Lung cancer surgery in the breathless patient – the benefits of avoiding the gold standard

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Abstract

Objective: Lung cancer resection in breathless patients with severe chronic obstructive pulmonary disease (COPD) remains controversial. Whilst open lobectomy remains the gold standard, alternative approaches have been described. We undertook a retrospective, observational study to compare the outcomes of a tailored strategy combining video-assisted thoracoscopic surgery (VATS) lobectomy and anatomical segmentectomy against open lobectomy in these patients. Method: Clinical outcomes were studied in 84 consecutive patients (male:female ratio was 56:28, mean age 69.0 years, median preoperative-forced expiratory volume in 1 s (FEV1) 41% with a predicted-postoperative FEV1 <40% (median 32.8% and range 14–40%) who underwent anatomical lung resection for lung cancer. The control group consisted of 35 patients who underwent open lobectomy. The study group comprised 27 patients who underwent anatomical segmentectomy, 18 who underwent VATS lobectomy and four who underwent VATS segmentectomy. Results: There were no significant inter-group differences in age (p = 0.87), gender (p = 0.49), preoperative FEV1 (p = 0.30) or cardiac co-morbidities (p = 0.78). There were more upper lobe resections in the control group (51% vs 94%, p < 0.0001). Tumour size tended to be smaller in the study group (p = 0.052). There were also more incidences of stage I cancers in the study group (90% vs 71%, p = 0.043). The median length of hospital stay was shorter in the study group (8 vs 12 days, p = 0.054). There was no significant difference in either in-hospital mortality (8% vs 14%, p = 0.48) or recurrence rate (26 vs 20%, p = 0.60). However, unadjusted survival was significantly longer in the study group (median survival 54 months vs 20 months, 5-year survival 42% vs 18%, p = 0.03). The survival benefit of this group remained significant in multivariate analyses (adjusted survival hazard ratio (HR) 2.39, 95% confidence interval (CI): 1.30–4.39, p = 0.005). A subgroup analysis on only uncomplicated stage I cancers found a similarly worse outcome in the control group (p = 0.002). After segregating surgical approach and the extent of resection, the VATS approach was identified as the critical factor conferring survival advantage to the study group (hazard ratio (HR) 2.78, 95% CI: 1.21–6.37, p = 0.016). Conclusions: Despite a tailored approach to patients with severe pulmonary dysfunction, there was still significant disparity in survival between groups. Patients who underwent open lobectomy have a worse outcome despite adjusting for confounders. This survival benefit was driven by thoracotomy avoidance through VATS resection. The use of operative techniques to reduce chest-wall dysfunction should be considered in the breathless patient.

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Keywords: Lung neoplasms; Pulmonary emphysema; Lung cancer surgery; Thoracoscopy/VATS; VATS lobectomy; Segmentectomy

1. Introduction

The best outcome for early-stage lung cancer is obtained by surgery [1–3]. Studies from patients in the 1970s undergoing lung resection have shown that those with severe chronic obstructive pulmonary disease (COPD) and airway obstruction are at highest risk of perioperative death [1]. These results have shaped many lung cancer management guidelines to date, including both the British Thoracic Society and the American College of Chest Physicians. In patients with a predicted-postoperative forced expiratory volume in 1 s (ppoFEV1) <40%, the current recommendations advise further investigations and consideration of alternative treatment beyond the ‘gold standard’ open lobectomy [1,3]. Unfortunately, epidemiological studies also revealed that lung cancer incidence is highest in COPD patients with the lowest FEV1 [4]; thus, these guidelines would potentially deny the best-available treatment to a significant proportion of patients. Thus, a modified surgical strategy, which allows lung cancer patients with severe COPD to receive the best curative treatment, would make a substantial impact on lung cancer outcomes.

The scope of lung resection has broadened over the last 20 years with new surgical approaches and resection techniques. Video-assisted thoracoscopic surgery (VATS) is now an established technique, which reduces surgical trauma with attendant benefits to postoperative recovery. Anatomical segmentectomy, on the other hand, spares functioning lung parenchyma whilst obtaining complete clearance of tumour...
2. Materials and methods

2.1. Study design

Over a 12-year period (April 1997–January 2009), 84 consecutive patients with lung cancer and severe pulmonary dysfunction as defined by a ppoFEV*1 < 40% underwent anatomical lung resection at a single institution. Together, they represent 5% of this institution’s anatomical resection for lung cancer practice. The variable ppoFEV*1 was estimated by segment counting allowing for obstructed segments [5]. Of these 84 patients, 35 patients underwent open thoracotomy and lobectomy (11 following initial thoracoscopy), 27 patients underwent open segmentectomy and 22 patients comprising 18 VATS lobectomies and four VATS segmentectomies underwent VATS anatomical resection.

