Patterns of Regional Ventilation in Patients with Cardiomegaly or Left Heart Failure

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Patterns of regional ventilation have been examined in 42 patients, the majority of whom had clinical evidence of left-ventricular or left-atrial dysfunction. Regional ventilation was studied with xenon-133 and regional perfusion with Tc-99m human albumin microspheres. The presence of a cardiac defect, seen in 54.8% of the washin images, was related to the depth of lung between the posterior heart border and the posterior lung border, but not to cardiac size. Washout patterns were fairly uniform in those patients (43%) who cleared their lungs within 3 min, but were remarkably variable in those with longer washout times. The presence of râles or clinical signs of a pleural effusion, and radiographic evidence of vascular redistribution or pleural effusion, were significantly associated with prolonged washout times. These observations suggest that the prolonged washout is due to edema in the walls of the smaller bronchioles, leading to airflow obstruction.

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Patients with shortness of breath due to heart failure are often referred for ventilation-perfusion imaging when there is clinical suspicion of pulmonary embolism. The patterns of blood flow seen in such patients have been described previously (*1,2*), but little has been written on their patterns of regional ventilation. Earlier studies using $C^{15}O_2$ (*3*), and more recent studies using xenon-133 (*4–6*), have provided conflicting information, some indicating that ventilation remains undisturbed, whereas others have shown a redistribution of ventilation that matches that of blood flow. These studies have concerned themselves largely with patients suffering from mitral stenosis and have for the most part been carried out with multiple-probe systems rather than a scintillation camera.

This paper reviews the patterns of regional ventilation observed in some patients with cardiomegaly alone, and in others with cardiomegaly and clinical evidence of left-heart failure.

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PATTERNS AND METHODS

The records of a consecutive series of patients with cardiomegaly (that is, a cardiothoracic ratio >50%) who also had ventilation-perfusion studies, have been reviewed retrospectively. Particular attention was directed to their presenting symptoms, final diagnosis, smoking history, and to any symptoms or other indications of chronic bronchitis, emphysema, or bronchial asthma. Clinical evidence of rhonchi (wheezes), râles (crackles) at the lung bases, pleural effusions, sacral or peripheral edema, and systemic blood pressure were noted. Arterial blood gases, if done within 24 hr of the ventilation-perfusion study, were also recorded. Chest radiographs, obtained within 24 hr of the ventilation-perfusion studies, were also reviewed and the presence or absence of vascular redistribution, infiltrates, pleural effusions, and Kerley 'B' lines noted. Radiographic evidence of chronic obstructive airways disease was also sought for, such as low flattened diaphragms, an increase in the retrosternal clear space, attenuated or irregular pulmonary vasculature, and bullae (*8*). Because more than half of the chest radiographs were portable films (23 of 42, 55%) the cardiothoracic ratio (CTR) was measured directly

from the anterior perfusion scans. In the 19 patients who had postero-anterior chest radiographs, the mean absolute difference between the CTR measured from the anterior perfusion scan and that measured from the chest radiograph was (4.2 ± 2.8%), with the measurements from the perfusion scans generally being the larger.

Each patient had a xenon-133 ventilation study followed by a perfusion scan using Tc-99m human albumin microspheres (Tc-99m HAM). For the ventilation study the patient either sat upright or lay supine with the back towards the gamma camera. Xenon-133 (10–20 mCi) was breathed from a simple rebreathing device (*7*) during 3 min of tidal breathing, and a single image was collected during the entire washin period. The subject then breathed air for 10 min or more for the washout procedure, during which serial 30-sec images were made for 2 min, followed by 1-min images until the washout was complete.

Technetium-HAM (2–4 mCi) was then given intravenously with the patient in the same position, and images were obtained in the anterior, posterior, and both lateral projections.

The images have been analyzed by careful visual inspection. No digital computer was available to process the ventilation studies, so we used the time-to-complete-clearance of a lung zone as an indication of the efficiency of ventilation. We divided the lungs into upper, mid, and lower zones as described previously (*8,9*).

A visual assessment was made of:

1. The distribution of xenon-133 during the washin period, particular attention being paid to the evenness of the distribution within each lung and to the presence or absence of a defect on the left side in relation to the heart.

