European Journal of Cardio-Thoracic Surgery 42 (2012) e22–e27
doi:10.1093/ejcts/ezs293

ORIGINAL ARTICLE

Risk factors for impaired lung function after pulmonary metastasectomy: a prospective observational study of 117 cases

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Received 7 February 2012; received in revised form 18 March 2012; accepted 29 March 2012

Abstract

OBJECTIVES: The prediction of postoperative preserved pulmonary function is essential for ascertaining the functional operability of pulmonary metastasectomy candidates. Formulae to predict pulmonary function after metastasectomy have not yet been described. This study was undertaken to provide data about the functional loss after a pulmonary metastasectomy, which often includes non-anatomical resections or combinations with anatomical resections.

METHODS: Pulmonary function tests were performed preoperatively, postoperatively and 3 months after a pulmonary metastasectomy, and the factors potentially influencing the functional outcome were prospectively collected in a database. The functional loss was calculated as the difference in the values between the follow-up visit and the preoperative values, and the influencing factors were tested using the Mann–Whitney test.

RESULTS: A total of 162 patients were prospectively included in the study and 117 completed the study protocol with a follow-up evaluation after a mean of 3.4 months. Of these, 33 patients had bilateral resections, 30 interventions were repeated resections and adhesions were removed in 46. The greatest lung resection performed was a lobectomy in 13, with segmentectomy in 27 and wedge resection in 77 patients. The mean overall functional loss was: forced vital capacity −9.2%, total lung capacity −8.8%, forced expiratory volume in 1 s −10.8% and diffusion capacity for carbon monoxide (DLCO) −9.7%, whereas the diffusion coefficient (KCO) and pO_2 remained unchanged after 3 months. This functional loss was significant ($P < 0.001$) for all the parameters mentioned. The two factors were inversely found to influence the functional outcome: bilateral resection reduced spirometry values ($P < 0.01$), postoperative chemotherapy reduced DLCO ($P = 0.011$) and KCO ($P = 0.029$).

CONCLUSIONS: A pulmonary metastasectomy leads to a significant loss of pulmonary function after 3 months in an average patient collective. The most important factors for deteriorating lung function are a bilateral operation and postoperative chemotherapy.

Keywords: Metastasectomy • Lung function • Bilateral metastasectomy • Functional impairment

INTRODUCTION

The resection of lung metastases from a wide range of primary tumours has become a routine part of daily practice in thoracic surgical units. Several selection criteria are well-accepted by thoracic surgeons: a definitely controlled primary tumour, completely resectable metastases limited to the lung, the lack of a better alternative treatment and the ability of the patient to tolerate the planned operation [1]. Due to the uncertain prognosis of these patients, parenchyma-sparing procedures such as segmentectomy or wedge resections are recommended whenever possible. As long as anatomical resections are planned, the loss of pulmonary function has been described and can be predicted [2]. But when wedge resections or a combination of anatomical and non-anatomical resections are planned, the degree of pulmonary impairment to be expected is unclear. Petrella *et al.* [3] found that the functional loss after three or more non-anatomical resections was comparable with that after a lobectomy. This would imply that the removal of >20 metastases would be fatal. Rolle *et al.* [4] reported the removal of >10 lesions in 57 patients and >20 lesions (up to 124 in one patient) in 25 patients by laser resection with no in-hospital mortality. In accordance with Rolle *et al.* [4], in our daily practice we find that most patients tolerate the removal of >10 bilateral metastases quite well, and only some experience a significant impairment of their lung function with shortness of breath after minor efforts. Also, whereas assessments of the completeness of resection and calculations of the anticipated amount of lung resection are minor problems for experienced thoracic surgeons, predicting postoperative (ppo) lung function after metastasectomy is difficult. We hypothesized that metastasectomy causes a significant deterioration in pulmonary function. Furthermore, we hypothesized that laterality and attendant chemotherapy and other possible factors may significantly influence the functional outcome. Therefore, we performed this prospective evaluation of standardized spirometric values before and after metastasectomy.