The choice of approach and extent of resection was at the discretion of one of the three surgeons. In general, a lobectomy was carried out if the tumour was located within a poorly perfused, emphysematous lobe, and an anatomical segmentectomy was carried out if the tumour was located within a well-perfused lobe and adequate resection margins could be obtained. A thoracoscopic approach is employed when the tumour size, anatomy and intra-operative findings permitted, but this could only be confirmed intra-operatively.

We examined the outcome measures of recurrence and survival retrospectively in these two groups of patients: those who ultimately underwent open lobectomy (the control group) and those who underwent open segmentectomy or VATS anatomical resection (the study group). We hypothesised that the survival of patients with severe COPD undergoing the less invasive or more parenchymal-sparing operations would be no worse than those undergoing the gold standard operation of open lobectomy.

2.2. Operative techniques

A thoracic epidural catheter was placed prior to surgery for perioperative analgesia in all patients. Intubation was carried out with double-lumen endotracheal tubes for single-lung ventilation. Open lung resections were carried out through a modified serratatus anterior-sparing posterolateral thoracotomy. VATS resections were performed using two ports and a 5-cm utility incision placed anteriorly at the fourth intercostal space without rib spreading. Both lobectomies and segmentectomies were carried out with individual division of hilar vessels and bronchi.

In segmentectomy, following division of the bronchi, the lung was partially re-inflated and the fissures and intersegmental divisions were completed with the use of staplers. The parenchymal resection planes were placed just distal to the intersegmental fissures to encompass the intersegmental veins and to obtain a wider margin. A systematic mediastinal lymph node dissection was routinely performed in all cases.

2.3. Statistical analysis

Analysis was performed on the demographic, pathologic and clinical data between the control and study groups. Continuous variables are expressed as mean (± standard deviation) if normally distributed, and otherwise by the median (range). Significance of inter-group differences was evaluated by the Fisher’s exact test for categorical variables, unpaired and paired Student’s t-tests for parametric continuous variables and Mann–Whitney U-test and Wilcoxon signed-ranked test for non-parametric variables. Follow-up was quantified with the reverse Kaplan–Meier estimator.

Recurrence was considered loco-regional when within the ipsilateral lung or mediastinum, and distant if contralateral, bilateral or in the presence of distant metastases. Probability of recurrence-free and overall survival was estimated with the Kaplan–Meier technique and the significance of differences was tested with the log-rank statistic. Multivariate Cox proportional-hazards regression models were constructed to adjust for the effect of different variables on survival. In the backward selection strategy, the least significant variables were eliminated and those significant at the 0.05 level were retained.

3. Results

3.1. Patients and treatment

There were 35 patients in the control group and 49 patients in the study group. The patient characteristics are given in Table 1. They comprise 56 males and 28 females with a mean age of 69.0 (±7.9). Fifteen (18%) patients had co-existent cardiac disease. The median preoperative FEV1 was 41% (range: 18–54%) predicted and the median ppoFEV1 was 33% (range: 14–40%). There were no significant inter-group differences in age, gender, FEV1 or history of cardiac disease. Two patients in the control group received neo-adjuvant chemotherapy prior to surgery.

There were significantly more upper lobe tumours in the control group (33 (94%) vs 25 (51%), p < 0.0001). There were 40 (49%) squamous cell carcinomas, 29 (35%) adenocarcinomas and 15 (17%) other primary lung cancers, with a similar distribution between the groups (p = 0.69). Tumours in the study group tended to be smaller (30.9 mm (±12.0) vs 39.9 mm (±24.6), p = 0.052), and there were significantly more pathological stage I lung cancers in the study group (44 (90%) vs 25 (71%), p = 0.043).

All cancers in the study group were completely (R0) resected, but there were three cases of R1 and one case of R2 resection in the control group. The R1 resections consist of two cases with extensive lymphovascular invasion and one with a focus on carcinoma in situ at the resection margin. The
R2 resection was in a patient who also underwent a chest-wall resection for a tumour, which infiltrated to the spine. Two of the R1-resection patients went on to have radio-therapy, and a further two patients with N1 disease (18%), one in each group, received adjuvant chemotherapy. One of these four patients died during the study period.