2. The washout time of xenon-133 from the various lung zones, using the time in minutes until the last washout image in which activity within a zone was still distinguishable from the blood and tissue background activity. The average of the washout times for the three zones in each lung was taken as the lung washout time. We have regarded a normal washout time as being 3 min or less, and a prolonged washout time as any greater than this.

3. The apparent matching or mismatching of ventilation in relation to blood flow in the various lung zones.

RESULTS

There were 32 women and 10 men in this study. Their ages ranged from 37–88 yr, with a mean of 65.5 yr. Fifteen patients suffered from hypertensive heart disease, 11 from ischemic heart disease, four from rheumatic heart disease, four from cardiomyopathies, and the remaining seven from miscellaneous problems (two arrhythmias, one pericarditis, one glomerulonephritis, one systemic lupus erythematosus, and two congestive heart failure of unknown cause).

Three patients had histories of bronchial asthma, and two had symptoms of chronic bronchitis. Six patients were cigarette smokers (two light, less than five cigarettes/day; one moderate, eight pack-years; three heavy, 27, 50, and 100 pack-years, respectively: 1 pack year = 365 packs/yr). Five patients were ex-smokers from 5 mo to 20 yr, 23 were nonsmokers, and the smoking habits of the other eight were not recorded.

Râles at the bases or signs of a pleural effusion were noted in 23 patients. Twenty patients had clinical evidence of peripheral edema, and this group had significantly larger hearts [CTR = (69.8 ± 6.3)%] than the 22 patients without edema [CTR = (61.4 ± 6.3)%, $t = 4.18$, $p < 0.01$]. The mean age and mean systemic arterial pressure of the patients with edema (66.5 ± 12.8 yr, and 104.3 ± 15.0 mm Hg) were not significantly different from those without edema (64.6 ± 15.7 yr, and 102.6 ± 16.9 mm Hg).

Fourteen of the 20 patients with clinical evidence of peripheral edema, and 12 of the 22 patients without edema, had blood-gas analysis within 24 hr of the ventilation-perfusion studies. None had an arterial CO_2 tension pressure (P_{aCO_2}) greater than 44 mm Hg. The mean values for the blood-gas analyses are shown in Table 1. Although the mean P_{aCO_2} appeared lower in the patients with peripheral edema, and the mean P_{aO_2} and mean pH higher, the differences were not statistically significant.

Chest radiographs. None of these showed radiographic evidence of chronic obstructive airways disease.

Evidence of vascular redistribution was seen in 22 of the 42 chest radiographs (52.4%), 11 in the patients with peripheral edema, (five were portable films), and 11 in the patients without peripheral edema (four were portable films).

Sixteen patients had radiographic evidence of pleural

TABLE 1. BLOOD-GAS ANALYSIS

		P_{aCO_2} ± 1 s.d. mm Hg*	P_{aO_2} ± 1 s.d. mm Hg†	pH ± 1 s.d.
Patients with peripheral edema	N = 14	30.7 ± 5.8	72.6 ± 12.9	7.52 ± 0.06
Patients without edema	N = 12	35.3 ± 6.9	66.9 ± 17.0	7.42 ± 0.07

* Carbon dioxide tension in the arterial blood.
† Oxygen tension in the arterial blood.

TABLE 2. VISIBILITY OF CARDIAC DEFECTS ON WASHIN IMAGE

	No cardiac defect, n = 8	Small cardiac defect, n = 9	Large cardiac defect, n = 8
Cardiothoracic ratio (±1 s.d.)	67.1 ± 8.0	66.9 ± 6.9	68.8 ± 6.0
Lung depth behind heart (cm ± 1 s.d.) on left lateral perfusion image†	2.78 ± 0.55	2.50 ± 0.55	1.63 ± 0.62*
Ratio of lung depth behind heart to total lung depth on left lateral perfusion image† (±1 s.d.)	0.65 ± 0.10	0.62 ± 0.09	0.43 ± 0.17*

* Significantly different ($p < 0.01$) from the group with no cardiac defect and from the group with a small cardiac defect.

† These measurements could be made in only 25 patients. Defects in blood flow in the regions of the lingula or the anterior basal segment of the left lower lobe, or the presence of a left-sided pleural effusion, prevented measurements in some patients and in others the scans were no longer available.

effusion, nine (four bilateral) in those with cardiomegaly and peripheral edema, and seven (one bilateral) in those without it. Kerley 'B' lines were recognized in only two radiographs, one from each group. Plate-like atelectasis was seen at the bases in three of the patients without peripheral edema.

