Original Research

Investigating The Prognostic Significance Of Simplified Wells And Geneva Characteristics In Ascertaining Hospital Mortality (Prognostic Factor) In Patients With Acute Pulmonary Embolism

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Abstract

Background: Pulmonary embolism is considered to be one of the most prevalent causes of death that can be prevented in patients who are hospitalized. By implementing appropriate measures of treatment, it is possible to significantly diminish the mortality rate. Various clinical diagnostic protocols have been introduced to ascertain the presence of acute pulmonary embolism, including the Geneva scoring system, PERC criteria, PISAPED criteria, and the Wells scoring system. Nevertheless, no definitive evidence has been provided to substantiate the supremacy of any one of these methods over the others. In pursuit of this, the present investigation aimed to determine the predictive worth of the simplified Wells and Geneva criteria in establishing the mortality rate within the hospital setting, specifically focusing on patients with acute pulmonary embolism and normal blood pressure.

Method: This particular cohort study conducted in the year 2017 encompassed a group of 133 individuals above the age of 18 who were deemed suitable candidates for a diagnostic examination regarding acute pulmonary embolism. The selection criteria for these patients involved a combination of clinical diagnostic criteria, laboratory criteria (specifically D dimer), and imaging techniques (such as color Doppler ultrasound and CT angiography of the lung). Only those patients who were diagnosed with acute pulmonary embolism based on the evaluation of CT angiography results by a proficient radiologist were included in the study. The progress of all patients was subsequently monitored for a period of 30 days. During the follow-up of the patients, the main outcome that was examined was the mortality of the patient. The follow-up process was conducted either through phone contact or, in cases of re-hospitalization, by reviewing the patient's file. Pertinent demographic details such as age, gender, and symptoms observed during the visit were documented in the checklist. Subsequently, the patients' score was calculated based on the simplified Geneva and WELLS criteria, utilizing the information from the patient's file or through a revaluation of their medical history by a trained researcher.

Results: The mean scores of Wells and Geneva in the examined individuals were 5.02 ± 2.3 and 3.13 ± 1.2, correspondingly. 34.6% of patients with pulmonary thromboembolism necessitated re-hospitalization. 26.3% of patients expired with the primary diagnosis of pulmonary thromboembolism, and one decease was unrelated to embolism. Based on the conclusive outcome, the mean scores of Wells and Geneva indicated a statistically significant disparity in the mean scores of patients based on the requirement for re-hospitalization (P=0.001). The average Wells score of patients, considering their mortality, exhibited a statistically notable variation (P=0.001). The analysis of regression unveiled that mortality was associated with demographic factors as well as Wells and Geneva scores. Notably, increases in the Wells score (every 0.229 score increase) are independently and positively correlated with an elevation in mortality.

Conclusion: The findings of the current investigation have revealed that the Wells criteria possess the capability to ascertain the prognosis of patients with a reasonably elevated level of precision. The principal merit of the present study, as opposed to prior investigations, lies in its capacity to establish the cut off for the Wells and Geneva criteria.

Keywords: Geneva Score, Wells Score, Pulmonary embolism, Mortality.

