EDITORIAL

The Low Probability V/Q Lung Scan: Can Its Credibility Be Enhanced?

The use of specific diagnostic algorithms to categorize lung scans as high, intermediate or low probability for pulmonary emboli as well as normal, was initiated by the late Dr. Dan Biello and his colleagues at Washington University in St. Louis in the late 1970s (*1*). Shortly thereafter, Dr. Barbara McNeil at Harvard University formulated an alternate, useful approach to lung scan interpretation (*2*). Both schema were based on retrospective reviews of lung scintigrams and angiograms at their respective institutions. In the early 1980s, the criteria for the prospective investigation of pulmonary embolism diagnosis (PIOPED) were formulated and adhered to during the study conducted at six medical centers in 1984–1985 and reported in *JAMA* in 1990 (*3*).

One key area in which the PIOPED criteria differed from those of Biello and McNeil was the erroneous placement of single moderate size V/Q mismatches (SSM) in the low rather than intermediate category. Although many have questioned the wisdom of this decision, Gottschalk (*4*) points out that the data from Rosen's study (*5*), showing a 50% incidence of emboli in SSM, was not available to the PIOPED investigators when they formulated their criteria. Nonetheless, PIOPED's finding of a 36% incidence of emboli in SSM has perpetuated a major credibility problem that had already existed for the low probability interpretation. Even prior to PIOPED, pulmonologists, such as Moser (*6*), had indicated that clinical needs were best served by eliminating low or intermediate probability interpretations and, instead, calling them "nondiagnostic." Hull and Raskob (*7*) echoed this sentiment and indicated that "reporting a lung scan pattern as being of low probability is no longer clinically correct." They expressed concern that "this report is frequently misinterpreted by the clinician as ruling out pulmonary embolism."

Pulmonologists' fear of misunderstanding the meaning of low probability interpretations is supported by the interesting survey of referring clinicians conducted by Dr. Harry Gray and his associates at Glasgow's Royal Infirmary (*8*). Although only 5% of clinicians felt a low probability interpretation made PE highly unlikely, an enormous 65% felt that it equated with a diagnosis of "PE uncertain." In this regard, they felt it was more of an indeterminate interpretation. In an associated survey, Gray et al. (*9*) found a wide variation in the way nuclear medi cine physicians interpret their own probability language. They conclude that "the use of verbal probability language complicates the communication of PE risk" and might best be replaced with actual likelihood ratios for or against the presence of PE.

Another interesting change that occurred between PIOPED and Biello's original criteria relates to the definition of a low probability interpretation in terms of its associated positive predictive value (PPV) for disease. Biello confined it to <10% whereas PIOPED broadened it to <20%. The latter decision was predicated on a desire to lower the number of intermediate interpretations. Recognizing that clinical decisions regarding anticoagulation are more confidently made on a 90% rather than 80% probability of the presence or absence of disease, it is certainly prudent to attempt to narrow the category to more closely fit Biello's originally proposed <10% predictive value for the low probability interpretation. Stein et al. (*10*) attempt to accomplish this in the accompanying article by their proposal of criteria for a very low probability category of interpretation.

The literature certainly suggests that we may have a "credibility gap" with our referring physicians in the area of low probability interpretations. Therefore, it is appropriate to examine what attempts already have been made and must be made in the future to try to rectify the situation.

MODIFICATION OF PIOPED CRITERIA

In a 1992 publication (*11*), the PIOPED investigators reviewed the data and modified the criteria, particularly those for low probability. Most notable among these modifications was the replacement of the SSM into the intermediate category in which Biello had originally placed it and from which it should never have been removed. The two other modifications were placement of multiple matched V/Q abnormalities with a *negative chest radiograph* in the *low probability* category and the suggestion that single matched defects might be *intermediate* rather than low probability. Sostman et al's. (*12*) use of these revised criteria found the modifications correct, with the exception of the intermediate category placement of the single matched defect. They found no PE in all eight patients with this finding. In the article by Stein et al. (*10*), their combined group revealed a PPV of 12% for single matched defects which places it in their low (10%–19% PPV) probability category. This is a revision downward from the disturbing 28% PPV found by the PIOPED investigators when they retrospectively revised their criteria (*11*). Stein et al. attribute this previously higher number to a more limited database. There does not appear to be any logical reason for the difference in categorizing single or multiple V/Q matches. It is my belief that further investigative work will allow placement of all V/Q matches (single or multiple) associated with a negative radiograph into a very low probability category of <10% PPV.

