Original Article

Which is Better - A Standalone Ventilation or Perfusion Scan or Combined Imaging to Predict Postoperative FEV$_1$ in One Seconds in Patients Posted for Lung Surgeries with Borderline Pulmonary Reserve

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Abstract

Introduction: Forced expiratory volume in one second (FEV$_1$) is an independent predictor for respiratory morbidity. Reports are varied and controversial substantiating the use of either lung perfusion (Q) or ventilation (V) scintigraphy as a single stage investigation to predict postoperative (ppo) FEV$_1$ in patients scheduled for lung resection surgeries. It is said that there is no additional benefit by performing both V/Q scan. As per one of the recommendations, no further respiratory function tests are required for a lobectomy if the postbronchodilator FEV$_1$ is >1.5 l. We wanted to study the ppo FEV$_1$ in patients with FEV$_1$ of <1.5 L scheduled for lung surgeries. Being a high-risk population, we wanted to assess (a) whether the ppo changes by this combined V/Q imaging and (b) whether the incidence of respiratory complication in the postoperative setting of this subgroup is different, (c) and study the short- and long-term clinical outcome. **Materials and Methods:** Fifty-two high-risk patients (with comorbidities) and borderline preoperative FEV$_1$ of 1.5 L or less planned for lung resection were enroled in this prospective study. V and Q scans were performed, and tracer uptake percentage was tabulated. **Results:** Tracer uptake in each lung was quantitated. Manual method of ROI drawing is preferred in high risk patients with reduced pulmonary reserve over the automatic method. Based on uptake patterns by V/Q scans, 4 different types of patterns were tabulated. Eighty-eight percentage of centrally placed tumors showed the difference in uptake patterns. Chronic obstructive pulmonary disease patients usually showed more modest ventilatory defects (categorised as type 2 or 3). Lung tumours produce erratic uptake patterns (Type 4) which depend heavily on their location and extent. The range of FEV$_1$ predicted was 0.6–1.38 L/min **Conclusion:** We recommend that combined imaging should be performed in patients with borderline pulmonary reserve to derive the benefit of surgery as it provides a realistic ppo FEV$_1$ in patients with moderate to severely damaged lung. Centrally placed hilar or bronchial tumors (even those <2 cm in size), produce discrepancies in V/Q distribution pattern. Patient who was thought ineligible for surgery due to low baseline FEV$_1$ may be actually be operable by this combined imaging if uptake pattern is better in V or Q scan with a good outcome. Accurate estimation of postop FEV$_1$ in fact helps the surgical team to implement measures to prepare high risk patients to reduce postoperative complications, enable faster weaning from ventilatory support and ensure favourable prognosis.

Keywords: *FEV$_1$, lobectomy, lung perfusion scintigraphy, lung resection surgery, lung ventilation scintigraphy, pneumonectomy*

Introduction

Measuring the forced expiratory volume in one second (FEV$_1$) and the diffusing capacity of the lung for carbon monoxide (DLCO) measurements are recommended for assessing risk related to pulmonary function. Measurement of the Dlco is generally recommended for patients who do not meet the FEV$_1$ cutoffs, or in those with unexplained dyspnea or diffuse parenchymal disease on chest radiograph or Computed tomography. FEV$_1$ is an independent predictor of respiratory morbidity. For every 10% drop in FEV$_1$, respiratory morbidity increases by 1.1.[1] Galvenze[2] has stressed that when FEV$_1$ is <30% there is a higher (43%) morbidity rate which decreases (12%) when respiratory function is better (FEV$_1$ is >60%). Thus, measurement of FEV$_1$ is of utmost importance, especially in those patients who actually may benefit from surgery but have borderline FEV$_1$ values which actually disqualifies them from going ahead with surgery.

