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MEASURES OF CLINICAL EFFICACY. III. THE VALUE OF THE LUNG SCAN IN THE EVALUATION OF YOUNG PATIENTS WITH PLEURITIC CHEST PAIN

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The usefulness of various modalities in evaluating pleuritic pain in young patients and in isolating cases of pulmonary embolism was assessed using likelihood ratios and the receiver operating characteristic (ROC) curve. History and physical, laboratory, and radiographic findings were used disjunctively to establish an ROC curve. The percentage of patients found to have pulmonary embolism increased monotonically with certain critical pieces of diagnostic data. For example, a history and physical examination alone detected 80% of patients with pulmonary embolism; a chest radiograph raised the percentage to 95%; and the addition of a lung scan increased the percentage to 100%. Thus, with proper interpretation of clinical and radiographic data, the lung scan has only a marginal impact upon the sensitivity ***with which pulmonary embolism is detected. Its major value is an increased*** specificity ***in the diagnosis of pulmonary embolism.***

Since the time of Hippocrates, physicians have recognized pleuritic pain as a symptom of significant disease. More recently, attention has been drawn to the frequency of this complaint in patients with pulmonary embolism and to the morbidity associated with failure to diagnose and treat the condition (*1–3*). In this investigation, we studied a group of patients with pleuritic pain to determine the relative usefulness of medical history, physical signs, laboratory tests, and radiographic examinations in distinguishing patients with pulmonary embolism from those with other disorders. We were also particularly interested in seeing to what extent performance of a lung scan in these patients improved the accuracy of diagnosis.

METHODS

Patient data: History, physical, and laboratory findings. We reviewed hospital records of 97 patients (72 women, 25 men) between 18 and 40 years of age who had had perfusion lung scans for evaluation of pleuritic pain. Patients were restricted to this age group in order to minimize abnormal findings deriving from long-standing chronic disease (e.g., obstructive lung disease). We correlated the history, physical, and laboratory findings with the final discharge diagnosis for each patient. On this basis, the patient population was divided into those with pulmonary embolism* (PE+) and those without pulmonary embolism (PE−).

Followup information was obtained for all but three patients 6–18 months after the initial episode of chest pain by (A) direct extraction from the medical record (73 patients), (B) letters to private physicians (12 patients), or (C) telephone calls to nine patients who had returned neither to the hospital clinic nor to their private physicians. In all cases, specific inquiries were made as to whether the patient had had a recurrence of pleuritic pain or had

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* During the study, an additional five patients under 40 years of age were discharged with the diagnosis of pulmonary embolism without having had a lung scan. All had angiographic evidence of massive disease (>50% occlusion of pulmonary vasculature) and all were treated with inferior venacaval ligation. Four of these five patients presented with syncope and one with pleuritic chest pain. These five patients were excluded from our data.

been seen at another medical facility after the first attack of chest pain.

Radiographic data. *Chest radiographs.* Chest radiographs for all patients were read by two observers who knew only the patient's age, sex, and chief complaint. When the observers disagreed, the interpretation was resolved by a third reader. The abnormal findings were tabulated for patients with pulmonary embolism, for patients with pneumonia, and for all others.

Pulmonary angiograms. Pulmonary angiograms were obtained on 23 patients. Only intraluminal filling defects or the clearly defined trailing edge of a thrombus were considered to indicate pulmonary embolism (*4*).

Lung scans. Lung scans for all patients were read by one observer who knew only the patient's age, sex, and chief complaint. Defects on the perfusion lung scan were categorized according to the bronchial anatomy (lobe, segment, or subsegment) and correlated with the appearance of an associated abnormality on the chest radiograph (*5,6*). Combined ventilation and perfusion studies were performed in 22 patients whose perfusion defects did not correspond to radiographic abnormalities and whose perfusion defects were large enough to resolve with ^{133}Xe (*6–8*). They were categorized as having normal or mildly reduced ventilation in a poorly perfused area ($\dot{V}/\dot{Q}$ mismatch) or poor ventilation in a poorly perfused area ($\dot{V}/\dot{Q}$ match).