FURTHER REFINEMENTS OF MODIFIED PIOPED CRITERIA

The PIOPED database was created to allow easy access for retrospective review. In their previous articles on patient stratification (*13*) and correlation with clinical assessment (*14*), Stein, Gottschalk and associates elegantly demonstrated how combining clinical information with lung scan interpretation can significantly enhance the PPV as compared to using the scan by itself. For example, a PIOPED low probability interpretation with its 14% PPV for PE dropped to 4% PPV when combined with a low suspicion of PE by clinical assessment. Stein et al. (*10*) sought to improve the value of low probability interpretations by identifying the criteria for a "very low probability" category with a <10% PPV. The importance of this concept is enhanced when one considers some of the PIOPED data associated with the gold standard, pulmonary angiography. With two experienced interpreters for each angiogram, the interobserver disagreement was 17%. With an adjudi-

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cator (third expert) involved, differences were resolved with a subsequent interobserver variation of approximately 9%. It therefore appears reasonable that a lung scan interpretation that would have a <10% PPV would approach the reliability of the gold standard.

In their "very low probability" category, Stein et al. (*10*) place three specific singular findings:

1. Nonsegmental abnormality (e.g., cardiomegaly, enlarged aorta, etc.).
2. Perfusion defect smaller than radiographic finding, e.g. infiltrate.
3. Matched V/Q abnormality in two or three zones of a single lung associated with a normal radiograph.

They also proposed one combination of findings for this category which was a nonsegmental abnormality associated with a perfusion defect less than the radiographic finding.

Multiple matched defects associated with a negative radiograph represent an area in which the revised PIOPED criteria and the original Biello algorithm differ somewhat. Whereas Biello did classify most V/Q matches with a negative radiograph as low probability, he did set up a special "diffuse severe airway obstruction" finding for particularly advanced abnormalities which he placed in the intermediate probability category. In patients with multiple (two or more) matches, Stein et al. (*10*) found that only 3% had PE. As mentioned earlier, single V/Q matches which fell into their low probability (10%–19% PPV) category will likely join multiple V/Q matches in the very low category when further investigative work is available.

USE OF ANCILLARY SCINTIGRAPHIC FINDINGS

Several ancillary findings have contributed significantly to lung scan diagnosis. One of these is the "stripe sign," described by Sostman and Gottschalk (*15*), which carries with it a 93% negative predictive value for PE. The presence of a stripe of normal parenchyma separating a perfusion defect from the lung surface is therefore a strong factor weighing against PE. Freitas et al. (*16*) recently completed a prospective study using two modifications to the PIOPED classification. These were the placement of moderate segmental perfusion mismatch in the intermediate category and using the stripe sign. By so doing, they were able to obtain better angiographic-proven PE discrimination between intermediate (31.8% PE prevalence) and low (5.5% PE prevalence) probability V/Q results than had been obtained for PIOPED intermediate (32.6% PE prevalence) and low (16.3% PE prevalence) probability interpretations.

The association of pleural effusions and their size is another example of useful ancillary information. Previous work by Bedont and Datz (*17*) as well as Gottschalk and Stein (*18*) suggest that large pleural effusions with corresponding V/Q matches could be categorized as low probability studies. Smaller effusions are more suspect and are to be placed in the intermediate category. The current work of Stein et al. (*10*) interestingly suggests that when combined with another finding, such as a nonsegmental abnormality or matched V/Q defects with a negative radiograph, smaller costophrenic angle effusions also may be considered low probability (10%–19% PPV).

UTILIZATION OF INFORMATION PROVIDED BY NONINVASIVE EVALUATION OF DEEP VENOUS SYSTEM

In addition to clinical assessment, the role of noninvasive examination of the lower extremities for deep venous system in patients with suspected PE is increasingly emphasized in the diagnostic algorithms proposed for this purpose. Currently, Impedence Plethysmography (IPG) and real-time (B mode) ultrasonography are used to accomplish this goal (*19,20*). By now, it is well established that anticoagulation is not indicated for patients with a low probability lung scan pattern for PE and a negative IPG or ultrasound exam. In contrast, patients with evidence of deep venous thrombosis are considered candidates for this type of therapy. The introduction of radiolabeled monoclonal antibodies targeted to specific sites on activated components of clotted blood provide a new and exciting approach to the diagnosis of deep venous thrombosis (*21*). Initial clinical trials have demonstrated excellent sensitivity and specificity with these preparations. The use of radiolabeled synthetic peptides may further simplify and enhance the utility of this approach (Alavi A, *personal communication*, 1995). It is conceivable that future application will include a perfusion scan followed by imaging with a thrombus-avid radiolabeled compound as a routine diagnostic approach for the management of patients with suspected PE. This may considerably improve the accuracy of the diagnosis and facilitate the timely workup of such patients.

