Prevalence and Predictors of Pulmonary Embolism in Patients with Acutely Decompensated Heart Failure

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Abstract

Background: The prevalence of pulmonary embolism (PE) has not been reported in patients hospitalized due to classical findings of decompensated heart failure (HF).

Objective: To describe the prevalence of PE and to assess the diagnostic accuracy of the Wells and Geneva scores in patients hospitalized due to HF.

Methods: Patients hospitalized primarily due to HF underwent systematic ventilation-perfusion lung scan, and PE was defined by a result of high probability. Aiming at interpreting, low clinical probability of PE was defined as prevalence < 5%, according to the literature. When calculating the sample size, 49 patients were required to provide a 95% confidence interval with ±10% accuracy, estimating an a priori prevalence of 15%.

Results: Of 51 patients studied, six had a high probability of PE on lung scan, resulting in 12% prevalence (95% CI = 5% - 23%). The Wells and Geneva scores had an area under the ROC curve of 0.53 (95% CI = 0.27 – 0.80; p = 0.80) and 0.43 (95% CI = 0.13 – 0.73; p = 0.56), respectively, indicating lack of accuracy for the diagnosis of PE. Alternatively, variables related to HF showed a tendency towards association with PE, and an exploratory model formed by that type of variable showed diagnostic accuracy for PE (ROC = 0.81; 95% CI = 0.66 – 0.96; p = 0.01).

Conclusion: (1) Despite the lack of primary suspicion, patients admitted with HF have intermediate clinical probability of concomitant PE; (2) the scores usually used to estimate the clinical probability of PE do not apply to the population with HF, and future predictive models should consider variables related to that syndrome. (Arq Bras Cardiol 2012;98(2):120-125)

Keywords: Pulmonary embolism / mortality; prevalence; heart failure; inpatients.

Introduction

Heart failure is a syndrome that predisposes to pulmonary embolism, because of venous stasis, increased blood viscosity, hypercoagulability, patients' immobility, and more advanced age than that of the general population[1]. Acutely decompensated heart failure is a highly lethal condition, whose prognosis is even worse when the patient develops pulmonary embolism[2]. A recent study has shown that 9% of the patients admitted with heart failure develop pulmonary embolism during hospitalization, which has been called incidence[3]. However, the prevalence of pulmonary embolism in patients admitted due to decompensated heart failure is unknown, because no study has been carried out with a systematic and independent diagnostic assessment of the clinical outcome. Knowing the prevalence of pulmonary embolism might influence the medical investigation management of those patients.

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Manuscript received July 01, 2011; revised manuscript received July 18, 2011; accepted July 20, 2011.

Part of the investigation of pulmonary embolism consists in assessing pretest probability. Predictive models, such as the Wells[4] and Geneva[5] scores, have derived from studies performed in patients suspected of having pulmonary embolism. Those scores, however, have never been validated in a specific population with heart failure, and the ideal model to clinically predict pulmonary embolism in that condition remains unknown.

This study aimed first at determining the prevalence of pulmonary embolism in patients primarily hospitalized due to heart failure, and second at testing the accuracy of the Wells and Geneva scores in that clinical condition. Thus, the patients admitted due to well-characterized decompensated heart failure underwent ventilation-perfusion lung scan.

Methods

Sample selection

This study included individuals consecutively admitted to the Coronary Unit primarily due to decompensated heart failure, for nine months, as of January 2009. To be included in the study, the patients had to have at least one of the three

following characteristics for at least two weeks: (1) dyspnea at rest associated with significant pulmonary congestion on chest X-rays; (2) evident peripheral congestion (edema); (3) low cardiac output evidenced by hypotension (systolic blood pressure < 90 mm Hg) associated with a reduction in the level of consciousness, oliguria (diuresis < 0.5 mL/kg/h) or metabolic acidosis demonstrated through laboratory exams. Those conditions should be clearly explained by heart failure, with no other alternative cause presenting itself as most likely. The following exclusion criteria were defined: (1) impossibility to undergo lung scan and (2) patient's refusal to participate in the study.

