Ventilation Perfusion Scintigraphy and Lung Function Testing to Assess Metal Stent Efficacy

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Stent implantation in malignant bronchial stenoses is a highly effective method of providing symptomatic relief by restoring bronchial patency. Whether an improvement in ventilatory conditions is paralleled by an increase in blood flow and gas exchange has not yet been determined. **Methods:** Fourteen patients with malignant, high-grade obstruction of bronchi who had metal stent implantation were investigated. Before the intervention and again 8 days afterward, both quantitative technegas ventilation and ^{99m}Tc-MAA perfusion scans (V/Q scans) and lung function tests were performed. **Results:** Stent implantation was successful in all patients, with a significant reduction in the degree of bronchial stenosis (prestent: 93% ± 1.5%; poststent: 16% ± 3.5%). After stent implantation, ventilation scintigraphy revealed an improvement in tracer deposition by 65% (prestent: 37% ± 8%; poststent: 61% ± 6%; p < 0.05) within the affected lung. A complementary increase of 71% by perfusion scintigraphy was obtained (prestent: 27% ± 4%; poststent: 46% ± 5%; p < 0.01%). Based on scintigraphic criteria, stenting was successful in 93% (n = 13) of all patients. Lung function studies performed after the intervention showed significant improvement in vital capacity (VC, p < 0.01), forced expiratory volume in 1 sec (FEV$_1$, p < 0.05), peak expiratory flow (PEF, p < 0.05), arterial oxygen (PaO$_2$, p < 0.05) and carbon dioxide (P$_a$CO$_2$, p < 0.05) tension, and oxygen saturation (p < 0.05). **Conclusion:** Stenting of malignant high-grade bronchial obstructions leads to an increase in bronchial patency and in activity distribution of both ventilation and perfusion scintigraphy of the affected lung, accompanied by significant improvement in lung function parameters.

Key Words: bronchial carcinoma; bronchial stenosis; ventilation perfusion scintigraphy; technegas; stents

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High-grade malignant bronchial stenosis can lead to a variety of complications in patients suffering from pulmonary neoplasms. Although surgical resection offers the best chance for curative treatment, only a minority of these patients are operative candidates, especially if respiratory symptoms have already occurred (*1,2*). The reduction in airway patency frequently causes severe dyspnea, stridor and impaired mucus expectoration that often leads to subsequent complications, such as pneumonia, atelectasis or lung abscess (*3,4*). Therefore, it is essential to reverse stenosis formation, usually through chemotherapy and radiation (*5,6*) as the treatments of first choice. Both treatment strategies can be combined effectively with endobronchial laser resection (*7*) or brachytherapy (*8*). Endobronchial stent implantation provides an additional tool to optimize and maintain restored bronchial lumen (*9–12*). In terminal cases, stenting sometimes represents the only therapeutic option left that is capable of giving relief. The value of stent implantation in patients with bronchial stenosis depends on the improvement in ventilation (*1,13*) and the normalization

of blood flow within the tumorous lung region. Impaired perfusion in the affected lung results from direct tumor infiltration and subsequent compression of blood vessels, which then leads to hypoxemia-induced vasoconstriction (*14,15*). However, to date it has not been determined whether restoration of airway patency will improve ventilation alone without affecting circulation, in other words, will simply lead to an increase in dead-space ventilation, especially if interruption in blood flow presumably has been chronic (*16*). In this regard, endobronchial stent implantation could improve ventilation in areas with a high degree of shunting or without blood flow due to decreased arterial oxygen tension (*17*). This study investigated if endobronchial stent implantation evokes a combined change in ventilation and perfusion (V/Q) scintigraphy parameters and if these changes are accompanied by corresponding changes in results obtained from lung function tests.

MATERIALS AND METHODS

Patients

Fourteen patients (age ± sem: 59 ± 4) with high-grade obstruction of the main (n = 9), intermediate (n = 3) and lower lobe bronchus (n = 2) by intraluminal or extraluminal tumor growth underwent fiberoptic bronchoscopic stent implantation because of severe dyspnea or symptomatically impaired ventilation (Table 1). One day before and 7 days after stent implantation, the effect of treatment was assessed by quantitative V/Q scintigraphy, lung function testing and arterial blood gas analysis. Informed consent was obtained in writing from all patients before the procedure.