Lung scans were considered abnormal when there were perfusion defects of any size. Abnormal lung scans were not considered indicative of pulmonary embolism when (A) the perfusion defects were subsegmental, (B) the perfusion defects were associated with a $\dot{V}/\dot{Q}$ match, or (C) the perfusion defects showed no changes in size and location when compared with a lung scan obtained during a temporally distinct illness at least 1 month earlier (*5,6*). Abnormal scans were considered highly probable for pulmonary embolism when (A) the perfusion defects were lobar or segmental, (B) the perfusion defects were of any size and were associated with a $\dot{V}/\dot{Q}$ mismatch, or (C) the perfusion defects had changed over a short time interval while the chest film remained normal in the involved area (*5,6*). Some abnormal lung scans could not be placed in either of these categories because the perfusion defects corresponded to radiographic abnormalities. These scans were called indeterminate for pulmonary embolism.

Method of data analysis. An IBM-370/168 computer was used for data storage and analysis. The true-positive (TP) and false-positive (FP) ratios* for each variable (i.e., each historical, laboratory, physical, or radiographic finding) were calculated for all patients. The likelihood ratio (i.e., TP ratio/FP ratio) was also calculated. Findings with high likelihood ratios are more reliable indicators of disease than those with lower likelihood ratios (*9*).

We calculated TP and FP ratios of new composite variables formed by the disjunction of several individual variables. These variables were disjoined in the order in which data are usually obtained in a clinical setting: case history, then physical findings, then laboratory tests, and lastly radiographic examinations. We searched for composite variables with higher likelihood ratios than the individual variables. Specifically, we started with the individual variable A_1 with the highest likelihood ratio. Our first composite variable was considered present if either variable A_1 was present or another variable A_2 was present. The next composite was considered present if variable A_1 or A_2 or A_3 was present, and the final one, if A_1 or A_2 or A_3 or . . . A_i was present. We displayed the TP and FP ratios of these composite variables using a receiver operating characteristic (ROC) plot (*10,11*).

Scintigraphic studies were included in the analysis in two ways. In the first method we analyzed all 97 lung scans and calculated TP and FP ratios for those lung scans categorized either as highly probable or indeterminate for pulmonary embolism. In the second method we calculated these same ratios using only lung scans performed on patients identified as positive by the preceding disjunctive process. For example, for the second step of the disjunctive process these new ratios were calculated for cases where either variable A_1 or A_2 was present *and* where the lung scan was indeterminate or highly probable for pulmonary embolism.

All TP ratios were recalculated for patients with angiographic confirmation of their diagnoses in order to ensure that these patients were similar to the entire patient population discharged with the diagnosis of pulmonary embolism. All FP ratios were recalculated for patients who had had a specific diagnosis or therapeutic maneuver performed in order to include or exclude a particular disorder. Pulmonary emboli were diagnosed by the above angiographic criteria (*4*) and excluded either by the presence of a normal pulmonary angiogram within 48 hr or by the presence of a normal lung scan (*12*). Other

* The TP ratio is the frequency of an abnormal result in patients *with* pulmonary embolism (i.e., the number of abnormal results in patients with pulmonary embolism divided by the total number of patients with pulmonary embolism). The FP ratio is the frequency of an abnormal result in patients *without* pulmonary embolism (i.e., the number of abnormal test results in patients without pulmonary embolism divided by the total number of patients without pulmonary embolism).

specific diagnoses were made by one of the following methods: (A) prompt response of patients to antibiotic therapy (pneumonia), (B) response of patients to antiasthmatic medications (acute asthmatic bronchospasm), (C) radiographic evidence of an acute bone trauma, (D) elevation of serum amylase levels from previously known normal values (pancreatitis), and (E) positive sputum cultures (tuberculosis, pneumonia).

Cost of diagnosing pulmonary embolism. In determining the financial costs of detecting patients with pulmonary embolism, we assumed the following average prices for radiographic procedures: chest radiograph $25, perfusion lung scan $125, ventilation study $35, and pulmonary angiography $300. The financial cost of finding a patient with pulmonary embolism in a young population was calculated for two situations, one for detecting 95% of patients with pulmonary embolism and the other for detecting all patients with pulmonary embolism. The additional cost of finding the last 5% of patients with pulmonary embolism was also calculated.

