Using Clinical Evaluation and Lung Scan to Rule Out Suspected Pulmonary Embolism

Is It a Valid Option in Patients With Normal Results of Lower-Limb Venous Compression Ultrasonography?

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Background: In patients with a low clinical probability of pulmonary embolism (PE) and a nondiagnostic lung scan, the prevalence of PE is theoretically very low. We assessed the safety and usefulness of this association for ruling out PE.

Methods: We analyzed data from 2 consecutive cohort management studies performed in 2 university hospitals (Geneva University Hospital, Geneva, Switzerland, and Hôpital Saint-Luc, Montreal, Quebec), which enrolled 1034 consecutive patients who came to the emergency department with clinically suspected PE. All patients were submitted to a sequential diagnostic protocol of lung scan, D-dimer testing, lower-limb venous compression ultrasonography (US), and pulmonary angiography in case of inconclusive results of noninvasive workup.

Results: The prevalence of PE was 27.6%. Empirical assessment was accurate for identifying patients with a low likelihood of PE (8.2% prevalence of PE in the low clinical probability category). One hundred eighty patients had a low clinical probability of PE and a nondiagnostic lung scan. Among these patients, US showed deep vein thrombosis in 5. Hence, PE could be ruled out by a low clinical probability, a nondiagnostic lung scan, and a normal US in 175 patients (21.5%). The 3-month thromboembolic risk in these patients was low (1.7%; 95% confidence interval, 0.4%-4.9%).

Conclusions: Anticoagulant treatment could be safely withheld in patients with a low clinical probability of PE and a nondiagnostic lung scan, provided that the US is normal. This combination of findings avoided pulmonary angiography in 21.5% of patients with suspected PE in this series.

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PATIENTS AND METHODS

PATIENTS

One thousand three hundred thirteen consecutive patients admitted to the emergency department of the Geneva University Hospital between October 1, 1992, and October 31, 1997, or to the emergency department of the Hôpital Saint-Luc, Montreal, Quebec, between November 1, 1996, and October 31, 1997, for clinically suspected PE were included in 2 successive trials on the diagnosis of PE.17,18 Patients were excluded if they met the following criteria: suspected PE during hospital stay (15); symptoms of deep vein thrombosis (DVT) (4); DVT or PE in the previous 3 months (10); refusal or inability to consent to care (21); contraindication to or impossible to undergo pulmonary angiography (14); ongoing anticoagulant treatment (5); blood sample to the laboratory. Ultrasonography was done within approximately 1 hour following the reception of the blood sample to the laboratory. The exact 95% CIs for incidence of thromboembolic and bleeding events during follow-up were calculated from the median of 2 years of postgraduate training) after filling out a standard checklist, including risk factors for venous thromboembolism, symptoms and signs frequently encountered in PE, blood gases, electrocardiogram, and a description of chest x-ray findings (Table). The checklist served as a reminder of useful information to the clinician, who then integrated it on an empirical basis (ie, without using a score or prediction rule). In the first study,16 clinical probability was rated between 0% and 100%. In the second study,6 it was rated low (≤20%), intermediate (21%-79%), or high (≥80%).

OUTCOMES

The usefulness of clinical probability was evaluated in terms of the proportion of patients in whom PE could be ruled out by the combination of a low clinical probability and a nondiagnostic lung scan. The safety of this combination was assessed by the upper limit of the 95% confidence interval (CI) for the 3-month thromboembolic risk.20,21

THREE-MONTH FOLLOW-UP

Venous thromboembolic events (DVT or PE) were recorded during the 3-month follow-up. Patients were followed up by their family physicians and were interviewed by telephone by one of the study coordinators at the end of the follow-up period. The family physician was contacted whenever a possible event was disclosed in the interim history, and the medical charts were reviewed if a patient was readmitted to a hospital for any cause. The death registries of the city of Geneva and the province of Quebec were consulted for patients who could not be traced after checking with the family physician. For patients who died, the cause of death was ascertained by either the autopsy or the death certificate.

