Stairs Climbing Test with Pulse Oximetry as Predictor of Early Postoperative Complications in Functionally Impaired Patients with Lung Cancer and Elective Lung Surgery: Prospective Trial of Consecutive Series of Patients

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Aim To test the predictive value of stairs climbing test for the development of postoperative complications in lung cancer patients with forced expiratory volume in one second (FEV_1)<2 L, selected for an elective lung surgery.

Methods The prospective study was conducted in 101 consecutive patients with an FEV_1<2 L selected for elective lung surgery for lung cancer. Preoperative examination included medical history and physical examination, lung function testing, electrocardiography, laboratory testing, and chest radiography. All patients underwent stairs climbing with pulse oximetry before the operation with the number of steps climbed and the time to complete the test recorded. Oxygen saturation and pulse rate were measured every 20 steps. Data on postoperative complications including oxygen use, prolonged mechanical ventilation, and early postoperative mortality were collected.

Results Eighty-seven of 101 patients (86%) had at least one postoperative complication. The type of surgery was significantly associated with postoperative complications (25.5% patients with lobectomy had no early postoperative complications), while age, gender, smoking status, postoperative oxygenation, and artificial ventilation were not. There were more postoperative complications in more extensive and serious types of surgery ($P<0.001$). The stairs climbing test produced a significant decrease in oxygen saturation (-1%) and increase in pulse rate (by 10/min) for every 20 steps climbed. The stairs climbing test was predictive for postoperative complications only in lobectomy group, with the best predictive parameter being the quotient of oxygen saturation after 40 steps and test duration (positive likelihood ratio [LR], 2.4; 95% confidence interval [CI], 1.71-3.38; negative LR, 0.53; 95% CI, 0.38-0.76). In patients with other types of surgery the only significant predictive parameter for incident severe postoperative complications was the number of days on artificial ventilation ($P = 0.006$).

Conclusion Stairs climbing test should be done in routine clinical practice as a standard test for risk assessment and prediction of the development of postoperative complications in lung cancer patients selected for elective surgery (lobectomy). Comparative to spirometry, it detects serious disorders in oxygen transport that are a baseline for a later development of cardiopulmonary postoperative complications and mortality in this subgroup of patients.

Surgical resection remains the best option for cure for patients with primary lung cancer. During the last few years, the survival improvement has been caused by an increase in the ratio of patients with early stage of disease, increase in the rates of complete tumor resection with lymph node dissection, and decrease in the rates of operation-related death (1). A negative aspect of lung cancer operation is a subsequent irreversible decrease in lung function. Thoracic and upper abdominal surgical procedures are associated with a high rate of postoperative cardiopulmonary complications, which prolong hospital stays and costs.

The population with lung cancer often develops concomitant diseases (2) and therefore has a reduced ability to tolerate further losses in lung function. The goal of the preoperative pulmonary assessment of individuals with resectable lung cancer is to identify the immediate perioperative risks from comorbid cardiopulmonary disease and long-term risks of pulmonary disability if surgical resection is performed.

Exercise testing is used in the preoperative evaluation of candidates for lung resection in order to uncover severe pathophysiologic abnormalities in systemic oxygen transport (3). Those patients who cannot generate high oxygen consumption on preoperative exercise testing may be similarly unable to do so in response to the hypermetabolic demands imposed by major surgery or its complications (4). Previous studies (5-7) assessing the ability of stairs climbing to predict postoperative complications were limited by small sample size or retrospective nature and were applied exclusively to patients undergoing lung resections. Stairs climbing is an economical and widely applicable test, and it has a long tradition among thoracic surgeons (8). The appeal of this symptom-limited test resides in its simplicity and safety, the familiarity of the patient with the exercise, and the need of a very limited staff, expertise, and equipment. The usefulness of this test resides in the capability of detecting patients with impaired aerobic capacity and subsequent increased risk of cardiopulmonary morbidity (9).

