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Prognostic value of the Geneva prediction rule in patients with pulmonary embolism

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ABSTRACT

Background: Assessment of pre-test probability of pulmonary embolism (PE) and prognostic stratification are two widely recommended steps in the management of patients with suspected PE. Some items of the Geneva prediction rule may have a prognostic value.
We analyzed whether the initial probability assessed by the Geneva rule was associated with the outcome of patients with PE.
Methods: In a *post-hoc* analysis of a multicenter trial including 1,693 patients with suspected PE, the all-cause death or readmission rates during the 3-month follow-up of patients with confirmed PE were analyzed. PE probability group was prospectively assessed by the revised Geneva score (RGS). Similar analyses were made with the *a posteriori*-calculated simplified Geneva score (SGS).
Results: PE was confirmed in 357 patients and 21 (5.9%) died during the 3-month follow-up. The mortality rate differed significantly with the initial RGS group, as with the SGS group. For the RGS, the mortality increased from 0% (95% Confidence Interval: [0–5.4%]) in the low-probability group to 14.3% (95% CI: [6.3-28.2%]) in the high-probability group, and for the SGS, from 0% (95% CI: [0–5.4%] to 17.9% (95% CI: [7.4-36%]). Readmission occurred in 58 out of the 352 patients with complete information on readmission (16.5%). No significant change of readmission rate was found among the RGS or SGS groups.
Conclusions: Returning to the initial PE probability evaluation may help clinicians predict 3-month mortality in patients with confirmed PE.

(ClinicalTrials.gov: NCT00117169)

Introduction

Pulmonary embolism (PE) is the third leading cause of mortality from cardiovascular disease, after coronary artery disease and stroke. The approach to diagnose PE has considerably improved over the past two decades and is nowadays mainly based on non-invasive diagnostic strategies including clinical probability assessment, D-dimer measurement and multidetector computed tomography (CT) angiography. Initial risk stratification of patients with confirmed PE is also recommended to distinguish between patients with high and non-high-risk of PE-related early mortality [1]. Several scores are available or have been recently proposed: the Geneva prognostic score [2], the Pulmonary Embolism Severity Index (PESI) [3] and its simplified version [4], and the PREP index [5]. All these scores are aimed at predicting adverse outcomes as 30-day mortality (PESI) [3] or combined outcomes at 30 days (death, secondary cardiogenic shock, or recurrent venous thromboembolism in the PREP Study [5]) or 3 months (death, recurrent thromboembolic event, or major bleeding in Wicki's Geneva prognostic score study [2]). Patients at high-risk (e.g. hemodynamic collapse) excepted, stratification is particularly aimed at identifying low-risk patients for whom ambulatory treatment may be considered [6]. However, despite international recommendations, this stratification process is

Abbreviations: CI, confidence intervals; CT, computed tomography; MDCTA, multidetector computed tomography angiography; OR, Odds Ratio; PE, Pulmonary embolism; PESI, Pulmonary Embolism Severity Index; RGS, Revised Geneva Score; SGS, Simplified Geneva Score; V/Q, ventilation-perfusion scintigraphy.

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far from being routinely used. There may be several reasons for this, such as the need for biological tests (e.g. troponin) or echocardiography data, lack of time, and often lack of awareness of scores… Alternatively, clinical probability assessment appears to be more frequently used in daily practice [7]. Several scores have been proposed: the Wells score [8,9], the Charlotte rule [10], the PISA score [11]. The Revised Geneva Score (RGS) is one well-validated diagnostic rule [12,13], allowing for objective clinical probability evaluation in patients with clinically suspected PE.

As some items of the RGS are also included in the above-mentioned prognostic rules, we studied whether this diagnostic rule was associated with the prognosis of non-high-risk patients with confirmed PE and especially 3-month mortality.

Material and Methods

Patients and setting

Data were collected in a prospective, randomized, multicenter clinical trial which evaluated a diagnostic strategy for PE, combining clinical probability assessment, plasma D-dimer measurement (ELISA) and multidetector computed tomography angiography (MDCTA) with or without lower limb venous compression ultrasonography [13] (see appendix for diagnostic algorithm).

Eligible subjects were consecutive adult outpatients admitted to the emergency department for clinically suspected PE (defined as acute onset of new or worsening shortness of breath or chest pain without any other obvious etiology) at six university hospitals in Switzerland, France and Belgium between January 1, 2005, and August 31, 2006. Exclusion criteria were: contraindication to MDCTA (i.e. allergy to iodine contrast agents, creatinine clearance of less than 30 ml/minute, or pregnancy), previous documented diagnosis of PE on presentation, terminal illness with expected survival of less than three months and ongoing anticoagulant therapy on presentation.

