receiver Operatic Characteristics (ROC)Curve

Table 6: Coordinates of the ROC curve

Positive if Greater Than or Equal To	Sensitivity (True Positive Rate)	1 – Specificity (False Positive Rate)
-2.00	1.000	1.000
-0.50	1.000	0.973
0.50	1.000	0.946
1.50	1.000	0.568
2.50	0.947	0.324
3.50	0.368	0.122
4.50	0.105	0.041
6.00	0.000	0.000

Test Result Variable: Modified Wells Score

a. The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

The table mentioned above depicts the relation between the value of the Modified Wells score and the corresponding Sensitivity and (1-specificity); we can see

a correlation between the Modified Wells score, true positive rate and false positive rate. Lower scores tend to have a very high sensitivity and a low specificity, while the higher scores have a low sensitivity and a high specificity. Sensitivity falls below 100, between a Modified Wells Score of 1.5 (100%) and 2.5 (94.7%).

Discussion

Deep vein thrombosis is one of the more complex diseases concerned with the peripheral venous system of the human body. The inherent homeostatic mechanism of clotting, which is undoubtedly essential in homeostasis and wound healing, is activated here with a deleterious effect that can ultimately end with mortality due to pulmonary embolism. Lower limb deep vein thrombosis is one of the most prevalent venous disorders with a significant financial and social burden. The major outcomes of lower limb venous thrombosis include recurrence, post-thrombotic syndrome, major bleeding due to anticoagulation, and death due to a massive pulmonary embolism in a few unfortunate cases. Thrombosis is also associated with poor quality of life, particularly when post-thrombotic syndrome develops. As the consequences of lower limb deep vein thrombosis are dreadful, it is imperative to rule out lower deep vein thrombosis if clinical suspicion arises. The clinical diagnosis of deep vein thrombosis is, at times, difficult and may also masquerade as another disease process. Due to this, a low threshold exists to order a doppler scan to rule out lower limb deep vein thrombosis. The wells /modified wells score was devised to reduce unnecessary imaging by determining a patient's pretest probability of having lower limb deep vein thrombosis. The modified wells score is calculated for patients with suspected deep vein thrombosis (as described in annexure-iii), and based on the score obtained; the patients are assigned one of the two pretest probability groups, viz. Likely and unlikely. Only those patients who belong to the "likely" group are subjected to a lower limb venous doppler, as the possibility of deep vein thrombosis in patients in the "unlikely" group is minimal. This intuitive test has stood the test of time and is still one of the west's most commonly employed clinical scoring tools. But if the patient has got access to an affordable healthcare system, it is best to rule out lower limb deep vein thrombosis, as even 1 in 100 patients, if missed, could end up with a potentially life-threatening condition or a complication with high morbidity, huge financial burden and decreased quality of life. At least in the major cities in india, due to affordable healthcare, deep vein thrombosis can be easily ruled out by ordering a venous doppler of the lower limbs in case of clinical suspicion of the lower limb deep vein thrombosis. But this is not the case in rural areas and smaller cities where ultrasound or venous doppler availability is a luxury. In those areas where the venous doppler is not readily available, protocols utilizing scoring systems should be set in place. And if the clinical scoring system points towards a likely risk of having lower limb deep vein thrombosis, such patients should be referred to the bigger cities for a doppler scan. Then unnecessary doppler scans can be avoided. In turn, this can significantly reduce the financial burden and the burden on our already overburdened healthcare system. There is much controversy about whether the modified wells score is valid, as different studies conducted in similar cohorts of patients across various geographical areas have yielded drastically different results. Especially in India, there is a gross lack of good research work that validates using the modified wells score in an Indian setup. But the noteworthy point is that the number