Determination of Stenosis

The degree of obstruction was calculated semiquantitatively by determining the remaining cross-sectional area bronchoscopically. Stenoses were classified into four ranges: 100% = occlusion; 99% = subtotal occlusion; 95% = high-grade stenosis; and 90% = moderately high-grade stenosis. Similarly, postinterventional results for the restored bronchial lumen were categorized as follows: 100% = complete restoration; 90% = nearly complete restoration; 75% = restoration; and 50% = incomplete restoration.

Stent Systems

The Strecker stent (Boston Scientific, Watertown, MA) is a passively-expanding wire mesh woven out of a knitted tantalum wire strand. The stent is mounted onto a 5 F balloon-tipped catheter (Fig. 1). After placement within the stenotic area, balloon insufflation at a pressure of 7 atm causes release of the stent from the insertion device. The stents used for the interventions had a final maximum diameter of 11 mm and a length of 4 cm.

The Accuflex stent (Boston Scientific, Watertown, MA) is a self-expanding device consisting of a single nitinol wire strand fixed onto the inner shaft of a guiding catheter. After its manufacture, the stent is compressed and covered by an outer sheath. For stent deployment, the proximal end of the inner shaft is held in position while the outer sheath is retracted (Fig. 2). On expansion, the stent assumes a tubular shape. The preset maximum diameter of

TABLE 1
Biographical Data, Site of Stenosis and Type of Stent

Subject no.	Sex	Age (yr)	Site of obstruction	Tumor growth (i/e)	Type of stent: Strecker (S) Accuflex (A)
1	f	60	RMB	i	S
2	m	43	LMB	i	A
3	m	67	LMB	i	S
4	m	68	LMB	i/e	A
5	m	67	IB	i/e	S
6	m	31	LLB	e	S
7	m	50	IB	i/e	S
8	m	75	RMB	i	A
9	m	55	IB	i/e	A
10	f	66	LMB	i	A
11	m	82	LLB	i/e	A
12	f	40	LMB	i	S
13	m	79	RMB	i	A
14	f	49	LMB	i/e	A

LMB = left main bronchus; LLB = left lower lobe bronchus; RMB = right main bronchus; IB = intermediate bronchus; i = intraluminal; e = extraluminal.

the Accuflex stent is 10 mm and it reaches a length of 4 cm after full expansion.

Stent Placement

Flexible bronchoscopy and stent placement were performed as recently described (17,18). Before starting the intervention, bronchoscopic intubation with a metal-reinforced silicone tube (Rüsch, Kernen, Germany) was performed. During the intervention, supplemental oxygen (8–10 l/min) was administered through a separate oxygen channel that ran parallel to the outside of the tube (Fig. 3). After the bronchoscope had gained access to the stenosis, the
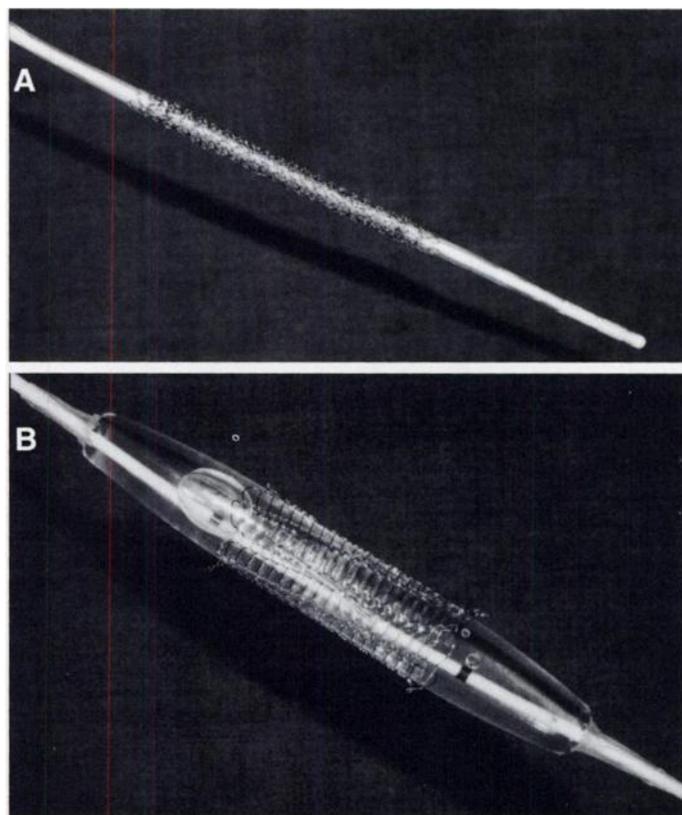

