The Effect of Lung Resection on Pulmonary Function and Exercise Capacity in Lung Cancer Patients

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OBJECTIVE: Prospectively to evaluate the effects of lung resection on lung function (as measured via spirometry) and exercise capacity (as measured via shuttle-walk test) in lung cancer patients. METHODS: We conducted pulmonary function tests and the shuttle-walk test with 110 consecutive patients, before and 1 month, 3 months, and 6 months after lobectomy ($n = 73$) or pneumonectomy ($n = 37$). All the patients underwent a standard posterolateral thoracotomy. Eighty-eight patients completed all 3 postoperative assessments. RESULTS: At 6 months after resection, the lobectomy patients had lost 15% of their preoperative forced expiratory volume in the first second (FEV_1) ($p < 0.001$) and 16% of their exercise capacity ($p < 0.001$), and the pneumonectomy patients had lost 35% of their preoperative FEV_1 ($p < 0.001$) and 23% of their exercise capacity ($p < 0.001$). CONCLUSIONS: Lobectomy patients suffered significant reduction of functional reserve, with almost equal deterioration between lung function and exercise capacity. Pneumonectomy patients had a more substantial loss of functional reserve, and a disproportionate loss of pulmonary function relative to exercise capacity. Therefore, pulmonary function test values considered in isolation may exaggerate the loss of functional exercise capacity in pneumonectomy patients, which is important because many lung cancer patients who require resection for cure are prepared to accept the risks of immediate surgical complications and mortality, but are unwilling to risk long-term poor exercise capacity. *Key words: pulmonary physiology, lung cancer, pneumonectomy, lobectomy, surgical resection.*
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Introduction

Lung resection remains the most effective treatment for non-small-cell lung cancer.[1,2] Although, there are many data available concerning various outcomes (eg, mortality and morbidity) after lung resection, there is a paucity of recent information concerning the postoperative recovery of pulmonary physiology. Resection of lung parenchyma reduces patient pulmonary functional reserve and exercise capacity, with potentially adverse consequences to the patient. This is particularly relevant because it has been consistently observed that these patients are prepared to risk immediate postoperative complications but are unwilling to accept the prospect of long-term pulmonary disability.[3,4] But few data have been published on which patients can base the decision of whether to proceed to lung resection.

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Table 1. Age, Sex, and Cancer Stage of the Participants

	Pneumonectomy	Lobectomy	Total
All Participants			
Number	37	73	110
Mean age (y, range)	67 (42–85)	68 (54–84)	68 (42–85)
Sex (M/F)	25/12	41/32	66/44
Cancer Stage (*n*)			
1	12	57	69
2	13	11	24
3	12	5	17
Participants Who Completed the 6-Month Follow-up Assessment			
Number	29	59	88
Age (y, range)	67 (42–85)	68 (54–84)	68 (42–85)
Sex (M/F)	19/10	32/27	51/37

Previous investigations of post-lung-resection pulmonary physiology usually examined postoperative changes in either pulmonary function[5,6] or exercise capacity in isolation.[7–10] However, the relationship between pulmonary function and exercise capacity is complex, and these essential variables have rarely been examined in combination.[11] Moreover, previous data were often retrospective and also originated from over a decade ago. The demographics of this surgical population have changed; today more lung-resection candidates are female and older. Furthermore, the surgical techniques for pneumonectomy and lobectomy have been refined. For these reasons we prospectively evaluated the effect of lung resection on both lung function and exercise capacity in our pneumonectomy and lobectomy patients.

Methods

Patients

Over 30 months, we prospectively recruited 110 consecutive patients who underwent potentially curative surgery for lung cancer. All patients underwent spirometry to assess lung function, and the shuttle-walk test as a surrogate for exercise capacity. Both tests were performed on the same day, prior to surgery, and then were repeated postoperatively at 1 month, 3 months, and 6 months. Table 1 shows the participants' age, sex, and cancer stages. Sixty-nine patients had stage 1, 24 patients had stage 2, and 17 patients had stage 3A lung carcinoma. Six patients met our lung-function criteria for airways obstruction: percent of predicted forced expiratory volume in the first second (FEV_1) $< 80\%$, and ratio of FEV_1 to forced vital capacity (FVC) $< 70\%$. No patients had criteria for heart failure. There was no formal rehabilitation program after surgery at our institution.