The anatomical extent of resection is given in Table 1. Whilst 28 (97%) right upper lobe tumours were treated by lobectomy, only 14 (48%) left upper lobe tumours were treated by lobectomy, the rest by segmentectomy, either by lingulectomy or by upper-division segmentectomy. Fifteen (63%) of all lower lobe tumours were resected by segmentectomy. The control group included two sleeve lobectomies and two bilobectomies — one with chest-wall resection.

### 3.2. Hospital outcome

There were nine in-hospital deaths (11%): four (8%) in the study group and five (14%) in the control group ($p = 0.48$; Table 2). The causes of death were pneumonia in seven, ischaemic bowel in one and bleeding in one. Fewer patients in the study group developed either respiratory complications (11 (22%) vs 18 (48%), $p = 0.019$) or non-respiratory complications (seven (14%) vs 12 (34%), $p = 0.037$). Five patients were admitted to intensive care (two (4%) vs three (9%), $p = 0.65$). The median length of hospital stay was shorter for the study group (8 days (range 3—31) vs 12 days (range 4—91), $p = 0.054$).

### 3.3. Recurrence

After a mean follow-up time of 56 months (56.0 vs 56.4 months, $p = 0.402$), recurrence was observed in 20 (24%) patients: 13 (27%) in the study group and seven (14%) in the control group ($p = 0.606$). Of these, nine were loco-regional and 11 distant.

Whilst the incidence of distant recurrence was similar in both groups, loco-regional recurrence occurred more frequently in the study group (Fig. 1). Distant recurrence occurred in five (14%) patients in the control group and six (12%) patients in the study group ($p = 1.0$), all were within the open segmentectomy group. Loco-regional recurrence occurred in two (6%) patients in the control group and seven (14%) patients in the study group ($p = 0.29$): of the seven, four were in the open segmentectomy group and one in the VATS segmentectomy group.

Of the 20 patients with recurrence, 17 (85%) died during follow-up. Despite a higher incidence of recurrence in the...
study group, recurrence-free survival was longer, although this did not reach statistical significance (median recurrence-free survival of 33 months for the study group vs 13 months for the control group ($p = 0.073$)).

### 3.4. Survival

During the follow-up period, 46 (55%) patients died: 25 (51%) in the study group and 21 (60%) in the control group. The median survival for the entire group was 39 months (95% confidence interval (CI): 26–51 months). All patients who underwent extended resections were alive without recurrence. Overall survival was significantly longer in the study group (median survival 54 months vs 20 months; 5-year overall survival 42% vs 18%, $p = 0.030$) (Fig. 2).

The cause of death differed between the two groups. Of the 46 deaths, only 17 (37%) were cancer related, whilst 18 patients (39%) died of pneumonia and respiratory failure and the rest died of other causes. Patients in the control group were more likely to die from non-cancer-related causes (42% vs 29%, $p = 0.14$) (Fig. 3).

As there were significant differences in the characteristics of the two groups, multivariate analysis was carried out to adjust for confounders and isolate the effect of the operation group. A multivariate Cox proportional-hazards regression model was constructed with the operation group along with variables known or expected to have an effect on survival: age, gender, preoperative FEV$_1$, disease stage, tumour histology and resection margins. In a model incorporating all the pre-specified covariates, only the operation group, age, preoperative FEV$_1$ and resection margin reached significance (Table 3(a)). A parsimonious model using a backward elimination strategy similarly retained only these four variables (Table 3(b)). The adjusted hazard ratio (HR) for overall survival for the study group was 2.39 (95% CI: 1.30–4.39, $p = 0.005$).