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Introduction

Venous thromboembolism is regarded as one of the most prevalent avoidable origins of fatality among patients who are hospitalized. Numerous factors that pose a risk have been suggested to account for the occurrence of venous thromboembolism. These factors encompass old age, a history of deep vein thrombosis in the past, any element that induces venous stasis, any affliction that results in harm to the endothelium of blood vessels, such as surgical intervention and trauma, escalated coagulability of blood, the utilization of estrogen, and the malignancies he has enumerated (1). According to the findings of epidemiology, individuals who engage in the habit of smoking are exposed to an elevated susceptibility of acquiring venous thrombosis. Conversely, over fifty percent of the individuals who have been diagnosed with pulmonary embolism lack any identifiable risk factor (2). The practice of conducting genetic tests for the purpose of diagnosing thrombophilias is not appropriate within the emergency room setting. Under normal circumstances, the right ventricle of the heart functions to propel blood into the pulmonary vessels, which are characterized by their low resistance. The occurrence of pulmonary infarction can result in the manifestation of severe pleural pain. Despite the fact that a specific portion of the pulmonary arteries represents merely one-sixteenth of the overall pulmonary vascular system, the entrapment of blood clots within these deeper sections has the potential to induce necrosis in the lung tissue (3). Unlike chest pain, when asked carefully, 80% of pulmonary embolism patients mention a feeling of shortness of breath. Shortness of breath can be continuous and uncomfortable, or it can be intermittent and aggravated with movement (4). Pulmonary embolism has the ability to induce hypoxia; however, the extent of this hypoxia remains indeterminable. Approximately fifty percent of individuals afflicted with pulmonary embolism do not exhibit hypoxia. In the emergency department, half of the patients demonstrate a tachycardia exceeding one hundred beats per minute. The occurrence of tachycardia in cases of embolism stems from diminished left ventricular filling and compensatory responses akin to those observed in haemorrhagic shock. Merely fifty percent of patients report a respiratory rate surpassing twenty breaths per minute. It is crucial to note that the presence of normal vital signs does not necessarily exclude the possibility of pulmonary embolism (5). The absence of a pulse in patients with pulmonary embolism and cardiac arrest is frequently observed in their heart's electrical activity. Despite the presence of a witness and the administration of fibrinolytics, the estimated survival rate for these patients is approximately 20% (6). The diagnostic approach is carried out in individuals who may have pulmonary embolism, relying on clinical suspicion and specific standardized criteria. The estimation of clinical suspicion can be determined through the healthcare provider's clinical assessment and the utilization of scoring systems like Wells, Geneva, and Charlotte (1-3). Studies indicate that relying solely on clinical judgment, particularly the doctor's assessment of the likelihood of pulmonary embolism in a specific patient, lacks the necessary accuracy to categorize individuals into low, medium, and high-risk groups. Due to the inability to standardize or teach this approach, it is advisable to replace empirical judgment with well-defined diagnostic methods. Numerous diagnostic techniques have been proposed in the literature for identifying pulmonary embolism, such as the Geneva score system, PERC (Pulmonary Embolism Rule-out Criteria), the prospective investigative study of acute pulmonary embolism diagnosis (PISAPED) criteria, and the Wells scoring system (7). The efficacy of any of these approaches in relation to the others has yet to be substantiated. Furthermore, the significance of these standards in assessing the prognosis of patients has not been ascertained. Estimating mortality subsequent to pulmonary embolism can be accomplished by taking into account the patient's hemodynamic

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condition, right ventricular function as observed in echocardiography, CT scan findings, and PRO-BNP levels. The presence of myocardial damage in these patients can be linked to an elevated likelihood of death, a correlation that can be to some degree determined by assessing the serum troponin level (8). Soares' study in 2012 showed that Pulmonary Embolism Severity Index scores can accurately predict 90-day mortality in patients with pulmonary thromboembolism (9). In a study in Shiraz in 2015, Estvan showed that the simple and modified PESI scoring system is very efficient for determining the one-year prognosis of patients with pulmonary thromboembolism (10). In a separate investigation, Ferrer demonstrated in 2013 that the uncomplicated PESI scoring mechanism is highly effective in ascertaining the one-month forecast for individuals afflicted with pulmonary thromboembolism (11). Some studies have suggested the use of Wells and Genova diagnostic criteria as cost-effective and expedient approaches for predicting the prognosis of pulmonary thromboembolism. Consequently, the objective of this investigation is to ascertain the hospital mortality rate (a prognostic indicator) in individuals with acute pulmonary embolism and stable blood pressure. Additionally, we aim to compare the simplified Wells and Geneva criteria in these patients and identify the most suitable cut-off for these criteria.

Method

Study design:

This study, which took place in the year 2017, involved a prospective cohort of individuals diagnosed with pulmonary thromboembolism. The patients were referred to the emergency departments of both Imam Reza Hospital and Qaem Hospital in Mashhad. The selection of participants was based on non-probability and goal-oriented sampling methods.

