Review of 6-Month Mortality Following Low-Probability Lung Scans

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Background: Ventilation perfusion lung scanning is widely used as a diagnostic method for evaluating patients suspected of having pulmonary embolism (PE). While lung scan interpretation is traditionally performed in terms of probability of PE (usually low, moderate or intermediate, and high), in recent years concern has been raised that the term low probability may be misleading because adverse and even fatal sequelae of PE occasionally occur in such patients. To assess these concerns, a review of mortality in a large series of patients following low-probability lung scans was performed.

Objective: To determine the 6-month mortality in a consecutive series of patients following low-probability ventilation perfusion (V/Q) lung scans.

Methods: Records of all patients who had low-probability V/Q scans during a 9-year period (1987-1995) were reviewed. Causes of mortality for those patients who died during the 6-month period after the index scan were established from patients’ charts, autopsy reports, and computer record data.

Results: Of the total 536 evaluable patients, 83 (15%) died within 6 months of the date of the lung scan; 73 (88%) died while inpatients at the Seattle Veterans Affairs Medical Center, Seattle, Wash, and the other 10 (12%) died at other facilities or at home. Pulmonary embolism was not reported as a suspected or probable contributing factor in any of the 83 deaths. Sixty-three patients (76%) who died had a diagnosis of either cancer (n = 32) or advanced cardiovascular disease (n = 31) at the time of their lung scans. Twenty-six patients (31%) underwent autopsies, and PE was not identified on examination of the lungs in any of them. Of the 27 patients who died within 1 month of the scan date, 17 (63%) underwent autopsies.

Conclusion: Review of data from all patients with low-probability V/Q scans and a follow-up of 6 months showed no documentation to attribute any deaths to PE.

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VENTILATION perfusion (V/Q) lung scanning is extensively used in the evaluation of patients with suspected pulmonary embolism (PE). While a normal perfusion scan effectively rules out significant PE, and the pattern of multiple segmental V/Q mismatches is associated with a high probability (>85%) for PE, most scans fall into the low- or intermediate-probability categories. An issue raised in recent years is whether the low-probability category falsely implies a benign clinical outcome in light of reports of serious or even fatal sequelae of undiagnosed PE in such patients.

Validation of V/Q lung scan results, both as applied to individual patients and to population reviews, is usually accomplished through comparison with the “criterion standard” of pulmonary angiography. Many such investigations have established a less than 20% prevalence of PE in patients with low-probability lung scans, including a prevalence of 16% of angiographically diagnosed PE in the PIOPED study. However, as angiography is not routinely performed in patients with low-probability lung scans, other indexes, such as rates of recurrence of fatal and non-fatal PE, are sometimes used to judge the appropriateness of this diagnostic classification. A number of such outcome analyses have reported infrequent occurrence of major adverse sequelae for these patients. One common feature of most of the previous reports, however, has been the relatively small number of patients examined. We sought to expand on those earlier observations by analyzing 6-month mortality, a commonly used statistic, in a larger consecutive series of patients with low-probability lung scans.
PATIENTS, MATERIALS, AND METHODS

During a 9-year period (1987-1995), 870 lung scans were performed for clinical suspicion of PE. Scans on 570 patients (66%) were interpreted clinically as low probability for PE. On initial review, 336 of these latter patients (94%) were evaluable; 34 were removed from the analysis for lack of follow-up information. The scan population consisted of 524 men and 12 women, with a mean age of 62 years (range, 23-98 years).

The scanning techniques used have been described previously. Briefly, ventilation lung scanning was performed first in the posterior projection, using 10 to 40 mCi (370-1480 MBq) of xenon 133 gas and a large field of view camera (GE 500, General Electric Co, Milwaukee, Wis) with low energy, all-purpose parallel hole collimator. A standard 8-view perfusion scan was then performed following the intravenous administration of 6 mCi (222 MBq) of technetium Tc 99m-labeled macroaggregated albumin (200 000-500 000 particles). Plain radiograph of the chest was obtained in all patients within 24 hours of the scintigraphic study.

The clinical interpretation of low probability was based on the criteria of Biello et al9 or those used in the original PIOPED study, modified as appropriate in the final several years based on the later recommendations from the PIOPED trial. However, virtually all scans interpreted using PIOPED criteria would have received the same low-probability designation using the criteria of Biello et al. An average of 64% (range, 32%-71%) of lung scans per year were interpreted as low-probability during the study period. Scans were not reexamined as part of our study analysis.