#### Table 3

<table>
<thead>
<tr>
<th>Variables</th>
<th>HR</th>
<th>CI</th>
<th>$p$-value</th>
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<tr>
<td>Operation group</td>
<td>2.506</td>
<td>1.334–4.771</td>
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<td>Gender</td>
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<tr>
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<td>1.016–1.113</td>
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<td>0.934–0.997</td>
<td>0.031</td>
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<td>Stage I disease</td>
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<td>0.297–2.175</td>
<td>0.666</td>
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<td>0.620</td>
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<td>Histology: miscellaneous</td>
<td>0.556</td>
<td>0.217–1.424</td>
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<td>Margins</td>
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<td>1.554–115.439</td>
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<td>(b) By study group: backward elimination model</td>
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<td></td>
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<td>(c) Approach versus extent of resection</td>
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<td>VATS versus open</td>
<td>2.782</td>
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<td>Segment versus lobectomy</td>
<td>1.643</td>
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<tr>
<td>Gender</td>
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<td>Preop FEV$_1$</td>
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<td>Stage I disease</td>
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<td>(d) Subgroup of uncomplicated stage I disease only</td>
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<td>VATS versus open</td>
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<td>0.034</td>
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<tr>
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<tr>
<td>Preop FEV$_1$</td>
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<td>0.930–1.000</td>
<td>0.050</td>
</tr>
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<td>0.746</td>
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<td>Histology: miscellaneous</td>
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<td>0.603</td>
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<td>Tumour size (mm)</td>
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<td>0.975–1.029</td>
<td>0.921</td>
</tr>
</tbody>
</table>
3.5. Is the effect driven by VATS approach or by segmental resection?

When patients were regrouped by extent of resection irrespective of surgical approach (Fig. 4: all lobectomies vs all segmentectomies), there was no significant difference in overall survival \((p = 0.99)\). This led us to hypothesise that the surgical approach (open vs VATS) was responsible for the observed difference in survival.

To test this hypothesis, we constructed a Cox regression model with separate variables for the surgical approach (open vs VATS) and the extent of parenchymal resection (lobectomy vs segmentectomy). In a model incorporating all the pre-specified covariates (Table 3(c)), the VATS approach conferred a 2.8-fold adjusted survival benefit over the open approach (HR: 2.782, 95% CI: 1.215—6.371, \(p = 0.016\)), whilst segmentectomy did not confer a significant benefit on survival.

3.6. Stage I cancers

We undertook an alternative approach to reduce inter-group differences in our comparison whilst also addressing survival in a clinically more meaningful subgroup of patients — those with uncomplicated stage I cancers.

We performed a subgroup analysis selecting only those patients with stage I non-small-cell lung carcinoma, which were completely (R0) resected. Patients with extended resections or those who underwent neo-adjuvant or adjuvant therapies were excluded.

There were 20 patients in the control group and 43 patients in the study group. Overall survival was significantly longer in the study group (Fig. 5) (median survival 23 months vs 9 months, \(p = 0.002\)). In a non-parsimonious multivariate Cox regression model (Table 3(d)), the VATS approach once again conferred a significant survival benefit (HR: 2.73, 95% CI: 1.076—6.926, \(p = 0.034\)), whilst the extent of resection was again not significant.

4. Discussion

Many studies have demonstrated the feasibility of anatomical resection of lung cancer in high-risk patients using minimally invasive and parenchymal-sparing techniques. Each of these studies tended to focus on only either segmentectomy or VATS lobectomy. In this study, we investigated the effect of tailored operations in a real-life ‘all-comers’ cohort of patients with severe pulmonary dysfunction. We found a significant and over twofold survival benefit when using these techniques compared with the gold standard thoracotomy and lobectomy, and this difference appears to be attributable to the beneficial effects of a VATS approach. This effect persisted when only uncomplicated stage I lung cancer patients were compared.

In this study, there were significant differences between the two groups. First, there was more stage I disease in the study group. Two factors contribute to this disparity: (1) a surgeon may be more likely to select patients with more extensive disease for open lobectomy and (2) it is possible that VATS or segmental resection may under-stage the study group. Nevertheless, a significant survival benefit remained with the study group after adjusting for stage in both subgroup and multivariate analyses. Furthermore, if the study group were genuinely under-staged, the effect on the adjusted survival benefit would be to underestimate it, and the conclusion would continue to hold.

Another factor, which is more difficult to adjust for, is selection bias by the surgeon. It is conceivable that a surgeon would choose an open lobectomy for subjectively less fit
patients to reduce anaesthetic and operating time. The prevailing higher risk of death of these patients could contribute to the poorer observed survival in the control group.

Respiratory failure is a significant competing cause of death in our study population as reflected by the findings that 63% of deaths were not cancer related, with many due to respiratory failure. This is consistent with the other reports in similar groups of patients [6]. Both the risk of respiratory failure and cancer progression are modified by the choice of operation. An open lobectomy, whilst minimising the risk of recurrence, could have negative impact on their respiratory reserve through pain, restrictive ventilatory impairment and parenchymal loss, rendering patients less able to withstand respiratory insults, with detriment to their survival. This effect is illustrated by the control group where the recurrence rate was lower but not of a sufficient magnitude to justify the increased incidence of non-cancer-related deaths, resulting in a worse overall survival.

