

with a negative PET scan, there is only $\leq 5\%$ probability of malignancy. Therefore, it may be economical to postpone or avoid surgery in this probable benign group.

CONCLUSION

FDG-PET is highly accurate in differentiating malignant from benign solitary pulmonary nodules (0.6–3 cm) when radiographic findings are indeterminate. The projected risk estimate for probability of cancer as well as detection of any involved lymph nodes could be very useful in the treatment of patients with solitary pulmonary nodules.

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EDITORIAL

Is PET Ready for Prime Time?

The practices for establishing medical insurance coverage policies include certain technology assessment steps and standards for evaluating the quality of supporting evidence from the medical literature. If we look at the standards for accepting evidence from the medical literature of some of the major insurance companies we find that they define the quality of the evidence. The Technology Evaluation Committee (TEC Committee) of Blue Cross/Blue Shield, for example, has very well-defined standards:

1. The study must be prospective.
2. There must be more than 10 patients in each study.
3. There must be a representative patient sample.
4. The imaging technique must be clearly specified.
5. The observers or independent readers must be blinded—not only to the reference standard but the alternative test.
6. There must be a clear and consistent use of the reference stan-

dard, e.g., either tissue sampling or biopsy.

7. There must be a within subject comparison between the imaging test and the alternative test.

Abstracts will not meet these criteria and only peer-reviewed publications are acceptable. Are these standards reasonable? Sackett and others from the Evidence-Based Medicine Working Group have established and published similar yet more rigorous guidelines for determining the quality of evidence for a diagnostic procedure (1,2). Table 1 is adapted from Jaeschke et al. (1) and presents their criteria for evaluating and applying the results of studies of diagnostic tests. An inspection of Table 1 and the primary guides for assessing validity reveals that they are quite similar, but more detailed than described above.

Unfortunately, many payers, including Blue Cross and Aetna, have not deemed PET oncologic studies as acceptable for payment and have not established policies for coverage of these studies. Their stated major reason for this decision relates to the lack of articles in the peer-review literature that meets their criteria for satisfactory quality of evidence.

In this issue of *JNM*, Gupta et al. (3) present their experience in the use of

TABLE 1
Evaluating and Applying Results of Diagnostic Tests

Are the results of the study valid?

Primary Guides:

- Was there an independent, blind comparison with a reference standard?
 - Did patient sample include appropriate spectrum of patients to whom diagnostic test will be applied in clinical practice?
- #### Secondary Guides:
- Did the results of the test being evaluated influence the decision to perform the reference standard?
 - Were the methods for performing the test described in sufficient detail to permit replication?
 - If the test requires observer interpretation, was there a measure of observer variability.

What were the results?

- Are likelihood ratios for the test results presented or data necessary for their calculation provided?

Will the results help me in caring for my patients?

- Are the results applicable to my patients?
- Will the results change my management?
- Will patients be better off as a result of the test?

FDG-PET studies in 61 patients with solitary pulmonary nodules. The results show PET to have a sensitivity of 93%, specificity of 88%, for detection of malignancy in solitary pulmonary nodules. This indeed sounds very

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good, but is it likely that this manuscript will meet the standards just described? If the answer is yes, it is then also likely the article will hasten the decision for a much-needed coverage policy.

The study design was prospective and involved a nonrandomized cohort of patients who consecutively presented for evaluation of indeterminate solitary pulmonary nodules that were 3 cm or less in size. Tissue was used as the independent reference test and obtained by thoracotomy in 43 subjects, needle aspiration biopsy in 13 and by bronchoscopy in 4. Follow-up for 2 yr was utilized as a reference test in one subject in whom tissue was not obtained. All patients had chest radiography and CT which were interpreted independently. A direct head-to-head intrasubject comparison between CT and PET was not made, as the criteria for selection already included the presence of a radiographically indeterminate (by chest radiographs and CT) solitary pulmonary nodule. In this regard, the population and the PET interpreters were somewhat biased in that selecting patients with radiographically indeterminate solitary pulmonary nodules increased the prevalence of malignancy to 73% in the study population. Thus, the PET observers had to be aware of a higher pre-existing probability of malignancy in the study population than that seen in all patients with solitary pulmonary nodules. Did the patient sample include an appropriate spectrum of patients to whom the diagnostic test will be applied in clinical practice? Certainly, the size of the solitary pulmonary nodules was appropriately limited to less than 4.0 cm and there was a good mix of small nodules, with one-fourth of the solitary pulmonary nodules less than 2.0 cm in size. If PET does *not* substitute for CT in the evaluation of solitary pulmonary nodules, this study population exactly represents the patient population that would be studied in most PET centers, i.e., those with radiographically indeterminate solitary pulmonary nodules. If PET would be used in place of CT in the evaluation of *all* patients presenting with solitary pulmonary nodules, the study population does not include an appropriate spectrum of patients that would be representative of the more general clinical population of solitary pulmonary nodules. The more general population would have a lower prevalence of malignant solitary pulmonary nodules.