The presence of vascular redistribution, or pleural effusion, or both, was significantly associated with prolonged washout times, and their absence with normal washout times ($\chi^2 = 3.95$, $p < 0.05$).

Washin images. A defect related to the heart was seen in the washin image in the left mid and lower zones posteriorly in 23 patients (54.8%). In 11 patients this cardiac defect was relatively small and extended less than half the width of the left lung from its medial border; in the other 12 patients the defect was larger. There was, however, no significant relationship between cardiac size as judged by the CTR and the presence or absence of cardiac defects on the washin image. The larger cardiac defects were related to the depth of the lung tissue, as measured on the left lateral perfusion scan, between the posterior border of the heart and the posterior border of the lung and also to the ratio of this distance to the depth of lung from the anterior margin of the left lateral perfusion scan to the posterior margin. These two measurements were significantly smaller ($p < 0.01$) in the patients with the larger cardiac defects compared with those with the smaller cardiac defects or none (see Table 2).

Washout images. Eighteen patients (43%) had washout times of 3 min or less (ten with cardiomegaly alone and eight with cardiomegaly and peripheral edema) while the other 24 patients (57%) had prolonged washout times (>3 min) (12 with cardiomegaly alone and 12 with cardiomegaly and peripheral edema).

There was no significant difference between the mean washout times for the patients with cardiomegaly alone and those for the patients with cardiomegaly and peripheral edema, although the latter appeared slightly shorter. For all 42 patients studied, there was no signif-

TABLE 3. MEAN LUNG WASHOUT TIMES

		Mean lung washout time (min ± 1 s.d.)					
		All patients		Patients with blood-gas analysis*		Patients without blood-gas analysis	
		n	min ± 1 s.d.	n	min ± 1 s.d.	n	min ± 1 s.d.
Cardiomegaly alone†	Left lung‡	22	4.2 ± 2.9	12	5.1 ± 3.0	10	3.3 ± 2.6
	Right lung		4.2 ± 2.8		5.0 ± 2.9		3.2 ± 2.4
Cardiomegaly and peripheral edema	Left lung	20	3.7 ± 2.3	14	3.8 ± 2.2	6	3.6 ± 2.6
	Right lung		3.6 ± 2.5		3.4 ± 2.2		4.2 ± 3.3
All patients	Left lung	42	4.0 ± 2.6	26	4.4 ± 2.6	16	3.4 ± 2.5
	Right lung		3.9 ± 2.6		4.1 ± 2.6		3.5 ± 2.7

† There are no significant differences between the mean lung washout times of the patients with cardiomegaly alone and those with cardiomegaly and peripheral edema.

‡ There are no significant differences between mean lung washout times in left and right lungs.

* There are no significant differences between the mean lung washout times of the patients who had blood-gas analysis compared with those who did not.

TABLE 4. MEAN WASHOUT TIMES BY LUNG ZONES

		Washout time (min ± 1 s.d.)	
		Left lung	Right lung
Upper zones	n = 42	3.8 ± 2.7	3.7 ± 2.9
Mid zones	n = 42	4.1 ± 2.8	3.9 ± 2.9
Lower zones*	n = 41	4.3 ± 2.5	4.1 ± 2.7

* In one patient the lower zones were not visualized due to bilateral pleural effusions.

icant difference between the mean washout time of the left lung compared with that of the right (see Table 3). Among the 26 patients who had arterial blood-gas analysis, there was also no significant difference between the mean washout times for those with cardiomegaly alone compared with those with cardiomegaly and peripheral edema, although the latter again seemed slightly shorter. There was also no significant difference between the mean lung washout times for the patients who had arterial blood-gas analysis compared with those who did not (see Table 4). There was a weak positive correlation between whole-lung washout times and P_{aCO_2} ($r = 0.37$, $0.1 > p > 0.05$).

There appeared to be a slight gradient (statistically not significant) of washout times between the upper, mid, and lower zones, with the lower zones having the longest washout times (see Table 4).

Among the 18 patients with washout times of 3 min or less, the pattern of regional ventilation was even in 13, i.e., no gradient could be appreciated between the upper, mid, and lower zones; and symmetrical in 15, i.e., the same pattern was seen in each lung. In two patients the lower zones could be seen to clear more slowly than the upper and mid zones, and in three others differences in washout times between other zones could be appreciated (Fig. 1).

