

Appropriate Use Criteria for Ventilation–Perfusion Imaging in Pulmonary Embolism: Summary and Excerpts

Alan D. Waxman¹, Marika Bajc², Michael Brown³, Frederic H. Fahey¹, Leonard M. Freeman¹, Linda B. Haramati⁴, Peter Julien⁵, Grégoire Le Gal⁴, Brian Neilly², Joseph Rabin⁶, Gabriel Soudry¹, Victor Tapson⁷, Sam Torbati³, Julie Kauffman¹, Sukhjeet Ahuja¹, and Kevin Donohoe¹

¹Society of Nuclear Medicine and Molecular Imaging; ²European Association of Nuclear Medicine; ³American College of Emergency Physicians; ⁴American Society of Hematology; ⁵American College of Radiology; ⁶Society of Thoracic Surgeons; and ⁷American College of Chest Physicians

From the Newslines editor: Appropriate use criteria (AUC) are statements that contain indications describing when and how often an intervention should be performed under the optimal combination of scientific evidence, clinical judgment, and patient values while avoiding unnecessary provisions of services. SNMMI is a qualified provider-led entity under the Medicare Appropriate Use Criteria program for advanced diagnostic imaging, allowing referring physicians to use SNMMI AUC to fulfill the requirements of the 2014 Protecting Access to Medicare Act. SNMMI follows a balanced multidisciplinary approach to guidance development by including various stakeholders in the development process. For background and a detailed explanation of this development process, see <http://www.snmmi.org/ClinicalPractice/content.aspx?ItemNumber=15665>. The complete text of the AUC is available at www.snmmi.org/auc.

EXECUTIVE SUMMARY

Perfusion lung imaging for diagnosing pulmonary embolism (PE) was introduced 50 y ago (1). At that time, it offered a noninvasive alternative to pulmonary angiography in patients with a clinical suspicion of PE. Because there are many causes of diminished regional blood flow in the lungs, particularly redistribution of blood flow away from regions with lung disease, the subsequent introduction of radionuclide ventilation studies added greater specificity to findings on radionuclide perfusion imaging. When appropriately used and interpreted, ventilation–perfusion (V/Q) scintigraphy is an important examination for the evaluation of patients suspected of having regional compromise of lung perfusion and ventilation.

The purpose of this document is to describe the appropriate use of V/Q scintigraphy in patients suspected of having acute PE. It is hoped that through these recommendations, V/Q scintigraphy will be appropriately applied to benefit patients.

Representatives from the Society of Nuclear Medicine and Molecular Imaging (SNMMI), the European Association of Nuclear Medicine (EANM), the American Society of Hematology (ASH), the Society of Thoracic Surgeons (STS), and the American College of Emergency Physicians (ACEP), as well as chest radiologists, emergency department physicians, pulmonary critical care physicians, and physician experts in thromboembolic disease, assembled as

an autonomous workgroup to develop the following appropriate use criteria (AUC). This process was performed in accordance with the Protecting Access to Medicare Act of 2014 (2). This legislation requires that all referring physicians consult AUC using a clinical decision support mechanism before ordering any advanced diagnostic imaging service. Such services are defined as diagnostic MRI, CT, nuclear medicine procedures (including PET), and others as specified by the secretary of Health and Human Services in consultation with physician specialty organizations and other stakeholders (2). These AUC are intended to aid referring medical practitioners in the appropriate use of V/Q scans in patients suspected of having PE (3).

INTRODUCTION

The following document describes the appropriate use of V/Q scans in patients suspected of having PE. The authors have tried to cover the most common clinical scenarios for this use. However, the reader is reminded that a patient may present with variations of the scenarios covered here, or with signs or symptoms not described, for which V/Q scanning may still be indicated. This document is presented to assist health-care practitioners considering V/Q scanning in patients suspected of having PE; however, each patient is unique, as is each patient's clinical presentation, and therefore this document cannot replace clinical judgement. V/Q scanning can also be used for other conditions. These other scenarios are beyond the scope of this document.