Outcome examined was 6-month mortality. Computer-based administrative and clinical records were first reviewed for all patients to determine survival status at 6 months after the index scan. All available medical records, including inpatient and outpatient charts, were then reviewed for the patients who had died during that period. For patients who died while hospitalized, causes of death were obtained from inpatient clinical charts and pathology and autopsy reports. Other deaths were attributed to known terminal diseases in the absence of contrary clinical information.

RESULTS

Eighty-three patients (15%) died within 6 months of the date of the lung scan; 73 (88%) died while inpatients at the Seattle Veterans Affairs Medical Center, Seattle, Wash, and the other 10 (12%) died at other facilities or at home. The age distributions of all patients and those who died are shown in Table 1. Data on principal diagnoses at the time of lung scanning are shown in Table 2.

Pulmonary embolism was not reported as a suspected or probable contributing factor in any of the 83 deaths. Twenty-six patients (31%) had autopsies, and PE was not identified on complete examination of the lungs in any of them. Of the 27 patients who died within 1 month of the scan date, 17 (63%) underwent autopsies. The number of deaths (with the number of autopsies within parentheses) in the second through sixth months after scanning were as follows: 20 (4), 14 (4), 11 (1), 6, and 5, respectively.

Sixty-three patients (76%) who died had a diagnosis of either cancer or advanced cardiovascular disease at the time of their lung scans. Three (4%) of the 83 patients underwent pulmonary angiography following the V/Q scans, all of which were negative.

Of the 10 patients (12%) who died outside the Seattle Veterans Affairs Medical Center, 8 had a diagnosis of advanced cardiovascular disease. Six of them died more than 1 month after the scanning date. No definite cause of death could be established from available records in 2 patients.

Record review did not identify any case in which the primary cause of death was different from the diagnoses at the time of index lung scan. Furthermore, no occult diseases were discovered in the autopsies performed and, therefore, the diagnoses listed in Table 2 reflect the best available information regarding the primary causes of death in the study population.

COMMENT

Pulmonary embolism is most often a systemic manifestation of deep venous thrombosis, with an estimated...
prevalence rate of 51 per 100,000. Untreated PE can be associated with a mortality rate as high as 26%. These observations, as well as the risks associated with anticoagulation therapy, have led to increased scrutiny of the reliability of noninvasive tests for the diagnosis of PE. Ventilation perfusion lung scanning, which has been in use for more than 30 years, has been extensively studied and continues to play an important role in the evaluation of patients suspected of PE. In a recent review, Henschke et al found the V/Q scan to be the single most common study undertaken in the evaluation of PE.

For several decades, V/Q scans have been classified as “normal,” “low,” “intermediate” (or moderate), and “high” probability for PE. More recently, a category of very low probability or near normal has also come into more common use. While the numeric equivalents of these categories have been remarkably consistent in various reviews, including PIOPED and those of Biello et al and McNeil, the weakness of this approach remains the poor predictive values of the low and intermediate categories. While normal- and high-probability interpretations have high-negative and positive predictive values for PE, respectively, the other categories do not, often leaving the clinician in need of further diagnostic guidance. Doubts about the safety of both the low and intermediate-probability categories have caused some authors to suggest a revision of the basic terminology, combining these 2 into a single category designated “non-diagnostic.” Before such an action is considered, however, it is necessary to establish whether patients with low- and intermediate-probability scans are clinically equivalent. A corollary question involves determining the actual risk to the tens of thousands of patients annually who have low-probability lung scans and neither undergo pulmonary angiography nor receive anticoagulation.

While the diagnosis of PE is most reliably established by pulmonary angiography, in practice this is rarely done in patients with low-probability scans. Outcome analysis, examining mortality and morbidity in such patients, represents a practical alternative means to judge whether undiagnosed or untreated PE is a significant problem. While there have been several small reports of significant mortality in patients with low-probability scans, most larger studies have not documented such adverse outcomes. The present results are germane to understanding this discordance in that while there was a significant 6-month mortality in our patients, no objective evidence associating the deaths to PE was found. One possible explanation may be that thromboembolism occurred among some of the 57 patients who died and did not have autopsies, certainly a plausible possibility given the high prevalence of risk factors such as malignancy and cardiovascular disease. While neither PIOPED nor the earlier report of Biello et al documented a significant mortality in patients with low-probability lung scans, these series examined patients who had undergone angiography and therefore were appropriately treated with knowledge of the presence (or absence) of PE. While our results add significant new data concerning clinical outcomes, they cannot definitely resolve the discrepancies among previous studies with regard to unsuspected and therefore typically undiagnosed recurrent PE.