In the current study, we sought to prospectively test the predictive value of stairs climbing in a patient population with lung cancer and a forced expiratory volume in one second (FEV_1) less than 2 L that were at risk for the development of postoperative complications after thoracic surgery.

Materials and methods

Patient selection

One hundred and one consecutive patients selected for elective lung resection for lung cancer with $FEV_1<2$ L were from 1998 to the end of 2002 prospectively enrolled in the study after giving informed consent. Patients were excluded if they could not benefit from lung resection because of the advanced staging of their lung cancer or if their cardiopulmonary status would be an excessive risk for perioperative mortality. Types of elective surgery were as follows: 55 lobectomies (54.5%), 14 bilobectomies (13.9%), 17 pulmectomies (16.8%), and 15 exploratory thoracic surgeries (14.8%). All patients underwent a complete history taking and physical examination on initial screening. Preoperative examination also included spirometry testing, electrocardiogram, laboratory, and radiological testing. Patients with $FEV_1<2$ L underwent stairs climbing testing with measurement of pulse oximetry (BCI International, Finger Print, Waukesha, WI, USA). Most of the patients (89%) had concomitant diseases as follows: chronic obstructive pulmonary disease (COPD) (34%), cardiomyopathy (26%), combination of COPD and cardiomyopathy (14%), hypertension (12%), and diabetes mellitus (4%).

Stairs climbing test

The stairs climbing test was performed before the operation. Patients were brought to a staircase, which consisted of 92 steps. Each step was 0.15 m in height. The patients were asked to climb the maximum number of steps, at a pace of their own choice, and to stop only if they start feeling exhaustion, limiting dyspnea, leg fatigue, or chest pain. They were instructed not to use railing for balance. The patients were accompanied by a physician during their exercise and encouraged to continue the test. During the exercise, pulse rate and capillary oxygen saturation were monitored by means of a portable pulse oximeter. The number of steps climbed and the time taken to complete the test was recorded. Oxygen saturation and pulse rate were measured every 20 steps.

Postoperative outcomes

Postoperative care was directed by the surgical intensive care unit team and the floor team without input from the research team, and oxygen use (during first 4 days after surgery) and prolonged mechanical ventilation (longer than 24 hours after surgery) were recorded. Postoperative complications were determined by the review of hospital records and chest radiographs, together with the early postoperative mortality (within 30 days after surgery).

Statistical analysis

Continuous variables with normal distribution were expressed as mean and standard deviation (SD). When Kolmogorov-Smirnov test showed that distribution was not normal, median and range were used. The comparison of the variables between subgroups was made by analysis of variance. The comparison between groups was made by means of χ^2 test, Fisher exact test, or Kruskal-Wallis analysis of variance (ANOVA) for categorical variables. Categorical variables were presented as frequencies (%). Discriminant analysis (univariate and multivariate models) was made in order to determine predictive value and boundary values, sensitivity, specificity, and accuracy of different predictive models. Multivariate models were designed based on univariate relationship of individual variables by gradually adding new variables with F>3.00 (forward stepwise analysis) because of the small sample size. Because incidence and severity of complications were associated with type of surgery, we made a separate analysis for two surgical types (lobectomy vs bilobectomy, pulmectomy, and exploratory surgery). A *P* value of <0.05 was considered statistically significant. The analysis was performed by STATISTICA, version 6.0 (StatSoft, Inc., Tulsa, OK, USA).

Results

Nineteen women and 82 men (44-87 years of age) were included in the study. The majority (69.3%) of these patients were active smokers. Eighty-seven of 101 patients (86%) had at least one postoperative complication. Arrhythmia was the most common postoperative complication with the incidence of 26% (Table 1). Only 4 patients out of 55 (13.8%) in COPD-cardiomyopathy as a concomitant disease had a diagnosed arrhythmia before operation. Age, gender, smoking status, postoperative oxygenation, and artificial ventilation were not significantly associated with incident postoperative complications. The only difference was found for the type of surgery – one quarter of lobectomy group did not have early postoperative complications (Table 1). When postoperative complications were analyzed according to the type of surgery and their severity, patients undergoing more extensive surgery had significantly more postoperative complications (Table 2). Seven patients died during the 30 days after elective surgery, giving the mortality rate of 6.93