of studies validating the modified wells score outnumbers those questioning its validity. Therefore, we conducted this prospective cross-sectional study to present our experience. In this cross-sectional study, the performance of modified wells criteria as a clinical tool for risk stratification of deep venous thrombosis was studied. All the inpatients and outpatients with clinical suspicion of lower limb deep vein thrombosis were stratified into the two pretest probability groups, and then all of these cases were followed up with a lower limb venous colour doppler. Then the efficiency and efficacy of modified wells criteria (see annexure- iii) were ascertained by statistical analysis of the data obtained. This study will indicate whether the modified wells score can be reliably used in an Indian scenario or not. However, as this is a cross-sectional study, the results of this study cannot be taken as foolproof evidence for the validity of the modified wells score in an Indian setup. Several good-quality prospective studies must be carried out in the reference population to validate a scoring system. Then the results of these studies must be analyzed by a meta-analysis. If the meta-analysis validates the scoring system, it would be safe to use such a scoring system to formulate diagnostic and treatment protocols. Diagnostic and treatment protocols formulated in the west advocate using the modified wells score in conjunction with the measurement of d-dimer levels to effectively rule out lower limb deep vein thrombosis in clinically suspected cases. However, the availability of d-dimer testing in non-tertiary care hospitals in India is rare. Hence d-dimer levels were not checked in the patients included in this study. In the following paragraphs, we will discuss the findings of our study under the following sub-headings; baseline characteristics of the patients, the pretest probability of the lower limb deep vein thrombosis, effectiveness of modified wells criteria, and the conclusion.

Baseline characteristics of the patients

In this study, a total of 93 patients were included. The type of study, study duration, inclusion criteria, exclusion criteria, sample size calculation, and statistical analysis method has been described in detail in the methodology section.

Age distribution of the patients

The mean age of the patients included in our study was 48.78 ± 1.62 years. The range of age variation was 65, with the youngest subject being 20 years old and the oldest one being 85 years old. Most of the patients included in this study (n=54, 58.7%) belonged to the age group of 30 to 50 years. There was no statistically significant correlation between increasing age and the probability of having a modified Wells score of more than 2 (p-value-0.104, CI=95%) or testing positive for deep vein thrombosis on a lower limb colour doppler (p-value-0.151, CI=95%). [p-value of less than 0.05 at 95% CI was considered statistically significant]

Gender distribution of the patients

In our study, males (n=51, 54.8%) were slightly more numerous than females (n=42, 45.2%). However, no statistically significant relation was found between gender and the likelihood of having lower limb deep vein thrombosis (p-value- 0.83, CI-95%) or a higher Wells score (p-value-0.673, CI=95%). There was no statistically significant association between gender and the likelihood of falling under either of the pretest probability groups (p-value=0.287, CI=95%).[Statistical significance was calculated using the 2-tailed test, a p-value of less than 0.05 would be considered statistically significant]

Individual parameters used to ascertain the Modified Wells score

Active cancer (ongoing treatment/treatment within the last six months or palliative)

In our study group, out of the 93 patients, twenty-three patients had active cancer (n=23, 24.7%).

Recently bedridden for ≥3 days, or major surgery within the last 12 weeks requiring general or local anaesthetics

Nineteen patients (n=19, 20.4%) were recently immobilized for more than three days or had undergone major surgery within the last 12 weeks.

Localized tenderness along the distribution of the deep venous system

Six patients (n=6, 6.5%) had localized tenderness along the distribution of the deep venous system.

Calf swelling >3 cm compared with the asymptomatic leg (measured at 10 cm below the tibial tuberosity)

More than a quarter of the 93 patients (n=25, 26.9%) had a significant calf swelling measuring greater than 3 cm compared with the asymptomatic leg (measured at 10 cm below the tibial tuberosity)

Pitting oedema (greater than on the asymptomatic leg)

All of the patients in our study group had pitting pedal oedema, which was greater than on the asymptomatic leg (n=93, 100%).

Previously documented DVT

Forty-two out of the 93 patients (n=42, 45.2%) had a previous history of deep vein thrombosis.

Entire leg swelling

Twenty-eight patients had (n=28, 30.1%) an entire limb swelling.

Intravenous drug abuse

None of the patients had a previous history of intravenous drug abuse.

An alternative diagnosis is more likely than DVT (e.g., muscular tear, cellulitis, etc.).

