Quality of life evolution after lung cancer surgery in septuagenarians: a prospective study

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Abstract

Objective: To prospectively evaluate quality of life (QoL) evolution after lung cancer surgery in a cohort of septuagenarians with the European Organisation for Research and Treatment of Cancer (EORTC) QoL Questionnaire-C30 and LC13.

Methods: Between January 2003 and December 2006, QoL was prospectively recorded in 60 consecutive septuagenarians undergoing lung cancer surgery. Forty-nine lobectomies and 11 pneumonectomies were performed. Questionnaires were administered before surgery and 1, 3, 6 and 12 months postoperatively (MPO) with response rates of 100%, 83%, 87%, 90% and 77%, respectively.

Results: After lobectomy, QoL scores returned to baseline 3–6 months after surgery, with the exception of a persistent decrease in physical functioning and an increase in dyspnea within the 12 months follow-up. In the 12 months follow-up period after pneumonectomy, there was no return to baseline in physical, role and social functioning. After pneumonectomy, most quality of life scores returned to baseline at 1-month follow-up, with the exception of dyspnea and general pain, which returned to baseline at 3 and 6 months, respectively. Comparing both resections, significant differences in evolution of physical functioning (6MPO \( p = 0.045 \)), role functioning (3MPO \( p = 0.035 \)), social functioning (6MPO \( p = 0.006 \), 12MPO \( p = 0.001 \)) and general pain (6MPO \( p = 0.037 \)) were reported in favor of lobectomy.

Conclusions: The present study documented QoL evolution profiles of septuagenarian patients after pulmonary surgery. The results indicate that both resections have a major impact on elderly patients, especially physical functioning and dyspnea status. If both resections are compared, lobectomy patients have a more favorable evolution in QoL subscales compared to pneumonectomy.

Keywords: Quality of life; EORTC; QLQ-C30; QLQ LC-13; Elderly patients; Septuagenarians; Lobectomy; Pneumonectomy; Lung cancer

1. Introduction

The incidence of lung cancer in the elderly continues to increase. Surgical resection is the mainstay of curative treatment with a favorable survival even in the elderly [1,2]. Given the increased risk of postoperative morbidity in the elderly, all efforts are made in order to avoid pneumonectomy by the use of parenchyma sparing procedures. Nevertheless, there are a proportion of elderly patients that require pneumonectomy for the cure of cancer [3]. The aim of any cancer treatment extends well beyond increasing survival. Palliation of symptoms and the maintenance or improvement of quality of life (QoL) are equally important goals of treatment. The benefits of existing cancer treatment need to be weighed against the side effects and possible impairment of patients’ QoL. In the last few decades, there has been an increased recognition of the need to complement follow-up of cancer patients with an assessment of QoL, in addition to the impact of treatment, survival and side effects [4–7]. Limited information is available regarding the long-term QoL evolution of septuagenarian patients who underwent pneumonectomy or lesser resections. Accurate identification of comorbidity is essential in assessing patient’s health status and quantifying risk of mortality and morbidity. The Charlson comorbidity index (CCI) is the weighted sum of all conditions that are known to significantly influence survival of cancer patients in the first month after treatment [8]. The CCI is strongly correlated with higher risk of surgery in primary non-small cell lung cancer patients and is a better predictor than individual risk factors [9]. The objective of the present study is to measure QoL evolution after lung cancer surgery in septuagenarian patients and to evaluate the usefulness of the CCI to predict postoperative QoL.

2. Patients and methods

From January 2003 to December 2006, 60 consecutive septuagenarians with a clinical diagnosis of non-small cell lung cancer (NSCLC) underwent lobectomy (\( n = 49 \)) or
pneumonectomy (n = 11). All patients were operated by an anterolateral muscle-sparing thoracotomy. Lobectomy was considered and performed in any case that could be completely resected.

2.1. Quality of life assessment

QoL was assessed using the Dutch version of the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ)-C30 (cancer core questionnaire) and the Dutch version of the EORTC QLQ-LC13 lung cancer-specific questionnaire module [4,5]. The questionnaires were administered one day before surgery and at 1, 3, 6 and 12 months postoperatively (MPO). The questionnaires were sent to the patients by mail, accompanied by a letter with general information and the aim of the study.