By contrast, the patterns of regional ventilation in the 24 patients with prolonged washout times, showed much more variability, both in the distribution between zones and between the two lungs. None of these patients had an even pattern of regional ventilation, that is the same washout time in each lung zone. In only six patients were the patterns of washout symmetrical between the two sides. By comparison with the patients with washout times of 3 min or less, this lack of symmetry between the ventilation of the two lungs was significantly associated with prolonged washout times ($\chi^2 = 6.13$, $p < 0.01$; Fig. 2).

The presence or absence of the cardiac defect on the washin image was not significantly associated with either normal or prolonged washout times ($\chi^2 = 0.05$, N.S.). In six patients the left lower zone cleared more slowly than the right, with a difference of more than 1 min between the washout times, but this was not associated with the degree of cardiomegaly. In three other patients the right lower zone cleared more slowly than the left.

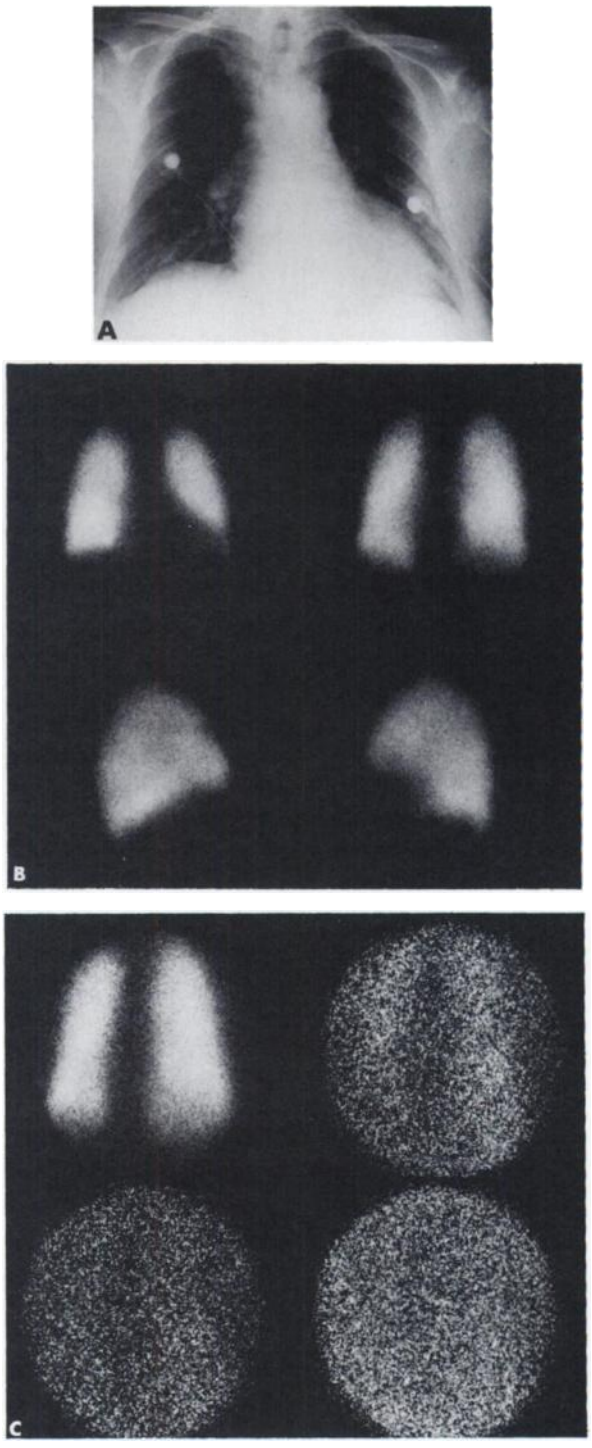
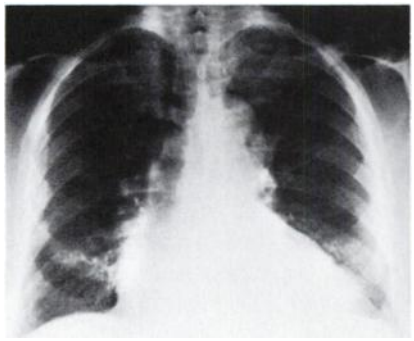


FIG. 1. (A) Portable chest radiograph of 65-year-old woman with arteriosclerotic heart disease. (B) Perfusion scans (anterior, posterior, and right and left lateral views) showing cardiomegaly (CTR = 65%) and a small defect in blood flow in anterior segment of right upper lobe. Distribution of blood flow is normal elsewhere. (C) Ventilation study: washin image (top left) and washout images at 1 min (top right), 2 min (bottom left), and 4 min (bottom right). No cardiac defect is visible in washin image, and both lungs clear rapidly, being clear by 4th minute.