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However, there is no clearcut directive from the literature search whether to perform a V or Q scan alone for the accurate prediction of FEV_1.[1,3] Various guidelines provided by reputed societies such as American College of Chest Physicians (ACCP), European Respiratory Society and the European Society of Thoracic Surgeons, and British Thoracic society (BTS) differ from one another in their algorithms for presurgical evaluation in patients planned for lung resection. Society guidelines like ACCP 2013, BTS and the Society of Cardiothoracic Surgeons of Great Britain and Ireland clearly recommends using quantitative perfusion scintigraphy to predict postoperative (ppo) lung function in lung cancer patients with borderline pulmonary function tests planned for pneumonectomy.[4.5]

Patients with either FEV_1 or DLCO or both <80% predicted should undergo an ergometric assessment (stair climbing or shuttle walk test). Spirometry is the first presurgical investigation performed to assess pulmonary function test. The recommendation for lobectomy is the postbronchodilator cutoff value of FEV_1 >1.5 L and for pneumonectomy value of >2 L, and >80% of predicted unless the patient has dyspnea or evidence of interstitial lung disease. Controversy exists regarding the use of ventilation and perfusion (V and Q) scan as a single stand-alone or combined investigation in the prediction of FEV_1 in patients undergoing lung resection.

We set out to assess if there is any uptake difference between both imaging techniques and if not, whether Q imaging is enough to proceed with surgical decision making in these patients. We also wanted to assess the cutoff limit of FEV_1 and tolerance level for patients undergoing lobectomy and pneumonectomy in our South Indian population. All patients undergoing segmental/lung resection were also observed for short (3 months) as well as long-term performances (1 year).

Materials and Methods

Fifty-two patients (M:F = 45:7) with borderline respiratory function (PFT, pulmonary function test showing FEV_1 1.5 L or less) scheduled for lung resection at Amrita Institute of medical sciences were enrolled. Patients were categorized high risk based on variables such as long-standing diabetes mellitus, hypertension, smokers, and postcoronary bypass surgery. Selected cases were grouped as those with proven lung malignancy and benign lung disease (obstructive airway disease). Lung ventilation (^{99m}Tc labeled Diethylenetriamine penta acetic acid [DTPA] aerosols), and perfusion (^{99m}Tc macroaggregated albumin [MAA]) scintigraphy were performed in all patients within 1 week interval. All patients were followed up for 6–12 months postsurgery.

For patients undergoing same day (V/Q) protocol, ventilation scan was the first imaging to be performed followed by perfusion imaging. For all other patients, both scans were performed within an interval of 7 days.

Ventilation scintigraphy

1665 Megabecqueral MBq of ^{99m}Tc DTPA was added to the aerosol delivery system to produce nebulisation. The patient receives approximately 37–74 MBq (1.0–2.0 mCi) of tracer into the lungs as radiolabeled aerosols. The aerosol is administered through a mouthpiece with the nose occluded while the patient is in the supine position and engaged in tidal breathing. The patient was familiarized with a few dry runs before the actual inhalation of labelled aerosols. Static anterior and posterior views of both lungs were acquired on a NM 640 gamma camera. Moreover, in those with better count statistics single photon emission computed tomography- computed tomography, SPECT-CT was also acquired.

Perfusion scintigraphy

74 MBq of intravenous ^{99m}Tc MAA was injected slowly during 3–5 respiratory cycles with the patient in supine position. Anterior and posterior planar images of both lungs and SPECT-CT were acquired.

Processing of ventilation and perfusion scans

After obtaining the planar V/Q scans, a region of interest (ROI) was drawn, and radioactive count distribution was calculated using manual and automatic methods. Vendor provided reference image with lung segmentation was used for delineating the bronchopulmonary segments for drawing the ROI as shown in Figure 1. Percentage uptake using manual and automatic methods were correlated. The drawing of ROI was based on the surgical technique contemplated, i.e., pneumonectomy/upper, mid, or lower lobectomy. Similarly, the uptake distribution on planar scintigraphy was correlated with SPECT-CT images for the accuracy of segmental delineation. In the automatic method, in