All patients gave their informed consent prior to participation in the study. This research had the permission of our institution's ethics board.

Thoracotomy

The routine surgical and anesthesia procedure included single-lung ventilation with a double-lumen endobronchial tube. All patients underwent standard posterolateral thoracotomy. Postoperative physiotherapy included respiratory exercises and early ambulation with every patient. There were 37 pneumonectomy patients, and 73 lobectomy patients, including 6 bi-lobectomies and 4 wedge resections.

Spirometry

The wedge bellows 12-second spirometer (Vitalograph, Ennis, Ireland) and recording system were calibrated each day, using a 3-L calibrated syringe (Vitalograph, Ennis, Ireland). Spirometry measurements were made with the patient seated, with a conventional flanged rubber mouthpiece and nose clip. At least 3 recordings were made, until the results were reproducible, and the best of 3 reproducible attempts was used for analysis. FEV_1 was calculated from the FVC. The absolute and percent-of-predicted values were recorded. The patient's height was carefully measured and the predicted values were taken from a well-known source.[12]

Shuttle-Walk Test

The shuttle-walk test was performed with methods previously described for measuring exercise capacity in lung cancer patients.[13] The patients walked between 2 cones, 10 m apart, at an incrementally increasing pace. Each increment was signaled by a fully calibrated audiocassette. To assist, the operator accompanied the patient throughout the test. The end point was reached when the patient could no longer maintain the required speed or became too breathless to proceed further. We also recorded the patient's recovery time and the reason for terminating the shuttle walk.

Table 2. Pulmonary Function Recovery After Lung Resection

	FEV_1 (L, range)	Percent of Preoperative FEV_1	Percent of Predicted FEV_1 (%, range)	FVC (L, range)	Percent of Preoperative FVC	Percent of predicted FVC (%, range)	Shuttle Walk Distance (m, range)	Percent of Preoperative Shuttle Walk Distance (%)
Pneumonectomy*								
Preoperative	2.3 (1.3–3.4)	100	87 (43–119)	3.6 (1.8–5.2)	100	108 (71–155)	435 (210–660)	100
1 month	1.4 (0.9–2.5)	61	55 (35–89)	2.0 (1.0–3.6)	56	62.5 (38–97)	259 (70–470)	60
3 months	1.5 (0.7–2.8)	65	59 (39–97)	2.2 (1.0–3.7)	61	66.2 (44–93)	309 (30–500)	71
6 months	1.5 (0.7–2.7)	65	59 (39–97)	2.2 (1.0–3.7)	61	66.2 (39–100)	333 (180–550)	77
Lobectomy†								
Preoperative	2 (1–4.7)	100	78.5 (40–119)	3.2 (1.7–6.0)	100	99.5 (71–149)	433 (190–780)	100
1 month	1.5 (0.5–3.8)	75	60.6 (32–113)	2.2 (1.0–4.5)	69	70.4 (36–105)	305 (30–650)	70
3 months	1.7 (0.8–4.1)	85	66.7 (46–119)	2.5 (0.8–4.1)	78	78.7 (33–121)	358 (180–670)	83
6 months	1.7 (0.8–4.2)	85	66.7 (34–125)	2.6 (1.2–5.2)	81	82.3 (46–119)	365 (110–670)	84

*$n = 29$
†$n = 59$
FEV_1 = forced expiratory volume in the first second
FVC = forced vital capacity

Statistical Analysis

Paired-sample *t* tests were made with statistics software (SPSS 2005, SPSS, Chicago, Illinois) to calculate the differences between the preoperative and postoperative values for both the lung function and shuttle-walk tests.

