

## Invasive exercise testing in the evaluation of patients at high-risk for lung resection

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*Invasive exercise testing in the evaluation of patients at high-risk for lung resection. J. Ribas, O. Díaz, J.A. Barberà, M. Mateu, E. Canalis, L. Jover, J. Roca, R. Rodriguez-Roisin. ©ERS Journals Ltd 1998.*

**ABSTRACT:** The aim of this study was to investigate whether invasive exercise testing with gas exchange and pulmonary haemodynamic measurements could contribute to the preoperative assessment of patients with lung cancer at a high-risk for lung resection.

Sixty-five patients scheduled for thoracotomy (aged  $66 \pm 8$  yrs (mean  $\pm$  SD), 64 males, forced expiratory volume in one second (FEV<sub>1</sub>)  $54 \pm 13\%$  predicted) were studied prospectively. High risk was defined on the basis of predicted postpneumonectomy (PPN) FEV<sub>1</sub> and/or carbon monoxide diffusing capacity of the lung (DL<sub>CO</sub>)  $<40\%$  pred. Arterial blood gas measurements were performed in all patients at rest and during exercise. In 46 patients, pulmonary haemodynamic measurements were also performed at rest and during exercise. Predicted postoperative (PPO) values for FEV<sub>1</sub> and DL<sub>CO</sub> were calculated according to quantitative lung scanning and the amount of resected parenchyma.

There were four postoperative deaths (6.2% mortality rate) and postoperative cardiorespiratory complications developed in 31 (47.7%) patients. Patients with respiratory complications only differed from patients without or with minimal (arrhythmia) complications in FEV<sub>1</sub>, PPO. Peak O<sub>2</sub> uptake and haemodynamic variables were similar in both groups. The four patients who died had a lower FEV<sub>1</sub>, PPO, a lower DL<sub>CO</sub>, PPO and a greater decrease in arterial oxygen tension during exercise, compared with the remaining patients.

In conclusion, the forced expiratory volume in one second, together with the extent of parenchymal resection and perfusion of the affected lung, are useful parameters to identify patients at greatest risk of postoperative complications among those at a high-risk for lung resection. In these patients, pulmonary haemodynamic measurements appear to have no discriminatory value, whereas gas exchange measurements during exercise may help to identify patients with higher mortality risk.

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Surgery alone or in combination with other strategies gives the best hope for lung survival in patients with resectable nonsmall-cell lung cancer [1]. Most patients with lung cancer are current smokers or exsmokers and often have associated chronic obstructive pulmonary disease (COPD) [2] and other comorbidity factors that increase the risk of postoperative complications and death. Pulmonary function tests (PFT) and split pulmonary function, as determined by quantitative macroaggregate lung scanning, are useful in identifying patients with impaired lung function who are at risk of postoperative complications [3]. To what extent further functional testing contributes to more accurate prediction of postoperative morbidity and mortality is unclear.

Some authors have recommended exercise testing as a useful tool in the assessment of operative risk in thoracotomy candidates [4, 5]. Impaired exercise capacity, as assessed by a low oxygen uptake ( $V'O_2$ ), has been proposed as a predictor of a poor postoperative outcome [4], but the usefulness of  $V'O_2$  measurements in patients with severely

impaired pulmonary function at increased risk remains controversial. While some authors have shown that the  $V'O_2$  value is useful in the prediction of surgical outcome in high-risk candidates [6–9], others have not confirmed such results [10, 11].

Furthermore, since pulmonary hypertension is a poor prognostic factor in COPD [12] and a decreased arterial O<sub>2</sub> saturation on exertion has been proposed as a predictor of postoperative complications [13, 14], it was hypothesized that among COPD patients who are at a high-risk for resectional lung surgery, those who develop gas exchange and/or haemodynamic abnormalities during exercise may be at greatest risk of morbidity and mortality after surgery. Accordingly, the present study was intended to evaluate the potential role of both gas exchange and pulmonary haemodynamic measurements during exercise in the prediction of early post-thoracotomy morbidity and mortality in patients with a high-risk for surgery as assessed by conventional PFT and lung scanning.