RESULTS

Final diagnosis. Of the 97 patients, 20 (11 women, 9 men), or 21%, were discharged with the diagnosis of pulmonary embolism. Fourteen of these 20 patients had angiographic confirmation of the diagnosis. In the remaining six patients, the diagnosis was established by the referring physicians on the basis of other criteria (i.e., clinical, laboratory, radiographic, and scintigraphic results). All 20 patients were treated with anticoagulants and were well at the time of followup. One developed recurrent pulmonary emboli documented by angiography.

Of the remaining 77 patients, 17 (18% of the study group) were discharged with the diagnosis of pneumonia; nine were women and eight were men. Only eight (8% of the study group) of the remaining 60 patients had specific diagnoses postulated: two patients with asthma, two with sickle cell crises, one with tuberculosis, one with pancreatitis, one with a ruptured aortic aneurysm, and one with a broken rib. No diagnoses other than pleuritis, pleurodynia, or costochondritis were made in the remaining 52 patients (53% of the group). At the time of followup (three could not be located), none in this group had suffered recurrence of the original symptoms.

History, physical, and laboratory findings. Mean values for several quantitative physical findings and most laboratory tests were not significantly different for patients with or without pulmonary embolism (Table 1). In particular, the mean heart rates and white blood counts were normal and the mean respiratory rates and arterial blood gases were abnormal for both groups. The serum enzyme LDH level was normal in both groups but the serum SGOT level was significantly higher and abnormal in patients without pulmonary embolism.

TABLE 1. SELECTED PHYSICAL FINDINGS AND LABORATORY RESULTS FOR YOUNG PATIENTS WITH PLEURITIC PAIN*

	Diagnosis	
	Pulmonary embolism	Other
Heart rate (min^{-1})	87 ± 2	88 ± 2
Respiratory rate (min^{-1})	23 ± 1	24 ± 1
Temperature (°F)	98.9 ± 0	98.2 ± 0
Systolic BP (mm Hg)	120 ± 3	126 ± 2
Diastolic BP (mm Hg)	77 ± 2	80 ± 2
pO_2 (mm Hg)	81 ± 2	77 ± 1
pCO_2 (mm Hg)	33 ± 1	34 ± 1
pH	7.46 ± 0	7.45 ± 0
WBC	9100 ± 500	9000 ± 450
% PMNs	67 ± 3	62 ± 2
LDH (Wacker units)	246 ± 19	247 ± 18
SGOT (Karmen units)	21 ± 2	40 ± 8

* Expressed as the mean value ± the standard error.

The relative occurrence of several case-history features, physical findings, and laboratory results differed for patients with and without pulmonary embolism (Table 2). The most discriminating fea-

TABLE 2. TP AND FP RATIOS OF CASE-HISTORY, PHYSICAL, AND LABORATORY FINDINGS AS INDICATORS OF PULMONARY EMBOLISM*

	TP ratio	FP ratio	TP/FP ratio
Case-History Data			
Postoperative history	.45	.09	5.0
History of venous disease or old pulmonary embolism	.20	.10	2.0
Medication: birth control pills	.55	.27	1.9
Pain less than 1 day	.27	.54	0.5
Physical Findings			
Phlebitis, leg edema without cellulitis	.35	.09	4.0
↓ Breath sounds	.40	.21	2.0
↑ RR (>20)	.45	.48	0.9
↑ HR (>100)	.10	.13	0.8
Rhonchi, rales	.10	.13	0.8
↑ Temperature (>99.7°F)	.15	.23	0.6
Point tenderness	.05	.13	0.4
Laboratory Data			
↑ LDH (>231 Wacker units)	.59	.48	1.2
↑ pH (>7.40)	1.00	.88	1.1
↓ pCO_2 (<40 mm Hg)	.94	.88	1.1
↓ pO_2 (<80 mm Hg)	.44	.66	0.7
↑ SGOT (>33 Karmen units)	.12	.25	0.5

* Only findings occurring in more than 10% of the members of either group (PE+ or PE—) are recorded here.

tures occurred at least twice as often in patients with pulmonary embolism: postoperative history (mean 7 weeks, range 1 week to 4 months), previous venous disease, new venous disease, and decreased breath sounds.