DIAGNOSTIC STUDIES

The techniques for performing and interpreting lung scan and pulmonary angiography have been described elsewhere.4,22 In both studies, plasma D-dimer levels were measured using the ELISA technique (Asserachrom D-Di enzyme immunoassay kit; Diagnostica Stago, Asnières-sur-Seine, France)4,16 and a rapid ELISA (Vidas DD; bioMérieux, Lyon, France)9 by a technician unaware of the clinical probability, the lung scan result, and the final diagnosis. The result of the blood test was transmitted to the physician in charge of the patient within approximately 1 hour following the reception of the blood sample to the laboratory. Ultrasonography was done by trained staff within 24 hours in all cases. The examination consisted of a real-time B-mode venous compression test of the common femoral and popliteal veins. The criterion for diagnosing DVT was noncompressibility of the vein.23

STATISTICAL ANALYSIS

The exact 95% CIs for incidence of thromboembolic and bleeding events during follow-up were calculated from the binomial distribution using computer software.24

In 2 recent trials9,10 at Geneva University Hospital, Geneva, Switzerland, on noninvasive diagnosis of PE, empirical clinical probability of PE was systematically assessed by internal medicine trainees before any specialized tests were performed. The combination of low clinical probability and a low-probability lung scan ruled out PE. These patients did not undergo anticoagulant therapy and were followed up for 3 months because untreated PE will result in a high frequency of recurrences.17,18 Because the proportion of such patients in each of these individual trials was too small to allow a definitive assessment of the safety of this potentially cost-saving diagnostic criterion, we performed a pooled analysis of both studies. Moreover, since the distinction between the low- and intermediate-probability lung scan categories is difficult and fraught with substantial interobserver disagreement,19,20 we merged these results into a single nondiagnostic category in this article. Hence, this article reports the efficacy and safety of a low clinical probability combined with a nondiagnostic lung scan to rule out PE.
diagnostic lung scan ruled out PE. In 5 of these patients, both a low clinical probability and a non-
of those, 309 underwent a lung scan. In 180 (58.2%) of
Of the 1034 patients, 428 had a low clinical probability;
patients with a low clinical likelihood of the disease.

US showed DVT. Therefore, the combination of a low
clinical probability and a nondiagnostic scan ruled out
PE in 175 (20.9%) of 837 patients. The D-dimer level was
normal in only 28 of these 175 patients vs 202 of the
patients with lung scan. There were 3 false-negative
results assessed by further testing (1 patient with an
abnormal pulmonary angiogram) or by follow-up (1 with
DVT and 1 with PE). Finally, a young female patient with
no risk factors for PE and a normal D-dimer level was lost
to follow-up. Hence, the proportion of thromboembolic
events missed by the combination of clinical and lung
scan probability was 3 (1.7%) of 175 patients (95% CI,
0.4%-4.9%) after US. This rate would have been higher
if US had not been performed in all patients (4.4%; 95%
CI, 1.9%-8.6%).

This pooled analysis shows that empirical assessment of
clinical probability of PE is accurate in identifying pa-
tients with a low clinical likelihood of the disease. More-
over, it confirms that ruling out PE in patients in the
emergency department with a low clinical probability of
PE and a nondiagnostic lung scan is both effective, avoid-
ing pulmonary angiography in 21.5% of patients, and safe,
provided US shows no DVT.

The main limitation of empirical clinical probability
assessment is potentially poor interobserver agree-
ment, since different clinicians may attribute different
weights to the same clinical elements. Several observa-
tions suggest that this is seldom a problem. First, a
previous trial20 showed that residents and senior residents
had a high level of agreement in establishing the clinical
probability of PE. Second, the Figure shows that the ac-
curacy of clinical assessment in our series was remark-
ably similar to that observed in the PIOPED study.3 de-
spite the fact that the latter study was conducted in several
centers in North America. The only difference was a higher
proportion of patients with a low clinical probability in

RESULTS

One thousand thirty-four patients with suspected PE were
included in the 2 trials and were available for assessing
the accuracy of clinical probability. In 197 patients from
the second trial,9 a lung scan was not performed be-
cause the diagnosis was already established by plasma D-
dimer level or US, which were performed before the lung
scan. Therefore, the usefulness and safety of combining
clinical and lung scan probability for ruling out PE were
evaluated in the subset of 837 patients who had under-
gone a lung scan. The prevalence of PE was similar in
the entire cohort and this subset of patients (27.6% and
28.9%, respectively).