METHODS

Patients of the Department of Thoracic Surgery who were scheduled for pulmonary metastasectomy were prospectively included in this study from April 2008 to April 2010. The inclusion criteria were the lungs as the only site of demonstrable disease, planned a complete removal of lung metastases and written consent. The day before the surgery, the patients were asked to provide written consent for a follow-up control after 3 months and for a later anonymized data evaluation and publication. The study protocol was approved by our hospital's review board. All metastasectomies were performed through an anterolateral muscle, and saving thoracotomy with thoracotomy was used for the systematic palpation of the entire lung. Lung resection was performed at the surgeon's discretion with staplers, electrocautery or laser, and was supplemented by lymph node sampling. One or two drains were placed before closing the thoracotomy. All patients received analgesia based on the hospital's standard protocol. A standard physiotherapy programme was also used to support the expiratory flow, lung expansion and coughing.

Pulmonary function testing

Standard respiratory function tests and diffusion capacity for carbon monoxide (DLCO) were measured preoperatively (t1), postoperatively the day before discharge (t2) and 3 months later at the follow-up visit (t3). Spirometry tests were performed using a ZAN® 500 Body Plethysmograph equipped with a ZAN® 200 SB CO-Diffusion module (Spire Health Ltd., Hertford, UK) according to the criteria of the American Thoracic Society. The measurements were taken after administering a bronchodilator. The carbon monoxide lung diffusion capacity was measured using the single-breath method. The forced vital capacity (FVC), total lung capacity (TLC), forced expiratory volume in 1 s (FEV1), DLCO and diffusion coefficient (KCO) were expressed as percentages of the predicted values for age, gender and height, according to the European Community for Steel and Coal Prediction equations [5]. After staged bilateral resections, patients received their follow-up pulmonary function tests (PFTs) 3 months after the last resection. The follow-up control was performed 3 months later with the same devices. All patients were questioned regarding persistent postoperative pain, analgesic intake, tumour recurrence and ongoing chemotherapy.

Evaluation

Lung function parameters, blood gas values and the percentage of carbon monoxide diffusion capacity before and after metastasectomy and at follow-up were entered into a database along with the number of resections, the type of resection, the laterality of the resection, the presence of adhesions, the performance of a postoperative pleurodesis for prolonged air leaks, the presence of any ongoing thoracic wall pain [post-thoracotomy pain syndrome (PTS)], tumour recurrence at any site and the use of chemotherapy within 6 months before the resection and at the time of follow-up.

Statistical analysis

The data were analysed using SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA). The differences between the preoperative and follow-up parameters were calculated and tested for significance using the Wilcoxon test. The influence of the aforementioned factors on the functional outcome was tested using the Mann–Whitney test. The values of 0.05 or less were considered significant.

RESULTS

During the study phase, 162 patients gave written consent and were entered into the database. A total of 45 were excluded from the analysis (Fig. 1); of these 45 cases, 16 could not be contacted within 6 months after metastasectomy and were therefore lost to the follow-up, 14 cases did not have metastasectomy due to the intraoperative detection of advanced tumour spread, 5 subjects refused participation in the follow-up control, 4 patients had complications under chemotherapy or major intestinal resections and refused further evaluation, 3 cases had incomplete functional data and 3 patients died during the study period. A total of 117 cases completed the study protocol and could be analysed. The patient demographics are shown in Table 1. Their median age was 61.8 (21.8–83.9) years and their Eastern Cooperative Oncology Group scale was 0 or 1. The greatest lung resection performed was a lobectomy in 13 (11.1%), with a segmentectomy in 27 (23.1%) and wedge resection in 77 (65.8%) patients. Of the 40 patients with an anatomical resection, 24 had further additional non-anatomical resections. Postoperative pleurodesis was performed in 4 (3.4%) cases in order to treat a prolonged air leak. The spirometry results were available from all patients preoperatively and at follow-up, but they were only available postoperatively from 81 subjects. The