2.2. EORTC QLQ-C30

The EORTC QLQ-C30 is a self-rating questionnaire composed of 30 questions/items and incorporates nine multi-item scales: five functional scales (physical, role, cognitive, emotional, and social), three symptom scales (fatigue, pain, nausea/vomiting), a global health/QoL scale, and several single items assessing additional symptoms (dyspnea, sleep disturbance, constipation and diarrhea). A final item evaluates the perceived economic consequences of the disease [5]. Reliability and validity of the EORTC QLQ-C30 questionnaires have been confirmed in international studies [5,6].

2.3. EORTC QLQ-LC13

The EORTC QLQ-LC13 is a supplementary questionnaire module that was designed for use among patients receiving treatment with chemotherapy and/or radiotherapy. It contains 13 questions/items assessing lung cancer-associated symptoms (cough, hemoptysis, dyspnea, and site-specific pain), chemotherapy/radiotherapy-related side effects (sore mouth, dysphagia, peripheral neuropathy, and alopecia), and pain medication [6]. Chemotherapy/radiotherapy-related side effects were not included in the analysis. Reliability and validity of the EORTC-LC13 module have been confirmed in international studies [4—6].

2.4. Charlson comorbidity index

Each patient was scaled on the CCI. Patients were considered to have a comorbid condition if a listed disorder was mentioned in the records or if the patient was treated for it. The modified CCI scoring was used, as proposed by Birim et al. [9]. The authors modified the CCI by scoring all forms of coronary artery disease (myocardial infarction, angina, coronary artery bypass graft, percutaneous transluminal coronary angioplasty) with a value of one, as it is associated with a higher risk of surgery in patients with lung cancer [9].

2.5. Statistical analysis

Statistical analysis was performed using statistical software (SPSS, version 15.0, Chicago, IL). In accordance with procedures recommended by the EORTC, scores were linearly converted to a scale ranging from 0 to 100 for each patient. For the global health/QoL and functional scales, higher scores represent a higher level of functioning. For the symptom scales, higher scores represent a greater symptom burden. Results were reported as mean. The Wilcoxon-signed rank test was used to compare the mean value before and after surgery. Student’s t-test was used to compare parametric data between groups. The Mann—Whitney U test and the Kruskall—Wallis test were performed to compare non-parametric data. Survival curves were estimated by the Kaplan—Meier method. A p value was considered statistically significant if lower than, or equal to 0.05.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Patients’ characteristics.</th>
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<tbody>
<tr>
<td></td>
<td>Lobectomy (n = 49)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>73.45 ± 2.81</td>
</tr>
<tr>
<td>Male/female</td>
<td>43/6</td>
</tr>
<tr>
<td>Mean FEV1 (l) (range)</td>
<td>3.186 (1.630—3.520)</td>
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<tr>
<td>Length of hospitalisation (days)</td>
<td>17.02 ± 5.86</td>
</tr>
<tr>
<td>Follow-up (months)</td>
<td>30.76 ± 16.9</td>
</tr>
<tr>
<td>TNM classification stage I</td>
<td>33 (67%)</td>
</tr>
<tr>
<td>Stage II</td>
<td>13 (27%)</td>
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<tr>
<td>Stage III</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Histology squamous cell carcinoma</td>
<td>22 (45%)</td>
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<tr>
<td>Adenocarcinoma</td>
<td>24 (49%)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Charlson comorbidity index grade 0</td>
<td>6 (12%)</td>
</tr>
<tr>
<td>Grade 1—2</td>
<td>31 (63%)</td>
</tr>
<tr>
<td>Grade 3—4</td>
<td>8 (17%)</td>
</tr>
<tr>
<td>Grade ≥5</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>Induction chemotherapy</td>
<td>5 (10%)</td>
</tr>
<tr>
<td>Adjuvant radiotherapy</td>
<td>20 (41%)</td>
</tr>
<tr>
<td>Adjuvant chemotherapy</td>
<td>6 (12%)</td>
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3. Results

3.1. Response rate to QoL questionnaire and comparison of patients’ groups

The preoperative response rate to the QoL questionnaire was 100%, at 1 month 83%, at 3 months 87%, at 6 months 90% and at 12 months 77%. The prevalence of comorbidity was 88% in general, 88% in the lobectomy and 91% in the pneumonectomy group. No statistical differences were observed between the lobectomy and pneumonectomy group regarding age, sex, adjuvant therapy, TNM classification, pulmonary function, tumor histology, preoperative comorbidity and response rate, with the exception of a borderline significant higher number of stage I tumors in the lobectomy group ($p = 0.023$). Patients’ characteristics for the two surgical procedures are listed in Table 1.

