Lung Resection Improves the Quality of Life of Patients With Symptomatic Bronchiectasis

Camilla Carlini Vallilo, MS, Ricardo Mingarini Terra, MD, PhD, André Luís Pereira de Albuquerque, MD, PhD, Milena Mako Suesada, MD, PhD, Alessandro Wasum Mariani, MD, PhD, João Marcos Salge, MD, PhD, Priscila Berenice da Costa, RN, and Paulo Manuel Pêgo-Fernandes, MD, PhD

Thoracic Surgery Division and Pulmonology Division, Heart Institute (INCOR) Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil

Background. Bronchiectasis is a significant cause of morbidity. Surgical resection is a treatment option, but its main outcomes regarding quality of life (QOL) and physiologic consequences have not been addressed previously, to our knowledge. We aimed to evaluate the effect of surgical procedures on QOL, exercise capacity, and lung function in patients with bronchiectasis in whom medical treatment was unsuccessful.

Methods. Patients with noncystic fibrosis in whom medical treatment was unsuccessful and who were candidates for lung resection were enrolled in a prospective study. The main measurements before lung resection and 9 months afterward were QOL according to the Short Form 36 Health Survey and World Health Organization Quality of Life Questionnaires, lung function test results, and the results of maximal cardiopulmonary exercise testing on a cycle ergometer.

Results. Of 61 patients who were evaluated, 53 (50.9% male, age 41.3 ± 12.9 years) underwent surgical resection (83% lobectomies), and 44 completed the 9-month follow-up. At baseline, they had low QOL scores, mild obstruction, and diminished exercise capacity. After resection, 2 patients died and adverse events occurred in 24.5%. QOL scores improved remarkably at the 9-month measurements, achieving values considered normal for the general population in most dimensions. Functionally, resection caused mild reduction of lung volume; nevertheless, exercise capacity was not decreased. In fact, 52% of the patients improved their exercise performance. Multiple linear regression analysis showed that low QOL before resection was an important predictor of QOL improvement after resection ($p = 0.0001$).

Conclusions. Lung resection promotes a significant improvement in the QOL of patients with noncystic fibrosis bronchiectasis without compromising their exercise capacity.

(Bronchiectasis is a heterogeneous disease with permanent abnormal dilation of central and medium-sized bronchi as a result of a vicious circle of impaired mucus clearance, increased microorganisms, transmural infection, and inflammation [1]. It is a chronic condition and represents a significant cause of morbidity [2].

Patients with bronchiectasis report worse quality of life (QOL) than do persons in the general population, particularly those with poor lung function, frequent exacerbations, bronchorrhea, chronic infection, and symptoms of depression and anxiety [3–6]. Most of them can be treated medically, but patients in whom medical treatment is unsuccessful may be eligible for surgical management to remove damaged areas of lung parenchyma that antibiotics penetrate poorly, changing the pattern of repeated infections and leading to relief from cough and sputum production. Operative intervention may also benefit patients with associated cavitary lung disease or recurrent hemoptysis [7]. Thus, the main purposes of the surgical treatment are to restore QOL and to prevent such adverse events as infections and bleeding.

Most studies of the role of surgical procedures in bronchiectasis focus on describing the surgical technique and its adverse events; other outcomes, especially with regard to QOL and the functional consequences of lung resection (pulmonary function and exercise capacity), are poorly addressed [8–10]. Therefore, this study aimed to evaluate the impact of lung resection on QOL in patients with symptomatic noncystic fibrosis bronchiectasis that had not responded to medical treatment. The secondary outcomes were to evaluate the impact of lung resection on pulmonary and exercise capacity and to find predictors of QOL improvement.

Dr Terra discloses a financial relationship with Johnson & Johnson.
Material and Methods

This was a prospective study conducted between 2010 and 2013 in a tertiary teaching hospital in Brazil. The ethics committee (#3490/10/079) approved this study (Clinicaltrials.gov: NCT01268475).