The patients' clinical probability of PE was initially assessed using the RGS [12] (Table 1), followed by the PE diagnostic work-up, detailed elsewhere [13] (see appendix for diagnostic algorithm). The patients analyzed were those with confirmed PE and where 3-month status was known (death or readmission).

In short, PE was confirmed in case of i) positive MDCTA (intraluminal defect or vessel totally occluded by low-attenuation material during MDCTA); ii) high-probability ventilation-perfusion (V/Q) scintigraphy in patients with inconclusive MDCTA or a high clinical probability with a negative MDCTA; iii) positive angiography; iv) proximal deep-venous thrombosis in a patient with clinically suspected PE (diagnostic algorithm shown in Appendix).

Table 1
Revised and Simplified version of the Geneva Score.

Items of the Revised Geneva Score	Points for Revised Version	Points for Simplified Version
Age > 65 years old	1.0	1.0
Previous history of PE or DVT	3.0	1.0
Surgery or fracture within 1 month	2.0	1.0
Active malignancy	2.0	1.0
Unilateral leg pain	3.0	1.0
Hemoptysis	2.0	1.0
Heart rate (bpm)		
75-94	3.0	1.0
≥95	5.0	1.0
Pain on lower-limb deep venous palpation and unilateral oedema	4.0	1.0
Low probability	0-3	0-1
Intermediate probability	4-10	2-4
High probability	≥11	≥5

The Simplified Geneva Score [14] (in which each item has the same weight) and the Pulmonary Embolism Severity Index (PESI) (for which all the items were prospectively collected) [3] were calculated *a posteriori* for each patient.

All patients underwent follow-up at 3 months. They were instructed to come back to the clinic in case of recurrent symptoms of the respiratory tract or legs. At the end of the follow-up, all the patients included were asked by telephone to declare any health-related events (in particular any admission to hospital) during the 3-month period. The family physician was contacted whenever a possible event was declared. Medical data were analyzed if a patient was readmitted to hospital for any cause or death during follow-up. Deaths were adjudicated as related, possibly related, or unrelated to pulmonary embolism. Death was judged to be related to pulmonary embolism if confirmed by autopsy, or if subsequent to clinically severe pulmonary embolism, either initially or after a recurrent, objectively confirmed event. Sudden or unexpected death was classified as possibly related to pulmonary embolism. Unrelated deaths were due to an obvious cause other than pulmonary embolism. Three blinded, independent experts adjudicated the outcome events.

Written informed consent was obtained from all patients. The study was approved by the Ethics committees of the Geneva and Lausanne University Hospitals for Switzerland, Brest University Hospital for the French centers and Saint-Luc University Hospital for Brussels. This study was registered at Clinical Trials.gov, number NCT00117169.

Study outcomes

The primary outcome was 3-month all-cause mortality, according to each probability category obtained with the RGS (low/intermediate/high), in patients with confirmed PE.

Secondary outcomes were 3-month all-cause readmission rates (according to each probability category obtained with the RGS).

Both primary and secondary outcomes were also analyzed according to each probability category obtained with the Simplified Geneva Score (SGS). Three-month rates of death were also calculated according to an *a posteriori*-calculated PESI, with patients dichotomised into low-risk and high-risk groups. However, as SGS and PESI were computed *a posteriori*, they were not considered as primary outcomes.

Data analysis

Categorical variables are presented as numbers and/or percentages, and continuous variables as means +/− standard deviations.

Patients were classified into 3 groups according to their Revised Geneva Score (RGS <4: low; 4 ≤ RGS < 11: intermediate; RGS ≥11: high). We calculated *a posteriori* the SGS for each patient and the proportion of patients classified within each SGS probability group (SGS < 2: low; 2 ≤ SGS < 5: intermediate; SGS ≥5: high). PESI score was also calculated for every patient. Patients were then classified into low-risk PESI (≤85 points) and high-risk PESI (>85 points) groups. Cut-offs were identical to those used in diagnostic studies.

Comparisons between groups were made using Chi-square tests to compare categorical variables and the Student t-test for continuous variables. Kaplan-Meier analysis completed the analysis of the 3-month all-cause mortality. We then used logistic regression to identify independent items of the score associated with the occurrence of an event (death or rehospitalization) at 3 months. Every item of the Geneva score was included both in univariate analysis and multivariate analysis.

Results were expressed as Odds Ratio (OR) and 95% confidence intervals (CI). A p value <0.05 was considered statistically significant. Statistical analysis was carried out with the Statview 5.0 software (v5, SAS Institute Inc., USA).