Routine Use of a V/Q SPECT/Low-Dose CT Hybrid System to Diagnose Pulmonary Embolism Seems Premature

TO THE EDITOR: Gutte et al. (*1*) reported on a novel, exciting concept to diagnose pulmonary embolism (PE) using a γ-camera integrated with a multidetector CT scanner. Interestingly, ventilation–perfusion (V/Q) SPECT alone had almost a 20% false-positive rate caused by interlobar fissures, pleural fluid, and pulmonary pathology, whereas CT of the pulmonary arteries (CTPA) had a 100% positive predictive value. This finding emphasizes that, like a conventional V/Q scan, a V/Q SPECT scan showing mismatched defects requires a recent chest radiograph or preferably a low-dose pulmonary CT (LDCT) scan, conveniently performed with the author's hybrid scanner. However, the value of the reported superior sensitivity of SPECT/LDCT relative to CTPA, and the drawbacks of CTPA due to renal impairment and radiation dose, may be debatable.

One hundred ninety-six patients were recruited during 20 mo, a remarkably low figure for the 2 hospitals mentioned. At the same time, 24% of the patients were excluded because of renal impairment. To me, this indicates that some kind of additional selection criteria were applied in choosing from among the general cohort of patients with suspected PE. For comparison, only 0.7% of patients were excluded because of a glomerular filtration rate of less than 30 mL/min in the large, multicenter Christopher study (*2*). It should also be noted that CTPA in azotemic patients may be performed with substantially lower contrast medium doses (*3,4*) than in the present study, therefore disqualifying only a minority of patients for CTPA.

Seven percent of the patients were excluded from CTPA because they were women less than 40 y old. The relatively high effective radiation dose (11 mSv) with the present CTPA protocol may have been the motive. The 2007 Fleischner Society Statement (*5*), representing a certain expertise in PE diagnosis, indicates that exposure parameters resulting in an effective dose as low as 3–5 mSv is sufficient for an adequate study. In fact, 80- to 100-kVp CTPA with effective doses in the same range as (3.3 mSv) (*6*) or actually lower than (1.3–2.3 mSv) (*6–8*) that of the present SPECT/LDCT (3 mSv) have been achieved with preserved or even improved diagnostic quality.

A composite reference standard including the index tests, that is, V/Q SPECT and CTPA, was used by Gutte et al. (*1*). This choice may introduce incorporation bias (item 7 in the Quality Assessment of Diagnostic Accuracy Studies [QUADAS]) overestimating the various measures of diagnostic accuracy (*9*). Specifically, mismatched defects of any size and number at V/Q SPECT may then have been taken as evidence of PE, partly explaining the relatively low sensitivity of CTPA while false-positive diagnoses at SPECT/LDCT may still have been present. To the best of my knowledge, there is to date not a single prospective study published adhering to the Standards for the Reporting of Diagnostic Accuracy Studies (STARD) (*10*), where defined SPECT criteria for a positive diagnosis of PE has been validated with a proper reference standard. Thus, the probability of PE, depending on the size and number or segmental equivalents of mismatched defects on SPECT combined with various clinical likelihoods of PE, is not known.

One may also speculate on whether the high sensitivity of SPECT may diagnose PE that does not need anticoagulation. Several well-conducted outcome CTPA studies (*2,11–13*) clearly demonstrate that patients with clinically likely PE or a positive D-dimer, with few exceptions, can safely be left without anticoagulation after a negative CTPA result, even if not combined with ultrasonography of the lower legs (*14*). Thus, the lower sensitivity of CTPA may actually be advantageous relative to SPECT, which may carry the risk of serious bleeding complications from treatment of clinically harmless PE. The potential problem with false-positive and harmless true-positive PE at SPECT/LDCT may not be solved unless we study the outcome of patients with mismatched SPECT/LDCT defects left without anticoagulation after a negative CTPA result.

In conclusion, although having interesting potential in diagnosing PE, hybrid SPECT/LDCT is still a research tool and has to undergo properly performed studies based on the STARD and QUADAS criteria before it can be recommended as the "first-line imaging test in the work-up of PE in most cases." The drawbacks of CTPA relative to SPECT/LDCT, with regard to contrast media and radiation, are today of minimal concern in nonpregnant patients (*15*) if contrast media and radiation exposure parameters are optimized.

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DOI: 10.2967/jnumed.110.077313

REPLY: We greatly appreciate the interest of Dr. Nyman in our study (*1*), in which we concluded that ventilation–perfusion (V/Q) SPECT in combination with low-dose CT without contrast enhancement has excellent diagnostic performance in patients suspected of having pulmonary embolism (PE).

All patients were referred for a V/Q SPECT scan and therefore, as stated by Dr. Nyman, were preselected from the general cohort of patients suspected of having PE. The prevalence of patients excluded because of renal impairment was 24%, which compared favorably with the PIOPED II study (19%) (*2*). The conclusions from our study applied strictly to patients who could safely undergo CT angiography. Thus, whether the same results would be obtained in patients who cannot undergo CT angiography is unknown.

Dr. Nyman points out that using a lower dose of contrast medium and a lower kilovoltage could be sufficient for diagnostic CT angiography of the lungs. However, we chose to use a CT protocol that was the state of the art at that time (*2*) in order not to jeopardize the quality of the CT scans.

The lack of an independent gold standard for establishing a diagnosis of PE poses difficulties for evaluating and comparing the diagnostic accuracy of different modalities in PE. To compare the diagnostic performance of the tested modalities, we used a combination of composite and head-to-head consensus reading as the criterion standard. The use of this combined method that includes all tested modalities to classify PE patients raises methodologic and conceptual problems and is controversial. It is important to keep in mind that some patients may be incorrectly assigned to a disease category by the modality that is being studied, producing exaggerated or underestimated accuracies. This concern was also commented on in an invited perspective (*3*) on our study (*1*), published in *The Journal of Nuclear Medicine.* However, we believe that as long as the results are viewed in that respect, our approach can be justified and was the best available criterion standard.

In our report, we conclude that V/Q SPECT in combination with low-dose CT without contrast enhancement has an excellent diagnostic performance in patients suspected of having PE. Dr. Nyman speculates on whether the lower sensitivity of CT angiography of the lungs could benefit patients. Thus, the lower sensitivity of CT may be advantageous relative to SPECT, which may carry the risk of serious bleeding complications from treatment of clinically harmless PE. Several other studies have shown that after a negative pulmonary CT angiography result, 3- to 6-mo mortality is low and an anticoagulant can be omitted. However, our study was not performed as an outcome study but to compare the diagnostic accuracies of V/Q SPECT, CT angiography, and V/Q SPECT in combination with low-dose CT.

The incidence of chronic thromboembolic pulmonary hypertension (CTEPH) is estimated at about 4% within 2 y for all patients surviving an episode of symptomatic idiopathic pulmonary embolism (*4*). Most cases of CTEPH may originate from asymptomatic venous thromboembolism (*5*), but it is not known how many patients with PE that is unobserved in the acute phase later develop CTPEH. We hypothesize that a more sensitive diagnostic modality has to be used in order for CTEPH not to develop.

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DOI: 10.2967/jnumed.110.077438