Can pneumonectomy for non-small cell lung cancer be avoided? 
An audit of parenchymal sparing lung surgery

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Abstract

Background: Lung cancer resection rates are suboptimal in the UK. Pneumonectomy has a higher perioperative mortality risk than lobectomy. To increase resection rates and improve outcomes we have implemented a policy of parenchymal sparing surgery for tumours involving a main stem bronchus. Methods: In a prospective 4 year study of 119 consecutive patients operated upon by a single surgeon the perioperative course, pathology and survival were compared for 81 patients undergoing pneumonectomy and 38 patients in whom pneumonectomy was avoided by bronchoplastic angioplastic procedures. Results: The rate of pneumonectomy decreased significantly with increasing experience with parenchymal sparing surgery ($R^2 = 0.98$, $P < 0.001$) with 21 of the last 30 patients (70%) avoiding pneumonectomy. There were no significant inter-group differences in patient characteristics, perioperative course or outcome. One-year survival was 64% after pneumonectomy and 73% after sleeve lobectomy. However the perioperative loss of respiratory function was significantly lower in the patients in whom pneumonectomy was avoided ($P = 0.0003$). Conclusions: Pneumonectomy can be avoided in a large proportion of patients with non-small cell lung cancer of a main stem bronchus without adversely affecting outcome but with preservation of lung function.

Keywords: Sleeve resection; Bronchoplasty; Non-small cell lung cancer

1. Introduction

Bronchoplastic resections have been widely employed for decades and it has been stated that sleeve lobectomy should be the procedure of choice for anatomically suited non-small cell lung cancer (NSCLC) and in cases of compromised respiratory function [1]. The complication rates and mortality of sleeve lobectomy are similar to those in pneumonectomy [2,3]. The long-term survival is at least similar [4,5], and it has been demonstrated that the preserved lung parenchyma contributes to the overall respiratory function [5,6] thus decreasing the perioperative loss of respiratory function.

Avoidance of pneumonectomy can be achieved in large proportion of cases with rates of sleeve lobectomy:pneumonectomy of up to 2:1 in some series without compromising outcome or survival [7]. However when the practice in the UK is analysed, the lack of enthusiasm for these procedures is patent. Over the last 10 years there has been no change in the number of bronchoplastic lobectomies (less than 2% of total procedures) and pneumonectomies are performed up to ten times more frequently [8].

We have implemented a policy of parenchymal sparing surgery for NSCLC in patients not resectable by standard lobectomy and we have analysed the results of our experience.

2. Methods

2.1. Patients/methods

Between 1997 and 2001, 459 patients were operated upon by a single surgeon for NSCLC. Of them, 119 patients: 90 male and 29 female, median age 63 (range 35–84) years were not resectable by standard lobectomy due to involvement of the main stem bronchus by either the primary tumour or hilar lymphadenopathy. In an attempt to improve clinical practice and resection rates with preservation of lung parenchyma the surgeon electively started to perform bronchoplastic lung resections for NSCLC. A total of 38 patients (32%) underwent broncho±angioplastic lobect-
omn. The perioperative course, histopathological characteristics, and follow-up data of these patients have been compared with the 81 patients (68%) who underwent pneumonectomy. The data was collected prospectively.

Operations performed for carcinoid tumours or non-malignant disease were excluded from this study.

2.2. Operative technique

All the operations were carried out under general anaesthesia, with a double lumen endotracheal tube to isolate the operated side, and through a posterolateral thoracotomy. A thoracic epidural infusion of bupivacaine and fentanyl was used for postoperative analgesia. The bronchial anastomosis was performed using interrupted 3/0 absorbable polyfilament sutures. Pericardial release maneuvers or bronchial anastomosis reinforcement were not routinely performed. Mediastinal lymphadenectomy of stations 2, 4, 6 and 7 was performed in all cases. Prior to closure of thoracotomy the stump/anastomosis was checked with inflation pressures of 40 cm H₂O. A single intercostal drain was used. Postoperative fiberoptic bronchoscopy was not used to assess the anastomosis. Patients were extubated routinely in the operating room and transferred to the recovery area.

2.3. Statistical analysis

Postoperative survival was plotted according to the Kaplan–Meier method and differences in survival between life tables were evaluated with the Log Rank test. Qualitative data was compared between the two groups with the Chi-square test and differences between means were analysed with the Student’s t-test. The cumulative number of procedures performed was plotted and the correlation coefficient ($R^2$) was calculated for the best curve fit. Statistical significance was defined by $P$ values of less than 0.05.

