Ventilation-perfusion lung scan for the detection of pulmonary involvement in Takayasu's arteritis

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Abstract. The aim of study was to analyse ventilation and perfusion (V/Q) lung scan findings in a series of Italian patients with Takayasu's arteritis. Eighteen consecutive patients underwent V/Q lung planar scintigraphy and single-photon emission tomography (SPET). Before perfusion scan acquisition was started, a first-pass study with ^{99m}Tc-macroaggregates of albumin was performed to assess the right ventricular ejection fraction (RVEF). All patients had normal chest X-rays and were symptom free at the time of the investigation. They also underwent echocardiography to evaluate pulmonary artery pressure and in 13 patients respiratory function tests were performed. In four patients, perfusion lung scan was repeated after 1 year. In 10/18 patients (55.5%), 43 unmatched lobar, segmental or subsegmental perfusion defects were found on planar images; ventilation scintigraphy was normal in all cases. On SPET images, 55 defects were found; no defects were found with SPET in the remaining patients who had normal planar images. All patients had normal RVEF and 5/13 patients had mild restrictive-obstructive lung disease. The pulmonary artery pressure was increased in two patients with perfusion defects. In the four patients who had repeat scintigraphy, all defects remained unchanged. The prevalence of lung perfusion abnormalities observed in Italian patients with Takayasu's arteritis is within the range of values reported in other countries, and V/Q planar scintigraphy is sufficient for the screening of patients.

Keywords: Takayasu's arteritis – Ventilation/perfusion lung scintigraphy – Lung involvement

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Introduction

Takayasu's arteritis (pulseless disease) is a chronic arteriopathy of unknown origin affecting the aorta and its main branches; it is prevalent mainly in Asia and South America [1, 2]. Besides involvement of the aortic arch and subclavian and carotid vessels, lesions in pulmonary arteries have also been described [3]. Over the years, many different imaging techniques including pulmonary angiography, computed tomography, magnetic resonance imaging (MRI) and perfusion lung scintigraphy have been used to detect pulmonary involvement [4, 5, 6, 7, 8]. In the course of a study designed to establish the prevalence of lung perfusion abnormalities in Takayasu's arteritis, pulmonary perfusion and ventilation were assessed by means of planar scintigraphy and single-photon emission tomography (SPET).

Materials and methods

This study was approved by the Ethics Committee of the Department of Nuclear Medicine at our hospital. Eighteen patients (17 females and 1 male; age 20–66 years, mean 41.5) affected by Takayasu's arteritis and diagnosed according to the criteria of the American College of Rheumatology [9] underwent V/Q lung planar scintigraphy and SPET. Six patients had had signs or symptoms of lung disease in the past (haemoptysis, dyspnoea or pleural effusion) but all were symptom free at the time of investigation. All patients were receiving treatment with antiplatelet drugs; 14 of them were also receiving prednisone, and ten, immunosuppressants (methotrexate, cyclophosphamide, cyclosporin or azathioprine). Mean lengths of these treatments before scintigraphy were 7, 4 and 2 years, respectively.

Ventilation planar and tomographic images were obtained after inhalation of approximately 74 MBq of graphite crucible microaerosol particles labelled with technetium-99m pertechnetate (Technegas), using a large field of view gamma camera (Picker Prism 2000) equipped with a low-energy, general-purpose parallel-hole collimator. Perfusion planar and SPET images were obtained the following day. A first-pass study, after injection of

259 MBq of labelled human serum macroaggregates of albumin, was performed to assess the right ventricular ejection fraction (RVEF) with a high-sensitivity parallel-hole collimator. Planar images were then acquired in the eight standard views with 700,000 counts per view. SPET was acquired collecting 60 views of 20 s per image; a series of transaxial images were reconstructed after prefiltered back-projection obtained with a low-pass filter (BT filter; order 5; cut-off 0.40). The number of segments with perfusion defects was assessed on planar and SPET images, as well as on three-dimensional display (3D display). Perfusion defects were classified as lobar, segmental, subsegmental or non-segmental, and the "match" or "mismatch" with the ventilation scan was recorded in each case. The extent of the defects was estimated according to the PIOPED (Prospective Investigation of Pulmonary Embolism Diagnosis) criteria for pulmonary embolism [10]. The images were interpreted by two experienced readers; in the event of discordant results regarding the site and extent of the perfusion defects, a consensus was reached. All patients had chest X-rays and colour Doppler echocardiography to detect parenchymal abnormalities and to evaluate pulmonary artery pressure (PAP) and valve insufficiency. The RVEF was calculated in ten patients with echocardiography. Thirteen patients underwent spirography for assessment of respiratory function. Four patients (three with an abnormal perfusion scan) were re-examined after 1 year because of an increase in PAP in two cases and the onset of pulmonary symptoms in the other two.