FIGURE 1. (A) The Strecker stent expands within the bronchus by the (B) inflation of the balloon.
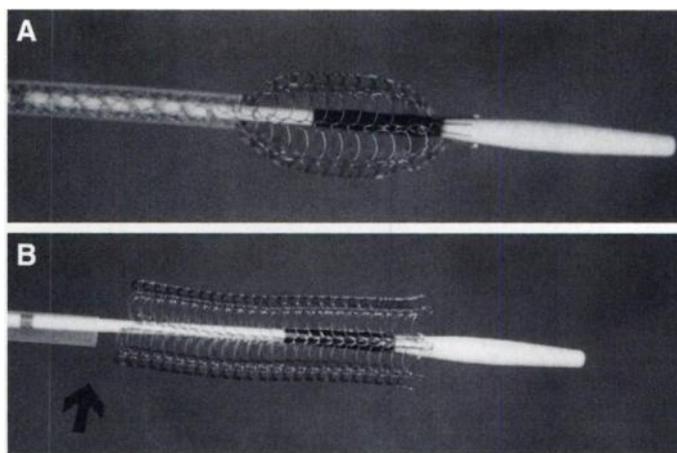

FIGURE 2. (A) The Accuflex stent unfolds by (B) retraction of the cover sheath.

lower border was delineated with radiopaque skin markers under fluoroscopic guidance. Next, the stent was advanced along the guidewire and positioned under fluoroscopic control and direct visualization through a 2.8-mm bronchoscope (Pentax FB 10X; Pentax, Hamburg, Germany). This procedure assured the most accurate placement of the prosthesis. Deployment of the stent was considered successful if the stent endings covered the stenosis by a minimum of 1 cm each, distal and proximal to the lesion, and if the stenosis could be crossed with a 5.8-mm bronchoscope after the intervention. The degree of bronchial stenosis before and after stent implantation was calculated semiquantitatively.

Lung Function Testing and Arterial Blood-Gas Analysis

Lung function testing consisted of spirometry and whole-body plethysmography (Bodyscreen, Jaeger GmbH & Co. KG, Würzburg, Germany). For spirometry, an open system was used with integration of the flow signal. Whole-body plethysmography was performed according to the constant volume method and the results obtained were compared with international protocols (20). Data were expressed as base value, deviation from base value in percent before and after stent implantation, and as the percentage of the predicted value. All blood-gas analyses were performed by an automatic blood-gas analyzing system (280 Blood Gas System, Ciba Corning Diagnostics, Fernwald, Germany).

Ventilation and Perfusion Scintigraphy

Technegas was used as the ventilatory agent because it allows for the acquisition of images in multiple projections after the administration of a single dose of radiotracer. This provides a higher degree of precision for comparison with the respective scans obtained in the scintigraphic perfusion studies. In addition, the ideal imaging energy of ^{99m}Tc avoids photon attenuation by overlying soft tissues (21,22).