Study Population

Consecutive patients with symptomatic bronchiectasis in whom medical treatment had been unsuccessful were included. The diagnosis of bronchiectasis was based on high-resolution computed tomographic (HRCT) scanning with cylindrical Bronchiectasis, varicose and cystic bronchiectasis, even when associated with healed tuberculosis cavities. We considered that medical treatment had failed when, after 1 year of adequate medication, patients still had frequent infectious exacerbations, chronic cough, or purulent sputum interfering significantly with their daily activities. Hemothysis and fungus ball were also considered to represent failure. Cystic fibrosis, active tuberculosis, immunodeficiencies, and lung cancer were already eliminated by a respiratory physician. We excluded individuals with comorbidities or lung function and cardiopulmonary capacity that precluded the planned resection based on the American Thoracic Society / American College of Chest Physicians statement on cardiopulmonary exercise testing [11], musculoskeletal impairment interfering with exercise performance, inability to understand QOL questionnaires, bleeding diathesis; active infection, or age above 80 years or below 18 years.

Outcomes

The main outcome was QOL improvement after resection. We assessed QOL before lung resection and 9 months afterward using Short Form 36 Health Survey Questionnaire (SF36v2) [12] and World Health Organization Quality of Life (WHOQOL) [13], both general questionnaires validated for the Portuguese language. Previously trained personnel applied all questionnaires.

The secondary outcomes were the impact of the resection on pulmonary and exercise capacity and the identification of predictors of QOL improvement. Demographic data, American Society of Anesthesiologist score, and Charlson Comorbidity Index were collected for later analysis. The same variables were analyzed as predictors of surgical adverse events. We defined as surgical adverse events those that prolonged hospitalization or required new procedures.

Intervention

At baseline, the study participants filled out QOL questionnaires and performed lung function tests (LFT) and cardiopulmonary exercise tests (CPET). When referred to our clinic, all patients already had undergone HRCT and bronchoscopy with bronchoalveolar lavage, new examinations were ordered only when necessary.

Pulmonary function tests (PFT) were performed in the 1085 ELITE system D (Medical Graphics Corporation St. Paul, MO), and CPET was performed with the Cardio2 System (Medical Graphics Corporation) on a cycle ergometer (CPE 2000, Medical Graphics Corporation). All measurements were obtained on the basis of recommended standards [11, 14–16]. CPET was performed with incremental load after a warm-up period of 2 minutes, and the load was increased every minute from 5 to 20 W/min (determined by the investigator according to value physical fitness reported by the patient) until the patient was exhausted. The predicted values for PFT and CPET were derived from the Brazilian population [17, 18]. Thoracic surgeons and pulmonologists decided together to send patients to resection, considering the extent of the resection and its risk based on LFT and CPET. High-risk patients [11] were excluded, and all others underwent lung resection. A double-lumen endotracheal tube was used, and pulmonary resection was achieved through a lateral thoracotomy. The surgical procedure was aimed at primary resection of the affected area, as assessed by HRCT. In case of multiple lesions, the resected region showed the most exuberant change, major bleeding, or the presence of fungal ball. The bronchial stump was closed with 4.0 polydioxanone (PDS II, Ethicon Cornelia, GA) suture and protected with a parietal pleural flap. After the operation, we collected information concerning the surgical procedure, admission time, postoperative adverse events, and readmissions. Nine months after the operation, the patients filled out QOL questionnaires and underwent repeated LFT and CPET. The patients were regularly seen at our outpatient clinic, and any event during follow-up was recorded.

Data Analysis

The results of the QOL, LFT, and CPET before and after lung resection were compared using Student’s t test or Wilcoxon rank sum test. Multiple linear and logistic regression analyses were performed to identify the variables independently related to the improvement of physical domain of QOL (SF36v2 and WHOQOL) and to the presence of postoperative adverse events. A p value <0.05 was considered significant, and SPSS v21.0 software was used.

Results

Participants

Sixty-one patients were enrolled in the study. The main symptoms at presentation were shortness of breath on moderate and minimum exertion (65.6%), hemothysis (57.4%), thoracic pain (50.8%), abundant purulent sputum (44.3%), cough (40.9%) and clubbing (13%).