3.2. Preoperative QoL

In general, patients complained of dyspnea, coughing and fatigue. Most patients had a median impaired physical, social and emotional functioning preoperatively. Patients reported significantly more coughing before pneumonectomy than lobectomy ($p = 0.015$). There were no other statistical differences in baseline QoL items between the two resection groups.

3.3. Operative morbidity and mortality

No operative mortality was observed, either after lobectomy or pneumonectomy. After a mean follow-up of 29.2 months (range 1—69 months), 5-year survival rates were 0.62 $\pm$ 0.12 in the lobectomy group and 0.36 $\pm$ 0.16 in the pneumonectomy group. There was no significant difference in 5-year survival between both groups.

3.4. QoL evolution after lobectomy

One month after lobectomy, physical, role, cognitive, social and general QoL functioning dropped significantly below baseline values ($p = 0.001$, $p = 0.001$, $p = 0.032$, $p = 0.021$ and $p = 0.030$ respectively). Role and cognitive functioning scales returned to baseline at 3 months after surgery. Social functioning returned to baseline at 6 months (3MPO $p = 0.014$). A persistent decrease in physical functioning was reported (3MPO $p = 0.001$, 6MPO $p = 0.001$, 12MPO $p = 0.001$).

After lobectomy, patients reported a persistent increase in dyspnea (1MPO $p = 0.001$, 3MPO $p = 0.004$, 6MPO $p = 0.001$, 12MPO $p = 0.001$). Patients did not report a significant increase in coughing after lobectomy. Patients reported a persistent increased in thoracic pain in the 12-month follow-up period. (1MPO $p = 0.003$, 3MPO $p = 0.002$, 6MPO $p = 0.018$ and 12MPO $p = 0.005$). Selected scales are shown in Fig. 1.

3.5. QoL evolution after pneumonectomy

In the 12 months follow-up period after pneumonectomy, there was no return to baseline in physical (1MPO $p = 0.042$, 6MPO $p = 0.018$ and 12MPO $p = 0.018$), role (1MPO $p = 0.017$, 3MPO $p = 0.017$ and 12MPO $p = 0.011$) and social functioning (6MPO $p = 0.024$ and 12MPO $p = 0.018$). General quality of life returned to baseline after 6 months (1MPO $p = 0.017$, 3MPO $p = 0.011$). After pneumonectomy, symptom scores returned to baseline at 1-month follow-up, with the exception of dyspnea (1MPO $p = 0.012$, 3MPO $p = 0.034$) and thoracic pain (1MPO $p = 0.046$), which returned to baseline at 6 and 3 months respectively. Selected scales are shown in Fig. 2

3.6. Comparing QoL evolution after lobectomy and pneumonectomy

Comparing both resections, significant differences in evolution of physical functioning (6MPO $p = 0.045$), role

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Fig. 1. QoL evolution after lobectomy: preoperatively, 1, 3, 6 and 12 months postoperatively (MPO). $p$ value $<0.05$ indicates significance between the baseline value and the value after 1, 3, 6 and 12 months. No significance indicates return to baseline values.
functioning (3MPO p = 0.035), social functioning (6MPO p = 0.006, 12MPO p = 0.001) and general pain (6MPO p = 0.037) were reported in favor of lobectomy. The evolution of postoperative coughing is more favorable after pneumonectomy (1MPO p = 0.049, 3MPO p = 0.012, 12MPO p = 0.022)

3.7. Influence of comorbidity grade on the postoperative QoL

With the exception of a significant correlation between the comorbidity index and postoperative dyspnea (p = 0.041) and fatigue (p = 0.034) at 3 months, no other correlations were seen.