In our study, eight out of the ninety-three patients (n=8, 8.6%) were more likely to have a diagnosis other than deep vein thrombosis. Similar to the previously conducted studies, we did not find a statistically significant association between age and gender vs the likelihood of being tested positive for deep vein thrombosis or scoring more than or equal to two on the Wells score. The commonest parameter present in the patients with clinically suspected lower limb deep vein thrombosis was pitting oedema (greater than on the asymptomatic side); it was seen in all of the patients in our study. Unilateral painful pitting oedema (especially associated with a history of recent air travel, long drive, and sedentary life) seldom makes a clinician think of a disease other than the lower limb deep vein thrombosis, even more so if the patient doesn't have diabetes mellitus or any other immunocompromised condition. About 42 patients (45.2%) had a previous history of deep vein thrombosis. More than a quarter of the patients included in our study (n=25, 26.9%) had asignificant calf swelling measuring greater than 3 cm compared with the asymptomatic leg (measured at 10 cm below the tibial tuberosity):- This was the third most common clinical parameter seen in patients suspected with the lower limb deep vein thrombosis. Nineteen patients (n=19, 20.4%) gave a history of recent immobilization/significant surgery within the preceding 12 weeks. Twenty-eight patients (n=28, 30.1%) had an entire limb swelling. However, localized tenderness along the distribution of the venous system was seen in relatively few patients (n=6, 6.5%). None of the patients in our study had a history of intravenous drug abuse. Eight patients (n=8, 8.6%) were more likely to have an alternate diagnosis

other than deep vein thrombosis. But interestingly, none of the reliable prospective studies or randomized control trials have looked in detail at the prevalence of individual parameters used in calculating Modified Wells score in patients with suspected lower limb deep vein thrombosis. This may indicate that the relative frequency of individual parameters across various institutions or geographical areas may vary significantly. Statistical analysis of each parameter may not yield helpful information as this is a non-randomized study without blinding and with an obvious one. Similar studies were done in the past; they solely looked at the correlation between the total calculated Modified Wells score and the incidence of lower limb deep vein thrombosis without correlating the likelihood of lower limb deep vein thrombosis and the individual parameters. Those studies also looked at the incidence of lower limb deep vein thrombosis in each of the pretest probability groups.

The Modified Wells score and the pretest probability of having lower limb deep vein thrombosis

In our study, based on the Modified Wells score, the patients were stratified into two groups, namely, "LIKELY" (if the score was more than or equal to two) and "UNLIKELY" (if the score was less than two). Thirty-two patients (n=32, 34.5%) had a score of less than two, and the remaining seventy-one patients (n=61, 65.6%) had a score of equal or greater than two, and hence they were grouped as "UNLIKELY" and "LIKELY" respectively. The mean Modified Wells score was 2.27

"Unlikely" group-_Of the 93 patients in our study, 32 (n=32, 34.5%) were unlikely to have lower vein deep vein thrombosis according to the Modified Wells Criteria. None of these 32 patients tested positive for lower limb deep vein thrombosis. The absence of false negatives is probably due to a relatively small sample size.

"Likely" group-A total of sixty-one patients (n=61, 65.6%) belonged to the likely group. Of these 61 patients, nineteen (n=19, 31.1%) were diagnosed with lower limb deep vein thrombosis on doppler scanning, and forty-two (n=42, 68.9%) did not show evidence of lower limb deep vein thrombosis on doppler scan.

Effectiveness of Modified Wells criteria in risk stratification of patients with suspected deep vein thrombosis

This study was conducted to determine the discriminatory accuracy of the Modified Wells Score for risk stratification of lower limb deep vein thrombosis. In this study, only nineteen patients had lower limb deep vein thrombosis out of the ninety-three patients. All these nineteen patients belonged to the "likely" group, and no patients in the "unlikely" group were diagnosed with lower limb deep vein thrombosis. The absence of false negatives is one of the significant drawbacks of this study, as it points toward an inadequate sample size. Otherwise, the lack of false negatives could also be attributed to operator bias. Tests of Normality showed normal distribution of the test variables (Pretest Probability of having deep vein thrombosis and deep thrombosis detected on colour doppler scan). Hence parametric measures were used for Statistical Analysis. Chi Square-test was then performed {Null Hypo- There is no relation between the pretest probability and lower limb deep vein thrombosis}; sensitivity and negative predictive value were 100% due to the lack of false negatives; Specificity and positive predictive value were 43.24% and 31.15%, respectively. All the obtained values were statistically significant [p-value<0.05 at