The study does not state explicitly that the two experienced PET observers providing qualitative visual analysis were blinded to the results of the reference test, although

this was presumably the case. An abnormal PET test was defined as focal uptake in suspected nodules or lymph nodes greater than background mediastinal activity. The study does not state whether consensus reading was used, nor does it provide information on reader agreement rates. Thus, while the study design does not support the rigid application of the above criteria, it is clear that an independent, blind comparison with a reference standard was made in this rather large series of patients. Furthermore, there was no verification or workup bias and the methods for performing the test as well as the criteria for a positive test were explicitly described. The results were presented using likelihood ratios as well as conventional methods of analysis.

The study concludes by indicating that PET can be useful in determining the probability of cancer in patients with radiographically indeterminate solitary pulmonary nodules. The study does not define a clear role for PET but suggests that the real value of PET would be in avoiding unnecessary thoracotomies in patients with benign nodules. Ultimately, this is what strikes at the heart of the matter, i.e., is PET valuable enough for insurers to pay for it? Will PET just add another high-tech cost to management of patients with solitary pulmonary nodules without effecting outcomes, or does it have the ability to appreciably modify the outcome in a beneficial way.

What would be a beneficial outcome? Based on evidence in the literature, current anatomic-based modalities may miss or result in delayed diagnosis (false-negative rate) in as many as 30% of malignant solitary pulmonary nodules. Similarly, as many as 30%–40% of benign solitary pulmonary nodule may be subjected to unnecessary thoracotomy because of the high false-positive rate of radiography and CT. A correction of either of these errors in diagnosis by PET would result in a better outcome for the patient.

It is generally believed that the concordance between CT and PET for “true-positive” studies is higher than the concordance between CT and PET for “true-negatives.” As “indeterminate” CT studies must be classified as “positive” studies, the concordance between the sensitivity of CT and PET is considerably higher than the concordance between their specificities. Although the specificity of PET is lower than its sensitivity and there will be fewer false-negative PET studies than false-positive PET studies, it is the improved specificity of PET over CT which will lead to its greatest potential utility in avoiding unnecessary surgery on patients with benign solitary pulmonary nodules. The true-negative

rate for PET is perhaps 35%–40% higher than CT. With these impressive performance characteristics, PET could be substituted for CT in the diagnostic evaluation of patients with solitary pulmonary nodules. However, a study design that includes an intrasubject direct head-to-head comparison of the two modalities may be needed to prove such hypotheses to payers.

As Dr. Gupta and his colleagues correctly point out, some 20,000–25,000 unnecessary thoracotomies per year could be avoided because of the lower false-positive rate of PET compared to CT. Translated into health care dollars, this could represent an expense avoidance of over \$250,000,000 per annum. Although PET is more expensive than CT, the additional cost of substituting PET would be minuscule compared to the cost savings recognized by the avoidance of unnecessary thoracotomy. If there is only a 1 in 20 chance that a patient with a negative PET study has a malignant solitary pulmonary nodule, most clinicians would opt for watchful waiting rather than proceeding immediately to an unnecessary “diagnostic thoracotomy.”

We often hear that the value of a diagnostic test can be described in terms of its ability to reduce diagnostic uncertainty. It is, however, often difficult to place a real dollar value in association with this reduction. In the case of PET in the evaluation of solitary pulmonary nodules, it would seem that we now have valid studies in the peer-review literature which establish that PET is now a procedure that should be routinely used in the assessment of patients with solitary pulmonary nodules. Compared to the current management paradigms which use chest radiographs, CT and biopsy, PET could substantially reduce the number of patients unnecessarily subjected to diagnostic thoracotomies and the expenditures associated with these surgeries.

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