Over the past half century, V/Q lung scintigraphy has been a sensitive and useful tool to detect the presence of PE. CT pulmonary angiography (CTPA) was introduced in the mid-1990s, and subsequently this technology demonstrated the ability to detect peripheral or subsegmental PE (4). CT scans are more commonly available 24 h a day, 7 d per week, as compared with nuclear medicine studies. In addition, CTPA diagnostic algorithms are simpler and able to depict pulmonary, pleural, mediastinal, and chest wall lesions that may cause symptoms similar to those of PE. With these attributes, CTPA has become the most common procedure for the diagnosis of PE. On the other hand, CTPA may be contraindicated in some patients, such as those with intravenous radiographic contrast reactions or renal failure. Therefore, in many patients, V/Q scintigraphy may be warranted as the primary imaging procedure when PE is suspected.

TABLE 1
Clinical Scenarios for PE in Adults

Scenario no.	Description	Appropriateness	Score
1	PE unlikely, D-dimer negative	Rarely appropriate	1
2	PE likely, D-dimer negative	Appropriate	8
3	PE unlikely, D-dimer positive	Appropriate	8
4	PE likely, male or nonpregnant female with normal chest radiograph	Appropriate	9
5	PE likely, male or nonpregnant female with mild abnormal chest radiograph	Appropriate	9
6	Suspected PE, male or nonpregnant female with significant abnormal chest radiograph	May be appropriate	5
7	PE likely, patient with abnormal renal function	Appropriate	9
8	PE likely, patient at risk for contrast complication	Appropriate	9
9	PE likely, patient who cannot cooperate for ventilation imaging, perfusion only	May be appropriate	5
10	PE likely, CTPA inconclusive or discordant with clinical probability	Appropriate	9
11	PE likely, hemodynamically unstable patient, portable V/Q equipment available	Appropriate	7
12	PE likely, hemodynamically unstable patient, portable V/Q equipment unavailable	Rarely appropriate	1
13	PE likely, ultrasound of lower extremity with clot	Appropriate	9
14	PE (clinically) unlikely, ultrasound of lower extremity with clot	May be appropriate	5
15	PE likely, pregnant patient with normal/mild abnormal chest radiograph, low-dose perfusion only	Appropriate	9
16	PE likely, pregnant patient with severe abnormal chest radiograph, perfusion only	Rarely appropriate	3
17	PE likely, patient ventilator-dependent	May be appropriate	5
18	Recent/prior documentation of PE with CTPA, suspected new PE	Rarely appropriate	2
19	Recent/prior documentation of PE with V/Q scan, suspected new PE	Appropriate	9
20	Recent documentation of PE by CTPA, patient now on anticoagulation; imaging to document disease status when clinically indicated	Rarely appropriate	2
21	Recent documentation of PE by V/Q scan, patient now on anticoagulation; imaging to document disease status when clinically indicated	Appropriate	9

PE likely or unlikely is determined by the referring clinician.

The exquisite anatomic detail of CTPA has raised concerns about the overdiagnosis and overtreatment of small, clinically insignificant PEs and the frequent reporting of new incidental findings that require further work-up (5,6). A third and even greater concern is the patient's CTPA radiation exposure, particularly to the radiosensitive breast tissue of young women.

To protect the systemic circulation, the pulmonary arteries and capillary beds uniquely possess properties that both trap and lyse small subsegmental clots, suggesting that small PEs are common physiologic phenomena (3,7). It is not, however, uncommon for radiologists viewing an abdominal CT examination to see incidental PEs at the lung bases. Physicians in the United States tend to treat these small PEs, although the wisdom for treating small, incidentally discovered PEs has been questioned. A recent policy statement from the American College of Chest Physicians (ACCP) (8) says that for subsegmental PEs and no proximal deep vein thrombosis (DVT), clinical

surveillance is suggested over anticoagulation when there is a low risk of recurrent venous PE (venous thromboembolism [VTE]) and anticoagulation is suggested over clinical surveillance when there is a high risk of recurrent venous PE. As stated by Goodman (3), the only 3 reasons to treat small PEs are inadequate cardiopulmonary reserve, coexisting acute DVT, and prevention of chronic PEs and pulmonary artery hypertension in patients with thrombophilia.

