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European Journal of Cardio-thoracic Surgery 27 (2005) 675–679

EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY

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A case-matched study of anatomical segmentectomy versus lobectomy for stage I lung cancer in high-risk patients☆

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Received 1 September 2004; received in revised form 30 December 2004; accepted 3 January 2005

Abstract

Objective: Sublobar resections may offer a method of increasing resection rates in patients with lung cancer and poor lung function, but are thought to increase recurrence and therefore compromise survival for stage I non-small cell lung cancer (NSCLC). To test this hypothesis we have compared the long-term outcome from lobectomy and anatomical segmentectomy in high-risk cases as defined by predicted postoperative FEV_1 ($ppoFEV_1$) less than 40%. **Methods**: Over a 7-year period 55 patients (27% of all resections for stage I NSCLC) with $ppoFEV_1 < 40\%$ underwent resection of stage I NSCLC. The 17 patients who underwent anatomical segmentectomy were individually matched to 17 patients operated by lobectomy on the bases of gender, age, use of VATS, tumour location and respiratory function. We compared their perioperative course, tumour recurrence and survival. **Results**: There were no significant differences in hospital mortality (one case in each group), complications or hospital stay. Overall 5-year survival was 69%. There were no differences in recurrence rates (18% in both groups) or survival (64% after lobectomy and 70% after segmentectomy). There was preservation of pulmonary function after segmentectomy (median gain of 12%) compared to lobectomy (median loss of 12%) ($P = 0.02$). **Conclusions**: Anatomical segmentectomy allowed for surgical resection in patients with stage I NSCLC and impaired respiratory reserve without compromising oncological results but with preservation in respiratory function.

Keywords: Lung resection; Outcomes; Thoracic surgery

1. Introduction

Anatomical lobectomy is the procedure of choice in stage I NSCLC [1]. Available data and guidelines for operability in the management of these patients state that patients with a predicted postoperative FEV_1 ($ppoFEV_1$) of less than 40% of predicted are at risk of complications if surgical resection is undertaken [2,3]. This group of patients with significant impairment of respiratory reserve may benefit of a limited resection [3–5]. Non-anatomical sublobar resections have been associated with an increase rate of local recurrence [1]. However, anatomical segmentectomies have been employed in high-risk cases and reported as case-control studies with similar results as lobectomy [6,7]. We have used anatomical segmentectomy with systematic nodal dissection as part of our commitment to provide the option of surgery in patients not fit for traditional lobectomy. We report a case-matched comparison between segmentectomy and lobectomy in high-risk cases ($ppoFEV_1 < 40\%$).

2. Methods

2.1. Design of the study

Over a 7-year period (April 1997–April 2004) 203 resections for stage I NSCLC were performed in a single-surgeon practice. A calculation of the predicted postoperative FEV_1 ($ppoFEV_1$) according to the number of segments to be removed [8] identified that 55 of these patients (27%) had a $ppoFEV_1$ of less than 40%. The 17 patients who underwent anatomical segmentectomy were individually matched to 17 patients operated by standard lobectomy on the bases of gender, age, use of Video Assisted Thoracic Surgery (VATS), tumour size and location, and $ppoFEV_1$. We compared their perioperative course, tumour recurrence and survival.

2.2. Operative technique

With the patient under general anaesthesia and double lumen endotracheal intubation and a thoracic epidural catheter the affected lung is deflated. The segmentectomy is performed with division of the segmental bronchi and vessels of the areas affected. The parenchymal excision is taken distal to the intersegmental fissures and normally performed with the use of staplers. When tumours were close to intersegmental fissures then a bi- or

☆ Presented at the joint 18th Annual Meeting of the European Association for Cardio-thoracic Surgery and the 12th Annual Meeting of the European Society of Thoracic Surgeons, Leipzig, Germany, September 12–15, 2004.

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doi:10.1016/j.ejcts.2005.01.006

tri-segmentectomy is performed to ensure complete excision with wide margins. A systematic nodal dissection is performed in all pulmonary resections (Naruke stations 2, 4, 7, 8, 9 and 10 in right sided resections and stations 5, 6, 7, 8, 9, and 10 in left sided ones). When VATS techniques were applied, the procedures were identical as when thoracotomy was used (individual division of vessels and bronchus, incorporating the intersegmental plane in the resected specimen) and a specimen retrieval bag was used.

Following the resection a single intercostal drain is inserted and connected to an underwater seal system. The endotracheal tube is removed at the end of the procedure and the patients are transferred to the High Dependency Unit in the Thoracic Ward. Early ambulation and physiotherapy are encouraged during the postoperative period and aided by the routine use of flutter-valve drain systems.