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## Methods

### Patients

Eighty-six patients referred to the Pulmonary Function Laboratory of the Hospital Clinic of Barcelona for pre-operative evaluation between March 1992 and March 1997 with diagnosed or suspected lung malignancy and impaired lung function were considered eligible for the study. The inclusion criteria were a predicted postpneumonectomy (PPN) forced expiratory volume in one second (FEV<sub>1</sub>) <40% predicted [15] and/or a PPN diffusing capacity of the lung for carbon monoxide (*DL*<sub>CO,PPN</sub>) <40% pred [16], calculated on the basis of the quantitative contribution of the affected lung to overall function [13]. These calculations may not provide a reliable estimate of the actual postpneumonectomy measurements [17] but in this study the estimates were used only for the purpose of identifying patients at increased risk. Poor FEV<sub>1,PPN</sub>, *DL*<sub>CO,PPN</sub> or *V*'O<sub>2</sub> during exercise were not considered to preclude resective surgery. The study was approved by the Ethical Committee of the Hospital Clinic and written informed consent was obtained from each participant.

### Pulmonary function tests

Functional measurements were made within the month prior to the intervention. Forced spirometry, body plethysmography and single-breath CO diffusing capacity were measured using the Pulmonary Function System 1070 (Medical Graphics, St Paul, MN, USA). Results were expressed as percentages of the values predicted from our own equations [15, 16]. The FEV<sub>1,PPN</sub> was calculated on the basis of quantitative technetium-99m macroaggregated albumin (<sup>99m</sup>Tc-MAA) lung scanning, as described previously [13]. After surgery, the FEV<sub>1</sub> expected to result from the resection that was actually performed (predicted postoperative (PPO) FEV<sub>1</sub>) was calculated using a formula that takes into account quantitative <sup>99m</sup>Tc-MAA lung scanning and the amount of resected pulmonary parenchyma:  $FEV_{1,PPO} = preopFEV_1 \times (1 - ((\%Q' \text{ affected lung} / 100) \times (\text{number of segments resected} / \text{total segments in affected lung})))$ , where preopFEV<sub>1</sub> is preoperative FEV<sub>1</sub> and *Q'* is perfusion. The same formula was used to calculate PPO forced vital capacity (FVC) and *DL*<sub>CO,PPO</sub>.

### Exercise testing

Initially, prior to catheterization, all patients performed an incremental (20 W·min<sup>-1</sup>), symptom-limited, exercise test on a cycle ergometer (Ergotest; Jäeger, Würzburg, Germany) to determine *V*'O<sub>2</sub> and workrate at peak exercise (*V*'O<sub>2,peak</sub> and *W*<sub>peak</sub>, respectively). Subsequently, all patients had an arterial catheter (Seldicath 3F; Plastimed, Saint-Leu-la Fôret, France) inserted into the radial artery for blood gas measurements. Additionally, in 46 of the patients, a triple-lumen Swan-Ganz catheter (Edwards Laboratories, Santa Ana, CA, USA) was placed into the pulmonary artery using pressure wave monitoring (M1166A; Hewlett-Packard, Boeblingen, Germany), for measuring haemodynamics and mixed venous blood gases.

After a resting period, all patients performed a second exercise test. Patients with only systemic artery catheterization followed a second incremental work-rate protocol, with gas exchange measurements performed at peak exercise. The 46 patients with both systemic and pulmonary artery catheterization followed a constant workload protocol (at 60% of *W*<sub>peak</sub>), with gas exchange and haemodynamic measurements performed at the end of 4 min of constant work-rate to ensure steady-state conditions. Arterial blood gas measurements from the two groups of patients were pooled for statistical analysis, as in the latter group there was no difference between *V*'O<sub>2</sub> at peak exercise and at the end of the constant workload protocol (16.3±3.3 versus 16.7±3.9 mL·kg<sup>-1</sup>·min<sup>-1</sup>, *p*=0.3; and 75±26 versus 76±26% pred, *p*=0.4, during steady-state and incremental protocols, respectively). *W*<sub>peak</sub> and *V*'O<sub>2,peak</sub> were expressed as percentages of the predicted values of JONES *et al.* [18]. Measurements of pulmonary pressure were taken at the end of expiration. Pulmonary and systemic vascular resistances were calculated using standard formulae [19].