Radiographic findings. Seventy-five percent of patients with pulmonary emboli, 88% with pneumonia, and 38% with neither diagnosis had abnormal chest radiographs (Table 3). The type of abnormality varied with the disease category. Infiltrates were seen in 35% of patients with pulmonary emboli, 82% with pneumonia, and 8% with neither diagnosis. Unilateral or bilateral effusions were seen in 60% of patients with pulmonary emboli, in 41% of patients with pneumonia, and in 15% of the remaining patients. Other findings occurred less frequently in all three groups.

TABLE 3. INCIDENCE OF RADIOGRAPHIC FINDINGS AND THEIR LIKELIHOOD RATIOS IN PATIENTS WITH PLEURITIC CHEST PAIN ACCORDING TO DISCHARGE DIAGNOSIS

Finding	Pulmonary embolism (%)	Pneumonia (%)	Other	TP/FP ratio
Abnormal chest radiograph	75	88	38	1.5
Infiltrate(s)	35	82	8	1.4
Effusion(s):	60	41	15	2.9
unilateral	35	35	12	
bilateral	25	6	3	
Atelectasis	15	18	6	1.7
Elevated hemidiaphragm	5	12	5	0.8
Hyperlucent areas	0	0	3	0
Enlarged pulmonary artery	0	5	5	0

Scintigraphic findings. None of the 20 patients with pulmonary emboli had a normal scan: 17 had scans regarded as highly probable for pulmonary embolism, and three had abnormal scans which were indeterminate (Table 4). Twelve of the former group and two of the latter had their diagnoses confirmed by angiography.

TABLE 4. SCINTIGRAPHIC FINDINGS IN PATIENTS WITH PLEURITIC CHEST PAIN

	Pulmonary embolism	Other
Normal scan	0	42
Abnormal scan:	20	35
low probability of PE	0	23†
high probability of PE	17*	0
indeterminate	3	12

* 15 with $\dot{V}/\dot{Q}$ mismatches.
† 7 with $\dot{V}/\dot{Q}$ matches.

Of the patients with diagnoses other than pulmonary emboli, 42 had normal scans and 35 had abnormal scans. Of these abnormal scans, 23 were not thought to represent pulmonary embolism and 12 were indeterminate; none were regarded as highly probable for pulmonary embolism. Angiography performed in three of the patients with low-probability scans and six of the 12 patients with indeterminate scans did not show pulmonary emboli.

Testing the reliability of the clinical diagnosis. Because there could be some uncertainty about diagnoses made in patients who did not have specific diagnostic or therapeutic procedures, the subgroup of patients who had such procedures was examined and compared with the total group. Both groups had approximately the same incidence of abnormal findings and the same mean values of laboratory results (Table 5). Therefore, all subsequent calculations were performed using the entire population of patients.

Methods for selection of patients with pulmonary emboli. The most concave ROC curve that could be constructed without scintigraphic data started with two pieces of case-history data, proceeded to one physical finding, and included one radiographic finding (Fig. 1, triangles). Postoperative history alone detected 45% of patients with embolism (TP ratio = 0.45). Either a postoperative history or previous venous disease (including old pulmonary emboli) identified 65% of such patients. When the presence of varicose veins, phlebitis, or leg edema was considered along with the preceding variables, 80% of patients with pulmonary embolism were detected. When the presence of unilateral or bilateral effusions on chest radiographs was also considered, the detection rate increased to 95%.

The major effect of the lung scan was an increase in specificity (i.e., a reduction in the FP ratio), shifting the ROC curve to the left (Fig. 1, circles). For example, detection of 19 of 20 patients with pulmonary embolism (TP ratio = 0.95) involved the faulty inclusion of 30 patients without pulmonary embolism when only history, physical findings, and laboratory data were evaluated (FP ratio = 0.39), whereas only four such patients were included when lung scans were also performed (FP ratio = 0.05).