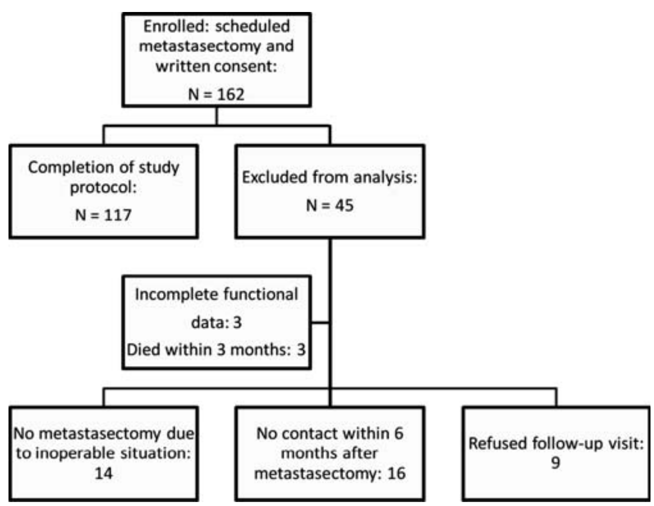

Figure 1: Flow chart: patient enrolment and exclusion.

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preoperative and follow-up DLCO values were available for 103 cases and postoperative DLCO values were available for 77. The mean preoperative lung function parameters expressed as percentages of those predicted [5] were: FVC 97.1%, TLC 94.1%, FEV1 87.0%, lung diffusion for carbon monoxide (DLCO) 82.7%, KCO 74.1% and $AaDO_2$ 22.1 mmHg (Table 2). At the postoperative control, the mean functional loss of the predicted values was FVC −34.4%, TLC −29.0%, FEV1 −28.8% and DLCO −24.3%, whereas $AaDO_2$ increased by 9.2 mmHg. At the follow-up control after a mean of 3.4 (±1.3) months, these values improved to a mean final functional loss of: FVC −9.2%, TLC −8.8%, FEV1 −10.8%, DLCO −9.7% and KCO −0.2%, and $AaDO_2$ returned to normal: −0.7 mmHg. The differences in the functional values between the preoperative and follow-up measurements were statistically significant for FVC, TLC, FEV1, FEV1/FVC and DLCO, whereas no significant difference was detected for KCO, pO_2, pCO_2 or $AaDO_2$ (Table 2). The separate calculations of the changes in lung function parameters in the subgroup of patients who only had wedge resections showed a significant reduction ($P < 0.001$) at the follow-up control, with mean losses of: FVC −7.5%, TLC −7.9%, FEV1 −9.2% and DLCO −8.8%.

The factors influencing lung function were investigated after 3 months. Repeated thoracotomy, PTS and the performance of pleurodesis had no significant influence on lung function. Furthermore, no significant difference was found between the lobectomy and segmentectomy patients concerning the functional outcome. The factors that significantly deteriorated pulmonary function were postoperative chemotherapy (DLCO%, $P = 0.01$; KCO%, $P = 0.029$ and $AaDO_2$ mmHg, $P = 0.047$) and bilateral versus unilateral thoracotomy (FVC%, $P = 0.007$; TLC%, $P = 0.003$ and FEV1%, $P = 0.004$) (Figs 2 and 3). Surprisingly, the patients with preoperative chemotherapy were found to have a smaller loss of diffusion parameters after 3 months (DLCO%, $P = 0.03$ and $AaDO_2$ mmHg, $P = 0.02$) than those patients without chemotherapy. This could possibly be explained by the adverse effect of chemotherapy on lung function reducing gas exchange parameters at the initial pulmonary function testing. On recovery from chemo side effects within the following 3 months, the resulting differences after metastasectomy were found to be less.