Ethical considerations:

Prior to enrolling the patients in this investigation, the procedural aspects were elucidated and informed consent was duly obtained. Throughout all phases of the inquiry, the researchers strictly adhered to the ethical principles outlined in the Declaration of Helsinki and ensured the confidentiality of patient data. The financial obligations associated with this endeavor were entirely borne by the researchers, thereby imposing no additional financial burden upon the patients. The ethics committee of Mashhad University of Medical Sciences granted approval (IR.MUMS. FM.REC.1396.834) for this investigation, in accordance with the prescribed code of ethics.

Selection of patients:

Patients who were above the age of 18 and deemed suitable for a diagnostic examination to detect acute pulmonary embolism (specifically, pulmonary CT angiography) based on a combination of clinical diagnostic criteria, laboratory criteria (D dimer), or imaging (Color Doppler ultrasound) were specifically chosen for this study. Only those patients who were diagnosed with acute pulmonary embolism, as confirmed by the report of CT angiography results provided by an experienced radiologist, were included in the study. Patients who exhibited signs of hemodynamic instability (specifically, systolic arterial blood pressure equal to or less than 90 mm Hg), were pregnant, had a known sensitivity to contrast material, had a glomerular filtration rate of less than 30 ml/min, had a previously confirmed diagnosis of acute pulmonary thromboembolism, or were currently undergoing anticoagulant treatment at the time of enrolment were excluded from the study.

Analysis method:

Demographic information of patients, including age, sex, and symptoms at the time of visit, were recorded in the checklist, and then the score of the patients was calculated based on the simplified Geneva and WELLS criteria according to the information of the patient's file or taking a history again by a trained researcher.

Follow up:

All patients were monitored for a duration of 30 days. The principal measure examined during the patients' follow-up period pertained to their

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mortality. The follow-up process was conducted either via telephone or by reviewing the patient's medical records in the event of re-hospitalization. Complying with the regulations regarding autopsy procedures in Iran, cases where the patient's death resulted from an evident cause other than pulmonary embolism were categorized as deaths unrelated to pulmonary embolism, while instances of sudden and unexpected patient deaths were classified as possibly related. As for the secondary outcome, re-hospitalization within the 30-day follow-up period was attributed to pulmonary embolism, encompassing secondary cardiogenic shock, significant hemorrhaging, and the like. The prognostic significance of the simplified Wells and Geneva criteria was assessed based on the aforementioned outcomes.

Statistical analysis:

The statistical data derived from the patients was gathered, encoded, and statistically examined through the utilization of SPSS software, specifically version 16. The depiction of the data was achieved by employing descriptive statistical measures, such as frequency and mean + standard deviation. The comparison of qualitative variables was conducted using the Chi-square test, while the evaluation of quantitative variables was accomplished via the t-student test. In instances where these variables did not adhere to a normal distribution, the Mann-Whitney test was implemented. Regression analysis, as well as univariate and multivariate evaluation, were carried out to assess each individual component within the simplified Wells and Geneva criteria. Additionally, Rock's curve was calculated to determine the optimal threshold for identifying hospital mortality, along with its corresponding sensitivity and specificity. Notably, a significance level of less than 0.05 was employed for all tests.

Results

A total of 133 individuals were enrolled in this particular investigation. The mean age of these participants was 61.3 ± 14.1 years. Roughly 50.4% of the subjects were male, while the remaining 49.6% were female. When examining the studied patients, it was found that the average scores for both Wells and Genova were 5.02 ± 2.3 and 3.13 ± 1.2, respectively. In terms of pulmonary thromboembolism, approximately 34.6% of the patients required re-hospitalization. Furthermore, 26.3% of the patients experienced mortality as a result of their primary diagnosis being pulmonary thromboembolism, with one death being unrelated to embolism. Upon analyzing the final outcome in the studied patients, the average scores for Wells and Geneva indicated a statistically significant difference (P=0.001) in terms of the need for re-hospitalization. Similarly, the mean Wells score of the patients displayed a statistically significant difference (P=0.001) in relation to mortality. (Refer to Table 1 for further details).