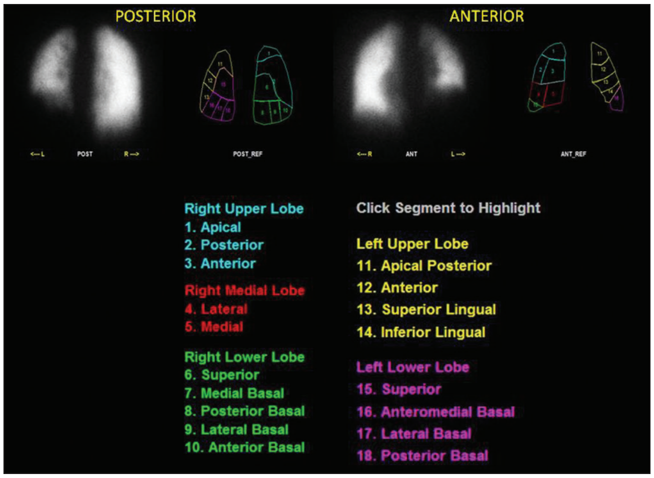


Figure 1: Vendor provided reference image with lung segmentation. This was used for manual region of interest delineation of the bronchopulmonary segments for FEV_1 calculation

both the anterior (*A*) and posterior (*P*) images, rectangular ROI (regions of interest), equal in size, were drawn over the whole lung as shown in Figure 4. Both lungs were divided into six regions of interest in the right upper, right middle, right lower, left upper, left middle, and left lower lung fields in each patient. Extrapulmonary radioactivity if present was excluded from the calculation. Using the geometric mean method, radioactive count distribution in lung segments was obtained. The percentage uptake obtained by manual/automatic method was reassessed by an experienced nuclear physician and the value reflecting the patients' disease pattern was tabulated.

Interpretation

Based on the patterns of V and Q findings as per Nakata *et al*.,[7] 4 types of distribution was observed.

Type 1– Congruent or matched reduction in V and Q of one or more lung segments and produces minimal V/Q mismatch [Figure 2].

Type II– Normal/near normal ventilation with larger perfusion defects and produces a dead space effect. This type shows a significant V/Q mismatch.

Type III– Larger V defects with normal or near normal perfusion signifies a low V/Q area or produces a "shunt effect," i.e., poor alveolar V compared to the degree of alveolar perfusion.

Type IV– Erratic (unmatched) distribution of both V and Q tracers [Table 1].

Spirometry

The FEV_1 was calculated from a record of forced vital capacity performed in our institute. Postbronchodilator FEV_1 is recorded and is considered to be the preoperative FEV_1 for that patient. At least 3 recordings were made until the results were reproducible. The best of the three reproducible attempts was then used for analysis. The FEV_1 was repeated 1-month and 3 months postsurgery. The predicted FEV_1, corrected for height, sex, and age, were calculated from the equation: $FEV_1 = 4.30 \times \text{height} - 0.029 \times \text{age} - 2.49$, with age in years and height in meters as described in the guidelines This value was regarded as 100% and the measured value was expressed as a percentage of the predicted normal value.

Predicted postoperative FEV^1 calculation

The predicted postoperative (ppo) FEV_1 is estimated by multiplying the preoperative FEV_1 by the residual V/Q territory percentage, as predicted on V/Q scintigraphy which will remain after resection. The calculation was performed as per the following example, if preoperative FEV_1 is 1 litre and surgery will result in the loss of 25% of lung segments, the ppo FEV_1 is said to be 750 ml.

For patients planned for lobectomy, segments with defects (which was considered as obstructed) in each technique (V/Q) were separately assigned as follows: right upper lobe 3; middle lobe 2; right lower lobe 5; left upper lobe 3; lingula 2; and left lower lobe 4 (total = 19). The calculation involves (a) number of obstructed segments to be resected (b) number of unobstructed segments to be resected (based on uptake seen by anyone study). Postbronchodilator FEV_1 of each patient was ascertained.

The calculation was based as per Brunelli *et al*.[6] on estimated postoperative FEV_1 in liters (epo FEV_1) = pre FEV_1 × [(19– a)– b]/19– a. Expression: epo FEV_1 (l) is expressed as % predicted.

Results

Fifty-two patients (M:F = 48:04, mean age 67.6 years, age range 32–73 years) with borderline preoperative pulmonary reserve (FEV_1 of 1.5 L and less) underwent combined V/Q scans**.** The automatic method of ROI did not provide an accurate estimation of FEV_1 in those patients showing uptake discrepancy on V/Q imaging. For patients with near-normal V/Q uptake patterns (Type 1), the automatic and manual ROI's matched well. The software automatically divides both lungs into three zones for calculation, in spite of left lung having 2 lobes. The surgical planes of lung resection are best depicted only by a manual method of ROI's. Being high-risk group with lower pulmonary reserve, we recommend a manual method of lung segmentation for FEV_1 prediction which is a practical approach based on the plan of surgery (lobectomy/pneumonectomy).