4. Discussion

Surgical resection remains the primary modality for the treatment of early stage lung cancer. The final aim is to obtain a complete resection, also after neoadjuvant or induction therapy. Definite indications for surgery include clinical stages I, II and resectable IIIA. Accurate peroperative or surgical staging is necessary, regarding the tumour as well as nodal factor, to determine the extent of resection [10]. Quality of life issues are becoming increasingly important, especially in relation to age and extent of resection. As a result of increasing life expectancy and a stable incidence of lung cancer, more elderly patients present with potentially resectable lung malignancy. The purpose of the present study is to measure the intermediate to long-term QoL evolution in elderly patients undergoing lung cancer surgery and evaluate the influence of comorbidity grade on the postoperative QoL.

Comorbidity in general has been considered to be an important prognostic factor in patients operated for lung cancer [9]. In this series of patients, the 88.4% prevalence of comorbidity is comparable with the comorbidity rate reported in other series of lung cancer in septuagenarians [9]. Birim et al. reported that the CCI was a valid predictor for major complications after lung cancer surgery [9]. In the present study, there was no significant correlation between the CCI grade and the immediate postoperative QoL, with the exception of dyspnea (p = 0.041) and fatigue (p = 0.034) at 3 months. The reported frequencies of postoperative complications are comparable with previous studies concerning this subject [11–12]. Histologic examination revealed that both adenocarcinoma (46.6%) and squamous cell carcinoma (48.3%) were seen in this septuagenarian population. The incidence of adenocarcinoma is significantly lower compared to a previously published younger population where incidences of 67.6% were seen [13]. This trend was also reported in other studies [14,15].

Although clinical research focuses on how to better identify the patient most likely to benefit from surgery in terms of survival, patients and caregivers also need information concerning the potential QoL outcomes after surgery. Despite the increasing focus of patients QoL assessment, there is no consensus about the definition of QoL and how it should be measured, although plenty of tools are available. Several instruments for the assessment of QoL have been validated, but none has been calibrated to the distinctive problems of elderly people [16]. Since survival benefits may decline and the risks of treatment progressively increase with age, preservation and improvement of QoL, should be one of the major goals of geriatric oncology [16]. A number of cohort studies with a younger population, has described a substantial decrease in physical functioning and an increase in symptoms after surgery [17–20]. In most publications a return to preoperative QoL levels is seen between 6 and 9 months [17,19]. Recent reports described the evolution of exercise capacity after different lung resections. Lobectomy patients experienced little or no persisting reductions in exercise capacity after surgery. Pneumonectomy patients had reductions of 16–30% [21–23]. The literature comparing QoL after pneumonectomy to lobectomy is scarce. Zieren et al. found more pronounced breathlessness on effort after pneumonectomy than after parenchyma sparing surgery such as lobectomy. Patients who underwent pneumonectomy had significantly lower physical

Fig. 2. QoL after pneumonectomy: preoperatively, 1, 3, 6 and 12 months postoperatively (MPO). ’p value < 0.05 indicates significance between the baseline value and the value after 1, 3, 6 and 12 months. No significance indicates return to baseline values.
functioning and more emotional complaints [20]. When compared to the preoperative assessment, QoL had deteriorated on discharge from hospital but was restored within 3—6 months after pneumonectomy. In a retrospective study by Myrdal et al., pneumonectomy patients had significantly lower physical capacity and more emotional problems. Decreased lung function after surgery was likely to contribute to both impairments [24]. However, some authors did not consider the type of surgery as predictive of lower QoL [18].

In this study, both resections were comparable in patient characteristics and baseline QoL, with the exception of a higher percentage of stage I tumors in the lobectomy group and a significantly higher percentage of coughing (p = 0.015) in the pneumonectomy group. During the 12 months follow-up after lobectomy, patients reported a lasting decline in physical functioning and a persistent burden of dyspnea. After lobectomy, quality of life, symptom and pain scores approximated baseline values 3—6 month after surgery. In contrast, pneumonectomy had a significant impact on physical and role functioning. In the 12 months follow-up period, there is no return to baseline in physical, role and social functioning. Most quality of life scores returned to baseline at 1-month follow-up, with the exception of dyspnea and general pain, which returned to baseline at 3 and 6 months respectively. Comparing both resections in QoL evolution, significant differences in physical functioning, role functioning, social functioning and general pain were reported in favor of the lesser resection. These results are in accordance with previous QoL studies in younger patients [20,24].