Table 1: Patient characteristics

Age		
Mean	59.3	
Range	21.8–83.9	
Gender		
Male	66	
Female	51	
Histology		
Colorectal	43	
Sarcoma	19	
Renal	16	
Breast	9	
Melanoma	6	
Germ cell	5	
Others	19	
	No	Yes
Chemotherapy		
Preoperative	91	25 (21.4%)
Postoperative	96	20 (17.1%)
Preceding lung resection	76	41 (35.0%) (15 bilateral)
Repeated thoracotomy	87	30 (25.6%)
Adhesions	71	46 (39.3%)
Laterality	84 unilateral	33 (28.2%) bilateral
Post-thoracotomy pain	107	10 (8.5%)
Analgesic consumption	98	19 (16.2%)
Tumour recurrence	100	17 (14.5%)

DISCUSSION

A pulmonary metastasectomy is a widely used therapeutic option for treating the oligo-metastatic stage IV disease of various primaries. It often requires multiple wedge resections or a combination of anatomical and non-anatomical resections as needed [6, 7]. The criteria for selecting the patients suitable for a metastasectomy include sufficient pulmonary function to tolerate the planned resection. The prediction of postoperative preserved pulmonary function is essential in order to ascertain the functional operability, especially when an operation is planned for the patients who have a cardiopulmonary impairment [8–10]. The prediction of postoperative pulmonary function is a routine measure before an anatomical lung resection for lung cancer [2, 9, 11]. A mortality rate of <5% can be achieved if the preoperative FEV1 is >1.5 l in patients undergoing a lobectomy and >2 l in patients undergoing a pneumonectomy [11, 12]. Besides the spirometry results, DLCO is also an excellent predictor of

Table 2: Lung function parameters, functional loss after 3 months and its significance

Parameter/time	t1 (SD)	t2 (SD)	t3 (SD)	Δt3 – t1	*P*-value
FVC (%)	97.1 (17.4)	62.5 (19.6)	87.4 (20.1)	−9.7	<0.001
TLC (%)	94.2 (16.1)	66.0 (15.6)	85.3 (17.4)	−8.9	<0.001
FEV1 (%)	87.0 (17.9)	56.2 (17.7)	76.2 (18.9)	−10.8	<0.001
FEV/FVC	71.6 (9.4)	72.5 (11.1)	69.8 (10.0)	−1.8	0.003
DLCO (%)	82.7 (16.2)	56.9 (16.9)	73.1 (14.8)	−9.7	<0.001
KCO (%)	74.1 (14.7)	71.8 (14.7)	73.3 (15.2)	−0.2	0.812
pO_2 (mmHg)	79.4 (8.3)	70.7 (9.1)	79.6 (10.2)	+0.2	0.725
pCO_2 (mmHg)	38.0 (3.2)	37.4 (3.4)	38.6 (3.4)	+0.5	0.759
$AaDO_2$ (mmHg)	22.1 (8.7)	31.5 (9.4)	21.4 (8.5)	−0.7	0.409

Predicted spirometry values at three time points: preoperative (t1), postoperative before discharge from the hospital (t2) and 3 months later at the follow-up (t3). Δt3 – t1 is the mean relative functional loss, which was significant for spirometry and DLCO values, but remained unchanged concerning blood gases and KCO.

