

## Assessment of pulmonary function and quality of life in patients submitted to pulmonary resection for cancer\*

Avaliação da função pulmonar e da qualidade de vida em pacientes submetidos à ressecção pulmonar por neoplasia

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### Abstract

**Objective:** To evaluate the effects that pulmonary resection has on pulmonary function and quality of life (QoL) in patients with primary or metastatic lung cancer. **Methods:** This was a prospective cohort study involving all patients submitted to pulmonary resection for cancer between September of 2006 and March of 2007 at the A. C. Camargo Hospital in São Paulo, Brazil. Patients underwent spirometry in the preoperative period and at six months after the surgical procedure. After a postoperative period of six months, the patients completed an overall QoL questionnaire (the Medical Outcomes Study 36-item Short-form Health Survey) and another one, specific for respiratory symptoms (the Saint George's Respiratory Questionnaire). The scores obtained in our study were compared with those previously obtained for a general population and for a population of patients with COPD. **Results:** We included 33 patients (14 males and 19 females), ranging in age from 39 to 79 years. All of the patients, smokers and nonsmokers alike, presented significant worsening of pulmonary function. The mean scores on the overall QoL questionnaire were approximately 5% lower than those obtained for the general population. The scores of various domains of the symptom-specific QoL questionnaire were 50-60% lower than those obtained for the general population and approximately 20% higher than those obtained for the population with COPD. **Conclusions:** Pulmonary resection has a direct negative impact on pulmonary function and QoL, especially on the QoL related to aspects directly linked to pulmonary function. We highlight the importance of preoperative assessment of pulmonary function in patients undergoing pulmonary resection, in order to predict their postoperative evolution.

**Keywords:** Thoracic surgery; Lung neoplasms/surgery; Spirometry; Quality of life; Questionnaires.

### Resumo

**Objetivo:** Avaliar as repercussões da ressecção pulmonar sobre a função pulmonar e a qualidade de vida (QV) de pacientes com câncer de pulmão primário ou metastático. **Métodos:** Estudo de coorte prospectivo que incluiu todos os pacientes que realizaram ressecção pulmonar por neoplasia no Hospital A. C. Camargo entre setembro de 2006 e março de 2007. Os pacientes foram avaliados no pré-operatório e após seis meses do procedimento cirúrgico através de espirometria. Após seis meses de pós-operatório, os pacientes responderam a um questionário de QV geral (*Medical Outcomes Study 36-item Short-form Health Survey*) e um específico para sintomas respiratórios (*Saint George's Respiratory Questionnaire*). Os valores de QV obtidos foram comparados a valores de uma população geral e aos de uma população de portadores de DPOC. **Resultados:** Foram incluídos 33 pacientes (14 homens e 19 mulheres), com idade entre 39 e 79 anos. Todos os pacientes, tabagistas ou não, apresentaram piora significativa da função pulmonar. Observamos uma redução de aproximadamente 5% na média dos escores do questionário de QV geral em comparação àquela da população geral. Houve uma redução de 50-60% nos vários domínios do questionário específico para sintomas, quando comparado aos resultados da população geral, e um aumento de aproximadamente 20%, quando comparado aos resultados da população com DPOC. **Conclusões:** Existe impacto direto da ressecção pulmonar na deterioração da função pulmonar e na QV com ênfase nos aspectos diretamente ligados à função pulmonar. Cabe ressaltar a importância da avaliação da função pulmonar destes pacientes no pré-operatório para se estimar sua evolução pós-cirúrgica.

**Descritores:** Cirurgia torácica; Neoplasias pulmonares/cirurgia; Espirometria; Qualidade de vida; Questionários.

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## Introduction

Surgery is considered to be the treatment that offers the greatest chance of cure for lung cancer patients. However, surgery is indicated for only approximately 20% of these patients, since most present an advanced anatomical stage or comorbidities that contraindicate surgery.<sup>(1,2)</sup> In this context, two aspects are vital: the determination of pulmonary functional reserve, which can determine candidacy for surgical resection; and evaluation of the effects that the proposed treatment has on patient quality of life (QoL).