2.3. Statistical analysis

The data is presented as median (range) and number (%) unless stated. Univariate analysis was performed using the χ^2 test for qualitative and Wilcoxon rank test for paired quantitative data. Postoperative survival was plotted according to the Kaplan–Meier method and any difference in survival between the groups was evaluated with the Log-Rank test. Statistical significance was defined by P values <0.05 throughout the study.

3. Results

3.1. Preoperative characteristics

The median age of the 22 male and 12 female was 70 (range 55–83) years. The mean FEV_1 was 43.7% (range 19–54) of predicted, with a mean ppoFEV1 of 32.6% (14–40%). The preoperative characteristics and operative details of the two groups were very similar as a result of the matching process (Table 1). All patients had undergone preoperative staging CT scan, but we did not routinely performed mediastinoscopy or PET scan in patients with radiological stage I lung cancer.

The distribution of the tumours was as follows: 6 in the left upper lobe, 5 in the left lower lobe and 6 in the right lower lobe in each group (Table 2). Four resections in each group (23.5%) were performed using VATS. Histology revealed adenocarcinoma in 10 cases (59%), squamous cell carcinoma in 6 (35%) and large cell carcinoma in 1 (5.8%) case in each group. Microscopic analysis confirmed complete excision of tumour (R0) in all cases. Seven patients in the segmentectomy and 6 in the lobectomy group had a pathological stage Ia while 10 and 11 had stage Ib, respectively. Complete follow-up was obtained in all patients and there were no patients in the study that received neo-adjuvant or postoperative treatment.

Table 1
Preoperative characteristics between the two groups: lobectomy and segmentectomy

	Lobectomy	Segmentectomy	P
Male:female	11:6	11:6	NS
Age (years)	69 (61–82)	70 (55–83)	NS
FEV_1	1.1 (0.80 1.7) l	1.0 (0.4-2.1) l	NS
$FEV_{1\%}$	44 (30–54) %	45 (19–54) %	NS
$PpoFEV_{1\%}$	35 (22–40) %	35 (14–40) %	NS
Body mass index	23 (18–30)	24 (18–33)	NS
VATS resection	4 (24%)	4 (24%)	NS
Tumour size	3.4 (1.5–4.3) cm	3.2 (1.4–4.1) cm	NS

Expressed as median (range) or number (%).

Table 2
Operative procedures performed in each group

	Lobectomy		Segmentectomy	
	Procedure	Number	Procedure	Number
Left upper lobe	Left upper lobectomy	6	Segments 4–5	3
			Segments 1–3	2
			Segments 1–2	1
Left lower lobe	Left lower lobectomy	5	Segment 6	4
			Segments 7–10	1
Right lower lobe	Right lower lobectomy	6	Segment 6	5
			Segments 7–10	1

3.2. Postoperative course

There was one postoperative death in each group (5.8%). The first death was of a 61-year old female with a $ppoFEV_1$ of 38% who died of acute renal failure 5 days after a right lower lobectomy. The second death was of an 83-year old male with a left lower lobe tumour and bullous emphysema in his left upper lobe with a $ppoFEV_1$ of 29% predicted who after an initial satisfactory recovery following a left apicolower segmentectomy combined with bullectomy of left upper lobe died of bronchopneumonia 8 days later. Complications (Table 3) were recorded in three more patients in each group (18%). The median length of intercostal drainage and hospital stay were 4 (1–30) and 6.5 (3–31) days, respectively. There were no significant differences between the two groups (Table 4).

3.3. Survival

Twenty-six patients (76.5%) were alive at the time of the study. With a median follow-up of 42 (range 2–83) months, the overall 5-year survival was 69.7 ($\pm$10) %. There were no significant differences in survival (Fig. 1), disease-free survival, or loco-regional recurrences between the two groups (Table 5).

3.4. Postoperative spirometry

Follow-up spirometry at a median of 4 (range 3–6) months after surgery was available in 11 patients of the segmentectomy group and 12 of the lobectomy group.

Table 3
Postoperative complications recorded in both groups (three patients in each group)

	Lobectomy	Segmentectomy
Pneumonia	2	1
Empyema	1	
Wound infection		1
Atrial fibrillation	1	1
Air leak	1	2

Table 4
Postoperative results

	Lobectomy	Segmentectomy	P
Hospital mortality	1 (5.9%)	1 (5.9%)	NS
Complications	3 (18%)	3 (18%)	NS
Hospital stay	6 (3-30) days	8 (4-31) days	NS
Drainage time	4 (2-13) days	3 (1-30) days	NS

Expressed as median (range) or number (%).

Table 5
Long-term results

	Lobectomy	Segmentectomy	P
Total recurrence	3 (18%)	3 (18%)	NS
Loco-regional recurrence	2 (12%)	0	NS
Actuarial 3-year survival	69%	94%	NS
Actuarial 5-year survival	64%	70%	NS

Expressed as median (range) or number (%).