Following that protocol, 73 consecutive patients met the inclusion criteria during the period studied. Of those 73 patients, 22 were excluded because they either refused to participate in the study, or had no clinical condition to undergo lung scan, or that exam was not available on hospital admission. Thus, 51 patients comprised the final sample of this study.

Study protocol

Data were prospectively collected, with a detailed recording of clinical history, physical examination, results of electrocardiography, and laboratory and imaging exams. After admission, the patients underwent ventilation-perfusion lung scan, whose interpretation was blind regarding the clinical findings and met the predefined criteria of the PIOPED study[6]. The results of the ventilation-perfusion lung scan were as follows: (1) normal; (2) low probability of pulmonary embolism; (3) moderate probability of pulmonary embolism; or (4) high probability of pulmonary embolism. Presence of pulmonary embolism was defined as the finding of high probability on scintigraphy[7], and any other result was considered negative for pulmonary embolism. High probability on lung scan was defined in the PIOPED study as at least two large perfusion defects, with no correspondence in ventilation, or one large perfusion defect and two moderate perfusion defects, with no correspondence in ventilation[6].

The Wells and Geneva scores, which represent validated models to estimate the clinical probability in patients with suspected pulmonary embolism, were calculated by using admission data. The Wells score comprises seven variables as follows: previous history of venous thromboembolism (1.5 point); recent immobilization (1.5 point); cancer (1 point); hemoptysis (1 point); heart rate > 100 bpm (1.5 point); clinical signs of deep venous thrombosis (3 points); alternative diagnosis less likely than pulmonary embolism (3 points). The interpretation of the Wells score is as follows: sum ≤ 1 point indicates low probability of pulmonary embolism; sum between 2 and 6 points indicates intermediate probability; and sum ≥ 7 points indicates high probability[4]. The Geneva score comprises eight variables as follows: age > 65 years (1 point); previous history of venous thromboembolism (3 points); recent immobilization (2 points); cancer (2 points); hemoptysis (2 points); heart rate ≥ 95 bpm (5 points) or between 75 and 94 bpm (3 points); clinical signs of deep venous thrombosis (4 points); and unilateral lower limb pain (3 points). The interpretation of the Geneva score is as follows: sum ≤ 3 points indicates low probability; sum between 4 and 10 points indicates intermediate probability; and sum ≥ 11 points indicates high probability[5].

Data analysis

The sample size was calculated aiming at determining the prevalence of pulmonary embolism. To obtain a 20% (± 10%) amplitude of the confidence interval of prevalence (accuracy), estimating an *a priori* 15% prevalence, we calculated that the minimal sample of 49 patients would be necessary to calculate a 95% confidence interval.

The prevalence of pulmonary embolism was represented as relative frequency, and the accuracy of that estimate was described by the 95% confidence interval. For interpreting the prevalence found, definitions originating from the validation study of the Wells score were used. In that study, the prevalence of pulmonary embolism in individuals with low probability according to the Wells score was 3.4%, with 95% confidence interval between 2.2% and 5%[4]. Thus, a confidence interval greater than 5% would represent a population with an at least intermediate pretest probability of pulmonary embolism.

To assess the diagnostic accuracy of the Wells and Geneva scores, Receiver Operating Characteristic (ROC) curves were drawn, considering the diagnosis of pulmonary embolism on scintigraphy as reference. An area under the ROC curve statistically different from 0.5 defined diagnostic accuracy. In addition, an arbitrary score was created based on variables of heart failure, which were more frequent in patients with pulmonary embolism, and one point was attributed to each variable present. That score was tested by use of the area under the ROC curve. That last analysis had a merely exploratory character, functioning as an initial test of the idea that a specific score of variables related to heart failure would be adequate to assess the probability of pulmonary embolism in that clinical setting.

As a general rule, numeric variables of normal distribution were described as mean and standard deviation, while those of non-normal distribution were described as median and interquartile range. Frequencies were described in a relative form, as percentages. The SPSS Statistical Software (Version 9.0, SPSS Inc., Chicago, Illinois, USA) and MedCalc Statistical Software (Version 9.3.2.0, MedCalc Software, Mariakerke, Belgium) were used for data analysis. Statistical significance was defined as p values < 0.05.