Technetium-99m-labeled ultrafine carbon particles (technegas, Medgenix, Belgium) were synthesized in a technegas generator by the complete evaporation to dryness of about 370 MBq of sodium ^{99m}Tc-pertechnetate that was contained in a graphite crucible filled with a total volume of 0.1 ml normal saline. The crucible (Tetley Crucible, Medgenix, Belgium) was heated at 2500°C under an atmosphere of pure argon, and the resulting vapor and argon mixture was used as the inhalation agent. Inhalation of the gas was performed with a mouthpiece that was attached to the generator by plastic tubing. While patients were in an upright position they inhaled slowly, then breathheld at maximum inspiration for several seconds. This was repeated up to eight times until an adequate counting rate was obtained. Static images in a seated position were acquired immediately after inhalation in the anterior, posterior, left and right posterior oblique and left and right lateral projections
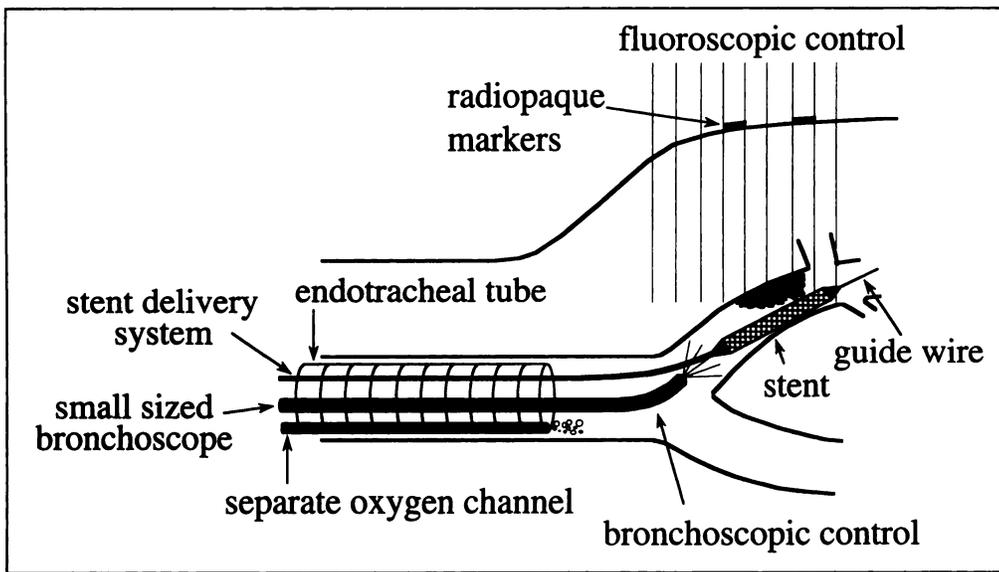
FIGURE 3. Schematic of the stent implantation procedure.

with a fixed total of 50.000 counts per frame (23). Ventilation scans were always performed first, and were immediately followed by the perfusion study.

For perfusion scintigraphy, about 185 MBq of ^{99m}Tc-macroaggregated albumin (SOLCO MAA, Sorin Biomedica, Saluggia, Italy) containing 100,000–500,000 particles were injected into an antecubital vein in the supine position and at maximal inspiration. Analog images were obtained in the same projections as for the ventilation studies with a fixed total of 400,000 counts per frame with the patient in a seated position. Subtraction of the technegas images from the perfusion images was not performed.

All ventilation and perfusion studies were performed using a large field of view gamma camera (Digital Dyna 4, Picker International, Munich, Germany) equipped with a low-energy, all-purpose collimator. The camera was linked to a Micro/Max DELTA computer (Siemens, Erlangen, Germany) that allowed quantitative analysis of the images obtained. For all ventilation and perfusion studies, the anterior and posterior projections were recorded digitally and analyzed by a region-of-interest technique using commercial software. In addition, the geometric mean of the counts acquired in the anterior and posterior projections was used for calculation of results. The geometric mean was used rather than the arithmetic mean as it provides for depth correction and, therefore, allows more accurate estimation of whole lung counts.

A fractional score (FS) of ventilation and perfusion was calculated to express the mean counts for the respective lung as a percentage of the total counts in both lungs:

$$FS = \frac{\text{mean counts from respective lung}}{\text{mean counts from both lungs}} \times 100.$$

To calculate the percent change in ventilation and perfusion of the stented lung after intervention, the proportional uptake of radioactive tracer by the healthy lung before and after stent insertion was regarded as fixed and was used as a reference value for the affected lung. Thus, a relative score (RS) of ventilation and perfusion of the affected lung was calculated as the ratio of FS of the affected lung to FS of the healthy lung:

$$RS = \frac{\text{FS of the affected lung}}{\text{FS of the healthy lung}} \times 100.$$

This RS was used for the calculation of the percent change (PC) in ventilation and perfusion of the affected lung after stent implantation:

$$PC = \frac{\text{RS before stent insertion}}{\text{RS after stent insertion}} \times 100.$$

Statistical Analysis

Data are expressed as mean ± s.e.m. Results obtained before and after stenting were compared using a Student's t-test for paired observations. Probability values of less than 0.05 were considered significant.