### Surgical procedures and definition of complications

All thoracotomies and pulmonary resections were performed by the same team of thoracic surgeons. The postoperative course of the patients was followed carefully, with daily assessment and recording of complications up to the discharge day. The survey of complications was limited to the hospitalization period after surgery because the vast majority of complications and postoperative deaths usually take place in the immediate postoperative period, and also because during this period the clinical follow-up can be performed more accurately. Complications were categorized as respiratory and cardiac. Respiratory complications were defined as: 1) lobar or whole lung atelectasis, requiring bronchoscopy; 2) prolonged mechanical ventilation for >24 h or requiring reintubation during the first 24 h; 3) acute respiratory failure, needing mechanical ventilation; and 4) pneumonia (temperature >38°C, compatible chest radiograph and purulent sputum). Cardiac complications were defined as: 1) cardiac arrhythmias requiring treatment; 2) symptomatic acute myocardial infarction; and, 3) left ventricular failure with cardiogenic pulmonary oedema. Some patients had more than one complication. Death was analysed as a separate complication.

### Statistical analysis

The results are presented as mean±SD. For quantitative variables, comparisons between patients with and without complications were performed using the unpaired two-tailed Student's *t*-test. The Chi-squared test was used for categorical variables. Comparisons between patients who died and the remaining patients were performed using the Mann-Whitney *U*-test. A *p*-value ≤0.05 was considered significant.

Receiver operating characteristic (ROC) curves were used to explore the performance of individual tests in the prediction of postoperative complications. ROC curves were analysed using a nonparametric approach. The area under the ROC curve (AURC) was estimated using the

Mann–Whitney U-test. Comparisons between ROC areas were performed using the test proposed by DeLONG *et al.* [20].

Multivariate analysis using stepwise logistic regression was performed additionally to explore the relative usefulness of the combination of variables for the prediction of postoperative complications.

## Results

Of the 86 patients who were evaluated initially, 21 were excluded from further study: 13 were considered inoperable by the attending physicians (six because of distant metastases and seven because of advanced age and poor general condition); in seven patients the surgical procedure performed was only an exploratory thoracotomy; and one patient refused surgical treatment. The remaining 65 patients (64 male) who underwent resectional surgery entered the study. Their demographic data, preoperative respiratory function, quantitative lung perfusion, and derived variables are shown in table 1. The surgical interventions performed were 26 lobectomies, 21 pneumonectomies, 11 bilobectomies and seven wedge resections. The mean hospital stay after surgery (follow-up period) was 14±9 days.

When the 13 patients excluded because of inoperability were compared with the 65 study patients, no significant differences were found in age, FEV<sub>1</sub>, DL<sub>CO</sub>, FEV<sub>1,PPN</sub>. Exercise capacity, as measured by V'O<sub>2,peak</sub>, was also similar in both groups of patients.

### Exercise study

The results of exercise tests and blood gas and haemodynamic measurements at baseline and during exercise are shown in table 2. Arterial carbon dioxide tension (P<sub>a,CO<sub>2</sub></sub>) increased significantly with exercise, while arterial oxygen tension (P<sub>a,O<sub>2</sub></sub>) remained unchanged. At rest, mean pulmonary artery pressure (PAP) was within normal limits in all patients and increased significantly during exercise (p<0.0001). Nevertheless, pulmonary vascular resistance (PVR) decreased moderately but significantly during exercise (p=0.002).