Pulmonary resection can be performed in patients with impaired pulmonary function if they are appropriately selected.<sup>(3)</sup> When selecting the candidates for pulmonary resection, the assessment of pulmonary reserve through pulmonary function tests is essential. Preoperative FEV<sub>1</sub> is a parameter commonly used to predict postoperative pulmonary function.<sup>(4)</sup>

Evaluating the functional effects of the disease, as well as the impact that the disease and its treatment have on patient QoL, has become increasingly necessary.<sup>(5-7)</sup> In general, QoL is influenced by various key aspects, such as functional status, physical aspects (somatic symptoms), psychological aspects and social relations.<sup>(8,9)</sup> Therefore, the diagnosis of cancer itself, together with the resulting anxiety and fear, as well as the subsequent manifestations of the disease and the repercussions of its treatment, can alter patient QoL.<sup>(10)</sup>

The objective of the present study was to evaluate the effects that pulmonary resection has on pulmonary function and on the QoL of patients diagnosed with primary or metastatic lung cancer.

## Methods

The present study was approved by the Research Ethics Committees of the A. C. Camargo Hospital and the University of São Paulo School of Medicine. All participating patients gave written informed consent.

We included patients diagnosed with primary or metastatic lung cancer and undergoing curative or palliative pulmonary resection in the Department of Thoracic Surgery of the A. C. Camargo Hospital between September of 2006 and March of 2007.

The exclusion criteria were as follows: dying within six months after the surgical intervention; lung cancer not having been confirmed histologically; undergoing a second surgical procedure within six months of the first; failing to appear for medical appointments; and not being re-evaluated within the first six months after having undergone the surgical procedure.

This was a prospective cohort study conducted in two phases. In the first phase, we searched the surgical archives of the Department of Thoracic Surgery of the A. C. Camargo Hospital for patients submitted to pulmonary resection between September of 2006 and March of 2007. The data were collected from the medical charts and transferred to an evaluation chart. In the second phase, the patients meeting the initial criteria were called to schedule a medical appointment with the physical therapist of the Department of Thoracic Surgery of the A. C. Camargo Hospital after a postoperative period of six months.

Spirometry was performed using a MicroLoop spirometer (Micro Medical Ltd., Kent, England), which is accepted by international guidelines, according to a procedure described elsewhere.<sup>(11)</sup> The values obtained in the evaluation after a postoperative period of six months were compared with those obtained in the preoperative period.

Two QoL questionnaires were applied, one specific for respiratory symptoms—the Saint George's Respiratory Questionnaire (SGRQ)—and the other, an overall QoL questionnaire regarding health care interventions—the Medical Outcomes Study 36-item Short-form Health Survey (SF-36). These questionnaires were administered only in the postoperative period. To administer the questionnaires, a medical appointment was scheduled. During this appointment, the patients completed the printed questionnaires, asking for clarification if necessary. All patients were literate and were able to read and interpret the questions. The level of education of the patients, however, was not determined.

The SGRQ addresses aspects regarding three domains: symptoms; activity; and psychosocial impact of the respiratory disease. Each domain has a maximum possible score. The scores obtained for all of the questions in a given domain are summed, and the total is expressed as a percentage of the maximum for that domain. Values greater than 10% reflect altered QoL in

**Table 1** – Analysis of preoperative and postoperative spirometry data of the population studied.

| Variable                        | Mean | n  | SD   | p      |
|---------------------------------|------|----|------|--------|
| FEV <sub>1</sub> Pre, L         | 2.43 | 26 | 0.75 | 0.0001 |
| FEV <sub>1</sub> Post, L        | 1.85 | 26 | 0.64 |        |
| FVC Pre, L                      | 2.96 | 26 | 0.86 | 0.003  |
| FVC Post, L                     | 2.66 | 26 | 0.83 |        |
| FEF <sub>25-75%</sub> Pre, L/s  | 2.43 | 26 | 1.06 | 0.0001 |
| FEF <sub>25-75%</sub> Post, L/s | 1.51 | 26 | 0.77 |        |

Pre: preoperatively; and Post: postoperatively.

that domain. Post-intervention variations equal to or greater than 4%, in any given domain or in the total score, indicate a significant change in patient QoL.<sup>(12)</sup>