While the median loss of FEV_1 after lobectomy was 12% (range 19-7%), there was an overall improvement of FEV_1 after segmentectomy [median of 12% (range from loss of 22% to gain of 47%)] ($P=0.02$).

4. Discussion

The rationale of performing sublobar resections for early stage NSCLC is based in the principle that surgery only aims to control local disease and that can be achieved with limited removal of lung parenchyma [6,9]. The same arguments that led to the replacement of pneumonectomy by lobectomy as the gold standard operation for early lung cancer (similar survival can be obtained with a less extensive resection) could be applied to sublobar procedures [10].

Jensik and colleagues [11] described the role of anatomical segmentectomy as the procedure of choice in patients with early NSCLC in a group of 69 patients achieving a 56% 5-year survival. The same group reported later on a 53% 5-year survival on 168 patients who underwent segmentectomy for stage I NSCLC [12]. Other authors have followed on their reports with variable results [13,14]. The best evidence available is currently the prospective randomized trial performed by the Lung Cancer Study Group [1]. It resulted of a significant increase in the rate of locoregional recurrence when non-anatomical wedge resections were performed instead of lobectomy. However, there were no significant differences between lobectomy and anatomical segmentectomy. In addition, there were no differences in survival between lobectomy and limited resections. The results confirmed other reports in that the oncological results with the use of wedge resection in patients with primary lung cancer were compromised, but not with anatomical segmentectomy [15-18].

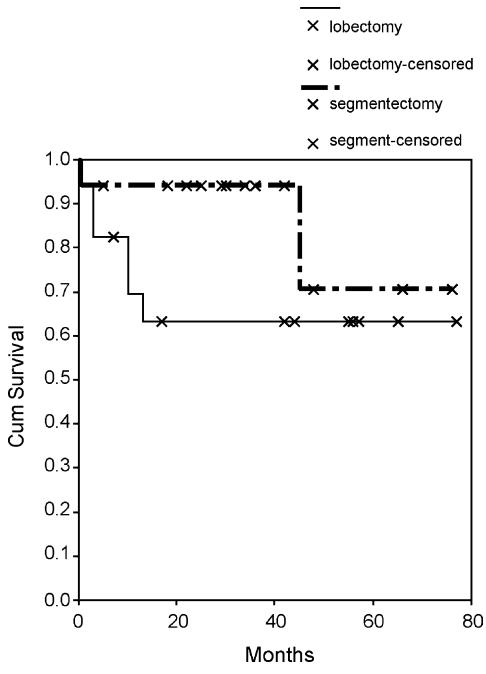

Fig. 1. Comparison of the actuarial survival in the two groups. Log-Rank $P=0.14$.

The use of segmentectomies has also been reported in the context of patients with compromised respiratory function, although the reports are mainly single series or case control studies with no randomization [19]. We were only able to find a comparison between individually matched cases undergoing lobectomy or segmentectomy for stage I NSCLC with similar 5-year survival between the groups in a report with similar methodology to our manuscript [20].

Our results in term of pulmonary function preservation after segmentectomy in relation to lobectomy in patients with stage I NSCLC coincide with a recent report [16]. In addition, the authors reported 4-year survival rates comparable with our results (62 and 67% after segmentectomy and lobectomy, respectively). The authors recommended the use of anatomical segmentectomy whenever anatomically feasible.

The loss of respiratory function after lobectomy (12%) in our report is greater than the ones reported by others [21,22]. This may be explained by the fact that there were no cases of right upper or middle lobectomy included in this study, which involve excision of less pulmonary segments.

We, like other authors, have already reported the benefit of performing lobectomy in patients with lung carcinoma within an emphysematous lobe with severely impaired respiratory function [23,24]. That experience mainly involved patients undergoing right upper lobectomy and resulted in an increased pulmonary function following surgery [25]. We therefore have not performed segmentectomies in the right upper or middle lobes.

We acknowledge are potential areas of bias in our work. It is the result of a retrospective study and in no way randomized, although being able to match individually patients in the two groups makes our manuscript more powerful than a case control-study. We were able to complete the data and the follow-up in every case but we cannot provide any information of patients not referred for surgery or those in which surgery was not performed. Also the use of other preoperative tests (although not proven to affect long-term survival) such as transfer factor measurement, exercise testing or nuclear perfusion scans were not obtained in all patients, so there are not included in our report. We unfortunately cannot comment on the quality of

life after surgery, as we do not perform health status measurements following lung cancer surgery. In addition, we do not perform routine CT scans during the follow-up period to exclude recurrences unless it is indicated by clinical examination, symptoms or new abnormalities on chest radiograph.