Results

The 6-month follow-up was completed by 88 patients: 29 pneumonectomy patients (10 right and 19 left) and 59 lobectomy patients (8 left lower lobe, 8 right lower lobe, 20 left upper lobe, 14 right upper lobe, 2 right middle lobe, 4 bi-lobectomy, and 3 wedge resection).

In the pneumonectomy group, 15 patients were current smokers and 14 were ex-smokers. In the lobectomy group, 19 patients were current smokers, 35 were ex-smokers, and 5 were non-smokers. The average smoking history (for both smokers and ex-smokers) was 41 pack-years (range 7.5–100 pack-years). All patients abstained from smoking postoperatively during the study period. One (pneumonectomy) patient underwent postoperative chemotherapy, and 7 (4 pneumonectomy and 3 lobectomy) underwent postoperative radiotherapy.

Lung Function Tests

Table 2 and Fig. 1 show the pulmonary function test results.

FEV_1

In the lobectomy patients ($n = 59$), the mean reduction in FEV_1 was 0.45 L (95% confidence interval [CI] 0.37–0.53 L, $p < 0.001$) at 1 month, and 0.30 L (95% CI 0.22–0.38 L, $p < 0.001$) at 6 months. In the pneumonectomy patients ($n = 29$), the mean reduction in FEV_1 was 0.84 L (95% CI 0.66–1.02 L, $p < 0.001$) at 1 month, and 0.74 L (95% CI 0.57–0.90 L, $p < 0.001$) at 6 months. The difference in mean FEV_1 reduction at 1 month and 6 months was significantly greater in the pneumonectomy patients than in the lobectomy patients ($p < 0.001$) during that time interval.

Between 1 month and 6 months the mean increase in FEV_1 was 0.15 L (95% CI 0.09–0.20 L, $p < 0.001$) in the lobectomy patients, and 0.11 L (95% CI 0.03–0.19 L, $p < 0.001$) in the pneumonectomy patients. There was no significant difference in the extent of improvement between the lobectomy and pneumonectomy groups during that period ($p = 0.395$).

FVC

In the lobectomy patients, the mean reduction in FVC was 0.94 L (95% CI 0.82–1.07 L, $p < 0.001$) at 1 month, and 0.58 L (95% CI 0.46–0.70 L, $p < 0.001$) at 6 months. In the pneumonectomy patients the mean reduction in FVC was 1.50 L (95% CI 1.26–1.74 L, $p < 0.001$) at 1 month, and 1.37 L (95% CI 1.13–1.61 L, $p < 0.001$) at 6 months. The FVC reductions were significantly greater in the pneumonectomy patients than in the lobectomy patients ($p < 0.001$).

Between 1 month and 6 months the mean increase in FVC was 0.36 L (95% CI 0.29–0.43 L, $p < 0.001$) in the lobectomy patients, and 0.13 L (95% CI 0.05–0.22 L, $p = 0.003$) in the pneumonectomy patients. The improvement in FVC during that period was significantly greater in the lobectomy patients than in the pneumonectomy patients ($p < 0.001$).