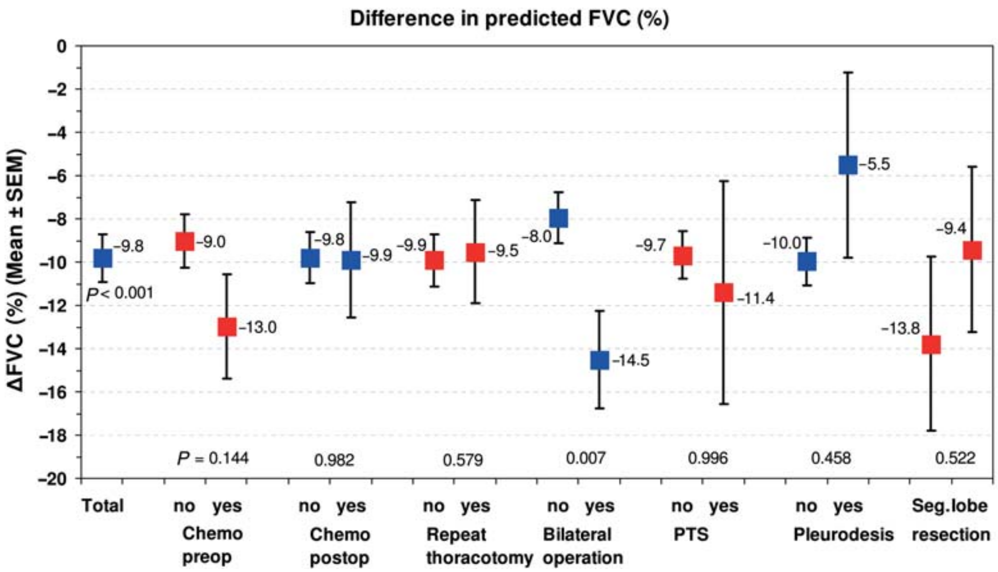

Figure 2: The influence of associated factors on FVC (expressed as percentage of predicated). Postop: postoperative; preop: preoperative; PTS: post-thoracotomy pain syndrome; SEM: standard deviation of the mean. The blue cubes are the mean loss of FVC depending on that variable. FVC is significantly reduced after 3 months as a consequence of bilateral resections.

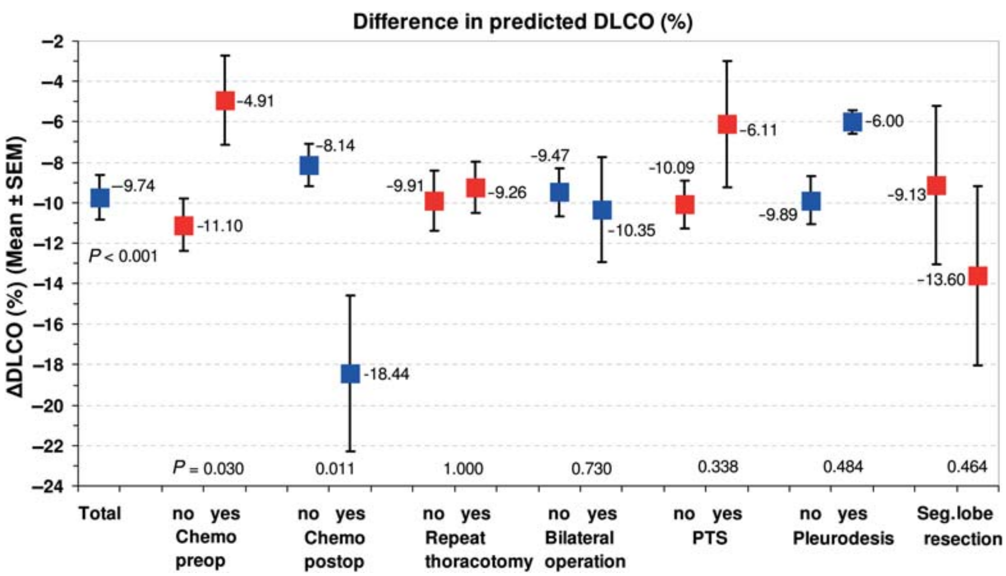

Figure 3: The influence of associated factors on DLCO (expressed as a percentage of predicated). Postop: postoperative; preop: preoperative; PTS: post-thoracotomy pain syndrome; SEM: standard deviation of the mean. The blue cubes are the mean losses depending on the variable. The fact that preoperative chemo leads to a smaller loss of DLCO than no chemo can be explained by the potential recovery from chemo side effects after resection in the first mentioned group.

postoperative mortality and morbidity rates [13–15]. Ferguson *et al*. [15] found that a predicted DLCO of <60% was associated with increased mortality and a predicted DLCO of <80% was associated with up to a 3-fold increased rate of pulmonary complications. None of these criteria was actually defined for wedge resections or combinations of anatomical and non-anatomical resections. To the best of our knowledge, no publications yet exist regarding the systematic evaluation of functional loss after a metastasectomy that allow a prediction of what a patient is going to lose when scheduled for a metastasectomy. In order to be able to provide the first answers to this question, we undertook this prospective evaluation of pulmonary function before and 3 months after a pulmonary metastasectomy.