Table 1. Clinical characteristics of patients according to the presence of incident postoperative complication (n = 101)*

		Complications (No., %)		
Variable†	total (n = 101)	No. (n = 14)	yes (n = 87)	*P*‡
Age (years, mean±SD)	61.1 ± 8.4	58.2 ± 8.7	61.6 ± 8.3	0.152
Active smokers (No., %)	70 (69.3)	8 (57)	62 (71)	0.287
Comorbidity	90 (89.1)			
Surgery type:				
lobectomy	55 (54.5)	14 (100.0)	41 (47)	0.002
bilobectomy	14 (13.9)	0	14 (16)	
pulmectomy	17 (16.8)	0	17 (20)	
exploration	15 (14.8)	0	15 (17)	
Mild postoperative complication:				
secretion retention	4 (4.0)	NA	NA	NA
local infection	6 (5.9)			
arrhythmia	26 (25.7)			
atelectasis	6 (5.9)			
Severe postoperative complication [early postoperative mortality]:				
bleeding	3 (3.0)	NA	NA	NA
pneumonia	18 (17.8)			
pulmonary edema	4 (4.0)			
stump fistula	7 (6.9)			
myocardial infarction	6 (5.9) [3]			
pulmonary embolism	6 (5.9) [3]			
uremia	1 (1.0) [1]			
Oxygenation during early postoperative period (days; median, range)	4 (2-9)	3 (2-8)	4 (2-9)	0.085
Need for mechanical ventilation (days; median, range)	1 (0-4)	0 (0-4)	1 (0-3)	0.079
Need for mechanical ventilation (%)	53 (52.5)	4 (28.6)	49 (56.3)	0.082

*Abbreviations: NA – not applicable.
†Results are presented as mean ± standard deviation for normally distributed data and median (range) for non-normally distributed data.
‡Analysis of variance or Fisher exact test for the comparisons between the subgroups with and without complications.

Table 2. Prevalence of postoperative complications according to surgery type in all studied patients (n = 101)

	Complications (No., %)				
	no (n = 14)	mild (n = 36)	severe (n = 44)	Early postoperative mortality (n = 7)	*P**
Type of surgery:					
lobectomy	14 (25.5)	26 (47.3)	13 (23.6)	2 (3.6)	<0.001
bilobectomy	0	4 (28.6)	10 (71.4)	0	
pulmectomy	0	2 (11.8)	12 (70.6)	3 (17.6)	
explorative surgery	0	4 (26.7)	9 (60.0)	2 (13.3)	

*Fisher exact test.

(95% confidence interval [CI], 3.03-13.71) with the marginal difference for mortality between the subgroups based on the type of surgery (other vs lobectomy, risk ratio, 1.64; 95% CI, 0.97-2.76; *P* = 0.070).

Although all patients had FEV_1<2 L, oxygen saturation before stairs climbing was not significantly disturbed. The mean±SD stair climbing test duration was 91 ± 17 seconds, and average number of the steps climbed was 88 ± 12. After and during stairs climbing test, all measured parameters (pulse rate, respiration rate, blood pressure, and oxygen saturation) significantly changed (Figure 1 and Table 3). There was a significant decrease in oxygen

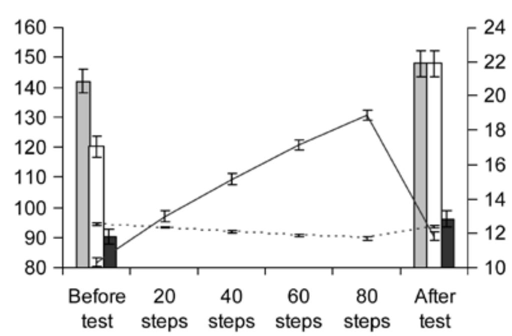

Figure 1. Changes in measured cardiopulmonary parameters according to stair climbing test phase in all studied patients (n = 101). Gray bars – systolic blood pressure (mm Hg); open bars – respirations (L/min); closed bars – diastolic blood pressure (mm Hg); vertical lines within bars – standard deviation; full line – pulse rate (L/min); broken line – oxygen saturation (%). All measured parameters significantly changed during stair climbing test performance (*P*<0.001 for all parameters; analysis of variance for repeated measurements).

