GUIDELINE

Guideline for Ventilation / Perfusion Scintigraphy

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Abstract

This paper is about the Guideline for Ventilation / Perfusion Scintigraphy. It has been developed by the Brazilian Society of Nuclear Medicine to be a best practices guide used in Nuclear Medicine. Its function is to be an educational tool to help the Nuclear Medicine Services in Brazil to guarantee a quality care to the patients.

Introduction

This guideline presents the best practices for carrying out and interpreting Ventilation / Perfusion Scintigraphy.

The main indication for Ventilation / Perfusion Scintigraphy is the detection of acute pulmonary thromboembolism (PE). It is characterized by acute obstruction of a pulmonary artery, or one of its sub-branches, caused by venous thrombus. The typical picture includes symptoms such as dyspnea without other cause, chest pain on inspiration and hemoptysis, accompanied by signs of low blood oxygen saturation and tachycardia. Loss of consciousness, hemodynamic instability and death may occur in more severe cases.[1]

The American College of Radiology (2011) guideline classifies Ventilation / Perfusion Scintigraphy as highly recommended, combined with CT pulmonary angiography (CTPA). Both studies are highly accurate in the diagnosis of acute PE and the choice for one or the other will depend on the availability of each service and may follow some specific recommendations, as in the case of patients with allergy to iodinated contrast or renal failure, in which scintigraphy should be preferred.[2]

If adequately used and interpreted, ventilation / perfusion scintigraphy is an important tool for the detection of regional abnormality of pulmonary perfusion and ventilation, allowing for the accurate diagnosis of pulmonary embolism with low radiation exposure and minimum risks of complications.

Keywords

Pulmonary Embolism/complications; Pulmonary Embolism/diagnostic imaging; Ventilation-Perfusion Ratio; Pulmonary Artery/pathology; Radionuclide Imaging/methods.

Objectives

The purpose of this guideline is to provide practical guidance on the indication, performance and interpretation of the results of Ventilation / Perfusion Scintigraphy.

General information about the exam

It is an imaging diagnostic procedure that uses ventilation and perfusion scintigraphy to assess pulmonary diseases.

Indications

The main indications for ventilation / perfusion scintigraphy are listed on Table 1.

Relative contraindication

Pregnancy and breastfeeding. One should weight the cost/benefit and, if the procedure has to be performed, it should be done in such a way that exposure to radiation be minimized and, whenever possible, it would be preferable to carry out only the perfusion phase. It is worth noting that, in pregnant women with suspected pulmonary embolism and normal chest X-ray, the American Thoracic Society and the Society of Thoracic Radiology Clinical Practice recommend the use of

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Table 1 - Indications for ventilation / perfusion scintigraphy

1. Diagnosis of acute pulmonary thromboembolism;
2. Diagnosis of chronic pulmonary thromboembolism;
3. Assesment of the rate of resolution of PE (compared to previous study);
4. Assessment and quantification of right to left shunt;
5. Differential quantification of pulmonary function before pulmonary resection;
6. Lung transplant evaluation;
7. Assessment of the etiology of pulmonary hypertension;
8. Assessment of chronic parenchymal diseases.

Table 2 - Modified Wells Score

Modified wells criteria	Points
Clinical symptoms of DVT	3
PE is more likely than other diagnoses	3
HR > 100 bpm	1.5
Prior DVT / PE	1.5
Hemoptysis	1
Malignancy	1

Clinical probability: High > 6; Intermediate: 2 - 6; Low < 2.

perfusion lung scintigraphy as the method of choice for the diagnosis of PE, because it has the advantage of less exposure of the mother to radiation.[2]

Exam duration

About 1 hour in total (acquisition of ventilation and perfusion images).