Study period

Our study did not include a second follow-up evaluation at 6 or 12 months because we found that the majority of patients had further treatment, such as chemotherapy, radiotherapy or major resections for liver metastases or recurrent primaries, which all have an important influence on the functional results. Therefore, we restricted the follow-up period to 3 months. Several publications underline our hypothesis that 3 months are enough to sufficiently evaluate the preserved lung function [16–18]. Functional recovery after a lung resection is rapid during the early postoperative phase and reaches a certain plateau after 3–6 months, being a function of time [16–18]. Brunelli *et al*. [16] observed

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Table 3: Significance of the factors found to inversely influence the functional outcome after pulmonary metastasectomy

	Significance (*P*-value)						
	No chemo preop	Chemo postop	Repeated thoracotomy	Bilateral resection	PTS	Pleurodesis	Segment/lobectomy
FVC (%)	0.144	0.982	0.579	**0.007**	0.996	0.458	0.522
TLC (%)	0.396	0.177	0.177	**0.003**	0.640	0.530	0.633
FEV1 (%)	0.128	0.745	0.231	**0.004**	0.925	0.195	0.457
DLCO (%)	**0.030**	**0.011**	1.000	0.730	0.338	0.484	0.464
KCO (%)	0.250	**0.029**	0.994	0.376	0.487	0.713	0.378
pO_2 (mmHg)	0.176	0.052	0.975	0.711	0.992	0.340	0.751
$AaDO_2$ (mmHg)	**0.022**	**0.047**	0.686	0.624	0.727	0.083	0.915

Preop: preoperative; postop: postoperative; PTS: post-thoracotomy pain syndrome.
Numbers in bold are significant.
Volume parameters (FVC%, TLC% and FEV1%) are significantly impaired by bilateral resections. Gas exchange parameters (DLCO, KCO and $AaDO_2$) are significantly reduced by chemotherapy. Due to the fact that patients with preoperative chemotherapy start with reduced gas exchange parameters, their final loss of gas exchange parameters is relatively small compared with those without preoperative chemotherapy.

FEV1 values that were 11% lower at discharge and 6% higher at 3 months after lobectomy compared with the ppoFEV1. The ppo FEV1 is usually calculated based on the number of non-obstructed pulmonary segments to be removed using the following formula: functional loss (%) = number of non-obstructed segments to be resected/total number of preoperative non-obstructed segments × 100 [8, 16]. Nosotti *et al*. [18] performed PFTs over 3 years in their randomized controlled trial with 100 patients comparing posterolateral thoracotomy with muscle-sparing thoracotomy. They demonstrated a continuous increase in FVC and FEV1 after lobectomy, reaching a plateau after 6 months. Unfortunately, values after 3 months were not available. The functional improvement between postoperative months 1 and 6 was ~7%, indicating that a further improvement after 3 months could be assumed to be <3%. The mean postoperative pain score (visual analogue score 1.0–5.0) showed a reduction from about 1.5 to 1.1 between postoperative months 1 and 6. All of these results indicate that the most important changes happen within the first 3 months, and only minor changes might occur later, up to 6 months.

Study results

Our results allow some very clear statements: pulmonary metastasectomy leads to a significant loss in spirometry and DLCO values of around 10% 3 months after the operation. A significant loss in the same parameters was also found in patients who underwent wedge resections only. The spirometry and DLCO values of the latter subgroup were reduced by around 8%. Petrella *et al*. [3] found a mean loss of 13.4% in FEV1 and 12.4% in FVC after a metastasectomy. The mean number of resections for the 66 patients in that study was three, and the authors concluded that the functional loss that occurs after three or more non-anatomical resections was comparable with the functional reductions that occur after a lobectomy. The mean interval between PFTs in this series was 54 days (23–1600), which is almost half of the time taken to obtain our results. In our series, the follow-up control took place within a mean of 3.4 months. That means a longer time to recover from surgery than in Petrella's series. Furthermore, Petrella *et al*. [3] found a significant difference concerning pulmonary function loss between these patients of <90 days or >90 days after resection, and none of the significant functional alterations they had observed in the early postoperative phase persisted >3 months after the procedure.