Of the 52 patients, 42 were lung malignancies planned for surgery with curative intent while remaining 10 were benign lung diseases (chronic obstructive pulmonary disease [COPD]) for volume reduction surgery [Figures 2-4].

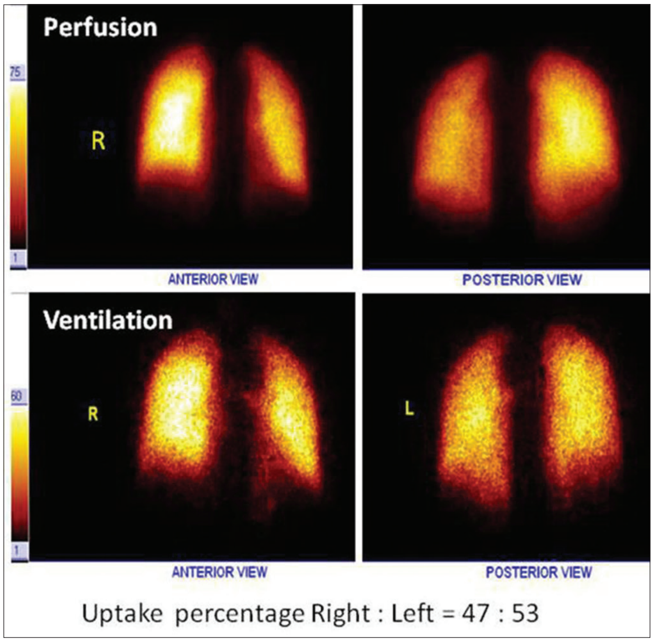


Figure 2: Near normal ventilation and perfusion imaging in a 49-year-old lady with small peripherally situated T1 lesion in left lung (category Type 1)

In this study, the majority of COPD patients (7 out of 10) showed larger V than Q abnormalities. They revealed predominantly a dead space effect and a shunt effect on scintigraphy (i.e., Type 2 and 3). In our results, peripherally placed lung tumors revealed Type 1 abnormality (i.e., in 5 patients) while centrally placed hilar or bronchial tumors (88% of patients) even T1 (<2 cm size) showed discrepancies in V/Q distribution pattern (Type 3/4) [Table 2]. This may be attributed to the severity of bronchial obstruction/bronchovascular cutoff with or without associated distal collapse of lung.

The ppo FEV$_1$ correlated well with actual postoperative lung function with no obvious difference based on the type of surgery performed (lobectomy versus pneumonectomy) [Table 3]. Two patients (with preoperative FEV$_1$ of <0.8 L) were not considered for surgery as they may not tolerate induction. Majority of patients underwent lobectomy. Two patients scheduled for pneumonectomy underwent management change to sublobar/wedge resection, as V/Q scan revealed ppo FEV$_1$ of 1.0 and 1.1 L, respectively. Sublobar resection or wedge resection is a useful option in patients with impaired pulmonary reserve. An absolute value of 800 ml for the ppo FEV$_1$ was the lower limit in our patients.

Based on the discrepancy of lung V and Q uptake pattern in 40 patients mostly categorized under Type IV, to predict accurately the FEV1 we resorted to the individual counting of lung segments with matching and nonmatching uptake patterns by V and Q scan separately [Table 4].

This high risk group had a larger number of uptake variance which were largely unmatched. This most probably is