The SF-36 is composed of 36 items. There are 35 questions grouped in eight scales or components—physical functioning (10 items); role-physical (4 items); bodily pain (2 items); general health (5 items); vitality (4 items); social functioning (2 items); role-emotional (3 items) and mental health (5 items)—and an additional question comparing current health conditions with past-year health conditions (self-reported health transition). The SF-36 evaluates the negative aspects of health (disease or illness), as well as the positive aspects of health (well-being).<sup>(13,14)</sup>

To evaluate the results of the SF-36, a score is given to each question; subsequently, the result is transformed into a scale ranging from 0 to 100, in which 0 corresponds to the worst health status and 100 corresponds to the best health status. Each dimension is analyzed separately. There is no single value that summarizes the entire evaluation or that translates to better or worse health status; using a mean value ensures that the real problems related to the health of

the patient are not overlooked or underestimated.<sup>(13-16)</sup>

For the statistical analysis of the SF-36, we compared our patients with a population of patients without cancer residing in the city of São Paulo.<sup>(17)</sup> For the analysis of the SGRQ, no reference values were found for Brazilians. Therefore, we used the values obtained in a study carried out in Spain, which compared a general population with a population of COPD patients.<sup>(18)</sup>

The paired t-test was used to compare the data obtained in the preoperative spirometry test with those obtained in the postoperative spirometry test for each group, since these data presented normal distribution. The analyses were made using the Statistical Package for the Social Sciences program (SPSS Inc., Chicago, IL, USA). A significance level of 5% was adopted.

## Results

Sixty patients who underwent pulmonary resection in the Department of Thoracic Surgery of the A. C. Camargo Hospital were included in the present study. Over the course of the study, 27 patients were excluded: 7 because they did not schedule the follow-up evaluation;

**Table 2** – Mean scores and variation in the scores of the components of the Medical Outcomes Study 36-item Short-form Health Survey for quality of life for the population studied and for a general population.

| Component            | Mean for the population studied | Mean for a general population | Δ     | Variation in comparison with the general population, % |
|----------------------|---------------------------------|-------------------------------|-------|--|
| Physical functioning | 74.24                           | 86.63                         | 12.39 | 14.30  |
| Role-physical        | 72.72                           | 90.00                         | 17.28 | 19.20  |
| Bodily pain          | 74.03                           | 76.65                         | 2.62  | 3.41   |
| General health       | 84.60                           | 81.47                         | -3.13 | -3.84  |
| Vitality             | 72.72                           | 67.93                         | -4.79 | -7.05  |
| Social functioning   | 81.21                           | 82.94                         | 1.73  | 2.08   |
| Role-emotional       | 75.75                           | 77.53                         | 1.78  | 2.29   |
| Mental health        | 77.33                           | 75.53                         | -1.80 | -0.23  |

**Table 3** – Domains of the Saint George’s Respiratory Questionnaire for quality of life regarding the patients who underwent adjuvant chemotherapy.

| Domain   | Adjuvant chemotherapy | Mean  | Standard error | p     |
|----------|-----------------------|-------|----------------|-------|
| Symptoms | no                    | 11.77 | 2.41           | 0.043 |
|          | yes                   | 24.74 | 7.29           |       |
| Activity | no                    | 15.54 | 3.51           | 0.225 |
|          | yes                   | 25.85 | 9.58           |       |
| Impact   | no                    | 8.25  | 3.56           | 0.538 |
|          | yes                   | 12.41 | 6.22           |       |
| Total    | no                    | 9.10  | 1.92           | 0.108 |
|          | yes                   | 18.35 | 6.98           |       |

4 because they died within six months of the surgical procedure; 4 because they were lost to follow-up; 3 because they declined to participate in the study; 3 because they had a benign tumor; 2 because they underwent a second operation within six months of the first; 2 because they lived in other cities, impeding outpatient follow up at our facility; and 2 because they scheduled the evaluation for a time after the end of the study period. Therefore, the final sample consisted of 33 patients, of which 14 were male (42.4%) and 19 were female (57.6%). Patient ages ranged from 39 to 79 years (mean,  $60.18 \pm 11.59$  years). Of the 33 patients assessed, 18 (54.5%) were active smokers and 15 (45.5%) were nonsmokers.