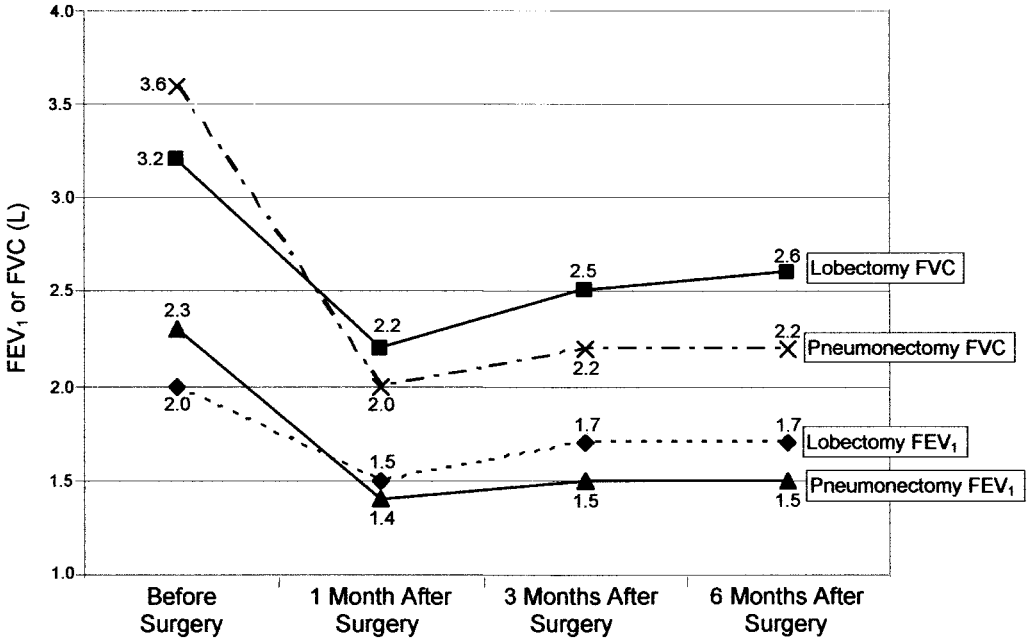

Fig. 1. Lung function recovery after pneumonectomy (n = 29) or lobectomy (n = 59).

After resection, 3 patients showed improved FEV_1 and FVC, compared to their preoperative state.

Percent of Predicted FEV_1 and FVC

The changes in percent of predicted FEV_1 and FVC showed a similar pattern to the absolute FEV_1 and FVC values (see Table 2).

Shuttle-Walk Distance

Fig. 2 shows the shuttle-walk distances. In the lobectomy patients the mean reduction in shuttle-walk distance was 125 m (95% CI 96–154 m, $p < 0.001$) at 1 month and 64 m (95% CI 33–95 m, $p < 0.001$) at 6 months. In the pneumonectomy patients the mean reduction in shuttle-walk distance was 181 m (95% CI 132–230 m, $p < 0.001$) at 1 month, and 99 m (95% CI 54–144 m, $p < 0.001$) at 6 months. The reduction in shuttle-walk distance was significantly greater in the pneumonectomy patients than in the lobectomy patients at 1 month ($p < 0.039$), but there was no significant difference in shuttle-walk deterioration between the lobectomy and pneumonectomy patients at 6 months ($p = 0.188$).

Between 1 month and 6 months, the mean increase in shuttle-walk distance was 55 m (95% CI 34–77 m, $p < 0.001$) in the lobectomy patients and 73 m (95% CI 36–111 m, $p = 0.001$) in the pneumonectomy patients. There was no significant difference in improvement in shuttle-walk distance between the lobectomy and pneumonectomy patients.

After resection, 16 patients showed improved shuttle-walk distance, compared to their preoperative state.

Effects of Sex, Operation Type, Smoking History, and Radiotherapy on Functional Recovery

Table 3 shows the differences in functional recovery between the male and female patients at 6 months. Table 4 shows the differences in functional recovery between the pneumonectomy and lobectomy patients at 6 months. There was a significant difference ($p < 0.05$) between left and right pneumonectomy for FEV_1 recovery, but not for shuttle-walk distance ($p < 0.25$). Between the male and female patients there was no significant difference ($p < 0.05$) in FEV_1 but there was a significant difference in shuttle-walk distance ($p < 0.05$). There was no difference in the pattern of recovery between current smokers and ex-smokers (eg, for deterioration at 6 months: FEV_1 $p = 0.62$, FVC $p = 0.783$, shuttle-walk distance $p = 0.11$. Subgroup analysis without the 7 patients who underwent radiotherapy did not alter the functional recovery findings.

Figures 3 and 4 show the correlations between the change in lung function and change in exercise capacity at 1 month and 6 months.