Table 1. – General characteristics and lung function data

	Mean±SD	Range
Age yrs	66±8	41–77
Weight kg	69±11	46–94
Height cm	166±7	151–185
FVC % pred	76±15	41–112
FEV <sub>1</sub> L	1.67±0.50	0.94–2.74
% pred	54±13	29–86
FEV <sub>1</sub> /FVC %	53±13	30–94
DL <sub>CO</sub> % pred	74±19	29–113
Perfusion of affected lung %	43±13	8–71
Predicted postpneumonectomy function		
FEV <sub>1,PPN</sub> L	1.02±0.30	0.39–1.90
% pred	33±9	13–52
DL <sub>CO,PPN</sub> % pred	43±15	17–88

FVC: forced vital capacity; % pred: percentage of predicted value; FEV<sub>1</sub>: forced expiratory volume in one second; DL<sub>CO</sub>: diffusing capacity of the lung for carbon monoxide; PPN: predicted postpneumonectomy.

Table 2. – Exercise data with gas exchange and pulmonary haemodynamics at rest and during exercise

	Rest	Exercise
Incremental exercise test		
W W	0	90±29
% pred	0	68±23
V'O <sub>2</sub> mL·kg <sup>-1</sup> ·min <sup>-1</sup>	4.2±1.0	16.4±4.0*
Gas exchange measurements		
P <sub>a,O<sub>2</sub></sub> mmHg	78±9	76±12
P <sub>a,CO<sub>2</sub></sub> mmHg	37±4	39±5*
P <sub>v̄O<sub>2</sub></sub> mmHg†	38±4	29±3*
Haemodynamic measurements†		
PAP mmHg	16±4	37±11*
P <sub>pcw</sub> mmHg	6±4	19±10*
CO L·min <sup>-1</sup>	6.62±1.36	12.67±2.45*
PVR dynes·s·cm <sup>-5</sup>	133±49	116±48*

Results are means±SD. W: workrate; % pred: percentage of predicted value; V'O<sub>2</sub>: oxygen uptake; P<sub>a,O<sub>2</sub></sub>: arterial oxygen tension; P<sub>a,CO<sub>2</sub></sub>: arterial carbon dioxide tension; P<sub>v̄O<sub>2</sub></sub>: mixed venous oxygen tension; PAP: mean pulmonary artery pressure; P<sub>pcw</sub>: pulmonary capillary wedge pressure; CO: cardiac output; PVR: pulmonary vascular resistance. \*: p<0.05 compared with resting conditions. †: n=46.

### Postoperative complications

Postoperative cardiopulmonary complications occurred in 31 (47.7%) patients. Of these, 16 (24.6%) patients suffered pulmonary complications (five atelectasis, three prolonged mechanical ventilation, eight acute respiratory failure, six pneumonia) only, four of them having more than one respiratory complication. Eleven (16.9%) patients developed cardiac complications (10 arrhythmia, one left ventricular failure) only and four (6.2%) patients had both respiratory and cardiac complications, the cardiac complication being arrhythmia in all cases.

There were only four postoperative deaths among the 65 patients (6.2% mortality rate). All had more than one respiratory complication simultaneously, and in one case these were accompanied by arrhythmia. All patients who died developed pneumonia, which was associated with atelectasis and prolonged mechanical ventilation in two cases, with acute respiratory failure in one patient and with acute respiratory failure and prolonged mechanical ventilation in the other. The operations performed in these four patients were pneumonectomy in two patients and bilobectomy in the other two. No deaths occurred among the seven patients who underwent wedge resections, of whom only two experienced postoperative complications (pneumonia and cardiac arrhythmia).