Table 3. Cardiopulmonary parameters at baseline, during and after steps climbing test according to type of surgery*

Parameter (mean±SD)†	Lobectomy (n = 55)	Other types of surgery (n = 46)	P
Blood pressure (mm Hg):			
systolic:			
before testing	139 ± 19	145 ± 19	0.118
after testing	146 ± 21	150 ± 23	0.391
diastolic:			
before testing	89 ± 13	92 ± 11	0.117
after testing	96 ± 13	97 ± 13	0.810
Respiration rate (min^{-1}):			
before testing	16.4 ± 2.1	17.8 ± 3.7	0.029
after testing	21.4 ± 3.3	22.5 ± 4.1	0.140
Pulse rate, (min^{-1}):			
before testing	80.1 ± 6.4	83.8 ± 8.9	0.017
after 20 steps	95.3 ± 8.7	99.0 ± 10.6	0.057
after 40 steps	107.5 ± 8.5	111.7 ± 9.9	0.023
after 60 steps	119.6 ± 8.1	122.2 ± 7.6	0.112
after 80 steps	129.7 ± 7.5	131.9 ± 7.9	0.204
after testing	89.4 ± 7.5	91.7 ± 7.9	0.145
Oxygen saturation (%):			
before testing	94.5 ± 1.2	94.2 ± 1.6	0.309
after 20 steps	93.5 ± 1.4	93.2 ± 1.8	0.401
after 40 steps	92.4 ± 1.9	91.7 ± 2.2	0.071
after 60 steps	91.1 ± 2.1	90.4 ± 2.4	0.091
after 80 steps	89.9 ± 2.1	89.5 ± 2.7	0.373
after test	93.7 ± 1.9	93.4 ± 2.0	0.378
Lung function:			
FVC (L)	2.66 ± 0.53	2.50 ± 0.51	0.110
FEV_1 (L/s)	1.85 ± 0.18	1.68 ± 0.32	0.001
MEF_{50} (L/s)	1.99 ± 0.73	1.69 ± 0.79	0.048
PEF (L/s)	3.13 ± 0.96	2.69 ± 0.78	0.014
RV (L)	1.20 ± 0.29	1.07 ± 0.26	0.020
Test duration (s)	91.9 ± 15.9	89.4 ± 19.1	0.476
Steps climbed	91.0 ± 5.8	83.8 ± 15.8	0.003
Oxygenation during early postoperative period (days; median, range)	3. (2-8)	5. (2-9)	<0.001
Need for mechanical ventilation(days; median, range)	0. (0-4)	1. (0-3)	0.001

*Abbreviations: FVC – forced vital capacity; FEV_1 – forced expiratory volume in 1 s; MEF_{50} – maximal expiratory flow at 50% of expired vital capacity; PEF – peak expiratory flow; RV – residual volume.
†Results are presented as mean ± standard deviation for normally distributed data and median (range) for non-normally distributed data.
‡Analysis of variance or Kruskal-Wallis ANOVA for the comparisons between the subgroups with different surgery types.

saturation for 1% and increase in pulse rate for 10 beats/min for every 20 steps (P<0.001).

Thirteen patients could not finish the test (were not able to climb all 92 steps) because they developed dyspnea during testing. Two of them underwent lobectomy and other 11 patients underwent other types of surgery. Dyspnea as a cause for preterm ending of the stair-climbing test was not considered as a cause for the change in the scheduled surgery type and did not have an influence on postoperative period.