Results

Forty-three perfusion defects were found on planar images in 10/18 (55.5%) patients. The defects were lobar, segmental or subsegmental and were all unmatched with the ventilation scan (Fig. 1). Fifty-five mismatched V/Q defects were seen with SPET and 3D display (Fig. 2); however, no perfusion defects were seen on tomographic images when planar scintigraphy was normal. The number of defects was larger in the right than in the left lung, and the upper and middle lobes were affected more often than the lower lobes. The number and sites of perfusion defects visible on planar and SPET images are reported in Table 1.

The mean age of the patients with perfusion defects was higher than that of patients with a normal perfusion scan, although the difference was not statistically significant (46±13 vs 35±11 years; P=NS). However, patients with an abnormal scan had a longer interval between the onset of symptoms of arteritis and lung scintigraphy (mean interval 15.8±9.7 years; range 1–30) than patients with a negative scan (mean interval 6.8±6.9 years; range 1–22; P<0.05). Five of the 13 patients who underwent spirography had mild restrictive-obstructive lung disease

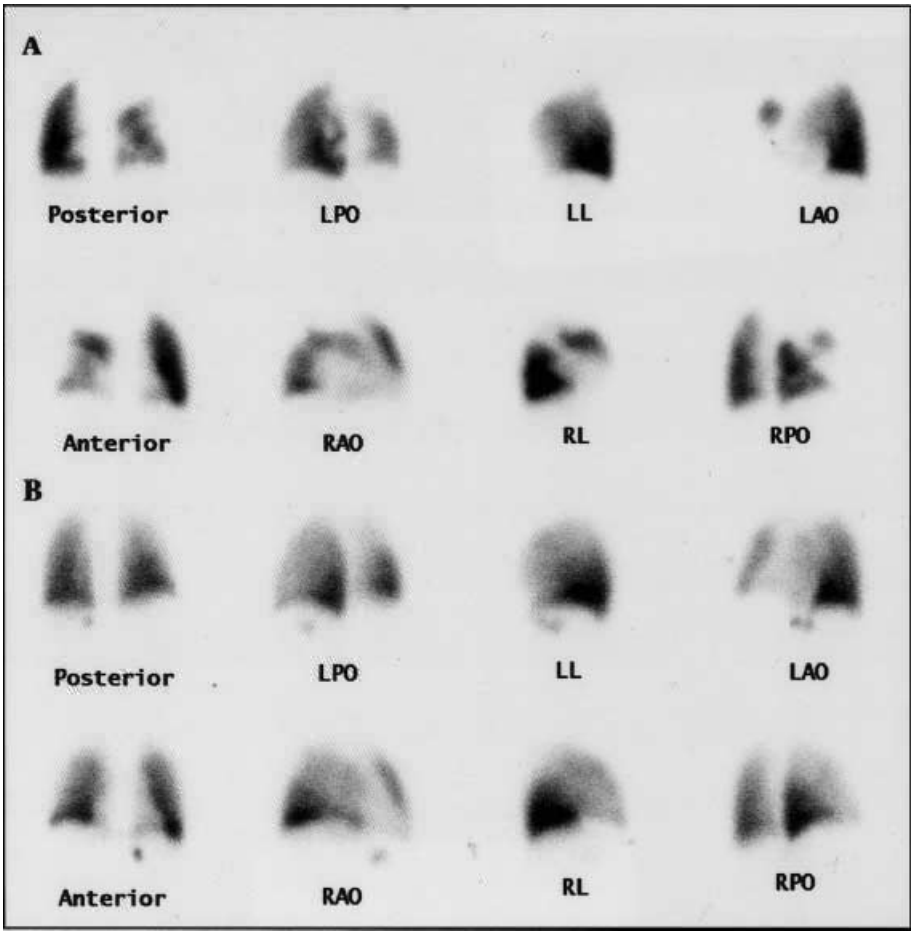

Fig. 1. Perfusion (**A**) and ventilation (**B**) planar scintigrams in a patient with Takayasu's arteritis. Multiple segmental and subsegmental mismatched V/Q defects are visible in both lungs