In order to increase the strength of the analysis and considering that arrhythmia is the least severe of the listed complications, patients without complications (n=34) and those in whom the only complication was arrhythmia (n=10) were pooled, after ensuring that there were no differences in the distributions of the variables between these two groups. The patient who suffered left ventricular failure was excluded from the final analysis, as the patient did not develop respiratory complications and could not be grouped with patients without complications or with only arrhythmia. Accordingly, on the basis of the presence or absence of respiratory complications during the postoperative period until hospital discharge, the final population of 64 patients was divided into two groups: those with no

Table 3. – Results of pulmonary function and haemodynamic responses to exercise in patients with and without postoperative respiratory complications

	Noncomplicated (n=44)	Complicated (n=20)	p-value
FEV <sub>1</sub> L	1.72±0.54	1.54±0.41	0.18
FEV <sub>1</sub> % pred	55±13	52±12	0.31
FVC % pred	76±16	75±15	0.66
DL <sub>CO</sub> % pred	74±18	76±23	0.74
Perfusion of affected lung %	42.4±13.8	43.8±10.8	0.70
Extent of resection no. of segments	5.6±3.1	6.0±2.8	0.66
FEV <sub>1,PPN</sub> L	1.05±0.34	0.92±0.20	0.10
FEV <sub>1,PPN</sub> % pred	34±9	31±7	0.24
FEV <sub>1,PPO</sub> L	1.42±0.39	1.20±0.29	0.03
FEV <sub>1,PPO</sub> % pred	46±10	41±10	0.05
FVC % pred	59±14	55±16	0.25
DL <sub>CO,PPN</sub> % pred	43±15	43±16	0.93
DL <sub>CO,PPO</sub> % pred	58±16	55±19	0.64
W <sub>peak</sub> % pred	67±21	67±25	0.93
V <sub>O<sub>2</sub>,peak</sub> % pred	74±22	83±33	0.27
V <sub>O<sub>2</sub>,peak</sub> mL·kg <sup>-1</sup> ·min <sup>-1</sup>	16.1±3.7	17.1±4.3	0.35
Change in P <sub>a,O<sub>2</sub></sub> with exercise mmHg	-1±9	-4±10	0.25
Change in P <sub>a,CO<sub>2</sub></sub> with exercise mmHg	1.7±3.4	2.5±3.7	0.37
PAP (exercise) mmHg*	38±11	35±11	0.40
P <sub>pcw</sub> (exercise) mmHg*	19±9	18±10	0.66
CO (exercise) L·min <sup>-1</sup>	13.3±2.3	11.8±2.2	0.06
PVR (exercise) dynes·s·cm <sup>-5</sup> *	111±43	122±58	0.50

Results are means±SD. FEV<sub>1</sub>: forced expiratory volume in one second; FVC: forced vital capacity; DL<sub>CO</sub>: diffusing capacity of the lung for carbon monoxide; PPN: predicted postpneumectomy; PPO: predicted postoperative; W<sub>peak</sub>: workrate at peak exercise; V<sub>O<sub>2</sub>,peak</sub>: oxygen uptake at peak exercise; P<sub>a,O<sub>2</sub></sub>: arterial oxygen tension; P<sub>a,CO<sub>2</sub></sub>: arterial carbon dioxide tension; PAP: mean pulmonary artery pressure; P<sub>pcw</sub>: pulmonary capillary wedge pressure; CO: cardiac output; PVR: pulmonary vascular resistance. \*: n=45 (30 noncomplicated versus 15 complicated). (1 mmHg = 0.133 kPa).

or minimal (arrhythmia) complications (n=44), and those affected by respiratory complications (n=20). No differences in FEV<sub>1</sub>, DL<sub>CO</sub>, % Q' of affected lung or extent of surgical resection were apparent between patients developing respiratory complications and those who did not (table 3). Interestingly, only FEV<sub>1</sub> corrected for the perfusion of the affected lung and the amount of parenchyma resected (FEV<sub>1,PPO</sub> in L or as %pred) was significantly different between patients with and without complications (table 3). The ROC curve of FEV<sub>1,PPO</sub> expressed as % pred, is shown in figure 1. Its AURC (0.66) was significantly larger than 0.5 (the result expected from a test without a discriminatory value) (p=0.01), although it was far from the ideal test (which would have AURC=1).