Sixty-three (76%) of 83 patients in our series who died had either cancer or significant cardiovascular disease at the time of lung scanning. Our study is in accord with others in suggesting that mortality in patients with low-probability scans predominantly reflects preexisting serious or terminal medical conditions. Symptoms mimicking PE can be caused by many other disease conditions, particularly advanced chronic obstructive pulmonary disease, cardiovascular diseases, and cancer, contributing to more frequent requests for V/Q scans in such patients. In studying clinical outcome following intermediate-probability lung scans, Jacobson et al found a low prevalence of new or recurrent thromboembolic disease (4%) in patients who did not undergo pulmonary angiography and were not anticoagulated, with no evidence of mortality secondary to untreated PE during 6-month follow-up.

The 31% (26/83) autopsy rate in our study is comparable with that in earlier series. In none of the autopsies in our study was PE reported as a contributing cause of death. Seventeen (63%) of 27 patients who died within the first month underwent autopsies and any significant residual PE would have been identified if it were present. The lower rate of autopsies in patients who died after 1 month (9 [16%] of 56) reflects that the known terminal conditions in most patients made confirmation of the cause of death only infrequently necessary. It is therefore unlikely that deaths occurring after the first month were caused by acute PE that was suspected but remained undiagnosed at the time of index scan.

Only 3 (4%) of 83 patients who died underwent pulmonary angiography following the V/Q scan. While a small number, it is not unexpected given that outside of controlled prospective trials, few pulmonary angiograms are performed in patients with low-probability lung scans. In a recent review of the diagnosis of pulmonary embolism in a teaching hospital, Schluger et al found that pulmonary angiograms were performed in only 5 (4%) of 118 patients with low-probability scans. This reflects both the low pretest suspicion of PE in most of this patient population and the reluctance of clinicians to request pulmonary angiography except in the occasional patient in whom the pretest suspicion is high. Although not directly contributing to low-angiography rates, it is also likely that many clinicians are aware that small peripheral emboli diagnosed angiographically have only a minor clinicopathologic impact on the immediate patient outcome.

The 6-month follow-up interval used in our study is longer than the recommended 3 months’ duration for continuation of anticoagulant therapy in the absence of continuing risk factors. Since thromboembolic recurrence is most common in the initial 4 to 6 weeks, it is unlikely that any significant recurrence of PE was missed during the 6-month follow-up in our review. Freitas et al found a 5.5% angiographic incidence of PE among 1000 patients with low-probability lung scans. Similarly, Trujillo et al report a 7% angiographic incidence of PE in patients with low-probability lung scans.
in an evaluation of aerosol ventilation scanning with di-
ethylenetriamine pentaacetic acid. These reports fur-
ther support the low likelihood of identifying thrombo-
embolism in patients with low-probability lung scans.

Our study has both the limitations commonly found
in retrospective reviews and several others. These in-
clude a small percentage of patients (6%) who were lost
to follow-up, incomplete follow-up data on the patients
who died at home or other facilities, and an autopsy rate
of only 31%. All these factors could contribute to an
underestimation of the occurrence of deaths attributable
at least in part to PE. In addition, original diagnoses in the
total population were derived primarily from computer
records, another possible source of error. However, causes
of death were derived from detailed patient chart review
and reflect the best information available to the treating
clinicians. Nevertheless, incomplete or inaccurate infor-
mation could have been recorded prior to the index scan
and then restated as fact later. The population reviewed
also reflects the typical composition of patients seen at a
Veterans Affairs Medical Center, primarily older men with
a high prevalence of chronic diseases such as obstruc-
tive lung disease, cancer, and coronary heart disease, there-
fore limiting the applicability of our findings to younger
or female patients or to those with less chronic cardio-
pulmonary diseases. While the large number of patients
in our review strengthens the validity of our data, the
generalizability of our observations is somewhat restricted
by the various limitations enumerated herein.

In summary, our analysis of 536 patients with low-
probability V/Q scans and a follow-up of 6 months iden-
tified no documentation of any deaths attributable to PE.
While these findings may reflect failure of clinicians to ad-
equately pursue or at least consider the diagnosis of PE in
patients with other major cardiorespiratory diseases, they
also do not provide objective evidence for replacing the term
low probability with nondiagnostic on the basis of mortality
attributable to PE. There remains the need to pursue
aggressively the diagnosis of PE in patients with high clini-
cal suspicion or major risk factors, regardless of the lung
scan categories or nomenclature used. Improving the com-
munication between imagers and referring clinicians with
regard to the significance of different lung scan findings
should also be a priority.20

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