Influencing factors

We evaluated the factors that potentially influence the functional outcome after a metastasectomy (Table 3). Repeated thoracotomy, PTS, pleurodesis and mode of anatomical resection were not found to be significant factors. Spirometry values were found to be significantly reduced by bilateral versus unilateral resections, and DLCO, KCO and $AaDO_2$ were only reduced by postoperative chemotherapy. Our results suggest that the repeated opening of the thoracic cage and adhesiolysis of the lung lead to the same functional loss as a first intervention. Whereas the preoperative impairment of DLCO by chemotherapy has been described by others [19, 20], to the best of our knowledge, the influence of preoperative chemotherapy on postoperative pulmonary function has not yet been described. Surprisingly, we found a reduced loss of DLCO after 3 months in patients who had preoperative chemotherapy and an increased loss in those having postoperative chemotherapy. We believe that this fact can be easily explained by the recovery from side effects: after resection, patients with preoperative chemotherapy recover from the surgery and from chemotherapy, and their final functional loss is small compared with the preoperative values. In contrast, patients with postoperative chemotherapy recover from the surgery, whereas the side effects from chemotherapy simultaneously reduce the diffusion capacity at the follow-up visit. Patients who do not undergo chemotherapy do not recover from the side effects and lose DLCO corresponding to the amount of lung tissue removed. Besides a shorter time after resection, the total volume of lung parenchyma resected was described as being the only factor to inversely affect pulmonary function in the series of Petrella *et al*. [3]. We found a similar association between the number of wedge resections and the loss in pulmonary function. Our results of the subgroup with wedge resections only are published elsewhere [21].

Surgical access

The surgical approach was the same for all patients in our series and was therefore not investigated as an influencing factor.

Other surgical approaches to the lung were described by Ninomiya *et al*. [22]. They found that thoracoscopic metastasectomy and metastasectomy through a median sternotomy cause a lower degree of restrictive respiratory dysfunction than metastasectomy through a posterolateral thoracotomy.

Despite the fact that this is the first prospective evaluation of the pulmonary function outcome 3 months after a lung metastasectomy, this study suffers from obvious limitations. It is a single centre result with different modes of resection, including the use of staplers, electrocautery and laser, at the discretion of each surgeon. Thus, differences in people and methods are reflected in the results, giving rise to a question regarding the amount of lung tissue removed. The lack of a further follow-up visit at 6 months is a disadvantage that we explained above. Finally, influencing factors such as a bilateral operation and the effects of chemotherapy need to be further investigated in a larger patient population.

CONCLUSION

Pulmonary function is significantly reduced 3 months after lung metastasectomy with an average reduction of around 10% in spirometry and DLCO values. The KCO and blood gases remain unchanged. The risk factors for an increased loss of function were found to be bilateral metastasectomy (lung volumes) and postoperative chemotherapy (gas exchange).

Conflict of interest: none declared.