Our strategy of performing lobectomy for upper lobe lesions in patients with heterogeneous upper lobe-predominant emphysema derived from our encouraging experience with lung volume reduction surgery (LVRS). We showed that a similar lung volume reduction effect was achieved by lobectomy, but with a shortened postoperative course compared with conventional LVRS techniques for emphysema [7]. For upper lobe tumours, a lobectomy would achieve both oncological control and symptomatic benefit through the volume reduction effect. The feasibility of a lobar volume reduction strategy, using the open approach to yield worthwhile long-term outcomes, has been previously demonstrated [6,8]. The current study takes this further and demonstrates the feasibility of ‘VATS lobar LVRS’ for lung cancer.

Our analysis suggested that VATS lobectomy is the principal driver of survival benefit in the study group: there was no significant survival difference when patients who underwent lobectomy were compared with those who underwent segmentectomy; however, a significant survival advantage appeared when the VATS lobectomy patients were regrouped with the segmentectomy patients (the study group). VATS, however, is not always possible. Our series had a conversion rate of 11 in 33 patients (33%) due to airtrapping, extensive adhesions and incomplete fissures.

Many recent studies have shown that concerns over operative safety and oncological adequacy of VATS lobectomy are unfounded [9,10]. Indeed, several studies including a systematic review have reported superior long-term survival in lung cancer patients who underwent VATS compared with open lobectomy, consistent with our findings [11–13]. The reasons behind the improved survival may relate to the evidence that VATS lobectomy reduces postoperative pain, preserves pulmonary function and provokes a milder systemic inflammatory response than open lobectomy [14–16]. Others have invoked the hypothesis that more extensive surgery causes more immunosuppression and impairs immunosurveillance [17]. The impact of the former physiological benefits would be most pronounced in borderline and high-risk patients who are particularly vulnerable in the early postoperative period [18]. Indeed, Garzon and colleagues have demonstrated that satisfactory short-term survival outcomes can be achieved with VATS lobectomy in patients with poor lung function [19]. This patient group therefore provides a sensitive model to demonstrate the benefits of VATS lobectomy.

In addition to a less traumatic surgical approach, parenchyma sparing with an anatomical sublobar resection can be carried out to reduce debility from surgery. Pulmonary function is indeed better preserved following anatomical segmentectomy than lobectomy [20]. Furthermore, a left upper lobe upper division segmentectomy may also provide similar lung volume reduction benefits to a right upper lobectomy. One of the major concerns regarding sublobar resection is a previously reported higher incidence of locoregional recurrence [21]. Our results show that a higher incidence of recurrence does not necessarily translate into worse survival. Many studies have since shown significantly better recurrence-free and overall survival with anatomical segmentectomy compared to wedge resection [22], whilst others have shown equivalent survival outcomes to lobectomy for T1a tumours [23,24], thus reviving interest in its role in lung cancer surgery. For the high-risk patients who constitute our study, concerns about marginal difference in recurrence may be immaterial compared with the impact of significant respiratory dysfunction from an open lobectomy. A similar effect has already been noted with age, where the benefits of lobectomy over sublobar resection disappeared in patients over the age of 75 [25].

The most significant limitation of the current study is its small size and retrospective design. Prospective data on diffusion capacity and functional status would lend more strength to the comparison between the two groups. Whilst data on diffusion capacity would be interesting, they would not detract from the findings of the study. Both FEV1 and diffusion capacity are surrogate markers of respiratory function; therefore, additional data on diffusion capacity would add only limited information to the study. There are also strong interactions between FEV1 and diffusion capacity; the resulting multicollinearity would make interpretation of the models unreliable. Another limitation of this study is the lack of postoperative data on health status. If the survival of patients between the control and the study groups were similar, such quality-of-life data would be pertinent to the choice of operation.

Whilst all efforts have been made to adjust for significant confounders, one critical variable is the choice of operation, which ultimately rests on the surgeon’s judgement. Having identified the VATS approach as the key driver behind better survival, the ideal study would be a randomised controlled trial to compare the gold standard open lobectomy to VATS lobectomy in these high-risk patients. Whilst the choice of operation may be dictated by the anatomy and size of the lesion (a large tumour, for example, may only be suitable for open lobectomy), where there is clinical equipoise, such as for most stage I tumours, such a study would inform decision making.