Regarding the anatomopathological diagnosis, 15 patients (45.5%) were diagnosed with primary lung cancer and 18 (54.5%) were diagnosed with metastatic lung cancer.

Regarding the type of surgical resection, 19 patients (57.57%) underwent segmentectomy, 7 (21.21%) underwent lobectomy, 6 (18.18%) underwent wedge resection, and 1 (3.03%) underwent pneumonectomy. The patients were distributed in two groups: the lobar group (lobectomy or pneumonectomy), comprising 8 patients; and the sublobar group

(segmentectomy or wedge resection), comprising 25 patients.

The type of surgery was correlated with the type of cancer (primary or metastatic). We observed that, of the 15 patients diagnosed with primary lung cancer, 9 were in the sublobar group and 6 were in the lobar group. Of the 18 patients diagnosed with metastatic cancer, 16 were in the sublobar group and 2 were in the lobar group. Therefore, we observed that most patients with metastasis were submitted to limited resection (sublobar group)—segmentectomy or wedge resection.

With regard to associated treatments (chemotherapy, radiotherapy or no treatment), we observed that 11 patients underwent adjuvant chemotherapy, 1 underwent neoadjuvant chemotherapy, 3 underwent adjuvant radiotherapy, 2 underwent neoadjuvant radiotherapy, and 16 did not undergo any of these treatments. In the present study, we found no significant differences between the patients receiving postoperative treatments and those not receiving such treatments.

Preoperative spirometry data were available for only 26 of the 33 patients studied. In those 26 patients, preoperative and postoperative spirometry data were compared. We observed

**Table 4** – Respiratory disease-specific quality of life (Saint George’s Respiratory Questionnaire scores) in the population studied and in a general population.

| Domain   | Mean for the population studied | Mean for a general population | $\Delta$ | Variation in comparison with the general population, % |
|----------|---------------------------------|-------------------------------|----------|--|
| Symptoms | 16.09                           | 7.06                          | 9.84     | 61.15  |
| Activity | 18.98                           | 10.11                         | 8.87     | 46.73  |
| Impact   | 9.64                            | 2.91                          | 6.73     | 69.81  |
| Total    | 12.19                           | 5.99                          | 6.20     | 50.86  |

**Table 5** - Respiratory disease-specific quality of life (Saint George's Respiratory Questionnaire scores) in the population studied and in a COPD population.

| Domain   | Mean for the population studied | Mean for a COPD population | $\Delta$ | Variation in comparison with the COPD population, % |
|----------|---------------------------------|----------------------------|----------|---|
| Symptoms | 16.09                           | 17.49                      | -1.40    | 8.70  |
| Activity | 18.98                           | 21.90                      | -2.92    | 15.38   |
| Impact   | 9.64                            | 10.43                      | -0.79    | 8.19  |
| Total    | 12.19                           | 15.36                      | -3.17    | 26.00   |

that pulmonary function worsened in all of the patients evaluated (Table 1).

In terms of the variations in spirometry data, there were no significant differences regarding gender, history of tobacco smoking, type of tumor (primary or metastatic) or the type of surgical procedure.

When analyzing the differences between preoperative and postoperative pulmonary function regarding the history of associated treatment (radiotherapy or chemotherapy), we observed that the reduction in postoperative pulmonary function was not affected by any of the associated treatments (adjuvant chemotherapy and adjuvant radiotherapy, respectively):  $\Delta$ FVC,  $p = 0.15$  and  $p = 0.94$ ;  $\Delta$ FEV<sub>1</sub>,  $p = 0.88$  and  $p = 0.32$ ; and  $\Delta$ FEF<sub>25-75%</sub>,  $p = 0.09$  and  $p = 0.17$ .

When comparing the results of the SF-36 questionnaire for the population studied with those for a general population, no significant differences were observed. The analysis of overall QoL in patients with cancer submitted to pulmonary resection showed values comparable to those of a control population, although the former presented role-physical scores that were 20% lower and overall scores that were 5% lower (Table 2).