95% confidence interval]. Finally, the area under the curve (AUC) of receiver operator characteristics (ROC) was obtained to check the discriminatory accuracy of the modified Wells score. AUC-ROC was 0.824 (S.E.=0.043). Coordinates of the ROC curve were marked at different values of Modified Wells Score, and as expected, lower scores tend to have a very high sensitivity and a low specificity, while the higher scores have a low sensitivity and a high specificity. Sensitivity falls below 100, between a Modified Wells Score of 1.5 (100%) and 2.5 (94.7%). Our study suggests that a modified Wells score of less than two can effectively rule out lower limb deep vein thrombosis in most (94.7% to 100%) patients. It is safe to assume that the Modified Wells score effectively predicts the presence of lower limb deep vein thrombosis. The findings of our study concur with several studies done in the past. The findings of a few of these studies have been described below.

Geersing et al. (2014), in their meta-analysis, concluded that lower limb deep vein thrombosis could be excluded in patients with an unlikely score (low probability) on Wells rule. A low probability score on Wells rule (<1) was associated with an extremely low probability of deep vein thrombosis (1.2%, 95% confidence interval 0.7% to 1.8%).[75] A meta-analysis conducted by Phillip Wells et al. (2006) showed that this criterion is very effective in risk stratification of patients with lower limb deep vein thrombosis. The prevalence of DVT in the low, moderate, and high clinical probability groups was 5.0% (95% CI, 4.0%-8.0%), 17% (95% CI, 13%-23%), and 53% (95% CI, 44%-61%), respectively.[75] However, a few studies suggest that the Modified Wells score is not very effective. In their prospective study, Ivan K P et al. Concluded that Wells score is slightly better than the chance of discrimination for determining the risk of lower limb deep vein thrombosis. In a study cohort of 1135 inpatients, 137 (12.1%) had deep vein thrombosis. Lower limb profound vein thrombosis incidence in low, moderate, and high pretest probability groups was 5.9% (8 of 135), 9.5% (48 of 506), and 16.4% (81 of 494), respectively (P < .001). The area under the receiver operating characteristics curve for the discriminatory accuracy of the Wells score for risk of proximal DVT identified on lower-extremity venous duplex ultrasound studies was 0.60. The failure rate of the Wells score to classify patients with a low pretest probability was 5.9% (95% CI, 3.0%-11.3%); the efficiency was 11.9% (95% CI, 10.1%-13.9%).[137] A prospective study done by Maelen Tagelagi et al. With a sample size of 432 patients concluded that the Wells rule had only moderate sensitivity and poor specificity and likelihood ratios, thereby inferring that the Wells score has limited use in the management of deep vein thrombosis. DVT was confirmed in 12% (39/327). Sensitivity was 82% (95% confidence interval [CI]: 67.3-91.0), and specificity was 22.5% (CI: 18.1-27.7). The likelihood ratio for a positive test was 1.06 (CI: 0.90-1.24), and for a negative test, 0.80 (CI: 0.39-1.61). [138]

Conclusion

- The modified wells score can effectively predict the probability of having lower limb deep vein thrombosis.
- The possibility of having lower limb deep vein thrombosis can be excluded in patients with an unlikely score on the wells rule.
- A higher score on the modified wells rule was associated with an increased probability of lower limb deep vein thrombosis.

- it is safe to assume that a score of <2 on the modified wells rule successfully rules out the possibility of having deep vein thrombosis in patients with clinical suspicion of deep vein thrombosis.
- The modified wells score has good efficiency. It successfully predicted the absence of lower limb deep vein thrombosis in 32 (43.40%) patients out of 74 who did not have deep vein thrombosis on a lower limb venous doppler scan.

Strengths of this study

It is one of the very few prospective studies conducted in India which studied the effectiveness of the modified wells score.

Drawbacks of this study

This was a cross-sectional study with a relatively small sample size. Randomization was not employed. Hence, further prospective studies and meta-analyses must be conducted in the Indian population to ascertain the validity of wells rule. Our study did not look at the confounding variables such as comorbid conditions. Effect of addition of d-dimer measurement wasn't studied.

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