In conclusion, we have shown that in patients with severe pulmonary dysfunction, despite a tailored approach, there was still significant disparity in survival between groups. Patients who underwent open lobectomy had a 2.4-fold higher hazard of death than patients who underwent VATS resection. The difference persisted after correction for
tumour stage. Further studies are required to fully evaluate the benefits of VATS lobectomy in this group of patients.

References


Appendix A. Conference discussion

Dr E. Lim (London, United Kingdom): I thought this was an excellent study and very informative, especially on the patients who only had VATS. I wonder what effect this would actually influence other surgeons or make any difference with our practice.

My first question is, given that there is no difference in survival in the lobectomy versus segmentectomy plot, I can only surmise that the main differences in survival was comparing VATS and open surgery, and although this was not included in the original manuscript, I’m very glad to see that my detective work proved right with your slide, which did show that in fact all the effects were the difference between VATS and open surgery and not on segmentectomy alone. If that is indeed the case, is it the mode of access that is important, that influences survival, or is it the characteristic of the tumour that influences survival? Your results suggest that the smaller peripheral tumours and the stage I tumours are the ones which undergo VATS resection, and probably that may have a stronger influence on survival rather than access itself.

Dr Lau: The mode of access is indeed important. The survival benefit presented here is adjusted for stage. Another reason why the open lobectomy group did worse is that there are patient factors independent of the operation. Whatever operation you throw at them, they do badly. These patients are a group which are relatively difficult to operate with VATS. There could also be a cost to them from conversion from VATS to open and that selects out the worst group back into the open lobectomy group. One way to look at this is by an intention-to-treat analysis to see what happens to all the VATS patients and the group back into the open lobectomy group. One way to look at this is by an intention-to-treat analysis to see what happens to all the VATS patients and the group back into the open lobectomy group. One way to look at this is by an intention-to-treat analysis to see what happens to all the VATS patients and the group back into the open lobectomy group. One way to look at this is by an intention-to-treat analysis to see what happens to all the VATS patients and the group back into the open lobectomy group.

Dr Lau: I thought this was an excellent study and very informative, especially on the patients who only had VATS. I wonder what effect this would actually influence other surgeons or make any difference with our practice.

Dr Lim: Given that this is a selection process, do you think that these results would actually influence other surgeons or make any difference with further patients? After all, the patients who only could qualify for a VATS really won’t influence how we change our practice for the future.

Dr Lau: I think so, absolutely. Whilst a lot of patients have anatomy and probably that may have a stronger influence on survival rather than access itself.

Dr Lim: So you would agree that it’s not access but it is the tumour characteristics that influences survival?

Dr Lau: I think they are both important factors but the tumour characteristics have already been adjusted for in assessing the benefits of access.

Dr Lim: Given that this is a selection process, do you think that these results would actually influence other surgeons or make any difference with further patients? After all, the patients who only could qualify for a VATS really won’t influence how we change our practice for the future.

Dr Lau: I think so, absolutely. Whilst a lot of patients have anatomy and disease which predetermines which operation they can have, these results are useful in patients who are candidates for several operations. Unfortunately many of these patients are still only being offered open lobectomy. Here we showed they would benefit from VATS.

Dr M. Dusnet (London, United Kingdom): If you believe Ferguson’s data, DLCO is what really matters, and, in fact, when he did his multivariate analysis,
FEV₁ fell out as a predictive factor for outcome. You don’t have DLCO data for these patients, so I really don’t know how to translate your data into my practice. Could you help me, please?

Dr Lau: I completely agree with you. However, this study is also useful in its own way, because even though FEV₁ drops out of a multivariate analysis, it doesn’t mean that it has no ability to discriminate between different prognostic groups to guide decision-making. FEV₁ fell out because of multicollinearity and that is a statistical artefact.

Dr Dusmet: What lesson do I take home? That’s the question. What lesson can I take home without DLCO data?

Dr Lau: I don’t think I fully understand what you mean in the absence of DLCO data you can’t draw a conclusion.

Dr Waller: We do have DLCO data, but not on all of the patients, Michael. I think the message is that we need to look at doing a trial of VATS lobectomy against open lobectomy but in the high-risk patients, and it would be easier to power that study on the basis of these results.