Preparation

The patient must be capable of tolerating the dorsal decubitus position necessary to perform the images and be cooperative enough to carry out the preparation for inhalation, as described hereafter. The patient's standard chest radiograph, preferably in both posterior–anterior and lateral projections, and recently acquired (within a few-day-period), should be reviewed. The authors indicate a maximum interval of 48 hours. A CT scan can substitute for the chest radiography. In the assessment of PE, the standard chest radiography must be the first exam used to exclude other pathologies.[5]

Relevant information to perform the procedure

The likelihood of the patient having pulmonary thromboembolism[6] should be assessed (through D-dimer testing or using the modified Wells score [Table 2], for instance), as well as by assessing the patient's medical history (history of deep venous thrombosis (DVP), previous PE, chest X-rays, use of anticoagulant or thrombolytic).[4,5]

The patient should be instructed about the exam and how to adequately perform the aerosol ventilation procedure, if possible practicing before the exam starts.

Radiotracers

Ventilation: Tc-diethylenetriaminepentaacetic acid (DTPA) labeled with ^{99m}Tc, ^{99m}Tc labeled microcolloid or solid ^{99m}Tc-labeled carbon particles in argon carrier gas. The latter should be preferred, as far as available, because it has a more uniform distribution in the lungs with lower retention in the airways and bronchi.[7]

Perfusion: ^{99m}Tc macro aggregated albumin (^{99m}Tc-MAA).

Marking and quality control

Marking and quality must always be done according to manufacturer guidelines. However, pharmacopoeial criteria must be respected (pH between 5.0 - 6.0 and radiochemical purity ≥ 90%).[4,5]

Adult activity

Ventilation: The usual dispensed activity of ^{99m}Tc DTPA or sulfur colloid is 900–1300 MBq (25–35 mCi) in the nebulizer, from which only approximately 20–40 MBq (0.5–1.0 mCi) will reach the lungs.[8]

Solid ^{99m}Tc-labeled carbon particles in argon carrier gas – the activity administered should be calculated according to the distributor manual.

Since it is more difficult to achieve higher activity in the lungs with inhalation, it should always be performed first. It is essential that the perfusion activity should be

at least three times the counting rate of the ventilation activity to ensure that the image shows pulmonary perfusion, because both agents are labeled with ^{99m}Tc.[4,5]

Perfusion: 40–150 MBq (3–4 mCi); depending on the number of particles administered, this value could be higher), and should be in the range of 200,000–700,000 particles. The particles administered should be within a size range of 15 to 100 micrometers. In Brazil, currently available preparations have at least 90% of MAA particles between 10-100 micrometers in size.[9] In certain clinical conditions, the number of particles must be reduced, such as pulmonary hypertension and presence of right to left shunting. In the case of right-to-left shunt investigation, the number of particles should be decreased to 100,000 - 150,000.

Pregnant women: as mentioned before, it is preferable to perform only the perfusion analysis with ^{99m}Tc macroaggregated dose reduction (0.5 to 1 mCi).[4,5]

Pediatric dosage

Ventilation: Minimum activity should be no less than 10 MBq (0.27 mCi) to allow for sufficient count statistics to achieve good quality images. Since approximately 10% is retained within the lungs, it is suggested to administer as much as 15 times the activity of the DTPA needed (4 mCi).[3]

Solid ^{99m}Tc-labeled carbon particles in argon carrier gas - the activity administered should be calculated according to the distributor manual.

Perfusion: 1.11 MBq/kg (0.03 mCi/kg), with a minimum of 14.8 MBq/kg (0.4 mCi) if no ^{99m}Tc ventilation study is performed or 2.59 MBq/kg (0.07 mCi/kg) if a ^{99m}Tc ventilation study is performed. The number of particles depends on the age and weight, according with the table below:

Parameter	Newborn	1 year	5 years	10 years	15 years
Weight (kg)	3.5	12.1	20.3	33.5	55.0
Dosage (mCi)	0.2	0.5	1.0	1.5	2.5
Particles	10-50	50-150	200-300	200-300	200-700

In case of pulmonary hypertension and cardiac shunt investigation, these values should be reduced, depending on the age and the weight of the patient.