3. Results

3.1. Preoperative characteristics

Demographic characteristics of both groups were similar. In the sleeve lobectomy group the proportion of patients with impaired respiratory reserve as stated by a preoperative FEV₁ of less than 70% of predicted was greater than in the pneumonectomy group (Table 1).

3.2. Operative details

Of the 81 pneumonectomies (28 right and 53 left sided), extended resection was required in 24 cases (30%). These include superior vena cava reconstruction in one case, en-bloc chest wall resection in three cases, and excision of pericardium in 20.

Indication for sleeve lobectomy was the involvement of the main stem bronchus by the primary tumour in 23 cases (60%) and by secondary hilar nodal disease in 15 (40%). In all cases sleeve resection was chosen electively, however in nine cases patients had been preoperatively deemed unfit for a pneumonectomy due to predicted postoperative FEV₁ of less than 40% of predicted. In another case a patient had undergone 1 year previously a video assisted contralateral lobectomy for a lung cancer of different cell type. The procedures carried out by bronchoplasty were: 28 upper lobectomy, six lower lobectomy and four bilobectomy. Pulmonary artery angioplasty (double sleeve) was required in six (16%) cases due to involvement by nodal disease, and additional en-bloc chest wall resection was performed in two cases. Operations are listed in Table 2.

3.3. Early outcome

Postoperative hospital mortality or 30-day mortality was similar in two groups. Eight of 81 (9.9%) patients died after pneumonectomy and four of 38 (10.5%) after sleeve lobectomy. The main causes of postoperative death were bronchopneumonia (seven cases), myocardial infarction (three cases), and pulmonary embolism (two cases).

We encountered two cases (2.4%) of bronchopleural fistula in patients undergoing pneumonectomy, and two late anastomotic complications after sleeve lobectomy (5%). These were the development of a bronchovascular fistula 2 months after bronchoplastic lobectomy secondary to ischaemic necrosis of the bronchus that resulted in the patient’s death, and one case of benign anastomotic stricture treated subsequently by bronchial stenting. The median postoperative hospital stay in both groups was 7 days. Since routinely admitting postoperative patients to a Thoracic High Dependency Unit 23% (14 of 61) of patients have been transferred to the Intensive Care Unit (ICU) after pneu-

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monectomy and 15.7% (six of 38) after sleeve resection with a median stay in ICU of 1 day in both groups (non-
significant).

3.4. Cumulative trends

The rate of pneumonectomy decreased with increase experience of bronchoplastic procedures ($R^2 = 0.98$, $P < 0.001$) (Fig. 1). Of the last 30 cases only nine required pneumonectomy (30%).

3.5. Histopathology

Squamous cell carcinoma accounted for 76% of the total cases and was similar in the two groups. Other cell types included Adenocarcinoma (12%) and undifferentiated types of NSCLC (12%). Complete local excision as defined by clear margins microscopically ($R_0$) was achieved in over 87% of cases in both groups (71 pneumonectomies and 34 sleeves). By stage, the distribution of patients undergoing pneumonectomy and sleeve resection was: Stage I 13 and 25%; Stage II 39 and 43%; Stage IIIa 32 and 28%; Stage IIIb 13 and 3%; and Stage IV 4 and 0%, respectively (non-significant). There were no differences in the nodal staging between the groups. $N_0$, $N_1$ and $N_2$ distribution was 25, 43 and 31% in the sleeve lobectomy group and 19, 54 and 27% in the pneumonectomy group.

3.6. Perioperative loss of lung volumes

Spirometry was performed 3 months after surgery on the most recent 20 consecutive patients undergoing sleeve resection. The perioperative change in spirometric variables was compared with the measurements on the most recent 14 patients who underwent pneumonectomy. The mean perioperative loss of FEV$1$ was 170 (range 0–500) ml in the sleeve lobectomy group and 620 (range 200–1400) ml after pneumonectomy ($P = 0.0003$). Similar significant differences were found in the FVC. The deterioration of

the pulmonary reserve was equivalent to a loss of 9% of the preoperative volumes after sleeve resection and 30% after pneumonectomy ($P = 0.0003$) (Fig. 2).

3.7. Survival

The Kaplan–Meier method was used to calculate the overall survival (Fig. 3). With a median follow-up of 31 months in the pneumonectomy group and 13 months in the sleeve resection group, the type of procedure performed did not significantly influence survival ($P = 0.6$). A total of 38 (47%) pneumonectomy and 28 (73%) sleeve lobectomy patients were alive at the time of analysis. One-year survivals were 64% (±5%) after pneumonectomy and 73% (±8%) after sleeve lobectomy.