Only a small gain in sensitivity was achieved when lung scans were performed on all patients rather than just on those selected by the presence of an abnormal historical, physical, or radiographic finding. The detection of patients with pulmonary embolism then increased from 95% to 100%, with accompanying false-positive ratios of 5% and 16%. Those patients

TABLE 5. INCIDENCE OF FINDINGS IN ENTIRE STUDY POPULATION AND IN SUBGROUPS

	PE+ group, % (n = 20)	Subgroup,* % (n = 14)	PE− group, % (n = 77)	Subgroup,† % (n = 65)
Abnormal history or physical examination	80	70	23	24
Abnormal history, physical exam, or chest radiograph	95	90	39	40
Lung scan highly probable or indeterminate for pulmonary embolism	100	100	16	17

* These patients had angiographically proven pulmonary emboli.

† These patients had either pulmonary embolism excluded by a normal pulmonary angiogram or another diagnosis included by specific diagnostic or therapeutic procedures.

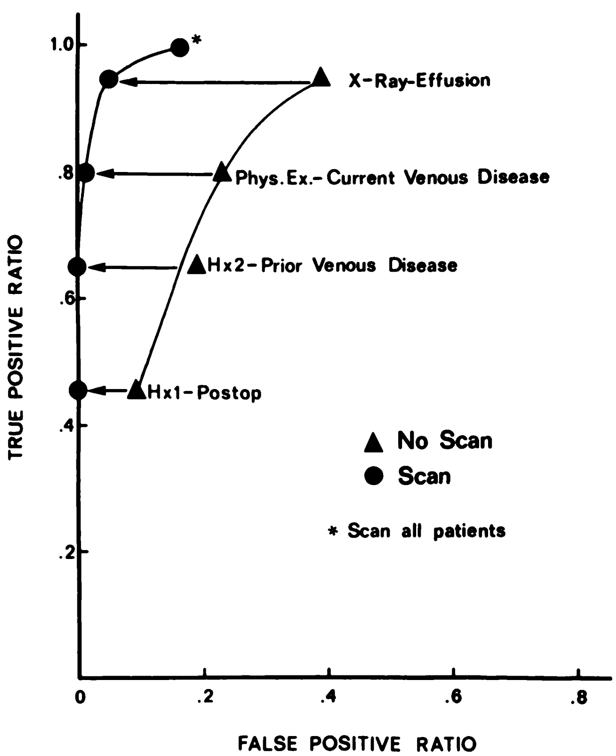

FIG. 1. Receiver operating characteristic curve. Vertical scale: true-positive ratio; horizontal scale: false-positive ratio. Triangles indicate new variables created by disjoining individual variables. These have likelihood ratios higher than either individual variables or other disjoined sets. Circles indicate that lung scans were performed only on patients belonging to groups created by above disjunctive process. Only lung scans read as highly probable or indeterminate are used to calculate true-positive and false-positive ratios.

who had indeterminate lung scans required another diagnostic procedure (angiography) to determine the origin of their chest pain. For example, of the 20 patients identified as having pulmonary embolism, 85% (17 patients) had lung scans highly probable for pulmonary embolism and 15% (three patients) had indeterminate scans. At the same time, 12 patients (16%) without pulmonary embolism also had indeterminate scans. Thus, in the group of 97 patients, 15 required angiography because of an indeterminate scan.

Cost of diagnosing pulmonary embolism. In order to identify all cases of pulmonary embolism, perfusion lung scans had to be performed on all patients, regional ventilation studies had to be performed when indicated, and pulmonary angiograms had to be performed on all patients with indeterminate lung scans. Because of the relatively high percentage of patients with pneumonia, chest films were also needed.

When all patients were detected, the cost of finding a patient with pulmonary embolism was $991 per patient (Table 6). When only 95% of patients were detected, the corresponding cost was 40% less: $596. The cost of finding the last 5% of patients with pulmonary embolism was $8,485.