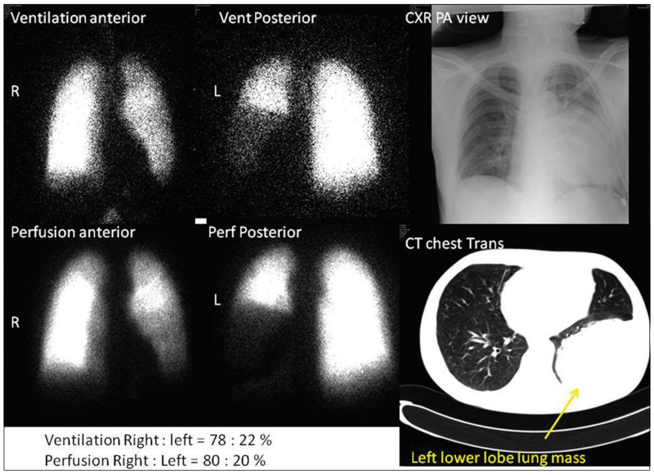
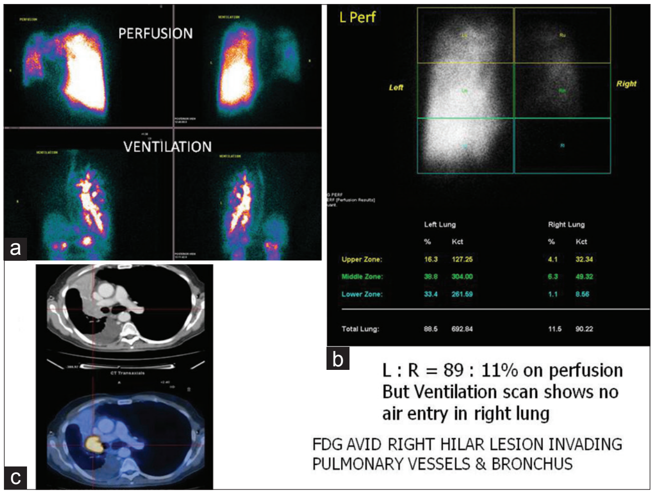


Figure 3: Congruent matching ventilation/perfusion defects in a patient with left lower lobe lung mass as seen on chest X-ray and Computed tomography



	Left Lung		Right Lung	
	%	Kct	%	Kct
Upper Zone:	16.3	127.25	4.1	32.34
Middle Zone:	38.8	304.00	6.3	49.32
Lower Zone:	33.4	261.59	1.1	8.56
Total Lung:	88.5	692.84	11.5	90.22

Figure 4: Discordant ventilation/perfusion scan findings (no ventilation but 11% perfusion) in a fluorodeoxyglucose avid right hilar mass invading right bronchus and pulmonary vessels. (a) V/Q planar scans of same patient, (b) lung quantitation of perfusion scan (c) FDG PETCT transaxial images showing the culprit small centrally placed tumour on right side - leading to significant discrepancy in MAA and DTPA aerosol distribution - Type IV A category

Table 1: Uptake patterns in ventilation/perfusion scans

	Ventilation	Perfusion
Type I	Abnormal Congruent matching defects	Abnormal Congruent matching defects
Type II dead space effect	Ventilation normal/near normal	Abnormal large perfusion defects
Type III low V/Q shunt effect	Larger ventilation defects	Normal/near normal perfusion
Type IV A	Larger ventilation defects	Perfusion is also abnormal
Type IV B	Abnormal ventilation	Larger perfusion defects

Table 2 : Listing of patients as per ventilation/perfusion scan uptake patterns

Types of uptake patterns scan encountered	Ventilation	Perfusion	Number of patients
Type I	Abnormal Congruent matching defects	Abnormal Congruent matching defects	5
Type II dead space effect	Ventilation normal/near normal	Abnormal large perfusion defects	3
Type III low ventilation/perfusion shunt effect	Larger ventilation defects	Normal/near normal perfusion	4
Type IV A	Larger ventilation defects	Perfusion is also abnormal	22
Type IV B	Abnormal ventilation	Larger Perfusion defects	18

due to the disruption of vasculature supplying the lung segments by a tumor or aerosol delivery due to damaged lungs in longstanding COPD. By performing a combined V/Q scanning technique, segments which show no MAA uptake may exhibit mild-to-moderate aerosol uptake (or vice versa). Thus, we found that by performing only one investigation (V or Q) patients with significant differences in uptake patterns can encounter three problems;

1. Patient who was thought ineligible for lung resection due to low baseline FEV1 may be actually operable [Figures 4 and 5]
2. There will be underestimation of the ppo FEV$_1$ values [Figure 6]
3. Patient who was thought to be in relatively safe zone as far as his respiratory reserve is concerned, may actually encounter major respiratory complications postoperatively. SPECTCT and three dimensional (3D) imaging help in better delineation of tracer uptake on V/Q scan [Figure 7].