Precautions to be taken during tracer injection

Since the particles tend to decant, the syringe should be gently rotated prior to use. Blood should not be drawn back into the syringe to prevent MAA aggregation, because it can cause damage to the images. It is important that a single dose be administered over 30 seconds. The patient is oriented to inhale and breathe deeply during the tracer administration, facilitating its uniform distribution.

Imaging acquisition

Nowadays, there are 3 possibilities to acquire the images: planar imaging, SPECT imaging and SPECT/CT imaging.

Several studies have demonstrated that SPECT imaging yields a higher sensitivity compared to planar imaging. Major segmental defects and more periferal defects are detected by planar imaging. However, especially mesial defects and subsegmental defects are more easily detected by SPECT imaging. SPECT imaging can detect around 50% more defects compared to inhalation imaging. Despite this, the recent Apropriate Use Criteria published by the Society of Nuclear Medicine and Molecular Imaging (SNMMI) recommends that both types of imaging (planar or SPECT) are valid in the clinical practice.[10,11] We recommend that SPECT imaging be performed whenever possible.

SPECT/CT combines increased sensitivity of SPECT imaging with high specificity of CT imaging. Several studies have shown that SPECT/CT provides increased sensitivity, specificity and accuracy compared to planar imaging. The improved specificity of SPECT/CT may reduce the number of false-positive results by 50%. Some studies have even demonstrated that SPECT/CT can increase specificity of scintigraphy to almost 100%, and make the study more accurate than CTA.[12-16] However, to our knowledge, there are no studies which assess the clinical impact on patient evolution when SPECT/CT is also used. Thus, the authors suggest that SPECT/CT imaging be performed whenever possible due to its higher accuracy, even though other studies are needed to confirm the impact on the clinical management of patients.

Ventilation:

Low energy high resolution collimator (LEHR), with an energy window of 20% centered at 140 keV.

Planar imaging must be obtained in anterior, posterior, left and right anterior and posterior oblique views, in addition to lateral views.

Counting recommendation:[8]

Posterior: 250,000 counts;

Other projections: use same time as the posterior view.

The following is a suggested protocol for image acquisition using SPECT/CT:

LEHR (Low Energy High Resolution) collimator;

64x64 matrix;

64 views (with a dual-head camera, 32 views per head);

20 sec acquisition;

Zoom 1.0

180 degrees (dual-head) or 360 degrees (single-head camera).

For CT image acquisition:

If the equipment allows it, the algorithm for dose reduction in CT (for example, CareDose, Auto mA);

130 kV;

5 mm slice thickness;

Pitch 1.8;

0.8 s rotation time;

Number of images = 61

Perfusion:

Low energy high resolution collimator (LEHR), with an energy window of 20% centered at 140 keV.

Planar imaging must be obtained in anterior, posterior, left and right anterior and posterior oblique views, in addition to lateral views.

Counting recommendation:[8]

500,000 to 750,000 counts per image.

In the case of perfusion SPECT with low-dose CT, perform tomographic imaging (see the acquisition protocol recommended above).

Acquisitions for other indications

Shunt investigation: the inhalation phase isn't performed. Following the administration of technetium Tc 99m injection, a whole-body scan should be performed in the anterior and posterior views; a static head imaging may be performed to better assess the brain.

Perform differential analysis of lung function prior to surgical procedure: the ventilation phase should not be performed; only lung perfusion imaging should be performed, as described above.

Assess lung transplantation: perfusion images and pulmonary ventilation.

Interpretation[4,5]

Acute PE Diagnosis:

The interpretation of ventilation/perfusion lung scans, both planar and SPECT/CT, is based on comparison. Thus, when there are ventilation-perfusion defects, a V/Q matched defect is characterized. When there is a defect in perfusion, but not in ventilation, it can be said that there was a mismatch defect. Thus, when there is a defect in ventilation, and there is not the same area in perfusion, we say that there was a reverse mismatch.