RESULTS

Reduction in Stenosis

Stenoses of 75% to 100% (mean 93% ± 1.5%) were treated by stent implantation. Stenting was successful in all 14 patients and led to a postinterventional reduction in stenosis of 16% ± 4% at minimum (Fig. 4).

Lung Function

In the majority of patients, total lung capacity (TLC) was in the normal range (93% ± 3%; range: 74% to 118%) due to at least some degree of residual bronchial patency for ventilation
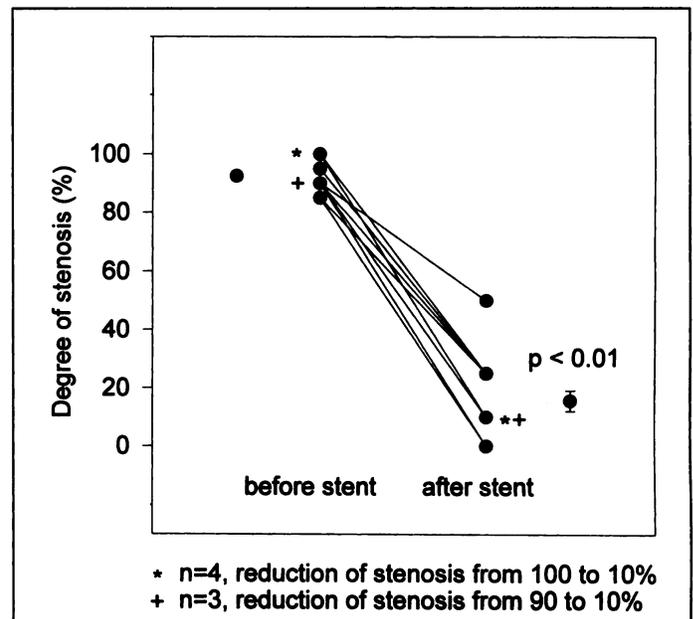

FIGURE 4. Degree of bronchial stenosis before and after stent implantation for all 14 study patients.

* n=4, reduction of stenosis from 100 to 10%
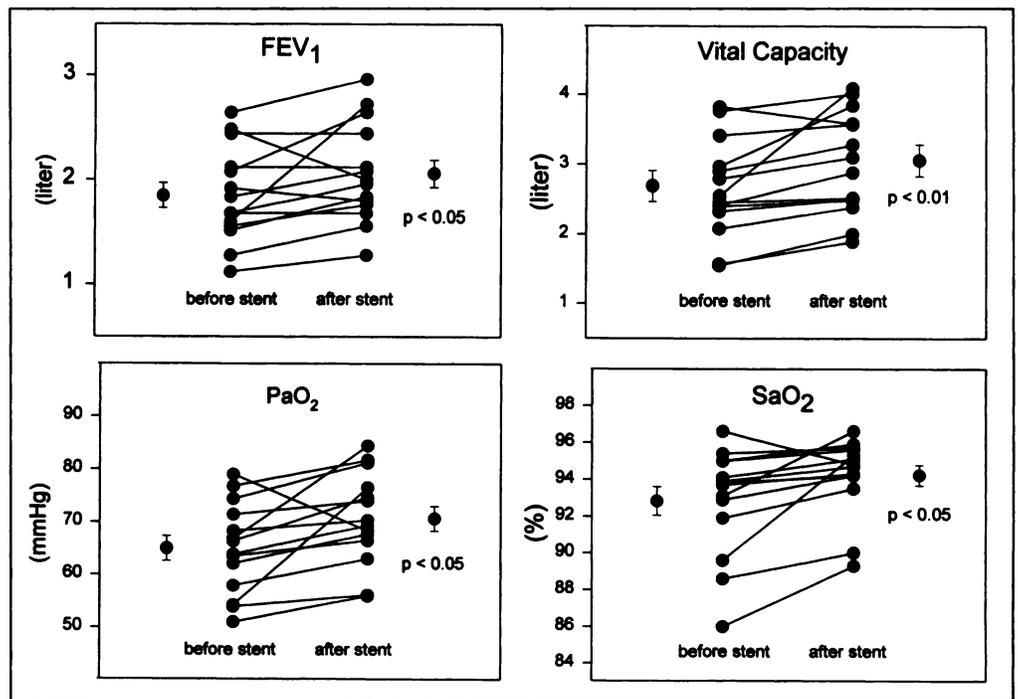+ n=3, reduction of stenosis from 90 to 10%