Table 3: Preoperative and predicted postoperative forced expiratory volume in one second chart

Techniques	Mean preoperative FEV$_1$ (L)	Percentage predicted FEV$_1$	*P*
Ventilation scan	1.09 + 0.19	76.8 + 10	<0.02
Perfusion scan	1.18 + 0.15	77.9 + 10	<0.03
Combined	1.23	68 + 10	<0.07

All correlations were statistically significant. FEV$_1$=Forced expiratory volume in one second

Table 4: Ventilation/perfusion scan uptake distribution patterns

Techniques	Correctly predicted number of patients	Matched segments	Unmatched segments
Ventilation scan	37	17	46
Perfusion scan	36	20	44

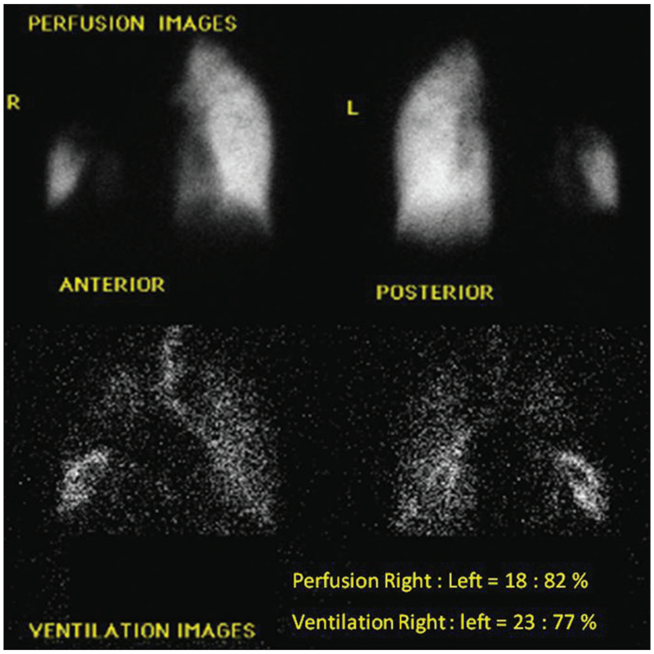
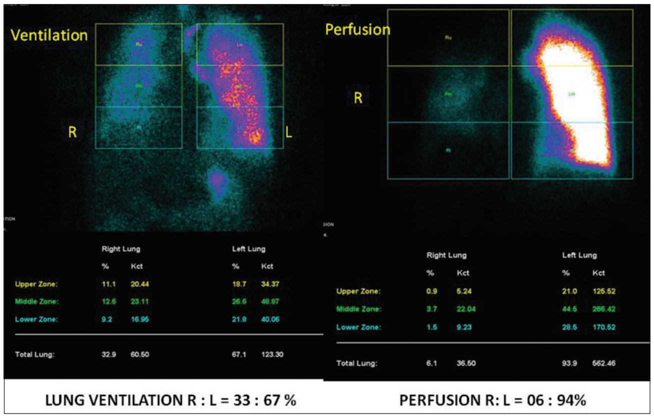


Figure 5: Discordant perfusion/ventilation scan findings in a high risk 56-year-old male with right lung lesion showing discrepant uptake patterns (18% and 23% uptake in right lung). This patient who was thought ineligible for lung resection due to low baseline FEV1 was taken up for surgery based on V/Q scan findings as the uptake variation between both imaging was not significantly different

Thus a higher accuracy in ppo FEV$_1$ is being suggested by this combined imaging technique. This is proved by the fact that patients tolerated the surgery well with no significant postoperative respiratory complications except for one patient. There was an improvement in their FEV$_1$ at 6 months follow-up. We also found that in patients with low FEV$_1$ (severe obstruction), aerosol distribution was extremely heterogeneous with predominately central airway deposition compared with the uniform distribution characteristic of patients with unobstructed airways. By performing both manual ROI, segment counting and SPECTCT the number of segments involved are clearly demarcated.