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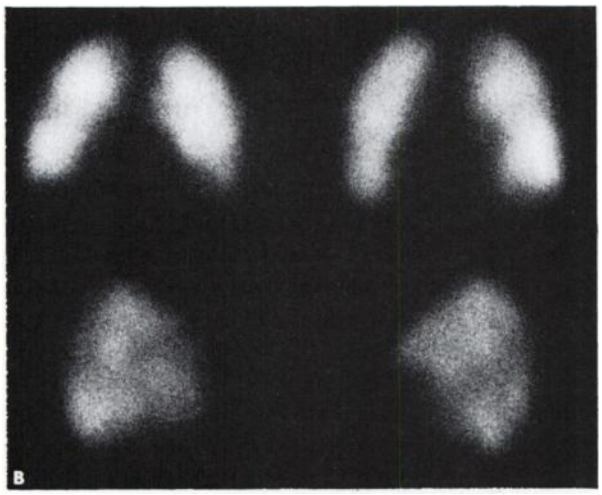

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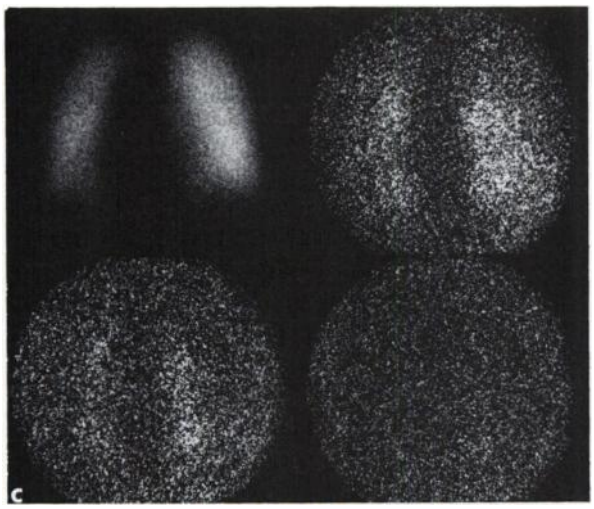

C

FIG. 2. (A) Postero-anterior chest radiograph of 77-year-old woman with diabetes mellitus, myocardial infarction, atrial fibrillation, and hypertension (B). Perfusion scans (anterior, posterior, and right and left lateral) showing marked cardiomegaly (CTR = 72%), with bilateral fissure signs and other ill-defined defects in blood flow. (C) Ventilation study: washin image (top left) and washout images at 1 min (top right), 4 min (bottom left), and 9 min (bottom right). There is a small cardiac defect on washin image. Washout of xenon-133 from both lungs is prolonged and irregular. Activity is faintly visible in right lung 9-min image but was not seen in 10-minute image.

The presence of râles at the bases or signs of a pleural effusion was significantly associated with prolonged washout times, and the absence of these findings with normal washout times ($\chi^2 = 6.74$, $p < 0.01$). This association remained significant ($\chi^2 = 5.36$, $p < 0.05$) when the three patients with a history of bronchial asthma and the two with symptoms of chronic bronchitis were excluded from the analysis.

The six smokers and five ex-smokers were fairly evenly divided between normal washout times (five) and prolonged washout times (six), while five of the eight patients whose smoking habits were unknown had prolonged washout times. There was no significant association between smoking habits, (smoker, ex-smoker, nonsmoker, or unknown) and normal or prolonged washout times ($\chi^2 = 1.09$, N.S.).