In summary, our results indicate that in the context of patients with severe impairment of their respiratory reserve anatomical resection of early stage NSCLC is feasible with good long-term outcomes. The oncological value of anatomical segmentectomy with systematic lymph node dissection is comparable to the one of lobectomy in these patients but with preservation of lung function. However, this conservation of lung function does not correlate with reduced morbidity or improved survival, although may equate to improved quality of life. As our efforts are targeted on increasing resection rates, we feel that anatomical segmentectomy should be considered among the alternative treatment options in this high-risk group of patients.

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Appendix A. Conference discussion

Dr W. Klepetko (*Vienna*, *Austria*): Was this a retrospective study or a prospective study?

Dr Martin-Ucar: This was a retrospective study.

Dr M. Dusmet (*London*, *UK*): Essentially you have patients with very poor function who actually are ideal patients for a lung-volume reduction procedure in terms of their type of emphysema, heterogeneity, et cetera, and have a cancer in the target zone for volume reduction, and you can do a combined lobectomy/lung-volume reduction procedure and get the benefits of both procedures in one operation. Did any of your patients fit into this category?

Dr Martin-Ucar: Yes, we are aware of that. We did publish our results in the past of especially right upper lobe tumors which underwent a lobectomy which were patients suitable for lung-volume reduction surgery. In this group of patients we were able to have perfusion data in about 90% of them, and none of these patients had heterogeneous emphysema with a target area in the lobe that was going to be resected. Most of them are lower lobes, but they don't get the benefit in the spirometry that you would expect in the lobar lung-volume reduction.

Dr A. Brutel de la Riviere (*Utrecht*, *The Netherlands*): You have spoken about segmentectomy versus lobectomy, but you haven't told us if any segmental resections had ever been converted to a lobectomy. What is your experience about conversion?

Dr Martin-Ucar: It wouldn't be figured in this retrospective series, obviously. Certainly if we weren't happy that we performed a complete excision, then we will do a lobectomy, without a doubt.

Dr Brutel de la Riviere: So you have no experience with starting a patient as a segmental resection and then being forced by, for instance, the tumor location to do a lobectomy, as I guess that would jeopardize the final result.

Dr Martin-Ucar: Oh, of course, yes. This is not a study of intention to treat. This is a retrospective study of the results.

Dr Brutel de la Riviere: Could you elaborate a bit for us on your technique of segmental resection? Is this blunt dissection, fingering out the segmental plane, or were any staple devices used?

Dr Martin-Ucar: We mainly used staples. We identified the segmental plane by the use of CPAP after the bronchus was dissected.

Dr P.L. Filosso (*Torino, Italy*): We recently reviewed our series of Stage I lung cancer and we observed the same results you present. From the oncological point of view, we noticed that there is not statistical significant difference between lobectomy and segmental or wedge resection. In our clinical experience, these limited surgical procedures are addressed to high-risk patients, only.

Otherwise we observed that the most important factors influencing prognosis are: (a) the presence of visceral pleural invasion; (b) the tumour size and (c) its histology. Did you observe the same results?

Dr Martin-Ucar: Yes, I agree with you. However, the type of tumor was similar in the two groups because of the matching system.

Dr H-B. Ris (*Lausanne, Switzerland*): Can you explain the difference in your results as compared to those published by the prospective Lung Cancer Study Group Trial? Is it a problem of patient selection, and, if so, what was the difference between your results and those reported by the lung cancer trial?

Dr Martin-Ucar: The lung cancer trial, the implications in terms of local resection and maybe survival were mainly due to the worse results in the wedge resection, in the nonanatomical sublobar resections. They did not find a statistical significance between anatomical segmentectomies and lobectomies, although obviously that paper is open to many discussions because of the methodology. Theirs was a randomized study, obviously, and this is probably the second best thing. We haven't suggested a randomized trial before because we didn't have any data of our own to support that, but I think a new one is warranted.

Dr Ris: But have you done some reflection as to why you have a difference as compared to these reported results?

Dr Martin-Ucar: I don't think there was a difference between the segmentectomy group in their trial and ours.

Dr W. Klepetko: I think the message you give us is that oncologically the segmentectomy is equal to the results of lobectomy. However, there is another message in your paper as well. If you look at it from the functional point of view, you could turn it over and say lobectomy in those patients who have pronounced hyperinflation has the same functional result as segmentectomy. And, in addition, I think we have to question the oncological result that you are presenting to us because the number of cases that you have been introducing in this study does not allow you to draw any meaningful statistical conclusions.

So my very last question is, how did you calculate the estimated difference between the two groups and what was the number of patients you calculated to meet the statistical significance?

Dr Martin-Ucar: That's the number of patients that we have available. Let's put it that way. We didn't have any power statistics performed. It is having this control group of the lobectomies, of the 38 lobectomies of the high-risk group/stage I lung cancer that allows us to do a matching process. So the answer is I don't know what the power statistics will be. I do agree with you, however, that certainly a lobectomy seems to be a good operation even in the high-risk cases. I don't have a problem with that. We fully support that.