Figure 1 depicts the flowchart throughout the study. Six patients showed maximum oxygen uptake (Vo2max) below 10 mL/kg · min at CPET and were excluded. One patient experienced supraventricular tachycardia during the CPET and was referred to the cardiology department, and 1 patient refused to undergo operation. Fifty-three patients underwent the operation, but 9 did not have the 9-month evaluation, 6 did not attend their second 9-month evaluation, and 1 experienced bleeding in the
contralateral lung and had to undergo another operation.
Two patients died. One had a failed extubation on the first postoperative day and had to be reintubated; then, after 13 days of unsuccessful weaning from mechanical ventilation, he underwent a tracheostomy, and on the 24th postoperative day he experienced multiple organ failure and died. The other patient died 3 months after operation.

Functionally, they had mild obstruction at spirometry and mild reduction in carbon monoxide diffusion capacity (DLCO) (Table 2). All patients stopped the exercise when they became exhausted, achieving a respiratory exchange ratio above 1.10. The exercise performance (mean peak VO$_2$) was also reduced, with 64% showing VO$_2$ lower than normal. The reason for exercise limitation was likely a combination of dyspnea and leg fatigue with similar Borg scale results for both components. There was a substantial ventilatory and cardiac reserve without considerable gas exchange impairment.

Most QOL scores were reduced in the preoperative evaluation. Figure 2 shows that the time 0 scores were below those of the general population 50th percentile according to SF36v2. This fact was also true for WHOQOL (Fig 3).

**Surgical Procedures**

Table 3 summarizes the surgical outcomes in the 53 patients who underwent pulmonary resection. Apart from the two fatalities previously described, 13 patients (24.5%) had at least one postoperative adverse event within 90 days. Eight had adverse events that required only clinical treatment: prolonged air leak (>7 days) in 2 patients, pulmonary thromboembolism in 2, and acute renal failure, sepsis, empyema (treated with antibiotics), and atelectasis (that resolved spontaneously) in 1 patient each. Adverse events that needed intervention were atelectasis requiring bronchoscopy (1 patient), pleural empyema on the 9th postoperative day (1 patient who underwent video-assisted thoracic surgery decortication), high-volume alveolar fistula (1 patient) and 2 bronchial stump fistulas, which were resolved with the use of a serratus muscle flap. The stepwise backward logistic regression analysis showed that only male gender was an independent predictor of postoperative adverse events (odds ratio 5.185; confidence interval 1.085–24.791, $p = 0.039$).

**Outcomes**

All patients with hemoptysis at presentation remained asymptomatic after intervention. Symptoms at the 9th month were shortness of breath on great effort (26.4%), sporadic dry cough (11.3%), and sporadic pain in the surgical wound (18.9%). Sputum production was present in only 1.9% of patients, whereas before operation it was present in 44.3%. We observed a significant improvement in all SF36v2 dimensions (Fig 2). The physical and mental components also improved ($p < 0.001$ for both components); it is interesting that after operation patients began to show values similar to those of the general population (Fig 2). In the WHOQOL, we observed significant improvement in the overall health, physical, and psychologic dimensions (Fig 3).

We built multiple linear regression models to evaluate the influence of several variables in the difference between QOL measurement at the 9th month and at baseline. Only low QOL before the operation surgery was found to be a predictor of improvement after resection ($p = 0.0001$ in all models).

Twelve patients had fungus ball as shown by HRCT; most were men with a history of tuberculosis. There was no difference between groups regarding length of
intensive care unit stay and hospital stay, readmission rate, adverse events, reoperation rate, fatalities, and LFT and CPET before or after operation. Although in some domains the patients experienced lower QOL before and after operation, we noticed an improvement in all of them at the 9th month but without statistical significance.