When the patients were analyzed regarding gender, smoking history, type of tumor (primary or metastatic) and extent of the resection, no significant differences were observed in the scores for the various domains of either of the two QoL questionnaires applied (general and specific). However, the symptoms domain scores were significantly higher among the patients who underwent adjuvant chemotherapy than among those who did not (Table 3).

When the SGRQ scores were analyzed, we observed that our patients scored higher in all domains than did a general population in Spain, but lower than did a population with COPD (Tables 4 and 5).

## Discussion

In the present study, we aimed at evaluating the effects that pulmonary resection has on spirometry values, as well as on QoL, in lung cancer patients.

Resection of the parenchyma causes a reduction in pulmonary functional reserve and in exercise capacity, leading to potentially adverse consequences for the patient. A thirty-month study investigated 110 consecutive patients submitted to curative lung surgery. Preoperatively and postoperatively (at one, three and six months after the surgical procedure), the patients were submitted to spirometry and, on the same day, a walk test.<sup>(19)</sup> The authors observed that patients submitted to lobectomy presented a mean reduction in FEV<sub>1</sub> of 0.45 L in the first month and of 0.30 L in the sixth month. In addition, FVC dropped from 0.94 L in the first month to 0.58 L in the sixth month. Similarly, in the present study, we observed mean postoperative reductions of 0.5 L in FEV<sub>1</sub> and of 0.4 L in FVC in patients submitted to lobectomy. This effect typically persists for six months after the surgical procedure and is directly related to the extent of the resection. In the present study, we also observed that surgical resection had a direct, negative impact on pulmonary function, and that the effect persisted for six months. However, no significant differences were observed in relation to the extent of the resection. The fact that the type of resection was found to have no impact on pulmonary function in the present study was likely due to the small number of patients evaluated. We believe that this question should be investigated in a subsequent study.

One group of authors reported the need for assessing QoL before patients are submitted to surgical treatment of bronchogenic carcinoma.<sup>(20)</sup> The authors found that, compared with preoperative values, QoL is lower in the immediate postoperative period but is restored by

three to six months after the surgical procedure. In the present study, the respiratory disease-specific QoL values for the patients undergoing pulmonary resection were comparable to those obtained for a population of patients with COPD but approximately 60% lower than those obtained for a general population.<sup>(18)</sup>

In a retrospective study carried out in Helsinki, postoperative pulmonary function and QoL were evaluated in 31 patients (9 women) with primary non-small cell lung cancer submitted to pneumonectomy.<sup>(21)</sup> In that study, females presented lower scores than did males in terms of their ability to perform activities of daily living. In addition, when the total score of a general health-related QoL questionnaire was correlated with the baseline dyspnea index, significant variations were observed, for both genders, in terms of respiration, usual activities, mental health, discomfort, symptoms, stress and vitality.

In a study involving 12 lung cancer patients submitted to chemotherapy alone, radiotherapy alone, or a combination of the two, no worsening of QoL or pulmonary function was observed.<sup>(22)</sup> However, in the present study, all patients presented a worsening of pulmonary function and of QoL. Patients who underwent chemotherapy presented a significant worsening of SGRQ symptoms domain scores. In another study,<sup>(23)</sup> it was shown that this worsening of QoL persists throughout the first postoperative month. In addition, the authors of that study observed no QoL improvement related to the use of radiotherapy, chemotherapy or a combination of the two. Furthermore, there was significant worsening in the following SF-36 components: physical functioning ( $p < 0.004$ ); role-physical ( $p < 0.024$ ); vitality ( $p < 0.025$ ); and social functioning ( $p < 0.006$ ).

Few authors have correlated QoL with pulmonary resection, and other authors have not regarded the type of surgery as a predicting factor for the worsening of QoL.<sup>(24)</sup> In the present study, no significant differences were observed when QoL was correlated with pulmonary resection. However, we believe that this was due to the small number of patients investigated.