With an increasing clinical consensus that not all PEs should be treated, it is clear that PE imaging is best evaluated on the basis of outcomes rather than accuracy. In a prospective study comparing V/Q and CTPA, Anderson et al. (9) showed that the outcomes (based on a 3-mo follow-up of negative cases) were similar (false-negative rate, $\leq 1\%$) despite the fact that more PEs were detected with CTPA than with V/Q scans (17.7% for CTPA and 11.7% for V/Q). Similar outcome data have also been described in a large retrospective analysis (10).

Many of the referrals for patients with suspected PEs are for the presence of shortness of breath or hypoxemia. Both V/Q scans and CTPA can assist in diagnosing the cause of hypoxemia or shortness of breath. This document is therefore written to assist all medical practitioners in the appropriate use of V/Q scintigraphy in all patients who present with signs or symptoms of PE.

The 2 basic methods used to perform V/Q studies are planar imaging and SPECT. SPECT combined with low-dose CT has gained some popularity as well. Both methods have excellent performance characteristics in the diagnosis of clinically significant PE. SPECT, similar to CTPA, may demonstrate the presence of small, subsegmental emboli, which, if uncomplicated, may not require treatment. There is regional variation in the choice of V/Q methodology, with V/Q planar imaging being the preferred study in the United States (11) whereas V/Q SPECT is favored by the EANM and preferred in Europe, Australia, and some countries in Asia (11,12).

V/Q Planar Imaging

The standard planar examination consists of 8 ventilation views and 8 perfusion views (anterior, posterior, both lateral, both anterior oblique, and both posterior oblique) obtained in the same orientation. The ventilation study generally precedes the perfusion examination. Several different radiopharmaceuticals have been used for ventilation imaging. ^{133}Xe gas was commonly used in the past; however, in many centers xenon has been supplanted by aerosols. Presently, the most commonly used aerosol is $^{99\text{m}}\text{Tc}$ -diethylene-triaminepentaacetic acid. $^{99\text{m}}\text{Tc}$ -pyrophosphate and $^{99\text{m}}\text{Tc}$ -sulfur colloid aerosols are also in use with similar success. Some centers are using krypton gas. Several different kits are commercially available to administer these aerosols. A promising new agent not yet approved for use in the United States is an Australian product, Technegas (Cyclomedica), which produces a fine carbonized particle suspension with deep alveolar penetration (13).

The perfusion study is performed with $^{99\text{m}}\text{Tc}$ -macroaggregated albumin. These albumin particles average 20–70 nm in size, which effectively allows them to lodge in the pulmonary capillaries and distal arteriolar tree. A typical 111–185-MBq (3–5 mCi) dose will contain 200,000–700,000 particles, which will embolize <1% of the pulmonary capillary bed (14). The package insert from the manufacturer (Jubilant DraxImage) cautions against use in patients with severe pulmonary arterial hypertension; alternatively, some investigators choose to reduce the number of administered particles in these patients (15).

In centers with mobile γ -cameras available, bedside V/Q studies may be performed even in severely ill and hemodynamically unstable patients.

In pregnant patients suspected of having PE, the use of a perfusion-only study using a reduced administered activity of 18.5–37 MBq (0.5–1 mCi) of $^{99\text{m}}\text{Tc}$ -macroaggregated albumin is suggested.

V/Q SPECT

Characteristics of V/Q SPECT include a high diagnostic sensitivity. V/Q SPECT allows identification of segmental and subsegmental perfusion defects typical of PE, particularly in the middle lobe and lingula (11,16). It also allows quantification of PEs, valuable for therapeutic decision making, follow-up, and research (11,17). In patients with suspected PE who have complex situations including comorbidities such as chronic obstructive pulmonary disease, left heart failure, pneumonia, and tumor, V/Q SPECT retains its diagnostic utility (11,18).