Patients in the lobectomy group had better cardiorespiratory status (respiration rate before testing, pulse rate before testing, FEV_1, maximal expiratory flow at 50% of expired vital capacity, peak expiratory flow, and residual volume prior to elective surgery. These patients required shorter oxygenation and mechanical ventilation in early postoperative period (Table 3).

Discriminant analysis based on forward stepwise analysis identified the best (independent) predictive parameter in lobectomy group of patients as quotient of oxygen saturation after 40 steps and test duration, which had a sensitivity of 60%, specificity of 75%, and accuracy for early severe postoperative complications of 70.9% with the cut-off value of 1.09. Positive likelihood ratio (LR) was 2.4 (95% CI, 1.71-3.38), negative LR 0.53 (95% CI, 0.38-0.76) with diagnostic odds (DO) of 4.5 (95% CI, 1.28-15.81). With the cut-off value 1.47, the sensitivity was 100%, specificity 98%, and accuracy 98% for the postoperative mortality. As the sensitivity was 100%, approximations of positive and negative LRs and DO were done accordingly (positive LR, 29.7, 95% CI, 14.3-61.8; negative LR, 0.17, 95% CI, 0.02-1.22; DO, 173, 95% CI, 15-1978) (10). In patients with other types of surgery (bilobectomy, pulmectomy, and exploratory surgery), the only significant predictive parameter for incident severe postoperative complications was the number of days on artificial ventilation (P = 0.006; Table 4).

Discussion

In our study we sought to find parameters or their combination (pulse rate, saturation with test duration) that would predict severe complications. Results show that each of the combined parameters was predictive for severe complications and mortality in patients with lobectomy. Quotient of oxygen saturation and test duration after 40 steps (that all the patients were able to climb) showed the

Table 4. Relevant parameters predictive for severe postoperative complications and mortality in two groups of patients according to type of surgery

	Lobectomy (n = 55)			Other types of surgery (n = 46)		
Parameter (mean±SD)*	without and minor complications (n = 40)	severe complications and mortality (n = 15)	P†	minor complications (n = 10)	severe complications and mortality (n = 36)	P†
Test duration (TD) (s)	96.1 ± 14.5	80.7 ± 14.2	0.001	89.2 ± 21.8	89.5 ± 18.7	0.969
Speed, steps (s)	0.49 ± 0.50	0.57 ± 0.41	0.001	0.48 ± 0.12	0.49 ± 0.14	0.821
Pulse rate after:						
20 steps/TD	1.01 ± 0.14	1.23 ± 0.35	0.002	1.15 ± 0.39	1.20 ± 0.42	0.739
40 steps/TD	1.14 ± 0.16	1.37 ± 0.33	0.001	1.30 ± 0.47	1.34 ± 0.44	0.794
60 steps/TD	1.27 ± 0.18	1.51 ± 0.34	0.002	1.49 ± 0.57 (n = 9)	1.44 ± 0.43 (n = 34)	0.761
80 steps/TD	1.38 ± 0.19 (n = 39)	1.59 ± 0.28 (n = 14)	0.003	1.42 ± 0.14 (n = 8)	1.54 ± 0.46 (n = 28)	0.482
Change in pulse rate/TD	0.53 ± 0.11	0.62 ± 0.14	0.013	0.58 ± 0.30	0.54 ± 0.16	0.524
Maximum pulse rate/TD	1.39 ± 0.20	1.63 ± 0.33	0.001	1.53 ± 0.54	1.55 ± 0.44	0.917
Saturation after:						
20 steps/TD	0.99 ± 0.15	1.20 ± 0.23	0.001	1.14 ± 0.41	1.10 ± 0.30	0.733
40 steps/TD	0.98 ± 0.15	1.19 ± 0.24	0.001	1.11 ± 0.39	1.08 ± 0.30	0.809
60 steps/TD	0.97 ± 0.15	1.17 ± 0.23	0.001	1.14 ± 0.38 (n = 9)	1.05 ± 0.29 (n = 34)	0.450
80 steps/TD	0.95 ± 0.15	1.13 ± 0.21	0.001	1.00 ± 0.11 (n = 8)	1.04 ± 0.34 (n = 28)	0.783
Minimum saturation during test/TD	0.95 ± 0.15	1.16 ± 0.23	0.001	1.08 ± 0.38	1.06 ± 0.32	0.839
Saturation <90% (%)	23 (57.5)	3 (20.0)	0.013	5 (50.0)	23 (63.9)	0.426
Mechanical ventilation(days; median, range)	0 (0-4)	0 (0-2)	0.602	0.0 (0-2)	1 (0-3)	0.006