Table 2 showed the regression analysis between mortality with demographic variables and Wells and Geneva scores. Changes in the Wells score (every 0.229 score increase) independently and positively cause an increase in mortality. The Pearson correlation coefficients between the final result factors and the Geneva and Wells scores were as follows:

Correlation between Wells score and mortality: P=0.001, r = 0.640 (Strong).

Correlation between Geneva score and mortality: P=0.001, r = 0.508 (Middle).

Correlation between Wells score and re-hospitalation: P=0.001, r = 0.415 (Weak)

Correlation between Geneva score and re-hospitalation: P=0.001, r = 0.438 (Weak).

And there was no correlation between the scores of Wells and Geneva with age and gender.

Figure 1 shows the rock curve for determining the appropriate cut-off point for the Wells and Geneva scores. ROC curve to investigate the sensitivity and specificity of the Wells score in predicting mortality (space under the curve 0.902). ROC curve to investigate the sensitivity and specificity of Geneva score in predicting mortality (space under the curve 0.819). Wells score of 5.75 with 88.6% sensitivity and 74.4% specificity predicts the death of patients. The Wells score of 11 with

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100% sensitivity and 98.8% specificity predicts the need to re-hospitalize patients. Geneva score of 3.5 with 74.3% sensitivity and 79.6% specificity predicts the death of patients. Geneva score 8 with 100% sensitivity and 100% specificity predicts the need to re-hospitalize patients. The area under the curve for the Geneva criterion is 0.819 and for the Wells criterion is 0.902, which indicates the higher accuracy of the Wells criterion in determining the mortality cut-off. According to the Rock curve, the Wells score has 100% sensitivity and 62% specificity for mortality, and a Wells score of 8 has 40% sensitivity and 100% specificity for mortality. In other words, in this study, all patients with a Wells score of 8 and above died within 30 days, and none of the patients with a Wells score of 3 and below died within 30 days (Figure 1).

Discussion

The area under the curve for the Geneva criterion is 0.819 and for the Wells criterion is 0.902, which indicates the higher accuracy of the Wells criterion in determining the mortality cut-off. Wells score of 5.75 with 88.6% sensitivity and 74.4% specificity predicts the death of patients. Wells score 8 has 40% sensitivity and 100% specificity for mortality. According to the data of this study, all patients with a Wells score of 8 and above died within 30 days, and none of the patients with a Wells score of 3 and below died within 30 days. Acute pulmonary thromboembolism is a significant cardiopulmonary disorder characterized by a broad spectrum of clinical manifestations, ranging from asymptomatic to life-threatening conditions. Numerous criteria have been established to assess the risk of pulmonary thromboembolism in patients, which can be valuable in predicting the prognosis of individuals with pulmonary embolism. The findings of the current investigation demonstrate that the Wells 8 score exhibits 100% specificity in prognosticating early mortality within the initial 30 days following the diagnosis of pulmonary thromboembolism. Furthermore, a Wells score of 5.75, accompanied by a sensitivity of 88.6% and a specificity of 74.4%, serves as a predictor for patient mortality. The prediction of patient mortality is facilitated by the Geneva score, which has a sensitivity of 74.3% and a specificity of 79.6%. In an extensive evaluation conducted by Shen in 2016, the Wells criteria demonstrated a sensitivity range of 63% to 79% and the Geneva criteria exhibited a sensitivity range of 55% to 73% for the detection of pulmonary embolism. However, Shen did not explore the prognosis of patients in this investigation (12). In a study by Angriman in 2015 in Argentina, high Wells scores were associated with mortality or recurrence of thromboembolic events (13), this finding is similar to the findings of the present study, but in Angriman 's study, unlike our study, no cut-off point was determined. In Tamizifar 's research in Isfahan, Geneva score did not play a role in determining the prognosis of patients with acute pulmonary embolism (14). In our investigation, a high Geneva score is indicative of the necessity for mortality with a considerable degree of sensitivity and specificity. In the preceding investigations, the original score of the indices was not employed, and the scores were categorized into two broad divisions of low probability and high probability, which holds the potential to exert an influence on the disparity observed in the outcomes. Furthermore, our investigation was conducted in an academic referral center and a substantial number of patients were admitted with elevated Wells and Geneva scores as well as a suboptimal general state, both of which may have an impact on the accuracy of the findings obtained. Based on the study population, the results obtained from the current investigation have the potential to be broadly applicable to patients with a high likelihood of developing pulmonary embolism. Presently, diagnosing pulmonary embolism is considered a critical matter, as healthcare professionals often struggle to make appropriate decisions regarding whether to continue hospitalization or discharge patients in a timely manner. The presence of straightforward criteria, such as the Wales and