Exercise performance, as assessed by V<sub>O<sub>2</sub></sub>, did not differ between the two groups of patients (table 3), its AURC being <0.5, thus indicating a poor predictive value of this variable in this series. Blood gas analysis during exercise failed to show significant differences between patients with and without complications (table 3). Although the exercise parameter with the greatest AURC was the change in P<sub>a,O<sub>2</sub></sub> from rest to exercise (AURC=0.60), it was not significantly larger than 0.5 (p=0.09). The change in P<sub>a,O<sub>2</sub></sub> during exercise correlated weakly with the percentage predicted DL<sub>CO</sub> (r=0.30, p=0.02). At rest, no differences in haemodynamic measurements were shown between patients with and without complications. During exercise, both the increase in PAP and the decrease in PVR were similar in the two groups (table 3), although there was a trend towards a lower cardiac output in patients suffering pulmonary complications (p=0.06).

Using stepwise logistic regression no model was found that, combining different variables, improved significantly

the prediction of complications provided by the univariate analysis. No attempt was made to perform a multivariate analysis to assess death as the dependent variable, owing to the small number of cases.

The four patients who died, compared with the remaining patients, had a lower FEV<sub>1,PPO</sub> (1.0±0.1 versus 1.4±0.4 L, p=0.006; 34±7 versus 45±10% pred, p=0.03, non-survivors and survivors, respectively), a lower DL<sub>CO,PPO</sub> (40±13 non-survivors versus 58±17% pred survivors,

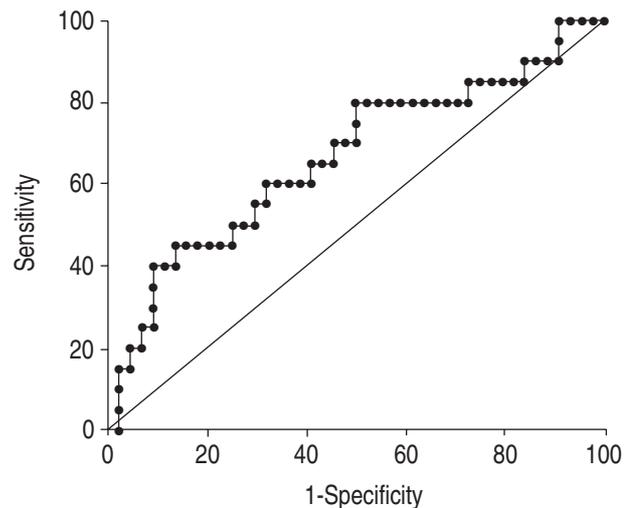


Fig. 1. – Receiver operating characteristic (ROC) curve and its corresponding area under the ROC curve (AURC) for per cent predicted post-operative forced expiratory volume in one second in the prediction of postoperative respiratory complications. The curve for a test with no discriminatory value would appear as a line of identity (AURC=0.5). p=0.01 (AURC=0.66 versus AURC=0.5).

$p=0.04$ ) and greater gas exchange impairment with exercise, as shown by a greater fall in  $P_{a,O_2}$  during exercise ( $-1.46\pm 1.20$  kPa ( $-11\pm 9$  mmHg)) compared with the survivors ( $-0.13\pm 1.20$  kPa ( $-1\pm 9$  mmHg)) ( $p=0.05$ ). Preoperative FEV<sub>1</sub> was not significantly different between survivors and nonsurvivors ( $1.34\pm 0.15$  versus  $1.69\pm 0.51$  L,  $p=0.13$ ; and  $47\pm 11$  versus  $55\pm 13\%$  pred,  $p=0.18$ , nonsurvivors and survivors, respectively).