4. Discussion

Our report shows that a policy of pneumonectomy avoidance and lung parenchyma preservation in NSCLC can be
implemented without compromising early outcome. Our experience includes cases in which the main stem bronchus was involved by either the primary tumour or metastatic nodal disease, and to date we have not seen any differences in early outcome between these two groups. Although the majority of the procedures involved an upper lobectomy, we have performed also bronchoplastic resections of the lower lobes in the same manner as others [1].

As in our case, most of the experiences reported in the use of bronchoplastic resections have reached similar results than their equivalent pneumonectomy [1,4,7] or even lobectomy control groups [5,7].

Once committed to implement a policy of surgical lung preservation using sleeve resections for NSCLC, there are two main areas of concern: (1) avoidance of anastomotic complications; and (2) obtaining complete local excision. The risk of anastomotic complications such as dehiscence or early stenosis has been reported to be of up to 7% after sleeve lobectomy [2] although the incidence of bronchovascular fistula is now rare and anastomotic stenosis rarely requires reoperation. We encountered two anastomotic problems in our experience: a bronchovascular fistula and a benign bronchial anastomotic stricture. The use of interrupted absorbable suture material for the anastomosis may reduce the incidence of strictures [1]. The case of fatal bronchovascular fistulae occurred in our series in a patient who underwent left upper sleeve lobectomy, and was the result of ischaemic necrosis. In cases in which bronchovascular sleeve is required we used a variety of interposition techniques to prevent development of fistula: azygos vein, intercostal muscle flap and pericardium. We did face bronchopleural fistula in 2.4% of pneumonectomies, which is comparable with literature reports [9].

In our experience complete local excision with clear microscopic margins was over 87% in both the sleeve resection (88.5%) and the pneumonectomy (87.5%) groups. This rate is comparable with reports in the literature that range from 81 to 93% [10–12]. The bronchial resection margin was clear in 100% of the cases undergoing bronchoplastic lobectomy. In the four cases with positive microscopic margins the vascular resection surface was the affected one. On three of these cases additional pulmonary artery angioplasty was not performed as macroscopic clearance was achieved. Perhaps this is also a reflection of a learning process in that more aggressive approach is taken on the bronchial than on the vascular excision. The good results reported by Rendina et al. [13] with the use of different techniques of pulmonary angioplasty after sleeve lobectomy: end to end, patch reconstruction, and conduit interposition with either prosthesis or pericardium suggest the effectiveness of aggressive management of cases in which pulmonary artery may be involved by metastatic nodes.

It seems clear in our experience that the preserved areas of lung parenchyma after reattachment do contribute to postoperative respiratory function, limiting the impact of pulmonary volume loss after surgery. These losses are equivalent to the deterioration of the total preoperative respiratory capacity of 9% after sleeve lobectomy and 30% after pneumonectomy. Our measurements were taken 3 months after surgery when the recovery of the respiratory function is estimated to be complete after sleeve lobectomy [6].

As experience in the use of the bronchoplastic techniques increases, the need for pneumonectomy declines. In the most recent cases we have achieved a rate of sleeve lobectomy: pneumonectomy of 2:1. We believe that it will increase even more in the future. When analysing the results to determine any possible impact of a learning curve we observed a trend of decreased postoperative mortality after bronchoplastic procedures as experience increases. Only one death has occurred within the latest 26 patients undergoing sleeve resection while the remaining three occurred within the first 12 cases.

There are potential positive implications in performing sleeve lobectomies for NSCLC. As the perioperative loss in pulmonary reserve is less than after pneumonectomy, some patients who would not tolerate pneumonectomy will still benefit of surgical resection. Severe complications that occur after pneumonectomy such as bronchopleural fistula and post-pneumonectomy pulmonary oedema (incidence of 4–5%) [14,15] are also avoided. Other possible consequences of pneumonectomy such as the cardiovascular impact of mediastinal shift [16] and right ventricular dysfunction due to raised pulmonary vascular resistance should not occur after sleeve lobectomy. Preservation of lung parenchyma also permits for patients who will develop a second lung malignancy (reported rates between 4 and 11%) [17] to be considered for surgery again. In a similar manner patients with previous pulmonary resections can undergo lung resection again as one of the cases in our experience [3].

We understand the limitations in our study, especially the short follow-up period after sleeve lobectomy. We are to continue collecting data from the patients included in this study with interest in the incidence and pattern of recurrence and longer survival periods. The small numbers do not permit at present a deeper analysis of the results in term of differences by nodal stage or the significance of a positive microscopic resection margin, both of them been isolated as predictors of survival [10,18].