Results

Characteristics of the sample

The study assessed 51 patients (41% males), whose mean age was 70 ± 15 years. The most frequent type of acute heart failure presentation was pulmonary congestion, observed in 88% of the cases. In the minority, the hospitalization was motivated by either systemic congestion (6%) or low cardiac output (6%). Thus, this sample is predominantly comprised by patients with left ventricular failure. The most frequent etiologies were hypertensive and ischemic heart diseases (35%

and 29%, respectively), and the least frequent etiologies were represented by those classified as idiopathic or patients with valvular or Chagas disease. According to the echocardiographic assessment, the sample was balanced between preserved left ventricular ejection fraction, present in 55% of the patients, and reduced ejection fraction in the remaining patients. Systolic left ventricular dysfunction at least of moderate degree (ejection fraction < 45%) was present in 37% of the sample. Thus, in this consecutive sample of patients admitted with typical findings of heart failure, those with preserved or slightly impaired systolic function predominated. The other clinical characteristics of the sample are shown in Table 1.

Table 1 – Clinical characteristics of the sample studied

Sample characteristics	
Sample size	51
Age (years)	70 ± 15
Male sex	21 (41%)
Chronic anticoagulation	7 (14%)
Clinical manifestation	
Pulmonary congestion	45 (88%)
Systemic congestion	3 (6%)
Low output	3 (6%)
Etiology of heart failure	
Hypertensive	18 (35%)
Ischemic	15 (29%)
Idiopathic	8 (16%)
Valvular	6 (12%)
Chagas disease	4 (8%)
Left ventricular function	
Ejection fraction ≥ 55%	28 (55%)
Ejection fraction = 45% - 54%	4 (8%)
Ejection fraction ≤ 45%	19 (37%)
Prothrombotic conditions	
Wells score	0 (0 – 1.5)
Cancer	2 (4%)
Previous thromboembolism	1 (2%)
Immobilization	4 (8%)
Chronic atrial fibrillation	12 (24%)
Obesity	2 (4%)

Wells score shown as median (interquartile range).

Prevalence of pulmonary embolism

The median time elapsed between admission and lung scan was two days (interquartile range = 1 - 3). Ventilation-perfusion lung scan was categorized as of high probability for pulmonary embolism in six patients, resulting in a 12% prevalence, with 95% confidence interval between 5% and 23%. That limit of accuracy is greater than the confidence interval of the pulmonary embolism prevalence of patients classified as of low pretest probability in the study that validated the Wells score[4]. Thus, the prevalence found indicates that the probability of pulmonary embolism in patients admitted with acutely decompensated heart failure is intermediate. In addition, two other patients had perfusion alterations compatible with intermediate probability on scintigraphy, and most of the remaining patients were classified as having low probability scintigraphy.

Prediction of pulmonary embolism

The Wells score had an area under the ROC curve of 0.53 (95% CI = 0.27 – 0.80; p = 0.80), indicating lack of the capacity to discriminate patients with or without pulmonary embolism, taking lung scan as the reference pattern (Figure 1). The median of that score was zero (interquartile range = 0 – 1.5). Regarding the probability of pulmonary embolism, no patient was classified as of high probability (≥ 7 points), only four patients (8%) were classified as of intermediate probability (2 – 6 points), and most patients were classified as of low probability (< 2 points). That resulted from the fact that the variables of the Wells score were less frequent in that population with well-defined criteria of heart failure. This is shown in Table 1, where all variables have prevalence lower than 10%, except for high heart rate, which occurred in 22% of the patients.

Similarly, the Geneva score showed no diagnostic capacity for pulmonary embolism, with an area under the ROC curve of 0.43 (95% CI = 0.13 – 0.73; p = 0.56) (Figure 1). The median of that score was 4 (interquartile range = 3 – 6). Only two patients (4%) were classified as of high probability, 63% as of intermediate probability, and the remaining as of low probability. According to the Geneva score, a larger number of patients was classified as of intermediate probability than in the Wells score, because of the presence of the variables age > 65 years and heart rate ≥ 75 bpm, whose frequencies were 73% and 81%, respectively. Nevertheless, those variables have not contributed to the discriminatory capacity of the Geneva score, whose area under the ROC curve was not greater than that of the Wells score.