In view of the zero mortality of patients who underwent lobectomy or wedge resections, the data in patients who underwent pneumonectomy or bilobectomy ( $n=31$ ) were analysed. When comparing patients with ( $n=10$ ) and without ( $n=21$ ) respiratory complications in this group, the results are in good agreement with those obtained in the whole population. In particular, FEV<sub>1,PPO</sub> in patients with complications was significantly lower than in those without complications ( $1.05\pm 0.20$  versus  $1.33\pm 0.28$  L,  $p=0.009$ ; and  $35\pm 6$  versus  $43\pm 8\%$  pred,  $p=0.02$ , complicated and noncomplicated patients respectively). When comparing survivors ( $n=27$ ) with nonsurvivors ( $n=4$ ) in patients following pneumonectomy or bilobectomy, the four patients who died also showed a lower FEV<sub>1,PPO</sub> ( $0.97\pm 0.10$  versus  $1.28\pm 0.27$  L,  $p=0.02$ , nonsurvivors and survivors, respectively) and a greater fall in  $P_{a,O_2}$  with exercise ( $-1.46\pm 1.20$  kPa ( $-11\pm 9$  mmHg) versus  $-0.13\pm 1.33$  kPa ( $-1\pm 10$  mmHg),  $p=0.037$  nonsurvivors and survivors, respectively).

### Discussion

One of the major findings of the present study was that in this group of patients at high-risk for lung resection, mortality was not much greater than that reported generally after thoracotomy [21]. This indicates that surgery can be offered to these patients with an acceptable rate of survival.

In this specific group of patients, preoperative lung function data and predicted postpneumonectomy variables were not useful in the prediction of postoperative complications, including death. Interestingly, only FEV<sub>1</sub> corrected for the amount of functional parenchyma resected (FEV<sub>1,PPO</sub>), calculated by the formula alluded to above, was significantly different between patients with and without complications. Furthermore, this variable had the greatest AURC, implying that it had the greatest overall accuracy in the prediction of complications, although the discriminatory value of the test was only moderate. This finding emphasizes the relevance of the amount of functional parenchyma resected surgically to the development of postoperative complications and supports the conventional approach to perform the minimal possible resection in this type of patient. Indeed, in this series no death occurred among patients who underwent lobectomy or lesser resections.

In the clinical setting the decision is usually whether a patient would tolerate pneumonectomy if this were the only way of resecting the tumour completely. In this regard, the analysis in patients who underwent major resections (pneumonectomy or bilobectomy) indicates that, even in this subset, a lower FEV<sub>1,PPO</sub> is indicative of both a greater morbidity and mortality risk and that a decrease in  $P_{a,O_2}$  with exercise is indicative of a greater risk of mortality.

In addition to a lower FEV<sub>1,PPO</sub> nonsurvivors had a lower  $DL_{CO,PPO}$  than survivors. The product of these variables, the predicted postoperative product, was calculated as recommended by PIERCE *et al.* [14]. This variable was not significantly different between patients with ( $2,283\pm 1,046$ ) and without ( $2,660\pm 934$ ) complications ( $p=0.15$ ), although nonsurvivors had a lower predicted postoperative product than survivors ( $1,426\pm 727$  versus  $2,616\pm 951$ ,  $p=0.02$ ). These results are in agreement with those reported by PIERCE *et al.* [14] and confirm the interest of the product of FEV<sub>1,PPO</sub> %  $\times$   $DL_{CO,PPO}$  % as a predictor of surgical mortality.

In the present series, exercise performance, as assessed by  $V'O_{2,peak}$  and  $W_{peak}$ , was not useful for the prediction of postoperative complications. Further, in relation to the most widely recommended threshold value for  $V'O_{2,peak}$ ,  $15$  mL $\cdot$ kg<sup>-1</sup> $\cdot$ min<sup>-1</sup> [4], a similar proportion of patients below and above this threshold (52 and 45%, respectively,  $p=0.1$ ) developed complications. Although previous studies in nonselected thoracotomy candidates have shown that  $V'O_{2,peak}$  is useful in the prediction of postoperative morbidity and mortality [4, 22–25], studies conducted specifically in patients already classified as being at higher risk have yielded conflicting results [6–11]. Accordingly, it could be inferred that in more selected populations with impaired pulmonary function, such as the present subjects, some functional variables shown to be useful in nonselected populations, *e.g.*  $V'O_{2,peak}$ , fail to show discriminatory power.