Table 4 summarizes the results at baseline and at the 9th month in the 44 patients who completed the follow-up. After lung resection, the patients had mildly lower values at spirometry but as a result of lower lung volumes, inasmuch as the forced expiratory volume at 1 second (FEV1) and forced vital capacity remained constant. DLCO was not changed, suggesting that predominantly nonfunctioning lung areas were resected. Exercise performance generally did not change, but approximately 52% of the patients improved their VO2 and workload. Sensorial discomforts (Borg scale) were not increased. All individuals persisted with a large cardiac and ventilatory reserve without gas exchange impairment. The hyperventilation during exercise and the tidal volume achieved after operation was maintained.

**Comment**

This study showed that lung resection significantly improved the QOL of patients with symptomatic bronchiectasis, and this was particularly relevant in the functional and physical QOL domains. We also observed a slight decrease in lung volumes after operation; nevertheless, this fact did not interfere with exercise capacity,
which remained unchanged in the 9th postoperative month when compared with baseline. In our sample, we could not identify predictors of improvement other than low preoperative QOL.

Our patients had significant impairment of LFT and CPET at baseline, but most importantly, they had a severe QOL impairment as measured by two validated questionnaires. Previous studies had already demonstrated decreased QOL in patients with noncystic bronchiectasis. Olveira and colleagues [5] showed, in patients with bronchiectasis, a positive correlation between the number of exacerbations and a poorer QOL on Saint George’s Respiratory Questionnaire. Interestingly, QOL was not associated with lung function and disease extent. Moreno and colleagues [19] found a significant correlation between anxiety scores and the amount of expectorated sputum and type of bacteria, especially *Pseudomonas aeruginosa*. Dyspnea, FEV_{1}, and daily sputum were independent determinants of QOL in patients with stable cystic bronchiectasis in another large series [20].

Despite the relevance of QOL in bronchiectasis, we found no studies evaluating such an outcome before and after lung resection; most studies addressed only control of symptoms or lung function behavior [21]. By contrast, several studies evaluated QOL after lung resection in lung cancer. Baldyuck and colleagues [22] and Brunelli and colleagues [23] applied European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-C30 + LC13 and SF36v2 questionnaires.
respectively, in patients with lung cancer who underwent pulmonary resection, and they observed low baseline QOL scores. In both studies, the authors observed an early decline in QOL, which returned to baseline after 3 months.

In our series, we observed a remarkable improvement of QOL, which returned to baseline after 3 months. In both studies, the authors observed an early decline in QOL, which returned to baseline after 3 months. In fact, patients had a decline of approximately 10% of baseline volumes. Even though this drop was statistically significant, this was just 300 mL for forced vital capacity and 200 mL for FEV1 and apparently did not lead to clinical deterioration. Similarly to studies addressing surgical resection in lung cancer, improvement in health status of our patients did not correlate with exercise and lung function response [24]. Interestingly, when all individuals were taken into account, mean exercise capacity was the same after lung resection; nevertheless, individually, 52% of them improved their oxygen consumption. Neither the behavior of ventilatory system nor gas exchanges changed after intervention. We can infer that the lung area resected had not contributed to ventilatory response during exercise before the intervention. Thus, patients were able to maintain their exercise performance (some of them even improved), with no impairment to the response of the ventilatory system during maximal testing.

The 30-day mortality rate was 1.8%, and the rate of adverse events was 24.5%. These are slightly higher than in other series, where we find 30-day mortality rates ranging from 0% to 1.1% and rates of adverse events ranging from 12% to 22.4% [25–28]. The large proportion (60.4%) of tuberculosis, a well-known risk factor for adverse events, might explain this fact [27]. In addition, many patients were colonized with *Pseudomonas* species and *Aspergillus* species, another important predictor of adverse events [28].