*Results are presented as mean ± standard deviation for normally distributed data and median (range) for non-normally distributed data; TD – test duration. Numbers in parenthesis for some variables represent the number of patients who were able to complete the stair climbing test.
†Analysis of variance or Kruskal-Wallis ANOVA for the comparisons between the subgroups according to type of complications in different surgery-type groups.

best predictivity for incident severe complications in patients with lobectomy. In contrast, patients who had FEV_1 lower than 2 L and were selected for an elective surgery more extensive than lobectomy, and with significant comorbidity, did not have any benefits from this test because their functional capacity was so damaged that they were expected to have higher postoperative morbidity and mortality. In these patients, other treatment options should be considered. In this patient group, duration of artificial ventilation was the only predictive parameter for postoperative complications with no preoperative parameters that could guide us through the decision process. This could be due to the extent of performed operation and previously mentioned damaged lung functional capacity.

Although all of our patients had lower functional capacity, their oxygen saturation was not dramatically impaired. This could be explained by lung function reserve that was still not preserved enough even in these conditions. During test performance, saturation was markedly lowered (1% for every 20 stairs). Brunelli et al (9) also performed similar stairs climbing test in patients with lung cancer. Their results showed that the decrease of oxygen saturation during preoperative stairs climbing test was an independent predictive factor for oxygen desaturation (saturation below 90%) (9). Desaturation during an exercise test was also mentioned in other studies where it has been associated with an increased risk for perioperative complications (11-14). Furthermore, oxygen desaturation greater than 4% indicates an increased risk for perioperative complications (15). Besides lower oxygen saturation, increase in pulse rate, blood pressure, and respiration rate was also recorded. This was expected as a compensatory mechanism of cardiopulmonary system for additional physical effort.

Girish et al (16) found that symptom-limited stairs climbing was predictive of postoperative complications and length of hospital stay. Olsen et al (6) performed a retrospective chart review of 84 patients who underwent stairs climbing test to a maximum of five flights. These authors reported that patients unable to climb three flights of stairs had a high number of postoperative complications, longer intubations, and longer postoperative length of the stay in the hospital than the patients able to climb three flights of stairs (6).

The significant predictor of incident postoperative complications in our study after lung resection was the type of surgery. Only in lobectomy group there were some patients without postoperative complications, which is logical because patients with lobectomy had less progressive disease and minor lung resection. Besides that, severity of complications in our study also depended on the surgery type performed. Lobectomy was associated with mild complications, while severe complications and greater mortality were associated with more extended operation types. Again, the explanation could be the same as before. In our study arrhythmia was the most common postoperative complication. Arrhythmia was also more prevalent after thoracotomy, especially in older patients (17). Furthermore, our patients had a greater need for postoperative artificial ventilation and oxygenation, which can be explained by markedly lower respiratory capacity of these patients than of patients who had undergone lung resection in other studies (18-20) or our patients with lung resective surgery with $FEV_1 > 2$ L operated in the same time period (28 patients on artificial ventilation of 2756 operated; unpublished data). The other reason could be an excess of anesthetic and relaxant agents during operation which caused delayed degradation and inability for spontaneous breathing after surgery.