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Geneva criteria, and the identification of an appropriate and precise cut-off point can significantly expedite patient assignments, particularly within the emergency department. The European Society of Cardiology has underscored the importance of utilizing Pro BNP, markers indicating myocardial damage, and indicators of right ventricular dysfunction as factors influencing the prognosis of individuals with pulmonary embolism (14). However, the cost of these invoices is high and they are not readily accessible in numerous healthcare facilities. Our research demonstrated that the clinical standards utilized in Wells and Geneva, despite their simplicity and cost-effectiveness, can be linked to a satisfactory level of precision in evaluating the outlook of individuals diagnosed with pulmonary embolism. In a separate study conducted by Hosseini, it was found that the overall mortality rate associated with pulmonary thromboembolism reached 17.6% (15). In our investigation, a mortality rate of 26.3% was observed among patients who were diagnosed primarily with pulmonary thromboembolism, with the exception of one fatality that was not attributed to embolism. In the research conducted by Soares, it was found that 6.3% of patients experienced fatal outcomes within a 90-day timeframe as a result of pulmonary thromboembolism (9). The potential cause of the observed discrepancies could potentially be associated with the specific research center and the methodology employed for patient screening. Considering the outcomes of this investigation as well as previous studies, and acknowledging the adverse effects and complications arising from the occurrence of thromboembolism in the pulmonary vessels, the following recommendations are proposed to mitigate the resultant fatalities and disabilities: a) Minimizing the duration of hospitalization for patients, particularly in cases involving complete immobility. b) Employing supportive interventions in hospitalized individuals, such as implementing physical therapy regimens for organ functionality. c) Utilizing anticoagulant medications in patients with prolonged hospitalization or those who possess risk factors for thrombosis. d) Promptly initiating therapeutic interventions in patients exhibiting potential diagnosis of pulmonary thromboembolism, thereby mitigating the ensuing impairments and averting supplementary financial burdens on both the patient and society (16). If the positive outcome of this investigation is validated, through broader multi-center investigations, the diagnostic criteria of Wells and Geneva, which are routinely employed to assess the likelihood of patients experiencing acute pulmonary thromboembolism, could be employed to categorize patients into high-risk and low-risk cohorts. Establishing the low-risk patients is particularly advantageous for continuing their treatment in an outpatient setting, thereby diminishing the treatment expenses and patient mortality rates. Moreover, it holds a distinct significance in conserving financial resources and reducing hospital bed occupancy. Conversely, recognizing the high-risk patients can facilitate their early transfer to specialized care units and curtail the mortality rate within this specific group.

Limitations and weaknesses and strengths:

1- Due to conducting the study in referral educational centers, the generalizability of the results is reduced.

2- Low sample size

3- Failure to examine the volume or size of the embolus, because it was mentioned as an effective factor in mortality in previous studies.