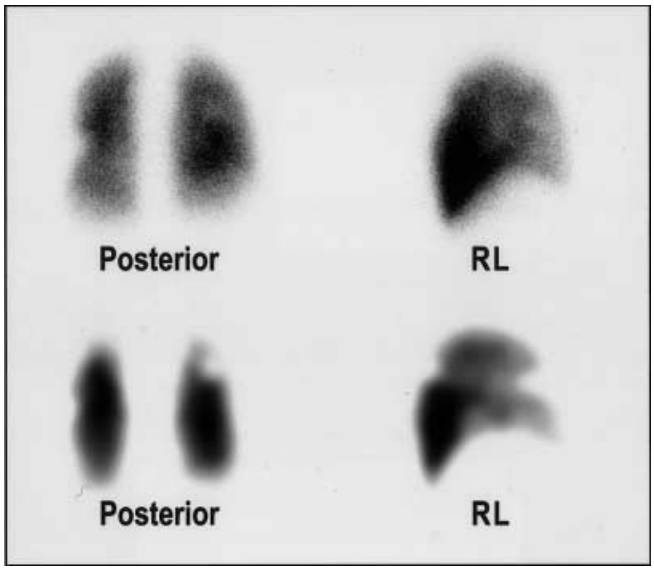

Fig. 2. One small perfusion defect not visible on planar images (*upper row*) is seen in the posterior segments of the upper right lung lobe on 10-mm SPET slices (*lower row*)

and three had perfusion defects; no matched V/Q defects suggestive of bronchopulmonary disease were found, and the number and size of the perfusion defects in these patients did not exceed those in patients with normal spirography. All patients had normal or borderline RVEF at both first-pass study and ultrasonography (54%±7% for first-pass study, range 47%–66%, and 49%±6% for ultrasonography, range 43%–67%; normal >45%); no correlation was found between RVEF and number and size of the defects. In two patients with perfusion defects (one with valvular prolapse and mitral valve insufficiency, and one with mild restrictive pulmonary disease) an increase in PAP (41 and 34 mmHg, respectively; normal ≤25 mmHg) was found.

The perfusion defects were unchanged in all four patients in whom follow-up studies were performed, although in two of them a diffuse decrease in segmental tracer uptake was seen.

Discussion

The involvement of the pulmonary arteries in Takayasu's disease has been reported in studies from different countries [2, 4, 5, 7, 11, 12, 13, 14, 15, 16] and its prevalence has been shown to vary widely among series (Table 2). Although racial or geographical predilection for the disease has been described, the sensitivity and specificity of the different imaging methods used may also be responsible for the observed differences in the prevalence of lung disease. For example, digital subtraction angiography is known to

Table 1. Number and sites of lung perfusion defects on planar and SPET images

	Upper lobe		Middle lobe		Lower lobe		Total	
	Planar	SPET-3D	Planar	SPET-3D	Planar	SPET-3D	Planar	SPET-3D
Right lung	12	15	9	13	5	5	26	33
Left lung	6[a]	5	8	8	3	9	17	22
Total	18	20	17	21	8	14	43	55

[a] One of these defects was located by SPET in the upper segment of the lower lobe

Table 2. Prevalence of lung involvement in Takayasu's arteritis in different studies

Source	Year	Affected pts/total pts	Country	Prevalence	Imaging technique
Suzuki et al. [4]	1973	12/15	Japan	80%	Pulmonary scintigraphy
Lupi-Herrera et al. [2]	1977	16/35	Mexico	45%	Pulmonary arteriography
Yamato et al. [12]	1986	18/21	Japan	86%	Pulmonary arteriography
Matsunaga et al. [5]	1987	16/32	Japan	50%	Digital subtraction angiography
Sharma et al. [14]	1990	4/9	India	45%	Digital subtraction angiography
Umehara et al. [13]	1991	91/120	Japan	76%	Pulmonary scintigraphy
Zheng et al. [11]	1992	40/75	China	53%	Digital subtraction angiography
Yamada et al. [15]	1992	21/30	Japan	70%	Pulmonary arteriography
Park et al. [16]	1992	24/54	Korea	44%	Digital subtraction angiography, pulmonary arteriography and scintigraphy
Yamada et al. [7]	1993	54/77	Japan	70%	MRI
Present series	2001	10/18	Italy	55%	Pulmonary scintigraphy
Total		306/486		63%	

miss certain stenotic, non-occlusive lesions that are detected with conventional pulmonary angiography [14].