In our study, the majority of patients were men. Rates of all lung cancer types among women and adenocarcinoma among men continue to rise despite declining cigarette use in many Western countries and shifts to filtered/low-tar cigarettes (21). A significant part of patients were active smokers. Concerning sex differences in smoking habits, not only has smoking been more common among men than among women, but also men smokers have generally had more dangerous smoking habits than women smokers (22-25). For example, among cigarette smokers, men smoke more cigarettes per day and more men inhale deeply (26). Cigarette smoking also predisposes these patients to other comorbid conditions, specifically atherosclerotic cardiovascular disease, which will further increase the perioperative risks. Consequently, the preoperative physiologic assessment of a patient being considered for surgical resection of lung cancer must consider the immediate perioperative risks from comorbid cardiopulmonary disease, the long-term risks of pulmonary disability, and the threat to survival due to inadequately treated lung cancer.

The potential limitation of our study is a relatively small sample size. Because of that, we could not provide data according to a specific type of lung cancer. Second, we did not assess the severity of concomitant disease or influence of the concomitant disease to outcome. Third, the age range of our patients was quite wide, which could be important for stairs climbing testing because younger patients could have better physical condition. Fourth, there was a significantly more men than women in our study sample so results should be carefully considered in female patients.

In conclusion, according to our results stairs climbing test has enough predictive power to detect serious disorders in oxygen transport that are the basis for the later development of cardiopulmonary postoperative complications and mortality. Therefore, it could be a valuable test in routine clinical practice to assess the risks of elective surgery (lobectomy) in patients with lung cancer with FEV_1 lower than 2 L and serve as a predictor for the development of postoperative complications.

References

1 Wada H, Tanaka F, Yanagihara K, Ariyasu T, Fukuse T, Yokomise H, et al. Time trends and survival after operations

for primary lung cancer from 1976 through 1990. J Thorac Cardiovasc Surg. 1996;112:349-55. Medline:8751502 doi:10.1016/S0022-5223(96)70261-1

2 Janssen-Heijnen ML, Schipper RM, Razenberg PP, Crommelin MA, Coebergh JW. Prevalence of co-morbidity in lung cancer patients and its relationship with treatment: a population-based study. Lung Cancer. 1998;21:105-13. Medline:9829544 doi:10.1016/S0169-5002(98)00039-7

3 Olsen GN. The evolving role of exercise testing prior to lung resection. Chest. 1989;95:218-25. Medline:2642409 doi:10.1378/chest.95.1.218

4 Gilbreth EM, Weisman IM. Role of exercise stress testing in preoperative evaluation of patients for lung resection. Clin Chest Med. 1994;15:389-403. Medline:8088100

5 Van Nostrand D, Kjelsberg MO, Humphrey EW. Preresectional evaluation of risk from pneumonectomy. Surg Gynecol Obstet. 1968;127:306-12. Medline:5662851

6 Olsen GN, Bolton JW, Weiman DS, Hornung CA. Stair climbing as an exercise test to predict the postoperative complications of lung resection. Two years' experience. Chest. 1991;99:587-90. Medline:1995212 doi:10.1378/chest.99.3.587

7 Holden DA, Rice TW, Stelmach K, Meeker DP. Exercise testing, 6-min walk, and stair climb in the evaluation of patients at high risk for pulmonary resection. Chest. 1992;102:1774-9. Medline:1446488 doi:10.1378/chest.102.6.1774

8 Souders CR. Clinical evaluation of the patient for thoracic surgery. Surg Clin North Am. 1961;41:545-56.

9 Brunelli A, Al Refai M, Monteverde M, Borri A, Salati M, Fianchini A. Predictors of exercise oxygen desaturation following major lung resection. Eur J Cardiothorac Surg. 2003;24:145-8. Medline:12853059 doi:10.1016/S1010-7940(03)00175-1

10 Glas AS, Lijmer JG, Prins MH, Bonsel GJ, Bossuyt PM. The diagnostic odds ratio: a single indicator of test performance. J Clin Epidemiol. 2003;56:1129-35. Medline:14615004 doi:10.1016/S0895-4356(03)00177-X