In a merely exploratory analysis, specific characteristics of the heart failure syndrome (contained in neither the Wells nor the Geneva scores) that could identify pulmonary embolism were more frequent in patients with the disease than in those without the disease as follows: inapparent cause of decompensation; lack of pulmonary congestion; lack of chronic anticoagulation; and right ventricular systolic dysfunction. Regarding the characteristics related to heart failure severity, serum sodium below the median value was more frequent in patients with pulmonary embolism, unlike moderate/severe left ventricular systolic dysfunction and chronic atrial fibrillation (Table 2). The characteristics associated with embolism were gathered as a score (1 point for the presence of each variable), which showed a satisfactory capacity for diagnosing pulmonary embolism on scintigraphy, represented by an area under the ROC curve of 0.81 (95% CI = 0.66 – 0.96; p = 0.01).

Discussion

The present study is the first systematic assessment of the presence of pulmonary embolism in patients admitted primarily due to decompensated heart failure. The two major and original observations of this study were as follows: first, the prevalence of pulmonary embolism is around 12%; second, the scores that estimate the pretest probability of pulmonary embolism do not apply to patients with acutely decompensated heart failure.

The greatest originality of this study lies in the target population assessed, which is not formed by patients suspected of having pulmonary embolism. On the contrary, the inclusion criteria were carefully defined so that the sample consisted of patients with classical findings of acutely decompensated heart failure. In that type of patients, neither the concomitance with the diagnosis of pulmonary embolism, nor the need for systematic investigation is known. The result found allows for some inferences regarding those questions.

Initially, we need to interpret the 12% prevalence of pulmonary embolism found, knowing that the sample size of the study allowed for a precision between 5% and 23% for that estimate. The study that validated the main model of the assessment of pretest probability in patients suspected of having pulmonary embolism has demonstrated prevalence of only 3.5% for patients defined as of low probability, with 95% confidence interval between 2.2% and 5%[4]. Thus, the limits of accuracy of the prevalence found in the present study indicate that having decompensated heart failure characterizes the patient as having intermediate probability for concomitant pulmonary embolism. Initially this might seem counterintuitive, because those patients meet clear criteria for heart failure. However, the diagnosis of pulmonary embolism does not exclude the presence of heart failure; it is a concomitant disease, which might even represent the decompensation factor of heart failure. In our study, the absence of an apparent cause for decompensation was more frequent in patients with pulmonary embolism. Thus, pulmonary embolism might be an occult factor for heart failure decompensation.