### Table 4. Baseline and Ninth Month Complete Pulmonary Function and Cardiopulmonary Exercise Test Results (44 Patients Completed Follow-Up)

<table>
<thead>
<tr>
<th>Tests</th>
<th>Variables</th>
<th>0 month</th>
<th>9th month</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>LFT (n = 44)</td>
<td>FVC (L)</td>
<td>3.15 ± 0.9</td>
<td>2.85 ± 0.8</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>(% predicted)</td>
<td>79.3 ± 17.9</td>
<td>71.4 ± 17.7</td>
<td>&lt;0.05</td>
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<tr>
<td></td>
<td>FEV1 (L)</td>
<td>2.21 ± 0.8</td>
<td>1.98 ± 0.8</td>
<td>&lt;0.05</td>
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<tr>
<td></td>
<td>(% predicted)</td>
<td>68.5 ± 21.4</td>
<td>61.1 ± 21.1</td>
<td>&lt;0.05</td>
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<tr>
<td></td>
<td>FEV1/FVC</td>
<td>0.7 ± 0.1</td>
<td>0.7 ± 0.2</td>
<td>0.400</td>
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<tr>
<td></td>
<td>DLCO (ml/min · mm Hg) (n = 37)</td>
<td>23.2 ± 7.6</td>
<td>21.7 ± 8.2</td>
<td>0.092</td>
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<tr>
<td></td>
<td>DLCO % predicted</td>
<td>92.1 ± 24.6</td>
<td>86.3 ± 27.1</td>
<td>0.340</td>
</tr>
<tr>
<td>CPET (n = 44)</td>
<td>Vo2max (ml/kg · min)</td>
<td>20.9 ± 7.4</td>
<td>20.2 ± 8.1</td>
<td>0.452</td>
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<tr>
<td></td>
<td>(% predicted)</td>
<td>69.9 ± 17.6</td>
<td>67.7 ± 17.7</td>
<td>0.269</td>
</tr>
<tr>
<td></td>
<td>VE (L/min)</td>
<td>52.1 ± 19.4</td>
<td>49.6 ± 17.6</td>
<td>0.510</td>
</tr>
<tr>
<td></td>
<td>VE/MVV</td>
<td>0.6 ± 0.1</td>
<td>0.7 ± 0.2</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>VTmax (L)</td>
<td>1.32 ± 0.4</td>
<td>1.25 ± 0.4</td>
<td>0.476</td>
</tr>
<tr>
<td></td>
<td>VE/VCO2</td>
<td>34.2 ± 4.8</td>
<td>35.7 ± 9.9</td>
<td>0.37</td>
</tr>
<tr>
<td></td>
<td>HRmax (beats/min)</td>
<td>151.9 ± 20.4</td>
<td>148.1 ± 17.7</td>
<td>0.172</td>
</tr>
<tr>
<td></td>
<td>(% predicted)</td>
<td>85.5 ± 10.3</td>
<td>83.4 ± 9.1</td>
<td>0.175</td>
</tr>
<tr>
<td></td>
<td>RER</td>
<td>1.21 ± 0.13</td>
<td>1.22 ± 0.2</td>
<td>0.833</td>
</tr>
<tr>
<td></td>
<td>Workload (W)</td>
<td>103.2 ± 38.9</td>
<td>100 ± 33.6</td>
<td>0.195</td>
</tr>
<tr>
<td></td>
<td>SpO2 %</td>
<td>93.7 ± 4.3</td>
<td>94.1 ± 4.2</td>
<td>0.690</td>
</tr>
<tr>
<td></td>
<td>Borg dyspnea</td>
<td>4.3 (IQR 1–7)</td>
<td>4.8 (IQR 3–7)</td>
<td>0.377</td>
</tr>
<tr>
<td></td>
<td>Borg lower limbs</td>
<td>4.3 (IQR 1–7)</td>
<td>4.9 (IQR 2–7)</td>
<td>0.231</td>
</tr>
</tbody>
</table>

Numbers expressed as mean and standard deviation, \( p \) value and interquartile range (IQR) 25–75.

Borg = modified Borg scale; CPET = cardiopulmonary exercise test; DLCO = carbon monoxide diffusion capacity; FEV1 = forced expiratory volume at 1 second; FVC = forced vital capacity; HRmax = maximum heart rate; LFT = lung function test; MVV = maximum voluntary ventilation; RER = respiratory exchange ratio; SpO2 = pulse oximetry; TV = total volume; VE = minute ventilation; Vo2max = maximum oxygen uptake.
Proportionally, the profile of adverse events in our study was quite similar to those in previous reports but for the high incidence of bronchial stump fistula (5.7%), which was experienced by 2 patients within a month and 1 patient after 2 months. All 3 patients had a particularly risky bronchial closure, and the stump was covered with a pleural flap. We were aware of the risks beforehand; maybe a pedicled muscle flap (either intercostal or serratus) should have been used in the first place.