FIGURE 5. Lung function parameters and results of blood-gas analysis, both of which improved significantly after stent implantation (PEF values are given in Table 2), shown for all 14 study patients.

of the affected lung or to a compensatory hyperinflation of the unaffected side (Table 2). Before stent implantation, vital capacity (VC) was decreased at 66% ± 3% of predicted values. In patients, a mean forced expiratory volume in 1 sec (FEV_1) of 61% ± 4% of predicted value was obtained; peak expiratory flow (PEF) was reduced as well at 54% ± 3%. Most patients suffered from moderate to severe hypoxemia before stent insertion, with an arterial oxygen tension (PaO_2) of 65 ± 2 mmHg. The mean arterial oxygen saturation (SaO_2) was to 93% ± 1%. As a consequence, the majority of patients presented with hyperventilation (mean $PaCO_2$ 33 ± 1 mmHg).

After stent implantation (Table 2, Fig. 5), a small but significant improvement in VC to 75% ± 4% (p < 0.01) of the predicted value resulted. Similarly, a significant increase in the airflow parameters FEV_1 to 67% ± 4%, and in PEF to 58% ± 4% occurred (p < 0.05). A trend towards reduction in specific airway resistance (1.5 ± 0.1 kPa sec to 1.3 ± 0.1 kPa sec) could be observed which did not, however, reach statistical significance. With the exception of one patient who showed a decrease

in PaO_2 (79–68 mmHg) 8 days after the intervention, all other patients demonstrated an improvement in arterial O_2-tension from 65 ± 2 mmHg to 71 ± 2 mmHg to (p < 0.05). In concert with the rise in PaO_2, an increase in $PaCO_2$ from 33 ± 1 mmHg to 35 ± 1 mmHg (p < 0.05) and an improvement in SaO_2 from 92% to 94% (p < 0.05) were observed.

Ventilation and Perfusion Scintigraphy

Before stent implantation, the perfusion scans of all patients revealed that the perfusion defects were clearly matched with the ventilation defects (Fig. 6).

After stent implantation, ventilation scintigraphy showed an

TABLE 2
Lung Function Test Parameters Before and After Stent Implantation for 14 Study Subjects

	Before stent	After stent
TLC (L)	6.1 ± 0.4	6.3 ± 0.3
% pred	92 ± 3	98 ± 3
VC (L)	2.6 ± 0.2	3.0 ± 0.2†
% pred	66 ± 3	75 ± 4
SRaw (kPa s)	1.47 ± 0.10	1.33 ± 0.11
% pred	144 ± 14	132 ± 10
FEV_1 (L)	1.9 ± 0.1	2.1 ± 0.1*
% pred	61 ± 4.0	67 ± 4
PEF (L s⁻¹)	4.1 ± 0.3	4.6 ± 0.3*
% pred	55 ± 3	58 ± 4
PaO_2 (mmHg)	65 ± 2	71 ± 2.4*
$PaCO_2$ (mmHg)	33 ± 1	35 ± 1*
SaO_2 (%)	93 ± 0.8	94 ± 0.6*

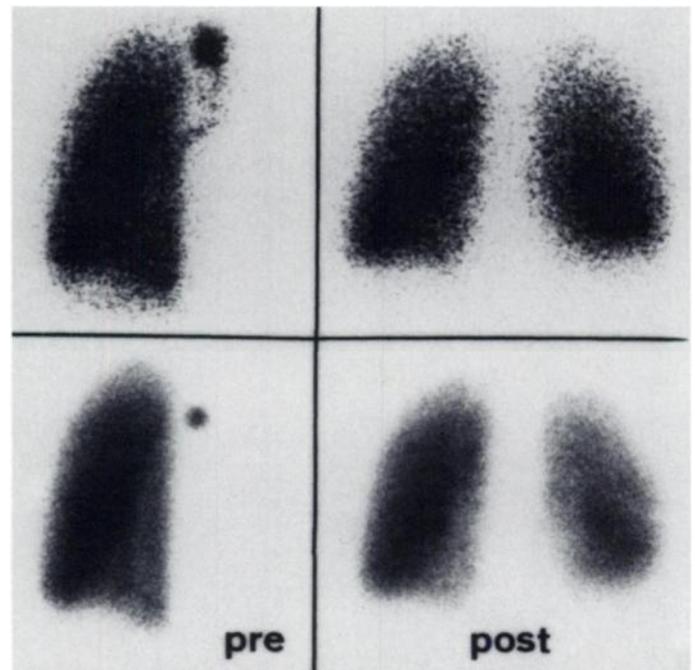*p < 0.05; †p < 0.01; % pred = percentage of predicted value. Values are mean ± s.e.m.

