

Latest highlight from literature review

Hess S, et al. State-of-the-Art Imaging in Pulmonary Embolism: Ventilation/Perfusion Single-Photon Emission Computed Tomography versus Computed Tomography Angiography - Controversies, Results and Recommendations from a Systemic Review. *Semin Thromb Hemost* 2016; 42: 833-845

V/Q SPECT/CT as first-line modality for PE diagnosis

Pulmonary embolism (PE) is a common and serious condition, potentially lethal if untreated. Because PE has no specific symptoms, diagnostic imaging is essential to avoid undertreatment as well as overtreatment which can result in an increased risk of serious adverse events¹.

Still, controversies remain regarding the first-line imaging for PE diagnosis even if the choice has narrowed to computed tomography pulmonary angiography (CTPA) and ventilation-perfusion single-photon emission computed tomography (V/Q SPECT)³ which has lately supplanted V/Q planar scintigraphy due to a better availability in clinical practice (particularly in Europe)⁴.

A more recent approach consists in fusing V/Q SPECT with low-dose computed tomography (V/Q SPECT/CT) to enable the acquisition of V/Q SPECT and CT scans of the lung in a single imaging session providing functional and anatomic data results⁵.

The introduction of SPECT and SPECT/CT has overcome limitations of planar scintigraphy by providing much simpler interpretation criteria based on a match– mismatch concept rather than on elaborate probabilistic interpretation with complicated algorithms⁶, and this has led to a very low degree of truly nondiagnostic results.

1. Konstantinides SV, et al. *J Am Coll Cardiol* 2016; 67(8): 976–990
2. Hess S, et al. *Adv Exp Med Biol* 2016; 1: 49–65
3. Stubbs M, et al. *Nucl Med Commun* 2017; 38(2): 135-140
4. Bajc M, et al. *Eur J Nucl Med Mol Imaging* 2009; 36: 1528-38
5. Mortensen J, et al. *Eur J Nucl Med Mol Imaging* 2014; 41(S1): S81–S90
6. Roach PJ, et al. *Semin Nucl Med* 2010; 40(6): 397–407

Aim of the study

Evaluate current evidence and controversy in the use and diagnosis performance of V/Q SPECT/CT, V/Q SPECT and CTPA as contemporary imaging modalities in suspected PE.

Design of the study

Systematic review of studies carried out with at least one of the following modalities to diagnose acute PE in a general population and compared with a predefined reference standard:

- CTPA
- V/Q SPECT or V/Q SPECT/CT
- Q SPECT or Q SPECT/CT

Analysis of diagnostic test characteristics including:

- Sensitivity
- Specificity
- Positive predictive value (PPV)
- Negative predictive value (NPV)
- Accuracy

Major findings

In patients suspected of PE, V/Q SPECT/CT was clearly the superior modality in most clinical settings with better overall diagnostic performance compared to CTPA which was less sensitive.

	V/Q SPECT/CT	V/Q SPECT	CTPA
Sensitivity	97.6%	93.3%	82.0%
Specificity	95.9%	93.0%	94.9%
PPV	93.0%	88.3%	93.8%
NPV	98.6%	96.1%	84.7%
Accuracy	96.5%	93.1%	88.6%

Clinical value for TECHNEGAS

By bringing further evidence on the overall diagnostic performances of V/Q SPECT/CT, this paper supports Cyclomedica's recommendation to use V/Q SPECT/CT with Technegas as the first-line imaging modality for pulmonary embolism diagnosis.

Early year literature review

Lung V/Q scan as diagnostic tool for PE

V/Q SPECT identifies (sub)segmental perfusion defects typical of PE. It also allows quantification of PE, valuable for therapeutic decision making, follow-up, and research. In patients with suspected PE who have complex situations (including comorbidities such as COPD, left heart failure, pneumonia, and lung tumor), radionuclide ventilation studies add greater specificity to perfusing findings allowing V/Q SPECT to retain its diagnostic utility.

Waxman AD, et al. J Nucl Med 2017; 58(5): 13N-15N

Although CTPA is the imaging of choice in diagnosis acute PE, V/Q is advocated in outpatients with low clinical probability and normal chest radiography, in young patients, in pregnancy, in severe renal impairment and in patients with history of contrast medium allergy.