Patients Who Failed to Complete the Study

Twenty-two patients (8 pneumonectomy and 14 lobectomy) failed to complete the study. Thirteen patients died: 5 with pneumonia, 4 from tumor recurrence, 2 from myocardial infarction, and 2 from unknown causes. Nine other

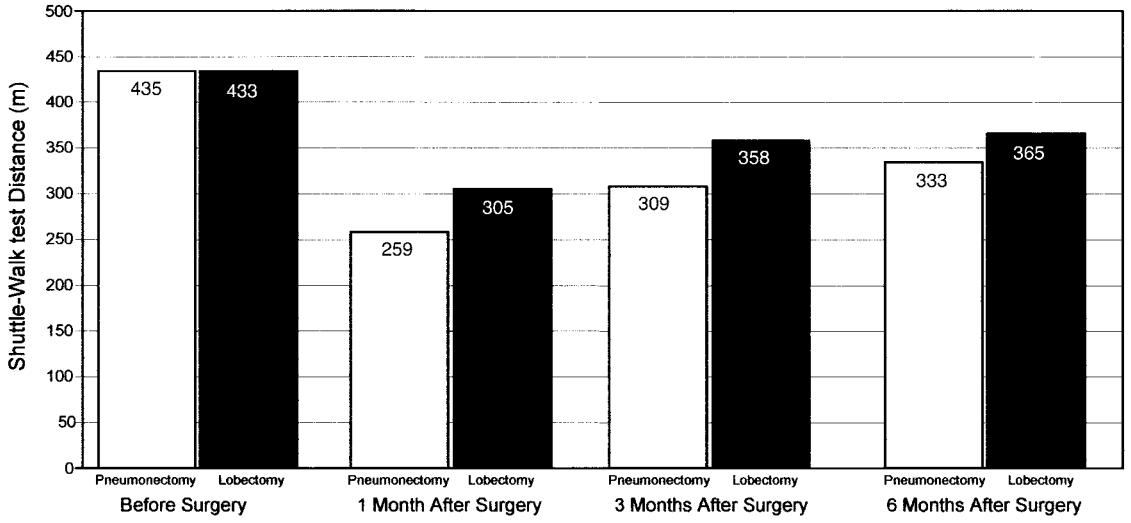

Fig. 2. Exercise recovery after pneumonectomy (n = 29) or lobectomy (n = 59).

Table 3. Difference Between Men and Women in Functional Recovery 6 Months After Pneumonectomy or Lobectomy

	Percent of Preoperative Value 6 Months After Surgery			
	Shuttle Walk Distance		FEV_1	
	Pneumonectomy	Lobectomy	Pneumonectomy	Lobectomy
Women	81	83	68	88
Men	74	85	68	86

FEV_1 = forced expiratory volume in the first second

Table 4. Effect of Operation Site/Type on Functional Recovery at 6 Months

	Percent of Preoperative Value			
	Pneumonectomy		Lobectomy	
	Right	Left	Upper	Lower
FEV_1 (L)	63	72	79	80
Shuttle walk distance (m)	73	78	81	80

FEV_1 = forced expiratory volume in the first second

patients also failed to complete the study (Table 5), none of whom had respiratory disability. There was no significant difference ($p = 0.15$) between the preoperative pulmonary function of the 22 patients who failed to complete follow-up (mean FEV_1 1.83 L) and the 88 patients who completed follow-up (mean FEV_1 2.06 L). Those who failed to complete the follow-up had a significantly lower exercise capacity (mean shuttle-walk distance 328 m) than those who completed follow-up (433 m, $p = 0.002$).