In this study, nonsurvivors had a greater decrease in  $P_{a,O_2}$  during exercise than did survivors. This is in agreement with previous studies [13, 14], which showed that a decrease in arterial O<sub>2</sub> saturation during exercise, measured by transcutaneous pulse oximetry, is useful in the prediction of postoperative complications, thus reinforcing the interest in gas exchange measurements during exercise in high-risk thoracotomy candidates. As information about arterial blood gases during exercise cannot be obtained from standard PFT and transcutaneous pulse oximetry provides an unreliable assessment of the actual arterial O<sub>2</sub> saturation during exercise [26], the placement of an arterial catheter for pulmonary gas exchange measurements during exercise in high-risk patients is recommended. This may allow the identification of patients at greatest risk among those with lower FEV<sub>1,PPO</sub>.

Measurements of pulmonary haemodynamics (PAP and PVR), both at rest and during exercise, were not useful for the prediction of postoperative complications, including death, although there was a trend towards a lower cardiac output during exercise in patients with complications (table 3). These findings are in agreement with previous studies in patients at high-risk for thoracotomy [27, 28], which showed that neither the haemodynamic effects of pulmonary artery clamping during thoracotomy [27] nor pulmonary haemodynamics measured on exertion [28], were useful for the prediction of postoperative complications. The fact that in the present series, detailed haemodynamic data have failed to show discriminatory power could be explained by the homogeneous haemodynamic response to exercise shown by the patients. Similarly, the good cardiovascular reserve for the whole population possibly compromised our ability to find differences between subsets of patients. Taking into account the present results in a large number of patients and considering the

invasiveness and the risk of the procedure, right heart catheterization is not recommended for the assessment of postoperative complications in lung resection candidates.

The large number of patients in this series and the fact that patients who would have been excluded in other series, on the basis of FEV<sub>1</sub>, PPN or V'O<sub>2</sub>,<sub>peak</sub>, were successfully operated on and followed an uneventful postoperative course adds valuable information which may be useful in preoperative decision making in such high-risk patients. Threshold values for functional variables should be interpreted cautiously, especially since lung volume reduction surgery for emphysema [29] may call into question the previous rules about operative candidacy [30]. With respect to the role of preoperative functional assessment, perhaps the most rational view would be to focus on the assessment of the capacity to tolerate complications rather than their prediction. In this regard, these results suggest that information on the behaviour of arterial blood gases during exercise provides useful data about the integrated response of the cardiopulmonary system when facing situations that require greater metabolic demand.

In summary, these data, obtained in a selected population of candidates for thoracotomy with severely impaired lung function, indicate that lung resection can be performed with relatively low mortality rate and an acceptable risk of survivable complications, provided that the minimal possible resection is performed. In these patients, the variables that may help to predict postoperative morbidity are percentage predicted forced expiratory volume in one second, the amount of perfusion of the affected lung and the amount of lung parenchyma expected to be resected. The fact that these variables alone did not discriminate complicated from noncomplicated patients, whereas the global parameter predicted postoperative forced expiratory volume in one second did, indicates that in the decision-making process, the relative value of each variable should be balanced against the others. Thus, patients with lower forced expiratory volume in one second will have a more favourable outcome if less parenchyma is resected and/or the perfusion of the affected lung is reduced. Furthermore, since a greater decrease in arterial oxygen tension during exercise may indicate a higher mortality risk during the immediate postoperative period, exercise testing with arterial blood gas measurements is recommended in the assessment of high-risk thoracotomy candidates especially in those with low predicted postoperative forced expiratory volume in one second and/or diffusing capacity of the lung for carbon monoxide.

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