Moreover, compared to V/Q planar scintigraphy, SPECT imaging improves the detection of subsegmental PE therefore reducing the frequency of inconclusive scans. The combination of low-dose CT and V/Q SPECT could be even more accurate than V/Q SPECT or CTPA alone, but more studies are still warranted.

Ruggiero A, et al. Clin Radiol 2017; 72(5): 375-388

Both CTPA and V/Q SPECT, when performed with optimized settings, are safe procedures regarding the radiation exposure to the embryo and fetus. However, regarding the important role of radiation burden, it is recommended to proceed with V/Q SPECT in follow-up studies and in young women patients due to the considerable lower radiation dose to the breast

committed by V/Q SPECT (0.8 mGy) compared to CTPA protocols (22-34 mGy). In addition, the extremely low radiation dose associated with ventilation SPECT scans highlights the importance of Technegas ventilation agent in offering additional clinical information for PE diagnosis.

Isidoro J, et al. Phys Med 2017; S1120-1797(17): 30112-6

Only a small fraction of patients undergoing a Technegas V/Q scan for PE diagnosis will require a CTPA to complete their investigation. This low rate of inconclusive study results also holds true in pregnant patients and in those with underlying chronic lung diseases supporting current guidelines recommending the use of V/Q scintigraphy in these patient populations.

Pelletier-Galarneau M, et al. Thrombosis 2017; 1623868

American College of Radiology Appropriateness Criteria

V/Q scans are the examination of choice in evaluating chronic thromboembolic pulmonary hypertension (CTEPH) from other causes of pulmonary hypertension as a normal or low-probability scan essentially excludes the diagnosis of CTEPH with a sensitivity of 90 to 100% and a specificity of 94 to 100%.

Sirajuddin A, et al. J Am Coll Cardiol 2017; 14: S350-61

Multidetector CTPA is the major modality used for PE diagnosis while the role of V/Q scans has considerably diminished even if it remains accurate and useful.

Kirsch, et al. J Am Coll Cardiol 2017; 14(5S): S2-12

Cyclomedica would like to shed light on recent studies showing a higher accuracy and fewer non-diagnosis cases of V/Q SPECT over CTPA imaging in diagnosing PE (Hall WB, 2009; Schatner A, 2009; Wiener RS, 2013; Morley NC, 2015).

It is also our view that introducing Technegas as ventilation imaging agent in the United States will increase the use of V/Q SPECT in diagnosing PE because of its lower radiation burden and absence of contraindication.

Other functional ventilation imaging tools

Xenon-enhanced ventilation and iodine-enhanced perfusion dual-energy CT technique showed that the ventilation and V/Q mismatch in patients with advanced emphysema improved after bronchoscopic lung volume reduction. This quantitative imaging technique-based approach may be a useful way to analyze the physiology of respiratory diseases, including COPD.

Lee SW, et al. Radiology 2017; 285(1): 250-260

Computed tomography ventilation imaging using four-dimensional CT (CTVI^{4DCT}) revealed good agreement with Technegas ventilation SPECT considered as the clinical gold standard for assessing regional lung function. Nevertheless, it is still needed to optimize the image quality of clinical 4DCT to further improve the accuracy of the modality.

Hegi-Johnson F, et al. Med Phys 2017; 44(8): 4045-4055

By deriving CTVI from 4D cone beam CT scans (CTVI^{4CBCT}) with iterative reconstruction and minimal truncation, it is possible to provide information on short timescale functional lung variations caused by breathing variability, changes in patient anatomy or radiation damage that are prone to occur in a longitudinal follow-up study. Therefore, this study demonstrated that CTVI^{4CBCT} can be applied clinically as part of the routine lung cancer radiation therapy workflow since it is equivalent to CTVI^{4DCT} which has been shown to correlate well with other ventilation imaging methods including PET-Galligas, SPECT-Technegas and MRI-3He.

Woodruff HC, et al. Med Phys 2017; 44(5): 1771-1781