11 Markos J, Mullan BP, Hillman DR, Musk AW, Antico VF, Lovegrove FT, et al. Preoperative assessment as a predictor of mortality and morbidity after lung resection. Am Rev Respir Dis. 1989;139:902-10. Medline:2930068

12 Pierce RJ, Copland JM, Sharpe K, Barter CE. Preoperative risk evaluation for lung cancer resection: predicted postoperative product as a predictor of surgical mortality. Am J Respir Crit Care Med. 1994;150:947-55. Medline:7921468

13 Ribas J, Diaz O, Barbera JA, Mateu M, Canalis E, Jover L, et al. Invasive exercise testing in the evaluation of patients at high-risk for lung resection. Eur Respir J. 1998;12:1429-35. Medline:9877504 doi:10.1183/09031936.98.12061429

14 Ninan M, Sommers KE, Landreneau RJ, Weyant RJ, Tobias J, Luketich JD, et al. Standardized exercise oximetry predicts postpneumonectomy outcome. Ann Thorac Surg. 1997;64:328-33. Medline:9262569 doi:10.1016/S0003-4975(97)00474-8

15 British Thoracic Society, Society of Cardiothoracic Surgeons of Great Britain and Ireland Working Party. BTS guidelines: guidelines on the selection of patients with lung cancer for surgery. Thorax. 2001;56:89-108. Medline:11209097 doi:10.1136/thorax.56.2.89

16 Girish M, Trayner E Jr, Dammann O, Pinto-Plata V, Celli B. Symptom-limited stair climbing as a predictor of postoperative cardiopulmonary complications after high-risk surgery. Chest. 2001;120:1147-51. Medline:11591552 doi:10.1378/chest.120.4.1147

17 Krosnick A, Wasserman F. Cardiac arrhythmias in the older age group following thoracic surgery. Am J Med Sci. 1955;230:541-50. Medline:13268433

18 Magdeleinat P, Seguin A, Alifano M, Boubia S, Regnard JF. Early and long-term results of lung resection for non-small-cell lung cancer in patients with severe ventilatory impairment. Eur J Cardiothorac Surg. 2005;27:1099-105. Medline:15896625 doi:10.1016/j.ejcts.2005.01.034

19 Bianchi RC, de Souza JN, Giaciani Cde A, Hoehr NF, Toro IF. Prognostic factors for complications following pulmonary resection: pre-albumin analysis, time on mechanical ventilation, and other factors. J Bras Pneumol. 2006;32:489-94. Medline:17435898 doi:10.1590/S1806-37132006000600004

20 Aguilo R, Togores B, Pons S, Rubi M, Barbe F, Agusti AG. Noninvasive ventilatory support after lung resectional surgery. Chest. 1997;112:117-21. Medline:9228366

21 Devesa SS, Bray F, Vizcaino AP, Parkin DM. International lung cancer trends by histologic type: male:female differences diminishing and adenocarcinoma rates rising. Int J Cancer. 2005;117:294-9. Medline:15900604 doi:10.1002/ijc.21183

22 Hammond EC. Smoking in relation to the death rates of one million men and women. Natl Cancer Inst Monogr. 1966;19:127-204. Medline:5905667

23 Cederlof R, Friberg L, Hrubec Z, Lorich U. The relationship of smoking and some social covariables to mortality and cancer morbidity. Stockholm: Department of Environmental Hygiene, Karolinska Institute; 1975.

24 Waldron I. What do we know about causes of sex differences in mortality? A review of the literature. Popul Bull UN. 1985;(18):59-76. Medline:12314310

25 US Department of Health and Human Services. The health consequences of smoking: cardiovascular disease. A report of the Surgeon General. DHHS publication No (PHS) 84-50204. Rockville (MD): US Department of Health and Human Services, Public Health Service, Office on Smoking and Health; 1983.

26 Perkins KA. Sex differences in nicotine versus nonnicotine reinforcement as determinants of tobacco smoking. Exp Clin Psychopharmacol. 1996;4:166-77. doi:10.1037/1064-1297.4.2.166