Conclusion:

A large number of investigations have been conducted on the Wells and Geneva criteria and their correlation with pulmonary thromboembolism. Multiple articles have demonstrated that the Wells score stands as a potent criterion for identifying individuals with pulmonary embolism. Our study reveals that this criterion possesses the capability to ascertain the prognosis of patients with a relatively high level of accuracy. The pivotal advantage of the current study lies in its ability to establish the cut-off point

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for the Wells and Geneva criteria, surpassing previous research endeavors.

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Table & Figure:

Table 1: Comparison of the average score of Wells and Genova patients based on the need for re-hospitalization and mortality

Mean score of Wells and Geneva based on the need for re-hospitalization and mortality			Mean ± standard deviation	**P value**
Wells	Need for re-hospitalization	Yes	6.3±1.6	0.001
		No	4.3±2.3	
	Mortality	Yes	7.4±1.8	0.001
		No	4.1±1.7	
Geneva	Need for re-hospitalization	Yes	3.8±1.1	0.001
		No	2.7±1.1	
	Mortality	Yes	4.1±1.1	0.001
		No	2.7±1	

Table 2: Regression analysis between mortality with demographic variables and Wells and Geneva scores

Regression analysis between mortality and demographic variables	Coefficient β	95% confidence interval	P-value
Wells score	0.229	0.006- 0.088	0.024
Geneva score	0.293	0.037-0.191	0.004

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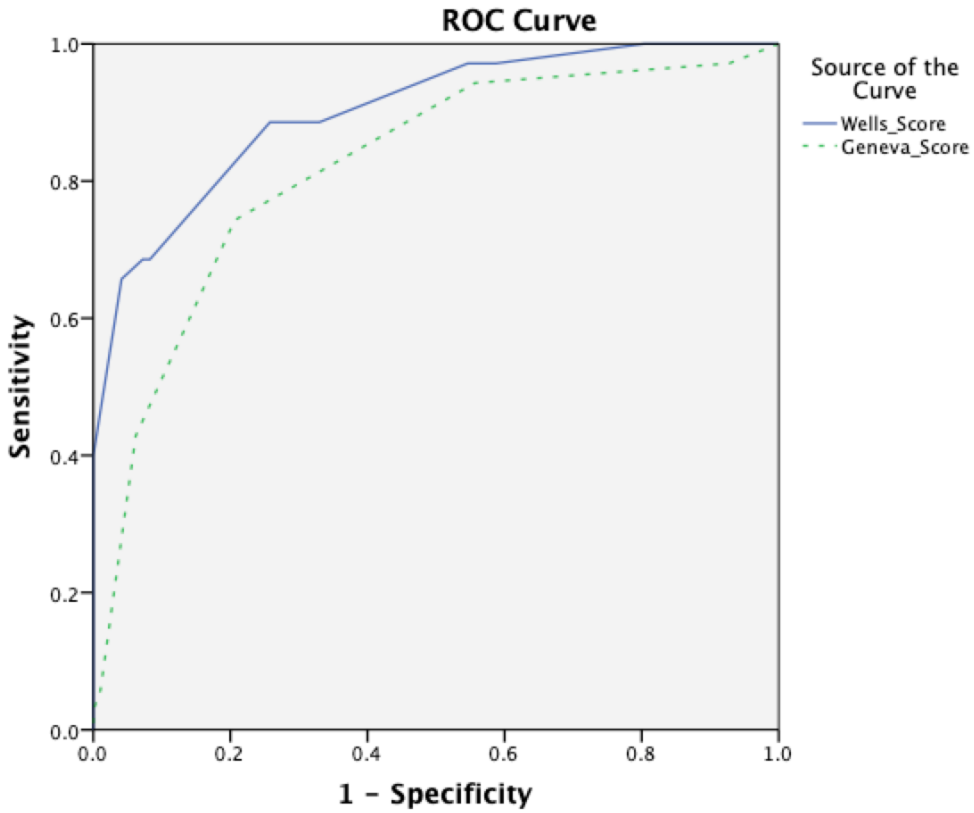


Figure 1: Rock curve for determining the appropriate cut-off point for Wells and Geneva scores

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