Despite the encouraging results of our study, some limitations should be recognized. First, our study had no control group, and we cannot rule out the possibility that the significant improvement in QOL after the operation resulted from the placebo effect of the procedure. Nevertheless, the large differences between QOL scores before and after the operation and the consistency of the results in two QOL instruments support our conclusions. Finally, although the number of patients was adequate to address our main objective, it was too small to identify predictors of adverse events and QOL improvement.

In conclusion, our results demonstrated that patients with symptomatic noncystic fibrosis bronchiectasis experience a significant improvement in their QOL after resection of compromised areas in the lung. Moreover, despite a slight decrease in lung volumes, a patient’s exercise capacity remains unchanged after operation. Our study highlights the role of surgical treatment of patients with symptomatic bronchiectasis that is refractory to clinical treatment or who experience such severe adverse events as hemoptysis.

References
reintubation, contralateral contamination of the lung. Did you have a chance to look at that readmission rate, not surgical readmission but medical readmission of those patients during the 9 months?

DR TERRA: Thank you so much for the question. Those results that I showed that 5% of the patients were readmitted—it was for both medical and surgical reasons. That was the number that we found in this cohort of patients.

DR DASILVA: So the readmission rate for treatment of pneumonias and so forth wasn’t changed after the operation? That’s my question.

DR TERRA: We didn’t know exactly the number of exacerbations they had before. These patients were sent to us after 1 year of treatment in the pulmonology department, and these numbers were not really reliable, and so we didn’t do that analysis. Anyway, none of our patients was readmitted because of pneumonia. That’s the answer I can give you.

DR JOHN MITCHELL (Aurora, CO): I have two quick questions. This was a nice study. First, did the extent of the resection influence your results—for example, pneumonectomy versus right middle lobectomy? Second, some of the medical regimens—the antibiotic therapy—associated with some of these diagnoses are pretty onerous. How did this influence your results?

DR TERRA: The first question, comparing pneumonectomy with lobectomy, we looked at these data, and actually the results were pretty much the same. We didn’t find any difference in regard to both quality of life and exercise and lung function capacity. That was a little bit surprising for us, but the sample size is small. Maybe those differences weren’t captured in our sample. The second question?

DR MITCHELL: The influence of the medical regimens on the quality of life outcomes.

DR TERRA: You mean before?

DR MITCHELL: And after as well. What was the timing of the medical treatment in relation to the data collection times?

DR TERRA: Well, these patients were treated for a year before operation. Some of them actually weren’t treated for a year because they had adverse events along the way, like hemoptysis, and so they were sent to us before. This is in more detail in the report. Because of time restrictions, we don’t have the time to show every single piece of data. These patients were treated for 1 year with medical therapy, like corticosteroids, physical therapy, and then sent to us if they were still symptomatic or having frequent exacerbations; and those who had some sort of adverse events, like hemoptysis and so on, they were sent to us earlier.

DR JOHN P. MAURICE (Newport Beach, CA): Congratulations on 9 months of showing all of your patients who got thoracotomies in this study who felt they had the same quality of life as the regular population. I wonder if you could give a little more detail on how you do your thoracotomies, and also if you have looked at a subset of patients who maybe got a thorascopic procedure instead.

DR TERRA: That is a very good question. Most patients undergo a muscle-sparing thoracotomy. Some of them—those who had lung cavities and the pleura was thoroughly obliterated may have had a larger thoracotomy. We looked at that, and there was no difference regarding quality of life and lung function. They could undergo thoracoscopy, but in our hospital we have some restrictions for using staplers and so on, and so we decided that we should spare the staplers for lung cancer patients, and that was an administrative decision.