ACCURACY OF CLINICAL
PROBABILITY OF PE

Physicians had a high accuracy for identifying patients
with a low likelihood of having PE (8.2% observed preva-
lence of PE in that category; Figure). Conversely, in the
high clinical probability category, physicians tended to
overestimate the likelihood of PE (Figure). To avoid in-
corporation bias,23 this analysis was also done in the sub-
set of patients in whom clinical probability did not in-
tervene in the final diagnosis (so-called certified diagnosis,
which relied solely on lung scan, D-dimer level, US, or
angiogram). The results were unchanged.

USEFULNESS AND SAFETY
OF CLINICAL PROBABILITY OF PE

Of the 1034 patients, 428 had a low clinical probability;
of those, 309 underwent a lung scan. In 180 (58.2%) of
these patients, both a low clinical probability and a non-
diagnostic lung scan ruled out PE. In 5 of these patients

COMMENT

The accuracy of clinical assessment in our series was remark-
ably similar to that observed in the PIOPED study.3 de-
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our series (40% vs 20%), probably due to inclusion of a significant proportion of inpatients in the PIOPED study. Indeed, hospitalization is by itself an important risk factor for venous thromboembolism. Therefore, clinical probability is more often high in that patient population. Third, clinical probability was assessed by more than 90 physicians throughout the study, all of whom were internal medicine residents in the second or third year of training. It is unlikely that this fair accuracy would have been observed if interindividual variability of empirical assessment were very important.

Admittedly, disagreement between physicians on clinical probability occurred occasionally. In our institutions, patients were treated by different teams in the emergency department and in the ward. Therefore, in 104 patients (7.9% of the entire cohort), clinical probability was either raised or, more often, lowered by the second team. Since physicians in the ward generally knew the results of the lung scan, D-dimer testing, or US when they modified the clinical probability and were likely to be influenced by that knowledge, such cases were excluded from our trials. Interestingly, the 3-month follow-up could be completed in the 74 patients who did not undergo angiography because their clinical probability was lowered by the ward physicians, and none had a thromboembolic event. Still, in case of a disagreement about clinical probability, it would be cautious to classify the patient in the higher clinical probability category and proceed to further tests. Obviously, a clinical prediction rule or score would allow a standardized estimate of clinical probability. However, existing scores are cumbersome and have not been prospectively validated in patient cohorts distinct from those in which they were established.

The 3-month thromboembolic risk was only 1.7% (95% CI, 0.4%-4.9%), comparable to that in patients who did not undergo anticoagulant therapy based on a normal lung scan. The 95% CI is still wide, due to the small size of this particular subset of patients. Studies by other groups to confirm our findings would verify the reliability of clinical assessment and increase the sample size to definitively ensure the safety of the strategy. Further study would be especially worthwhile, considering the potential contribution of clinical probability to noninvasive diagnosis of PE. In this study, the combination of a low clinical probability and a nondiagnostic lung scan was found in 21.5% of patients consecutively admitted to the emergency department, while in the PIOPED study,3 which included both inpatients and outpatients, this association was present in 18% of the cohort. This combination was associated with a normal US in 21.5% of patients in our series, allowing us to rule out PE. Admittedly, in institutions using ELISA to measure D-dimer levels and a normal US. Clinical assessment could avoid a pulmonary angiogram in as many as 21.5% of patients. An angiogram is still required in patients with inconclusive results of the noninvasive workup, and further tests are needed in case of a disagreement between physicians on the clinical probability of PE. These findings should be confirmed by other groups, and the validation of clinical prediction rules should be encouraged.

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REFERENCES