Clinical Scenarios and AUC Scores

Clinical scenarios for the use of V/Q imaging in PE and final AUC scores are presented in Table 1.

REFERENCES

1. Wagner HN, Sabiston DC, Iio M, McAfee JG, Meyer JK, Langan JK. Regional pulmonary blood flow in man by radioisotope scanning. *JAMA*. 1964;187:601–603.
2. Protecting Access to Medicare Act of 2014. Congress.gov website. <https://www.congress.gov/113/plaws/pub193/PLAW-113pub193.pdf>. Accessed March 7, 2017.
3. Goodman LR. Small pulmonary emboli: what do we know? *Radiology*. 2005;234:654–658.
4. Remy-Jardin M, Remy J, Wattrin L, Giraud F. Central pulmonary thromboembolism: diagnosis with spiral volumetric CT with the single-breath-hold technique—comparison with pulmonary angiography. *Radiology*. 1992;185:381–387.
5. Hall WB, Truitt SG, Scheunemann LP, et al. The prevalence of clinically relevant incidental findings on chest computed tomographic angiograms ordered to diagnose pulmonary embolism. *Arch Intern Med*. 2009;169:1961–1965.
6. Schattner A. Computed tomographic pulmonary angiography to diagnose acute pulmonary embolism: the good, the bad, and the ugly—comment on “The prevalence of clinically relevant incidental findings on chest computed tomographic angiograms ordered to diagnose pulmonary embolism.” *Arch Intern Med*. 2009;169:1966–1968.
7. Gurney JW. No fooling around: direct visualization of pulmonary embolism. *Radiology*. 1993;188:618–619.
8. Kearon C, Akl EA, Ornelas J, et al. Antithrombotic therapy for VTE disease: CHEST guideline and expert panel report. *Chest*. 2016;149:315–352.
9. Anderson DR, Kahn SR, Rodger MA, et al. Computed tomographic pulmonary angiography vs ventilation-perfusion lung scanning in patients with suspected pulmonary embolism: a randomized controlled trial. *JAMA*. 2007;298:2743–2753.
10. da Silva R, Shah M, Freeman LM. Ventilation-perfusion (V/Q) lung scintigraphy: a long journey to a renewed position of prominence in diagnosing pulmonary embolism. *Clin Transl Imaging*. 2014;2:369–378.
11. Bajc M, Neilly JB, Miniati M, et al. EANM guidelines for ventilation/perfusion scintigraphy: part 1—pulmonary imaging with ventilation/perfusion single photon emission tomography. *Eur J Nucl Med Mol Imaging*. 2009;36:1356–1370.
12. Le Roux PY, Pelletier-Galarneau M, De Roche R, et al. Pulmonary scintigraphy for the diagnosis of acute pulmonary embolism: a survey of current practices in Australia, Canada, and France. *J Nucl Med*. 2015;56:1212–1217.
13. Freeman LM, Blaufox MD. SPECT V/Q imaging of the lungs. *Semin Nucl Med*. 2010;40:393–394.
14. Weibel ER. *Morphometry of the Human Lung*. Berlin, Germany: Springer-Verlag; 1963.
15. DRAXIMAGE MAA [package insert]. Kirkland, Québec, Canada: Jubilant DraxImage Inc.
16. Grüning T, Drake BE, Farrell SL, Nokes T. Three-year clinical experience with VQ SPECT for diagnosing pulmonary embolism: diagnostic performance. *Clin Imaging*. 2014;38:831–835.
17. Elf JE, Jogi J, Bajc M. Home treatment of patients with small to medium sized acute pulmonary embolism. *J Thromb Thrombolysis*. 2015;39:166–172.
18. Begic A, Opankovic E, Cukic V, Lindqvist A, Miniati M, Bajc M. Ancillary findings assessed by ventilation/perfusion tomography: impact and clinical outcome in patients with suspected pulmonary embolism. *Nuklearmedizin*. 2015;54:223–230.