At present we have made of bronchoplastic lobectomy our procedure of choice in all the cases of central tumours in which lung parenchyma is unaffected and can be preserved. Although there is no conclusive evidence on either way, we will also continue to favor these procedures in cases with metastatic hilar nodal involvement either affecting the main bronchus or the main pulmonary artery as other authors have performed [1,5]. We are still performing pneumonectomy in cases in which lung parenchyma cannot be spared due to tumour involving all the pulmonary lobes so local clearance cannot be guaranteed with a more limited resection.
Appendix A. Discussion

Mr G. Ladas (London, UK): We do ourselves perform roughly 10% of resections for lung cancer as sleeve resections at the Royal Brompton. I was very surprised though by the very high mortality. I mean, you had a 40% mortality 1 year after the operation, which went down to 30% for sleeve resections, and I was puzzled until I saw your case mix. You operate on a lot of people with IIIa and even IIIb disease and do pneumonectomies in these patients.

So my question would be, what kind of staging do you use preoperatively, because it has been proven 30 years ago that resection alone as the primary treatment choice for N2 disease basically does not work. So how do you stage your patients, first of all?

And also can I put to you that with these results it would be advisable not to operate on these patients. Otherwise they are going to do slightly better than if they had a pneumonectomy but still very badly. And also you didn’t give us a breakdown on the cause of death in the two groups.

Mr Martin-Ucar: With respect to the staging question, we do perform a CT scan in all the patients, staging CT scan, including the liver and the adrenals, a CT scan of the brain or bone scan only when clinically indicated. On mediastinoscopy, which I am sure that is a question that you were going to ask, we perform it when the lymph nodes in the mediastinum are enlarged as per CT scanning standards, not routinely.

Mr Ladas: So can I then assume that all these N2 or IIIa, and the IIIb cases as far as nodal involvement was concerned because you didn’t give us the numbers, we didn’t see how many were N2 or N3 disease, but let’s assume that they were, they were all unsuspected N2 disease then, were they?

Mr Martin-Ucar: Yes.

Mr Ladas: Because the literature clearly shows that unsuspected N2 disease has a 5-year survival of around 25–28%. So if you end up with a 60% 1-year survival, you must be doing something very wrong.

Mr Martin-Ucar: No. I do acknowledge that the 1-year survival of 72 and 75%, that includes every patient, including the operative or in-hospital mortalities. You have seen the type of patients that we operate on. Some of them fall out of resectability or operability guidelines, however, the hospital mortality is not significantly different from the UK mortality.

Mr Ladas: You didn’t show this, and if they fall outside the resection criteria then you shouldn’t resect them.

Mr Martin-Ucar: The operability criteria.

Mr Ladas: Yes. If they are inoperable, why operate on them?

Mr Martin-Ucar: Why not?

Mr Ladas: You don’t help them. You just kill them.

Mr Martin-Ucar: No, we are not.

Mr D. Waller (Leicester, UK): Can I answer that question? The cause of mortality, as you say, a short follow-up, it is non-cancer-related mortality, and, as George points out, a lot of these patients would have fallen outside the Brompton’s resection criteria for operability. But I would have to ask him in his series of patients what is the overall mortality, including those patients who don’t receive surgery, presumably they have radiotherapy or chemotherapy, and what are his 1-year survival figures for that entire group?

Mr Ladas: Well, as you know, the mortality rates per surgeon in the UK are now submitted to the Society, and if you are interested, I will be happy to give you the numbers.

Mr Waller: You will have no data on the patients you don’t operate on.

Mr Ladas: Yes, but if I end up not operating on them it will be because they would fall in a category which has been shown by large series of patients to not benefit from surgery, and I could give you a very good example. You told us about patients with satellite nodules, Stage IIIb. I assume that these were satellite nodules in the same lobe, classified as T4 disease.

Mr Martin-Ucar: Otherwise he wouldn’t be IIIb.

Mr Ladas: Okay. Let’s assume that PET scan was not available, so you end up in a thoracotomy and you then find a satellite nodule. In my practice, if I was to find that someone has a tumour and a satellite nodule which on frozen section is shown to be really a satellite nodule, I would definitely not do a pneumonectomy. If I could do a lobectomy, obviously you have got someone with their chest open, you want to take the primary out as long as you don’t inflict unnecessary morbidity and mortality. But if you do a pneumonectomy in someone who has T4 IIIb disease, well, I wouldn’t do it, and you have to prove that you are going to help the patient by doing it.