DISCUSSION

This study presents a general technique which can be used to evaluate the impact of a diagnostic examination on clinical outcome. We were particularly concerned with the lung scan and its use in the work-up of young patients presenting with pleuritic pain. Our approach employed likelihood ratios and the receiver operating characteristic (ROC) curve in order to quantitate diagnostic accuracy when certain critical pieces of case-history information, physical findings, or radiographic data were disjoined. After considering each of the points generated in the disjunctive process as a subgroup, we combined the results of another diagnostic examination (the lung scan) with these data. Thus, the history, physical, and radiographic findings are the analogue of a preliminary screening examination performed on the total population. At its best operating position along the ROC curve, this "screening examination" was highly sensitive in that 95% of patients with pulmonary embolism were detected. However, it was also nonspecific, having a false-positive ratio of 39%. Other composite criteria, which embraced fewer pieces of his-

TABLE 6. COST OF FINDING A PATIENT UNDER 40 YEARS OF AGE WITH PULMONARY EMBOLISM

100% Detection (20 of 20 Patients Found)	
97 chest radiographs	$ 2,425
97 perfusion scans	12,125
22 ventilation studies	770
15 pulmonary angiograms for indeterminate scans	4,500
	$19,820
	($991 per patient found)
95% Detection (19 of 20 Patients Found)	
97 chest radiographs	$ 2,425
50 perfusion scans	6,250
16 ventilation studies	560
7 pulmonary angiograms for indeterminate scans	2,100
	$11,335
	($596 per patient found)

tory data or physical findings along the ROC curve, had correspondingly lower sensitivities and higher specificities. As the plot of these subgroups along the ROC curve shows, the addition of a more definitive diagnostic examination (the lung scan) maintained the same degree of sensitivity established by the "screening examination" but increased the specificity considerably. The ROC curve shifted markedly to the left when lung scans read with strict criteria (i.e., only scans highly probable or indeterminate for pulmonary embolism were called abnormal) were combined with the "screening examination" (Fig. 1).

The difference between these two curves can be used to measure the impact of a new test (as in this case, diagnosis of pulmonary embolism with and without lung scanning) or it can be used to compare the utility of two tests. The two curves in Fig. 1 show the impact of the lung scan in young patients with pulmonary embolism. Clearly, this examination does make a significant difference in the accuracy of diagnosis, thereby reducing the number of patients who would otherwise need to be admitted for further diagnosis and treatment. Moreover, in general this disjunctive and conjunctive method of analysis may permit the evaluation of diagnostic tests without recourse to a prospective random allocation of patients.

Several interesting points pertaining to the problem of diagnosis of pulmonary embolism in young patients emerged in the course of this analysis. Perhaps the most striking is the distribution of final diagnoses in the study group. Only 47% of all patients had diagnoses other than pleuritis or costochondritis: 21% were pulmonary embolism, 18% pneumonia, and 8% miscellaneous diagnoses. The absence of a clear-cut diagnosis in the remaining 53% may be inconsequential because most of these patients were well several months after presentation.

Several laboratory tests considered useful in identifying pulmonary embolism with older patients were not discriminating in this group (*13*). In our study, most laboratory test results had similar mean values for patients with and without pulmonary embolism. For example, patients with and without pulmonary embolism had a mean arterial pO_2 near 80 mm Hg. Moreover, although both elevated respiratory rates and elevated serum LDH levels were observed in patients with pulmonary embolism, these indicators were also observed with approximately equal frequency in other conditions.

The cost of finding a young patient with pulmonary embolism by our methods was of the same order of magnitude as the cost involved in other diseases requiring analogous techniques. For instance, the cost calculated in this study (about $600–$1000 per patient found) is comparable to a cost of about $2000 per patient found to have renovascular disease using the intravenous pyelogram as a screening test or to the cost of about $4000 per patient found to have an abnormal mammogram (*14*).

The marginal cost of performing a lung scan on all young patients with pleuritic pain, as opposed to those with significant case history, physical, or radiographic findings, raises the cost per patient from $596 to $991. This incremental cost is offset by the benefits gained in finding and treating the additional 5% of patients with pulmonary embolism. Currently we lack the information to calculate this benefit.

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