Discussion

The present study combines results from pulmonary function tests and exercise tests, which is important because pulmonary function test results alone do not necessarily correlate with exercise capacity, and vice versa. The 2 previous studies[10,11] that simultaneously investigated pulmonary function and exercise capacity after lung cancer surgery both assessed exercise capacity with a formal cardiopulmonary exercise test to measure maximum oxygen uptake. We measured exercise capacity with the shuttle-walk test, which is less time consuming, easier to perform, and mimics daily activity better. The shuttle-walk test reproducibly measures functional capacity in lung cancer patients[13] and closely correlates with maximum oxygen uptake.[14]

As the measure of lung function, we measured FEV_1 and FVC and calculated percent-of-predicted FEV_1 and FVC. This spirometry technique is simple to perform, tolerated by patients, and is the most helpful measurement for predicting tolerance of surgery.[4] Evaluating patients at 1 month, 3 months, and 6 months allowed us to directly compare our results with those of other studies.[9–11] We included the few patients who underwent radiotherapy, because that therapy was applied to only a tiny field, mainly localized to the remaining bronchial stump, and was performed at least 6 weeks after surgery. The fact that removing these patients from the analysis did not alter the results tends to support their inclusion.

We found that right-sided pneumonectomy had a greater adverse effect on both lung function and exercise capacity than left pneumonectomy (see Table 4) in keeping with the fact that the right lung is anatomically larger than the left. Interestingly, the female patients had better recovery of exercise capacity than did their male counterparts, but sex had

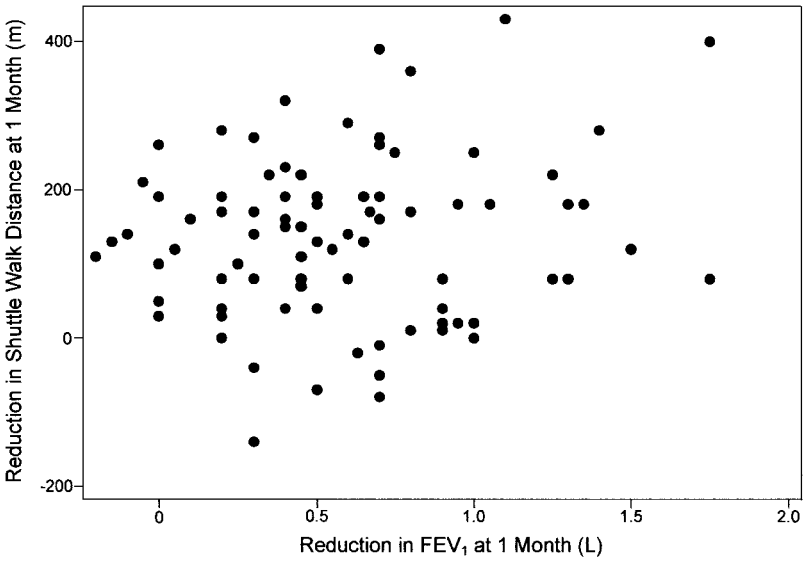

Fig. 3. Correlation between change in forced expiratory volume in the first second (FEV_1) and change in shuttle-walk distance, 1 month after lobectomy or pneumonectomy.