In the past, the PIOPED criteria were widely used. These are old criteria based on planar images. In addition, their classification as high, intermediate, and low probability does not meet clinical needs. It is also important to take into consideration the pretest clinical probability calculated using the modified Wells score (see below) and assess the laboratory tests. The observer's experience will also be an important factor. Thus, we believe that the report must be as accurate as possible, providing a "yes or no" response for the presence of acute PE. Below are the criteria used by the EANM, which are similar to the ones we use in our clinical practice.

The SNMMI has recently published an important document on appropriate use criteria for lung scintigraphy. The diagram below corresponds to the proposed investigation of pulmonary embolism in patients with low to moderate risk of PE (Wells Criteria: < 6). The presence of normal chest x-ray combined with increased D-Dimer values is associated with an accurate indication for ventilation/perfusion lung scintigraphy. In these patients the D-Dimer values are crucial to continue the investigation using imaging methods.

Thus, according to the SNMMI document, in patients with higher likelihood for PE (Wells Criteria: > 6), there is no clinical impact associated with the use of the D-Dimer assay for the diagnosis of PE (Figure 2). In these patients, imaging methods must be requested regardless of the D-Dimer values. In the same way, patients with normal chest x-ray are candidates for lung scintigraphy as diagnosis method of choice to CT pulmonary angiography. Lung scintigraphy will

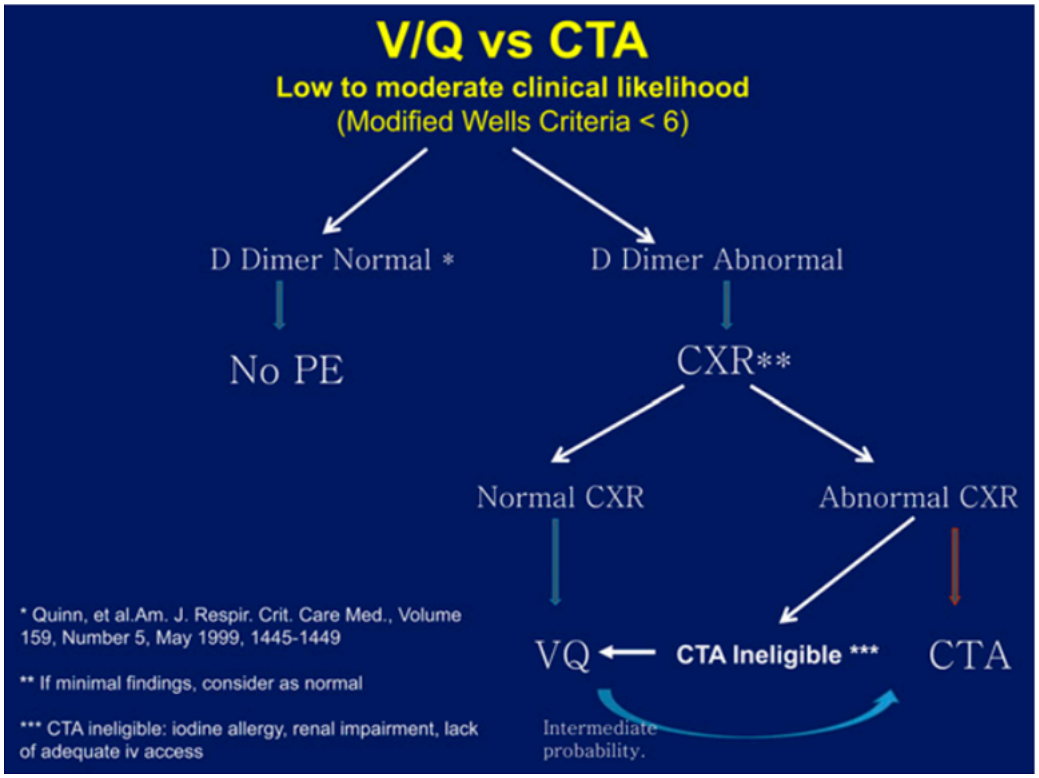

Figure 1 - Adapted from Waxman, et al. Appropriate Use Criteria for Ventilation–Perfusion Imaging in Pulmonary Embolism.

be the imaging modality of choice for investigation of suspected PE in patients with allergy to iodine, renal failure and inadequate venous access, even with abnormal chest x-ray.