There is general agreement that surgical intervention should be the choice of treatment for elderly patients with bronchogenic carcinoma, provided that the indication is appropriate and that the selection of patients is adequate [1]. In recent studies the long-term survival of septuagenarian patients has been shown to be comparable to that of younger patients [1,2]. Nevertheless, the probabilities of long-term disease free survival ought to be weighed against the risks of a surgical treatment in elderly patients. The British Thoracic Society noted that pneumonectomy is associated with a higher mortality risk in the elderly and that age should be factor in deciding suitability for pneumonectomy [25]. Considering the poorer survival and the impaired QoL evolution compared to lobectomy, elderly patients should be considered for pneumonectomy very cautiously and carefully.

The present study has several limitations. A valid and reliable measurement of QoL is of utmost importance. In the present study, QoL was assessed by the QLQ-C30 and LC-13. The reliability and validity of the EORTC questionnaires have been confirmed in stage III and IV lung cancer patients only [4,6]. It is unknown whether these standardized questionnaires are also applicable to patients who undergo thoracic surgery. In the present study, 23% of data were missing at one-year follow-up in both groups. This could introduce a certain bias. The results of the present study need to be interpreted with caution because of the rather limited number of patients included in the study. Larger multi-center prospective studies comparing both resections need to be planned. In addition, the patients were not randomized between the two treatment groups.

This prospective study represents a first step in documenting intermediate- to long-term QoL evolution in elderly patients undergoing lung cancer surgery. The results are not intended to influence the choice of resection technique, which depends mostly on the specific presentation. Despite the mentioned limitations, the findings of the study offer valuable information in understanding the evolution in QoL in septuagenarians and in that way may create realistic postoperative objectives for patients.

In conclusion, the present pilot study prospectively documents quality of life evolution profiles comparing preoperative status with deficits and changes at 1, 3, 6 and 12 months after lobectomy and pneumonectomy. After lobectomy, QoL scores returned to baseline 3—6 months after surgery, with the exception of a persistent decrease in physical functioning and an increase in dyspnea within the 12 months follow-up. In the 12 months follow-up period after pneumonectomy, there was no return to baseline in physical, role and social functioning. Most quality of life scores returned to baseline at 1-month follow-up, with the exception of dyspnea and thoracic pain, which returned to baseline at 6 and 3 months respectively. Comparing both resections, significant differences in evolution of physical functioning, role functioning, social functioning and general pain were reported in favor of lobectomy.

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References


Appendix A. Conference discussion

Dr E. Black (Nottingham, United Kingdom): I’m a little confused about the outcome on the pneumonectomy side. You said there was no return to role functioning?

Dr Balduyck: Yes.

Dr Black: I’m not sure what that means, and there was one other point that didn’t return, and yet the quality of life showed that they did feel the same after 1 month.

Dr Balduyck: Yes.

Dr Black: Is this a problem with the quality of life method that you’ve used as opposed to, say, many of the others that are available?

Dr Balduyck: Yes.

Dr Black: My second question about that is, why did you choose this particular scoring system? I was interested in this myself and I haven’t really made a decision on which method to use.

Dr Balduyck: Concerning your first question. The content areas covered by the questionnaire reflect the multi-dimensionality of the quality of life construct. Role functioning and general quality of life are two separate items in the questionnaire. Role functioning asks if the patients are limited in doing either their work or other daily activities. The quality of life item isn’t a synthesis of the other items, but an item in itself. It asks how the patient would rate his overall quality of life and health during the past week.

Concerning your second question: the choice of an appropriate quality of life instrument is defined by several conditions that have to be fulfilled, the questionnaire has to be validated, accepted by elderly patients and the time to complete the questionnaire has to be acceptable. The reliability and validity of the EORTC questionnaires have been confirmed in stage III and IV lung cancer patients only. It is unknown whether these standardized questionnaires are also applicable to septuagenarians who undergo thoracic surgery. Elderly patients can cope with the questionnaire if the scoring system is explained to them. As the questionnaire contains only 43 questions, the majority of the patients complete the questionnaire within 10–15 min.