The mean preoperative FEV$_1$ for ventilation scan was 1.09 + 0.19 (76.8% + 20% predicted). For perfusion scan, mean preoperative FEV$_1$ for found to be 1.18 + 0.15 (77.9% + 20% predicted). The mean measured postoperative FEV$_1$ among patients who underwent lobectomy and pneumonectomy was 0.9 + 0.69 L (69.5% + 20.5% predicted) and 0.89 + 0.13 L (36.3% + 8.5% predicted) respectively. The range of FEV$_1$ predicted was 0.6–1.38 L/min in our series.

After anatomical lobectomy, patients with normal or mildly diseased lungs have the greatest postoperative decrease in FEV$_1$, whereas those with poor baseline function present minimal change or even improvement in postoperative



	Right Lung %	Right Lung Kct	Left Lung %	Left Lung Kct
Upper Zone:	11.1	20.44	18.7	34.37
Middle Zone:	12.6	23.11	26.6	48.87
Lower Zone:	9.2	16.95	21.8	40.06
Total Lung:	32.9	60.50	67.1	123.30

	Right Lung %	Right Lung Kct	Left Lung %	Left Lung Kct
Upper Zone:	0.9	5.24	21.0	125.62
Middle Zone:	3.7	22.04	44.5	266.42
Lower Zone:	1.5	9.23	28.5	170.52
Total Lung:	6.1	36.50	93.9	562.46

LUNG VENTILATION R : L = 33 : 67 %

PERFUSION R: L = 06 : 94%

Figure 6: Another case of Type 4b findings with discrepancy in ventilation/ perfusion scan showing right lung uptake to be 6% and 33% on perfusion and ventilation scans respectively. Inspite of scan showing better percentage uptake on ventilation, predict postoperative based on lung perfusion was not significantly higher (as loss calculated was only 6%). But patient had stormy postoperative period and longer ventilator support was needed as ventilation scan showed he had preserved ventilation (33%) which he lost by penumonectomy

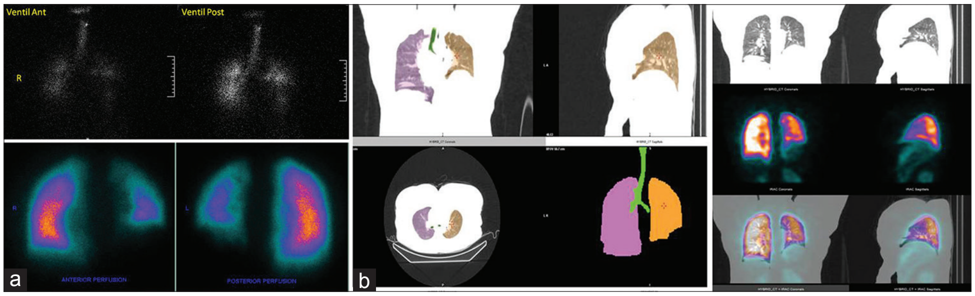


Figure 7: (a and b) (Planar, SPECTCT and 3D image reconstruction) Images of a 52-year-old patient with solitary lung nodule positive for malignancy. Aerosol distribution in left Lung on planar scan appears suboptimal. SPECTCT and 3D images are useful in delineating the segmental distribution of tracer in both lungs

FEV_1 which correlates with our study. In our series, we found a sustained functional improvement (extending upto 1 year) in selected patients postlobectomy with preoperative FEV_1 of around 1 L. Others showed a gradual improvement over a few weeks. One patient expired and three had a protracted recovery. At 3 months, there were excellent correlations (absolute/predicted values) in rest of the patients for FEV_1 with $r = 0.78$ and 0.81, respectively. Accurate estimation of postoperative pulmonary function by nuclear techniques takes into account the effect of deflating the over-expanded thorax and reinflating perfused lung areas. This can be possible by performing both V/Q scan in all patients.