In a study investigating the type of approach employed in thoracotomy (anterolateral, 79%; posterolateral, 13%; and video-assisted, 8%) and the type of surgery performed (lobectomy, 61%; wedge resection, 22%; and pneumon-

ectomy, 17%),<sup>(25)</sup> differences were observed among the types of approach and among the types of surgery in terms of the evolution of patient QoL. They used a questionnaire specific for cancer patients (European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire) and an additional module specific for patients with lung cancer (the LC13 lung cancer module). The patients submitted to lobectomy presented less thoracic pain than did those submitted to pneumonectomy. The results of the anterolateral thoracotomy were similar to those of the posterolateral thoracotomy regarding evolution of QoL. However, patients who underwent posterolateral thoracotomy had more pain and dyspnea in the postoperative period. In addition, physical function and QoL were improved and pain was reduced in the patients submitted to video-assisted thoracic surgery (VATS).<sup>(25)</sup>

In a cross-sectional cohort study that assessed QoL in patients submitted to pulmonary resection for cancer,<sup>(26)</sup> the authors compared lobectomy through thoracotomy with lobectomy through VATS and reported that there was a tendency toward higher scores among patients submitted to VATS, who also presented better QoL, reduced symptoms and better overall functioning.

Most studies report a worsening of various aspects of QoL after the surgical procedure; however, from the third month onward patients present an improvement in QoL, especially regarding social functioning.<sup>(23,27)</sup> One study demonstrated that, within one month of the surgery, lower values are obtained for most scales, and that these values return to preoperative levels from the third month onward.<sup>(28)</sup> The authors of that study also reported that cancer patients presented a worse initial QoL than did the general population, and that, except for general health, the scores on all scales remained below 50% in cancer patients even after the third postoperative month, which is in accordance with our results. In addition, those authors found that physical functioning, social functioning and mental health did not change over time.

The results of the present study show that there was a clear worsening of respiratory symptom-specific QoL in the patients analyzed, which was confirmed by the pulmonary function tests. This calls for the development of

viable strategies of treatment and intervention to prolong the rehabilitation time of these patients. Among such strategies, respiratory therapy is mandatory. Few authors have reported the need for preoperative or postoperative respiratory therapy. However, at the A. C. Camargo Hospital, all patients are routinely submitted to motor and respiratory therapy, two to four times a day, according to patient needs and medical prescription. Few studies have reported the use of physical therapy or have described in detail the regimen and procedures of the treatment performed.<sup>(19,23)</sup> In one study, it was reported that respiratory therapy (a program of pulmonary rehabilitation) was employed in all patients during hospitalization and for at least two months into the postoperative period.<sup>(23)</sup> The authors observed a reduction in postoperative pulmonary complications and in the length of hospitalization stays.

Due to the potential for reducing pulmonary complications, as well as for preventing the worsening of pulmonary function, after pulmonary resection, formal rehabilitation programs should be employed in patients with lung cancer, in order to diminish the deleterious effects of the surgery, the disease and the proposed treatment.

We believe that preoperative and postoperative strategies for pulmonary rehabilitation need to be developed. However, it is difficult to implement programs for pulmonary rehabilitation at public and private institutions. Together with the rehabilitation program, it is necessary that patients be adequately monitored by pulmonologists, that bronchodilator administration be optimized, that strategies for smoking cessation be implemented, and that associated acute respiratory symptoms be promptly treated.

In the present study, we observed that pulmonary resection has a direct, negative impact on spirometry values in cancer patients. This effect persists for at least six months after the surgical procedure and does not depend on gender, smoking history, type of cancer (primary or metastatic), associated treatment or extent of the resection.

The overall QoL values in cancer patients submitted to pulmonary resection were comparable to those observed in a control population. However, scores for the role-physical domain were 20% lower and overall scores were 5%

lower among the cancer patients. Regarding respiratory disease-specific QoL, the patients analyzed in the present study were more severely affected, scoring 50-60% lower in the various domains of the questionnaire in comparison with the general population and approximately 20% higher in comparison with the COPD population. When the patients were analyzed regarding gender, smoking history, type of cancer (primary or metastatic) and the extent of the resection, no significant differences were observed in the domains of either of the two questionnaires employed (specific and general). However, patients submitted to chemotherapy presented significantly higher symptoms domain scores.

We concluded that patients submitted to pulmonary resection present deterioration of respiratory function, which directly affects their QoL. Such patients require specific and intensive care.

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