REFERENCES

[1] Rusch VW. Pulmonary metastasectomy. A moving target. J Thorac Oncol 2010;5(Suppl. 2):130–1.
[2] Bolliger CT. Evaluation of operability before lung resection. Curr Opin Pulm Med 2003;9:321–6.
[3] Petrella F, Chieco P, Solli P, Veronesi G, Borri A, Galetta D *et al*. Which factors affect pulmonary function after lung metastasectomy? Eur J Cardiothorac Surg 2009;35:792–6.
[4] Rolle A, Pereszlenyi A, Koch R, Richard M, Baier B. Is surgery for multiple lung metastases reasonable? A total of 328 consecutive patients with multiple-laser metastasectomies with a new 1318-nm Nd:YAG laser. J Thorac Cardiovasc Surg 2006;131:1236–42.
[5] Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC. Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. Eur Respir J 1993;16:5–40.
[6] Rusch VW. Pulmonary metastasectomy. Current indications. Chest 1995; 107:322S–31S.
[7] Pastorino U, Buyse M, Friedel G, Ginsberg RJ, Girard P, Goldstraw P *et al*. Long-term results of lung metastasectomy: prognostic analyses based on 5206 cases. The International Registry of Lung Metastases. J Thorac Cardiovasc Surg 1997;113:37–49.
[8] Nakahara K, Moden Y, Ohno K, Miyoshi S, Maeda H, Kawashima Y. A method for predicting postoperative lung function and its relation to postoperative complications in patients with lung cancer. Ann Thorac Surg 1985;39:260–5.
[9] Kearney DJ, Lee TH, Reilly JJ, DeCamp MM, Sugarbaker DJ. Assessment of operative risk in patients undergoing lung resection. Importance of predicted pulmonary function. Chest 1994;105:753–9.
[10] Colice GL, Shafazand S, Griffin FP, Keenan R, Bolliger CT. Physiologic evaluation of the patient with lung cancer being considered for resectional surgery. ACCP evidenced-based clinical practice guidelines (2nd edition). Chest 2007;132:161S–77S.
[11] British Thoracic Society, Society of Cardiothoracic Surgeons of Great Britain and Ireland Working Party. Guidelines on the selection of patients with lung cancer for surgery. Thorax 2001;56:89–108.
[12] Miller JI Jr. Physiologic evaluation of pulmonary function in the candidate for lung resection. J Thorac Cardiovasc Surg 1993;105:347–51.
[13] Wyser C, Stulz P, Soler M, Tamm M, Müller-Brand J, Habicht J *et al*. Prospective evaluation of an algorithm for the functional assessment of lung resection candidates. Am J Respir Crit Care Med 1999;159:1450–6.
[14] Brunelli A, Refai MA, Salati M, Sabbatini A, Morgan-Hughes NJ, Rocco G. Carbon monoxide lung diffusion capacity improves risk stratification in patients without airflow limitation: evidence for systematic measurement before lung resection. Eur J Cardiothorac Surg 2006;29:567–70.
[15] Ferguson MK, Little L, Rizzo L, Popovich KJ, Glonek GF, Leff A *et al*. Diffusing capacity predicts morbidity and mortality after pulmonary resection. J Thorac Cardiovasc Surg 1988;96:894–900.
[16] Brunelli A, Refai M, Salati M, Xiumé F, Sabbatini A. Predicted versus observed FEV1 and DLCO after major lung resection: a prospective evaluation at different postoperative periods. Ann Thorac Surg 2007;83: 1134–9.
[17] Varela G, Brunelli A, Rocco G, Marasco R, Jiménez MF, Sciarra V *et al*. Predicted versus observed FEV1 in the immediate postoperative period after pulmonary lobectomy. Eur J Cardiothorac Surg 2006;30:644–8.
[18] Nosotti M, Baisi A, Mendogni P, Palleschi A, Tosi D, Rosso L. Muscle sparing versus posterolateral thoracotomy for pulmonary lobectomy: randomised controlled trial. Interact CardioVasc Thorac Surg 2010;11: 415–9.
[19] Takeda S, Funakoshi Y, Kadota Y, Koma M, Maeda H, Kawamura S *et al*. Fall in diffusing capacity associated with induction therapy for lung cancer: a predictor of postoperative complication? Ann Thorac Surg 2006;82:232–6.
[20] Rivera MP, Detterbeck FC, Socinski MA, Moore DT, Edelman MJ, Jahan TM *et al*. Impact of preoperative chemotherapy on pulmonary function tests in resectable early-stage non-small cell lung cancer. Chest 2009; 135:1588–95.
[21] Welter S, Cheufou D, Sommerwerck U, Maletzki F, Stamatis G. Changes in lung function parameters after wedge resections: a prospective evaluation of metastasectomy patients. Chest 2012; [Epub ahead of print] PMID: 22267678.
[22] Ninomiya M, Nakajima J, Tanaka M, Takeuchi E, Murakawa T, Fukami T *et al*. Effects of lung metastasectomy on respiratory function. Jpn J Thorac Cardiovasc Surg 2001;49:17–20.

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