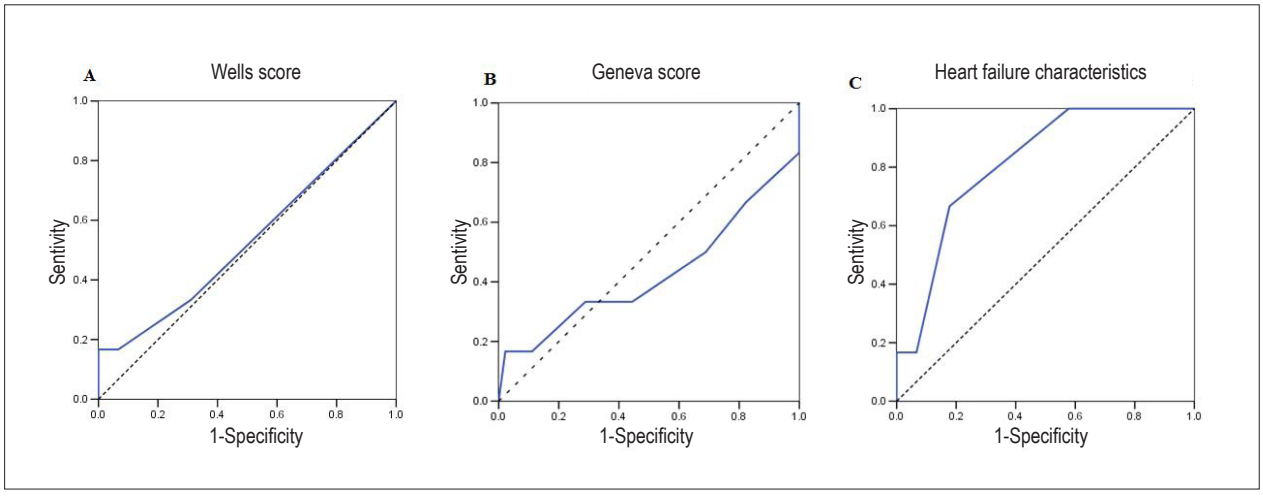

Figure 1 – *Panels A and B indicate the lack of diagnostic accuracy of the Wells and Geneva scores: area below the ROC curve of 0.53 (95% CI = 0.27 - 0.80; P = 0.80) and 0.43 (95% CI = 0.13 - 0.73; P = 0.56), respectively. Panel C indicates that the model created based on the characteristics of heart failure has diagnostic accuracy (ROC = 0.81; 95% CI = 0.66 - 0.96; P = 0.01).*

Table 2 – Exploratory analysis of the characteristics of heart failure related to the diagnosis of pulmonary embolism

	Lung scan diagnosis	
	With embolism	No embolism
Age (years)	69 ± 16	70 ± 15
Inapparent cause of decompensation	4 (67%)	17 (38%)
No pulmonary congestion	2 (33%)	4 (9%)
No chronic anticoagulation	1 (25%)	6 (16%)
RV systolic dysfunction	2 (33%)	6 (13%)
Serum sodium < median	4 (67%)	16 (36%)
Ejection fraction < 45%	2 (33%)	17 (38%)
Atrial fibrillation	1 (17%)	11 (24%)

RV - right ventricle.

Secondly, the implication of that prevalence in clinical practice should be inferred. Considering that patients with decompensated heart failure have an intermediate probability of pulmonary embolism, the indication of imaging tests to investigate that condition should be more frequent than it usually is for those individuals. Because of the lack of findings like the one presented in this study, the search for embolism is not routinely recommended in patients with classical acute heart failure[8,9], but it is recommended in those whose clinical findings are dubious regarding the primary origin of symptoms. The indication might not exist for any patient with heart failure, but for a subgroup of patients in whom the concomitance of embolism is frequent. In an exploratory and only preliminary form, our findings suggest that characteristics such as lack of apparent cause for decompensation, right ventricular dysfunction, and lack of pulmonary congestion (findings of systemic congestion or low output) can be predictive variables.

Regarding the identification of patients predisposed to concomitant pulmonary embolism, Piazza and Goldhaber[10] have recently suggested the application of the Wells score to those with heart failure, aiming at identifying the group to be investigated with imaging tests. Our findings are contrary to that recommendation, which has not been based on evidence of accuracy of the Wells score. We demonstrated that the classical scores to estimate the probability of pulmonary embolism (Wells and Geneva) do not have diagnostic accuracy in patients with heart failure, and this finding has not been reported in the literature. This is due to the fact that the presence of the variables of those scores is low in patients with acutely decompensated heart failure, suggesting that the predictive variables of embolism in that type of patient might be different. Thus, the identification of a subgroup to be investigated should not consider those scores, and predictive models should derive from populations with heart failure. Only for the purpose of preliminary analysis, we simulated a model based on the characteristics of the heart failure syndrome that were more associated with embolism. This analysis suggested that this is the way to find a probabilistic score. Given that the score assessed suggested the concept of risk prediction in that clinical context, it should not be considered since it has not been validated for clinical use.

Regarding studies previously published about that issue, Darzé et al[3] have originally reported the incidence of pulmonary embolism in patients admitted with acutely decompensated heart failure. Those authors have described the appearance of pulmonary embolism during hospitalization, and, thus, the investigation depended on new symptoms appearing over disease progression. Thus, the search for embolism was not systematic, and prevalence on admission was not the focus of that study. Gromadzinski et al[11,12] have carried out a systematic research on embolism with tomography, but the sample was not characterized by overt heart failure, but by cases whose diagnoses of embolism and heart failure were concomitant, and the probability of the former was at least intermediate. The present study is the first to systematically study embolism, and it reassures the importance of the problem in an original form, demonstrating that the condition can be present since admission, regardless of the appearance of new symptoms. In fact, some incident cases of embolism can be truly prevalent cases since admission.