Comparisons of regional ventilation and perfusion. There was an apparent match between ventilation and perfusion in 26 patients (62%). In six patients (14%) there were regions in the lungs where perfusion appeared diminished in comparison with local ventilation. Only one of these patients was considered to have pulmonary embolism on the basis of the ventilation-perfusion study. In the other five, the defects in blood flow were small and ill-defined or subsegmental, and were reported as having low probability for pulmonary embolism. They were thought to be due to the underlying heart failure. In the remaining ten patients (24%)—including two with a history of bronchial asthma—there were regions where ventilation appeared more disturbed than perfusion.

DISCUSSION

The patients with cardiomegaly in this study were all referred for ventilation-perfusion scans because of clinical suspicion of pulmonary embolism. None had radiographic evidence of chronic obstructive airways disease and only five had histories of it.

The underlying cardiac conditions, which affected mainly the left side of the heart, the finding of râles at the bases, the presence of pleural effusions, and the radiographic evidence of vascular redistribution, provide strong clinical evidence of compromised left-ventricular or left-atrial function in the majority of these patients.

The absence of an elevated P_{aCO_2} in those patients who had blood-gas analysis makes the presence of peripheral edema on the basis of cor pulmonale due to chronic obstructive airways disease most unlikely, for peripheral edema in this condition is almost never seen until the P_{aCO_2} is elevated (*10*).

As might be expected, the patients with peripheral edema had significantly larger hearts—and presumably more severe left-sided heart failure—than the patients with cardiomegaly alone. We had expected that the larger the cardiac size, the more apparent would be the cardiac defect seen in the washin image, and the more likely that there would be abnormalities of ventilation

at the left base; nevertheless, neither of these expectations could be substantiated.

The washout patterns were fairly uniform in the patients with washout times of 3 min or less, and almost completely uniform in those patients with washout times of 1.5 min or less. However, in the patients with prolonged washout times there was remarkable variability in the patterns of washout. Only one quarter (6 of 24) of these patients showed symmetrical washout patterns, whereas the other three quarters often showed differences between the two lungs and also between the regions within each lung.

Prolonged washout times were not significantly associated with smoking habits, and two of the five patients with asthma or chronic bronchitis had normal washout times, so in the majority of our patients, prolonged washout times could not be ascribed to diseases involving chronic airflow obstruction. In two independent long-term prospective studies, Fletcher and Peto (*11*) and Bates et al. (*12*) have observed that it is only a minority of cigarette smokers who develop serious airflow obstruction, so our failure to show an association between smoking habits and delayed washout times is not unexpected.

The presence of râles at the bases or signs of a pleural effusion were significantly associated with prolonged washout times, and so were the radiographic findings of vascular redistribution and pleural effusion. The finding of râles indicates that the underlying lung is less compliant than normal, and in the clinical context of cardiomegaly and heart failure it suggests the presence of interstitial edema. In these circumstances the excess fluid oozing from the pulmonary capillaries escapes from the interstitial spaces through the perivascular and peribronchial lymphatics, and the terminal airways may become edematous (*13*). Small-airway dysfunction has been demonstrated in patients with ischemic heart disease, who tend to have larger closing volumes than normal (*14,15*).

The reversal of the normal gradient of ventilation seen in our patients, with the slightly longer washout times at the bases compared with the mid and upper zones, is consistent with the observations of Jebavý et al. (*5*) and Ishii et al. (*6*), who have described similar alterations in the distribution of regional ventilation in relation to increases in left-atrial pressure. These considerations suggest that edema in the smaller bronchioles caused airflow obstruction that led to the prolonged washout times we observed.

Visual comparisons of regional ventilation and regional perfusion showed that in the majority of these patients (36 of 42, 86%) ventilation and perfusion were either matched (26 patients) or ventilation was more impaired than perfusion (ten patients). Only one of the remaining studies was sufficiently characteristic of pulmonary embolism to suggest that diagnosis (*16–18*). We cannot check the accuracy of the ventilation-perfusion interpretations in these patients, because none went on to have pulmonary angiograms.

From our observations of regional ventilation in these patients with cardiomegaly or heart failure, we conclude that a wide range of washout patterns may be seen. These vary from rapid symmetrical clearance to prolonged and uneven washout patterns. Together with the clinical finding of râles or the signs of a pleural effusion, as well as with radiographic evidence of vascular redistribution or pleural effusion, the significant association of prolonged washout times for xenon-133 suggest that the impaired exchange of air seen in these circumstances is related to edema of the small bronchioles rather than damage to these airways as a result of the diseases of chronic airflow obstruction.

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