Negative Acute PE:

Normal perfusion pattern conforming to the anatomic boundaries of the lungs;

Matched or reversed mismatch V/P defects of any size, shape, or number in the absence of mismatch;

Mismatch that does not have a lobar, segmental or subsegmental pattern, such as a stripe sign (perfusion defect with a normal perfusion stripe sign interposed between the defect and the adjacent pleural surfaces).

Positive Acute PE:

V/P mismatch of at least one segment or two subsegments that conforms to the pulmonary vascular anatomy (peripheral wedge-shaped defects – pleural based defects, and that conforms to the pulmonary vascular anatomy).

Inconclusive study:

Presence of multiple abnormalities identified in the images that do not correspond to any specific disease.

There are some causes for false-positive results. The main cause is an old or chronic PE. At the end of a hospital stay in which the patient was diagnosed with PE, it is recommended to perform a Ventilation/Perfusion Scintigraphy for this study to serve as reference for future suspicion of a PE. That is because, in some patients, the defect observed in the perfusion image may not normalize and remain as a mismatch defect. Nevertheless, in the vast majority of cases in which acute PE does occur, or the scintigraphy normalizes after treatment, or an infarction occurs in the region of the PE, the defect is regarded as a matched ventilation-perfusion defect. Other reasons for false positive results are: certain rare cases of pulmonary and mediastinal tumors, vasculitis and arteriovenous malformations; however, these possibilities, in general, do not represent a diagnostic problem when the overall patient's data is considered.