FIGURE 6. Anterior projections of radionuclide ventilation (upper panels) and perfusion scans (lower panels) 1 day before and 7 days after implantation of a nitinol stent within a subtotally-obstructed left main bronchus. After treatment, corresponding improvement in both ventilation and perfusion scans was observed.

TABLE 3
Quantitative Scintigraphic Ventilation and Perfusion Data of the Affected Lung Before and After Stent Implantation

Subject no.	Ventilation before stent (%)	Ventilation after stent (%)	Perfusion before stent (%)	Perfusion after stent (%)
1	28	38	19	27
2	1	53	7	26
3	1	24	11	24
4	1	83	18	78
5	84	65	40	37
6	70	88	43	76
7	56	72	41	48
8	52	69	59	71
9	76	95	47	62
10	17	36	22	30
11	30	33	19	25
12	33	35	25	32
13	66	67	23	41
14	1	89	1	67
Mean ± s.e.m.	37 ± 8	61 ± 6*	27 ± 4	46 ± 5†

*p < 0.05; †p < 0.01.

improvement in the deposition of radionuclides within the diseased lung by 65%, which was calculated from a mean increase in deposition from 37% ± 8% to 61% ± 6% (p < 0.05). Only one patient showed a decrease in tracer deposition of 7% after stent implantation (Table 3, Fig. 7).

By perfusion scans, a significant improvement from 27% ± 4% to 46% ± 5% (p < 0.01) was shown in all but one patient after stent implantation. Thus, relative perfusion increased by a mean of 71%, even in those patients with initially complete airway obstruction. Corresponding to the results obtained during ventilation scintigraphy, Patient 5 exhibited a decrease in the deposition of radioactivity during perfusion scanning (Table 3, Fig. 7). By comparing the incremental changes in ventilation scores with the incremental changes in perfusion scores a positive correlation was obtained with a correlation coefficient of 0.77.

DISCUSSION

This study used lung V/Q scintigraphy to show that both impaired ventilation and perfusion in patients with malignant obstruction of the central airways can be improved by endobronchial stent implantation and, consequently, can lead to an improvement in gas exchange.

The use of endobronchial stents is indicated for the reduction of high-grade stenoses of the large airways by extraluminal or endobronchial tumor growth (2,12,24). In most cases, stent implantation leads within a short time to substantial improvement in bronchial narrowing and to an immediate relief of dyspnea. Similarily, laser resection and, after some delay, radiotherapy can relieve dyspnea by reducing infiltration and compression of airways and blood vessels (17,25). It has been suggested that this improvement in gas exchange is the consequence of an increase in blood flow after correction of reduced reflex regional perfusion (26). Thus, an increase in ventilation within a completely or partially obstructed lung can fail to result in any improvement in gas exchange if recanalization is not accompanied by an increase in arterial pulmonary blood flow (17). This failure to improve can be a consequence of tumor mass, which compresses or distorts either arterial or venous blood vessels or both. Unfortunately, such disturbances in perfusion cannot in many cases be predicted from chest radiographs (15). In up to one third of patients with bronchogenic carcinoma, the radiographic appearance of the tumor is deceptive, and unexpected abnormalities of perfusion will be found (26). Hence, restoration of bronchial patency may simply increase dead-space ventilation or shunting within the appropriate lung areas but will not lead to an increase in arterial oxygen tension (27). To determine whether such a functional V/Q mismatch is induced or increased by endobronchial stent implantation, quantitative V/Q scintigraphy was performed 24 hr before and 1 wk after stent placement. Lung function studies were also performed.