IMPROVING THE UNDERSTANDING OF LUNG SCAN LANGUAGE

All the effort expended in refining our scintigraphic criteria will be for naught unless we correct the problems existing in the communication between the nuclear medicine physician and referring clinician. It is our policy to verbally communicate all lung scan interpretations immediately upon completion of the study with an explanation as to what the report means. For the past several years, all low probability interpretations end with the statement: "Low probability lung scans may be associated with a 10%–15% incidence of pulmonary emboli."

How else can we best communicate exactly what is meant by verbal probability categories of lung scan interpretation? Gray (*9*) has suggested using more specific likelihood ratios instead of probability categories. A 10% probability of PE would be expressed as a 9:1 likelihood ratio for no PE, whereas a 5% probability would make the likelihood ratio 19:1 for no PE. On the other end of the diagnostic spectrum, a 9:1 or 19:1 likelihood ratio for PE (high probability) would correspond to 90% and 95% probability of PE, respectively.

CONCLUSION

It is clear that low probability V/Q scan interpretations are often not welcomed by many of our clinical colleagues who would prefer that we lump them with the intermediate class and call them nondiagnostic. Continuing prospective and retrospective investigations refining the criteria to narrower categories, use of ancillary scintigraphic findings, noninvasive evaluation of the deep venous system, incorporation of clinical data and the potential incorporation of likelihood ratios into the report should go a long way in helping to restore the confidence of pulmonologists in low probability interpretations of V/Q studies. Rapid and continued communication with the clinician is an integral part of the reporting process and should help avoid any misunderstanding.

Drs. Stein and Gottschalk are two of several individuals who have contributed enormously to our understanding of lung scan interpretation. Their current effort, along with Dr. Relyea, to further refine the low probability category is most appreciated and should prove useful in helping us address some of the gray areas existing in lung scan interpretation.

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Radiation Pneumonitis Imaged with Indium-111-Pentetreotide

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Early recognition of radiation pneumonitis enables adequate treatment with a reasonable chance to prevent late sequelae. The feasibility of ^{111}In-pentetreotide in detecting this condition was explored in this study. **Methods:** The degree of lung uptake of ^{111}In-pentetreotide, evaluated both visually and quantitatively by irradiated-to-nonirradiated area ratios (INIA ratio) from planar images after 24 hr, was analyzed in relation to the radiation field and compared with ventilation/perfusion (V/Q) images and chest radiographs or CT in 11 patients who had received radiotherapy to the mediastinum or to the internal mammary nodes, 10 of whom were suspected of having clinical radiation pneumonitis. Additional SPECT studies were used to map lung uptake distribution. **Results:** Indium-111-pentetreotide scans were positive in nine symptomatic patients examined 2–5 mo after radiotherapy; strongly or moderately positive in eight patients, one of whom was receiving steroid therapy without clinical response; and weakly positive in one patient with good steroid response. Indium-111-pentetreotide studies were negative in one asymptomatic patient examined 1 mo after radiotherapy and in one symptomatic patient, with subsequent diagnosis of aspecific viral pneumonitis, examined 4 mo after irradiation. Positive ^{111}In-pentetreotide scans delineated areas of radiation pneumonitis that adequately correlated with areas of decreased ventilation/perfusion and x-ray abnormalities. INIA ratios varied from 1.01 to 2.16 and, in irradiated areas with visible uptake, the lowest value was 1.29. SPECT showed lung uptake in both superficial and deep lying areas in patients with mantle irradiation fields, whereas distribution was limited to anterior areas in internal mammary lymph node chain irradiation. **Conclusion:** Indium-111-pentetreotide can detect radiation pneumonitis and may have a role in both the differential diagnosis of patients who have complaints after radiotherapy, and when supported by quantification in the monitoring of response to steroid therapy.

Key Words: radiation pneumonitis; indium-111-pentetreotide; lung uptake assessment

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In radiation therapy of the thorax, radiation pneumonitis may occur 1–8 mo after treatment, varying from mild symptoms, such as fever, dyspnea and cough, to respiratory distress (*1,2*). From 8 mo onwards, lung fibrosis may appear. Although this condition remains mostly subclinical, it may lead to progressive impairment of pulmonary function.

Early assessment of radiation pneumonitis enables adequate treatment with a reasonable chance to prevent or limit late sequelae. Treatment includes prompt and maintained use of corticosteroids, which usually results in an effective suppression of complaints associated with the above mild symptoms (*3*). A delay in the start of steroid therapy may lead to a less effective clinical response.

Recognition of clinical manifestations, together with find-

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