Discussion

For patients with localized lung cancer or severe COPD, lung resection provides the highest likelihood of a cure. However, only about 20% to 30% of patients are potential candidates for surgical resection due to the stage at which the disease is diagnosed or due to comorbid conditions.[8]

To critically estimate the probable effect on respiration that a segmental lung or a larger resection can cause, one must understand the disruption of blood flow or aeration that can occur by a tumor or localised benign lung pathology. This will relate to the size, location of lung pathology, blood supply pattern and pre- or co-existing lung diseases such as COPD. Regional differences due to gravity (supine/prone position) and weight of each lung does not influence radionuclide distribution pattern as both the V/Q scans are performed in supine position. Factors which also needs consideration is the anatomic variability of bronchial and pulmonary circulation and the fact that lung perfusion can get augmented in underlying inflammatory, infective, and coexisting disease states like bronchiectasis (the rise can be from 1% to as much as 30% of cardiac output).[9] Normally, the alveolar region and respiratory bronchioles are supplied by the pulmonary circulation while blood flow to the larger airways (trachea to terminal bronchioles) is through the systemic circulation and these airways receive approximately 1% of the cardiac output. Mechanical factors such as the downstream pressure and alveolar pressure also influence the distribution of blood flow through the tracheal bronchial vasculature. Apart from the pulmonary risk factors, underlying cardiac problems can independently accentuate the postoperative risk.

ACCP guidelines[1] advocate performing lung perfusion scintigraphy as part of the preoperative physiologic assessment of a patient being considered for surgical resection of lung cancer.

Thida *et al*.[10] in their study conversely conclude that V scintigraphy alone provides the best correlation between the predicted and actual postoperative values and recommend its use to ppo lung function which we disagree. British thoracic society of cardiovascular surgeons[5] does not recommend any further respiratory function tests for a lobectomy if the postbronchodilator FEV_1 is >1.5 l and for a pneumonectomy if the postbronchodilator FEV_1 is >2.0 l, provided that there is no evidence of interstitial lung disease or unexpected disability due to shortness of breath.

It is well known that a preoperative FEV_1 of <60% of predicted is the strongest predictor of postoperative respiratory complication. Stephan *et al*.[11] reported that in postoperative states, pulmonary complication in patients with FEV_1 < L was 40%, while 19% for those with FEV_1 >2 L. In our series, only one patient died within 1st year of follow-up and 3/52 patients had prolonged recovery of respiratory function. Thus, quantification of lung function is of utmost importance in deciding the extent of surgical resection in each patient, especially those with lung cancer with curative intent. Variations in lung V and Q can alter the FEV_1 values. Patients with tumors obstructing the bronchus/hilum showed an increased deposition of labeled aerosols in the central airway. It was also found that clearance of the labeled aerosol inversely correlated with FEV_1. Patients with a lower FEV_1 (0.9 L) showed delayed tracer clearance on V imaging when compared to better clearance in patients with FEV_1 of >1.5 L.[12]

There is a clear correlation between the extent of resection and postoperative morbidity and mortality. Segmental or wedge resections have the lowest and pneumonectomies the highest risk. The estimation of the amount of lung tissue which can safely be removed is very important in the preoperative evaluation. The development of split-function studies has made it possible to calculate the relative function of the tissue to be removed to the total function of both lungs, and thereby to ppo function. Resections involving not >1 lobe usually lead to an early functional deficit followed by later recovery. Their permanent functional loss in pulmonary function is small (≤10%) and their exercise capacity is only slightly reduced, or not at all. Pneumonectomy, on the other hand, leads to an early permanent loss of about 33% in pulmonary function and 20% in exercise capacity.[13]

Thus, pulmonary function tests alone overestimate the functional loss after lung resection. Knowledge of these changes depending on the extent of resection is useful for the preoperative counselling, including the estimation of a patient's postoperative working capacity.

Conclusion

Our study suggests that combined V/Q scans are recommended in patients with borderline low respiratory reserve for postoperative FEV_1 prediction. Being inexpensive and easy to perform investigations, V/Q scans can be used to accurately estimate the surgical operability in these patients. V/Q scans accurately define the edges of the lungs and quantify amounts of MAA/DTPA aerosol penetration beyong the occluded lung regions. Planar and SPECTCT techniques appear robust and avoid errors from extrapulmonary activity. This allows one to decide on functional operability in patients with severe lung disease and comorbidities. Further, postoperative performance is accurately predicted by radionuclide investigations by providing anatomical delineation of the exact lung tissue to be resected.

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Conflicts of interest

There are no conflicts of interest.

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