Although scintigraphy cannot provide data on the absolute amount of ventilation and perfusion, calculation of relative changes in the degree of functional impairment is possible by the technique of serial scintiscanning (28). Using this approach, it was demonstrated that endobronchial stent insertion leads not only to a significant improvement in relative distribution of ventilation, but also to an increase in distribution of pulmonary arterial blood flow within the affected lung, even in patients who suffered from complete tumor occlusion of the bronchus. Only one patient suffered from a rapid increase in tumor growth which penetrated throughout the wire mesh in a short period of time, and was associated with an increase in mucus retention
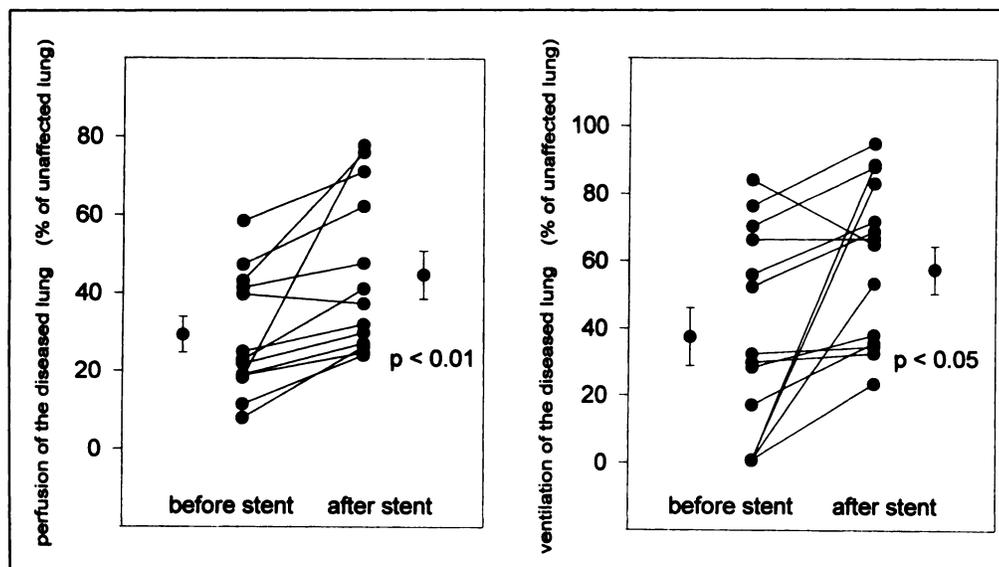

FIGURE 7. Perfusion and ventilation in the affected lung before and after bronchial stent implantation. Pretreatment and post-treatment values for all 14 study patients are given as mean ± sem. Ventilation and perfusion in the unaffected lung was used as a reference value and set to 100%.

and deterioration in the patient's physical condition. Scintigraphically, this was manifest by a decrease in tracer deposition in both ventilation and perfusion scanning. All other patients showed a parallel improvement in both ventilation and perfusion after stenting, in spite of the chronic neoplastic changes in the affected lung parenchyma. Similar results have been shown 2–4 days after laser resection in patients with bronchial carcinoma. However, in these patients, ventilation improved more than perfusion scores, and changes in gas exchange did not attain statistical significance (27).

In contrast, in this study, the parallel improvement in ventilation and perfusion scintigraphy was further substantiated by the significant improvements seen in lung function tests. A significant improvement in lung function parameters was intimately associated with success of stent implantation as evaluated by radionuclide lung scans and changes in arterial oxygen tension, in other words, only two patients showed discrepancies between their scintigraphic and lung function data.

CONCLUSION

This study demonstrates, by means of V/Q scintigraphy and lung function tests, that endobronchial stent implantation for the treatment of obliterating, centrally-located tumors is efficient and leads to overall improvement in pulmonary blood flow distribution, lung function parameters and gas exchange. Even after total bronchial occlusion, reduction in alveolar hypoxia leads to an increase in reflex regional vasodilatation. Both ventilation and perfusion scintigraphy proved congruent in the objective evaluation of the efficacy of endobronchial stent implantation and provided clear evidence that reopening of occluded or tumor-altered bronchi will not result in a significant increase in dead-space ventilation. Further studies are needed to investigate the duration in which pulmonary vessel occlusion might limit the beneficial effect of restoring bronchial airway patency.

ACKNOWLEDGMENTS

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