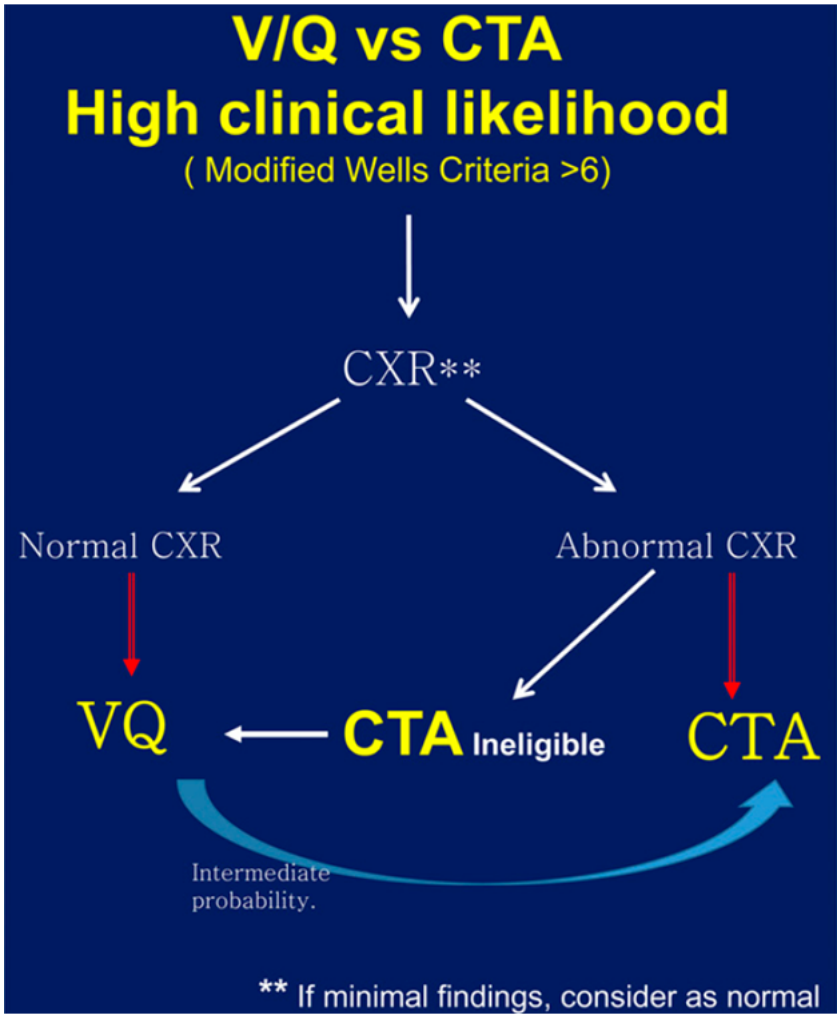

Figure 2 - Adapted from Waxman, et al. Appropriate Use Criteria for Ventilation-Perfusion Imaging in Pulmonary Embolism.

In cases in which the ventilation cannot be performed, only the perfusion phase may be performed, keeping good accuracy, with a sensitivity of 86% and a specificity of 93% compared to CTA;[17] and 80% and 96%, respectively, when combined with the interpretation of the chest x-ray.[18]

Evaluation of right to left shunts:

The presence of right to left shunts is detected through the presence of a tracer in extrapulmonary tissue, primarily in the brain. An image of the head complements the evaluation and helps detect small shunts. The presence of the radiopharmaceutical in the brain helps distinguish between a right-to-left shunt and free Tc-99m pertechnetate due to kit unlabelling, for instance, since the free Tc-99m pertechnetate would not be present in the brain.

The calculation of percentage shunts can be assessed using regions of interest (ROIs) drawn over the whole body and the lungs, in both anterior and posterior images, and through comparison of the radioactive activity in the lungs in relation to the whole body, resulting in a percentage number. Usually, it is considered as positive if the difference between the activity present in the lungs compared to the whole body is greater than 10%, following the formula:[19] (total number of whole body counts, including the background – total counts in the lungs) / total number of whole body counts, including the background x 100 = percentage of R-L shunt. Attention should always be drawn to radiopharmaceutical quality

control to ensure that the labeling efficiency is greater than 90%. Due to the presence of free Tc-99m pertechnetate. It should be remembered that visual analysis is always paramount and the presence of tracer in the brain and in renal cortex should be verified.

Perform differential analysis of lung function prior to surgical procedure:

The aim of this indication is to help predict the lung function reduction in the postoperative period following lung resection (e.g. lung cancer). This is particularly important in those patients who already have a reduced function in the preoperative period. The differential function is calculated by drawing ROIs on each lung in the anterior and posterior views. The lung can also be divided into three equal rectangular ROI: top, middle, and bottom. Alternatively, posterior oblique views can be used to assess lobar segmentation, assisting in cases of segmentectomy or lobectomy.[20]

Postoperative evaluation of lung transplantation

Evaluate the feasibility of vascular anastomosis. It is also possible to assess rejection, when there are matched defects suggestive of obstructive lung disease or changes in the perfusion between both lungs (in the case of unilateral transplantation).

Important observations

There may be hot spots on perfusion images, in case blood coagulation occurs in the syringe during injection of the tracer, which may occur when blood is aspirated into the syringe during injection.

The acquisition of images with the patient in different positions (dorsal decubitus or supine position) may hinder the comparability of the studies.

The unilateral absence of one of the lungs in the perfusion imaging, with normal ventilation, is not an indicative of PE. In these cases, the chest CT scan must be assessed in order to look for tumors, aortic aneurysm, vascular defects or other pathologies.

Author contributions

Conception and design of the research: Rigolon MY, Amorim BJ. Acquisition of data: Rigolon MY. Analysis and interpretation of the data: Rigolon MY, Mesquita CT, Amorim BJ. Writing of the manuscript: Rigolon MY. Critical revision of the manuscript for intellectual content: Mesquita CT, Amorim BJ. Supervision / as the major investigador: Amorim BJ.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any thesis or dissertation work.

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