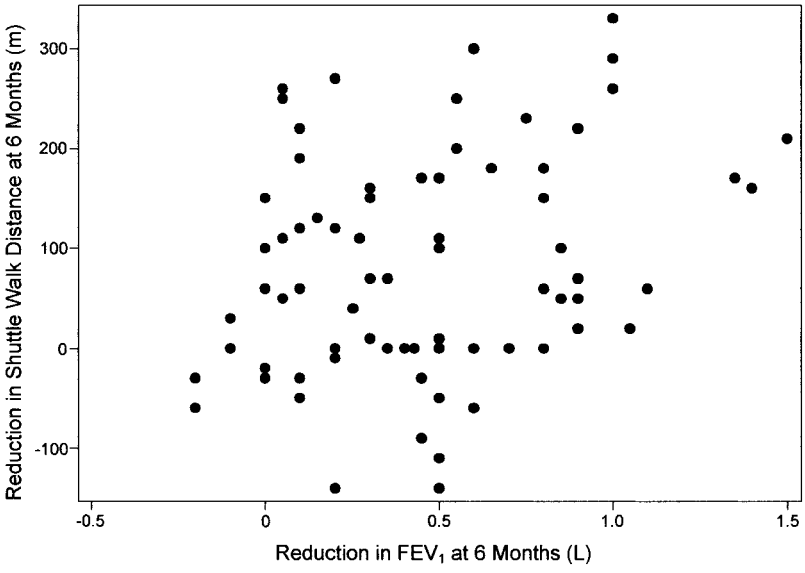

Fig. 4. Correlation between change in forced expiratory volume in the first second (FEV_1) and change in shuttle-walk distance, 6 months after lobectomy or pneumonectomy.

no effect on recovery of lung function. This finding is somewhat difficult to explain and may warrant further research.

At 1 month there was considerable reduction in both FEV_1 and exercise capacity. Much of this reduction has been previously attributed to the pain and thoracic wall restriction after thoracotomy, rather than the direct effect of lung parenchyma loss.[15] In the period between 1 month and 3 months there was improvement in both lung function and exercise capacity, although the lung-function improvement was more marked. However, lung function did not improve further after 3 months. A similar pattern was seen with respect to exercise capacity in the lobectomy patients. In contrast, in the pneumonectomy patients, exercise capacity continued to improve between 3 months and 6 months.

At 6 months, both exercise capacity and lung function were significantly worse than their preoperative values: lobectomy patients had lost 15% of FEV_1 and 16% of exercise capacity; pneumonectomy patients had lost 35% of FEV_1 and 23% of exercise capacity. The functional recovery of our pneumonectomy patients was generally better than that of patients in previously reported studies,[9,16] which could be explained by improvement in surgical techniques. The deterioration in respiratory physiology of our lobectomy patients was more severe than was seen in previous studies.[9,10,16,17] This may reflect that our

Table 5. Reasons for Noncompletion of Study

Reason	Number of Patients
Death	13
Well but refused to participate further	2
Radiotherapy	2
Chemotherapy	1
Multiple comorbidities	1
Musculoskeletal limitation to mobilization	1
Severe persistent postoperative pain	1
Treatment for concomitant bladder carcinoma	1
Total	22

patients were older than those in previous studies, and these surgeries were performed in an era of different surgical population demographics. Another plausible explanation for the differences between the present findings and those of previous studies could relate to the sometimes paradoxical effects of lobectomy. This could occur when patients undergo lobectomy of lung segments that contain severe disease. This is the basis for lung-reduction surgery in patients with localized emphysema and, indeed, in our cohort there were several patients who had improved performance following lobectomy.

In our study, all the patients abstained from smoking and there was no formal rehabilitation program, which might partly explain the slight difference between our results and those of previous series.

Limitations to our study included the assumption that a 6 month follow-up adequately reflects long-term recovery. This is not necessarily the case, but the majority of previous studies also adopted a 6 month end point. Our study suffered from the fact that 20% of the patients failed to complete the follow-up. Although, this is not a small number, it is similar to other investigations,[9–11] and it should also be appreciated that the patients who failed to complete follow-up had preoperative pulmonary function similar to those who completed the study. It could also be suggested that our data are limited by lack of multicenter recruitment, but a single-center trial helps maintain the reproducibility of the methodology.

Conclusions

The pattern of respiratory physiology recovery after lung resection showed some differences from previous studies. This may reflect the considerable changes in modern-day surgical population demographics, as well as some refinements in surgical techniques. Lobectomy patients suffered significant reduction of functional reserve, with equal fractional deterioration of lung function and exercise capacity. Pneumonectomy patients had a more substantial loss of reserve, as well as a disproportionate loss of pulmonary function relative to exercise capacity. The use of pulmonary function tests in isolation may therefore exaggerate the loss of functional exercise capacity in pneumonectomy patients, which is important, because many lung cancer patients who require resection for cure are prepared to accept the risks of immediate surgical complications and mortality but are unwilling to risk long-term poor exercise capacity.[3,4]

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