Although pulmonary angiography is considered to be the gold standard for the diagnosis of pulmonary arteritis, it was not performed in our study since we considered it unethical to submit asymptomatic patients with a hypercoagulable status to an invasive and potentially hazardous procedure [7, 17, 18]. Furthermore, lung scintigraphy is a sensitive imaging method for the assessment of pulmonary involvement, although its specificity for perfusion defects has been questioned [4, 13].

Planar scintigraphy revealed lobar, segmental or subsegmental perfusion defects in 55% of patients and neither tomographic nor 3D images were able to detect abnormal lung perfusion in other patients. However, the greater number of defects visible with SPET and 3D display suggests that tomographic images may provide a better definition of very small lesions, particularly in the lower lobes, where the large volume requires an increased contrast between the perfusion defect and the background activity for the detection of abnormalities [19, 20]. In our series, segmental or subsegmental defects accounted for about 90% of perfusion abnormalities; this finding is probably related to the frequent involvement of segmental pulmonary branches by arteritis [16]. Nevertheless, the predilection of defects for the right lung and upper and middle lobes remains unexplained, although similar findings have been reported by others [4, 11, 13, 21, 22].

Perfusion abnormalities were found mainly in older patients and in patients with a significantly longer interval between the onset of clinically overt arteritis and lung studies. These findings confirm the generally late involvement of the lung by Takayasu's disease, though a few cases of early pulmonary involvement have been reported [23, 24].

Although a normal ventilation pattern in a patient with lung perfusion defects from Takayasu's arteritis has been described [25], the analysis of ventilation pattern has not been previously applied to a large series of patients. Since large V/Q mismatches are considered to be suggestive of thrombo-embolism [10], the differential diagnosis with Takayasu's lung involvement may be difficult, particularly when the lung symptoms are early manifestations of arteritis. Moreover, even though angiographic findings suggest that Takayasu's disease usually involves more distal arteries than is the case with embolism, coagulation abnormalities recently demonstrated in this type of arteritis might be responsible for an overlap between the two scintigraphic patterns [26, 27, 28]. In our experience, patients with pulmonary embolism have more perfusion defects than those with arteritic lesions, and almost all of these defects clear or shrink over time. Moreover, no predilection for any segment or for the right lung is found. Since no reduction in defect size occurs in lung arteritis, repeat perfusion lung scintigraphy within 1 month may represent an additional criterion enabling differential diagnosis with acute pulmonary embolism, although persistent V/Q mismatches may occur in the chronic evolution of pulmonary embolism, as in Takayasu's lung disease [29, 30, 31]. Further scintigraphic evaluation of lung perfusion could be performed at longer intervals to check the progression of arteritis, especially when lung symptoms or pulmonary hypertension appear.

Systemic-pulmonary shunts able to preserve the parenchyma from infarction have been described [32], explaining the maintenance of the normal ventilation pattern observed in our patients. In fact, normal results or only mild abnormalities were found on spirography, confirming the uncommon and limited involvement of the lung parenchyma.

Finally, the lack of pulmonary hypertension at colour Doppler echocardiography in all patients but two (one with mild restrictive-obstructive pulmonary disease and one with valvular prolapse associated with mitral insufficiency) and the normal RVEF registered on first-pass study and by ultrasonography in all patients suggest that the high compliance of pulmonary vessels may delay the onset of pulmonary hypertension, preserving right ventricular function even in the event of extensive lung involvement.

In conclusion, V/Q planar scintigraphy is a useful and simple method for the screening of pulmonary involvement in patients with Takayasu's arteritis. The large size of the perfusion defects limits the usefulness of tomographic images to the better assessment of the extent of perfusion abnormalities. However, the similarity of scintigraphic findings observed in pulmonary embolism necessitates caution in the interpretation of the scan, particularly when lung symptoms are the first manifestation of the disease.

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