The major limitation of this study is the sample size. That is why we reported, in addition to punctual prevalence, its confidence interval, which provides the exact notion of the accuracy of our estimate. The accuracy presented allowed some original inferences about the pretest probability of embolism. However, we should recognize that those are preliminary data, and future studies should confirm our conclusions. In addition, the diagnosis of pulmonary embolism should result from the interaction between data of clinical presentation and results of imaging tests[6]. However, the clinical findings were not part of the definition of pulmonary embolism in the present study. Although this might seem a methodological bias, there is no model of pretest probability definition for a population with typical manifestation of heart failure. As demonstrated, if classical pretest probability was used as part of the definition of the disease, the diagnostic conclusion would always be undefined. In fact, the low pretest probability common to patients of a sample characterized by typical manifestations of heart failure would lead to a post-test probability at most intermediate.

In conclusion, the present study originally suggests that patients admitted with acutely decompensated heart failure have an intermediate probability of concomitant pulmonary embolism. The classical models for estimating the pretest probability of pulmonary embolism are not applicable to the type of patients in question. Future studies are required to validate new predictive models and assess the benefit of systematic research on embolism in subgroups of patients primarily admitted due to heart failure.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any post-graduation program.

References

1. Gibbs CR, Blann AD, Watson RDS, Lip GYH. Abnormalities of hemorheological, endothelial, and platelet function in patients with chronic heart failure in sinus rhythm: effects of angiotensin-converting enzyme inhibitor and beta-blocker therapy. Circulation. 2001;103(13):1746-51.

2. Darzé ES, Latado AL, Guimaraes AG, Guedes RA, Santos AB, de Moura SS, et al. Acute pulmonary embolism is an independent predictor of adverse events in severe decompensated heart failure patients. Chest. 2007;131(6):1838-43.

3. Darzé ES, Latado AL, Guimaraes AG, Guedes RA, Santos AB, de Moura SS, et al. Incidence and clinical predictors of pulmonary embolism in severe heart failure patients admitted to a coronary care unit. Chest. 2005;128(4):2576-80.

4. Wells PS, Ginsberg JS, Anderson DR, Kearon C, Gent M, Turpie AG, et al. Use of a clinical model for safe management of patients with suspected pulmonary embolism. Ann Intern Med. 1998;129(12):997-1005.

5. Le Gal G, Righini M, Roy PM, Sanchez O, Aujesky D, Bounameaux H, et al. Prediction of pulmonary embolism in the emergency department: the revised Geneva score. Ann Intern Med. 2006;144(3):165-71.

6. Value of the ventilation/perfusion scan in acute pulmonary embolism: Results of the prospective investigation of pulmonary embolism diagnosis (PIOPED). The PIOPED Investigators. JAMA. 1990;263(20):2753-9.

7. Stein PD, Fowler SE, Goodman LR, Gottschalk A, Hales CA, Hull RD, et al. Multidetector computed tomography for acute pulmonary embolism. N Engl J Med. 2006;354(22):2317-27.

8. Sociedade Brasileira de Cardiologia. II Diretrizes brasileiras de insuficiência cardíaca aguda. Arq Bras Cardiol. 2009;93(3):2-65.

9. Weintraub NL, Collins SP, Pang PS, Levy PD, Anderson AS, Arslanian-Engoren C, et al. Acute heart failure syndromes: emergency department presentation, treatment, and disposition: current approaches and future aims: a scientific statement from the American Heart Association. Circulation. 2010;122(19):1975-96.

10. Piazza G, Goldhaber SZ. Pulmonary embolism in heart failure. Circulation. 2008;118(15):1598-601.

11. Gromadzinski L, Ciurzynski M, Januszko-Giergielewicz B, Targonski R, Cyganski P, Pruszczyk P. Diagnostic value of mitral and tricuspid annular excursion in the diagnostics of acute pulmonary embolism patients with chronic heart failure. Int J Cardiol. 2011;149(1):118-9.

12. Gromadzinski L, Targonski R. The role of tissue colour Doppler imaging in diagnosis of segmental pulmonary embolism in congestive heart failure patients. Kardiol Pol. 2007;65(12):1433-9.