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At the 17th Congress of the Asian Pacific Society of Respiriology held on 14-16 December 2012 in Hong Kong, I was kindly invited to give a presentation entitled "Current Trends in Lung Cancer Surgery". Of the countless developments in Thoracic Surgery today, four trends were highlighted as being of particular interests for respirologists, oncologists and non-surgical members of any multi-disciplinary team managing lung cancer. These were:

Sublobar resection – There is growing interest amongst surgeons to consider segmentectomy or wedge resection for selected patients with lung cancer. Encouraging results are reported for patients with adenocarcinoma-in-situ or minimally invasive adenocarcinoma, and for patients otherwise unfit for lobectomy.

Minimally Invasive Surgery and Immuno-surveillance – Surgeons increasingly believe that the immune system may have a role in regulating tumor cells shed into the circulation during cancer surgery. Minimally invasive surgery may be advantageous in this regard by causing less immune-disruption.

Proceeding to surgery with no pre-operative tissue diagnosis – Surgeons are often prepared to offer minimally invasive thoracic surgery for suspected lung cancer even when a tissue diagnosis is unavailable pre-operatively. Recent results suggest this practice is safe and may reduce intervals between presentation and therapy.

Expanding candidacy for lung cancer surgery – By reducing surgical morbidity, minimally invasive surgical techniques are now allowing many lung cancer patients previously regarded as 'unfit for surgery' to be considered as potential candidates for curative resection.

In this edition of the APSR Update, I have selected a number of the most recently published papers that can reflect and illustrate the above trends.

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1. Sublobar resection

Oncologic efficacy of anatomic segmentectomy in stage IA lung cancer patients with T1a tumors

Authors: Donahue JM, *et al.*

Reference: Ann Thorac Surg 2012; 93:381–388.

URL: <http://ats.ctsnetjournals.org/cgi/content/full/93/2/381>

Comments: The Mayo Clinic presents its own series of 113 consecutive patients who underwent pulmonary segmentectomy for lung cancer. The median forced expiratory volume in 1 second was 1.53L (range: 0.5L to 3.27L), and the median diffusion capacity of lung for carbon monoxide was 69% predicted (range: 23% to 129%). Significant comorbidities were present in 62 patients (55%). This cohort clearly contains many patients who normally would not be candidates for lobectomy. Yet despite this, there was no perioperative mortality and major morbidity only occurred in 28 patients (25%). Overall 5-year survival was 79% for stage IA patients. For stage IA patients with T1a lesions, the five-year recurrence-free survival of these patients was 69% - which approximates that seen after lobectomy. This report is typical of recent publications showing that segmentectomy offers good safety and long-term survival in selected lung cancer patients.

Is limited pulmonary resection equivalent to lobectomy for surgical management of stage I non-small-cell lung cancer?

Authors: De Zoysa MK, *et al.*

Reference: Interactive CardioVascular and Thoracic Surgery 2012; 14:816–820.

URL: <http://icvts.oxfordjournals.org/content/14/6/816.full>

Comments: This recent paper attempts to answer an important clinical question: ‘A 74-year old chronic smoker with early-stage NSCLC but an FEV1 of 1.1L and diffusing capacity of 40% is not a candidate for a lobectomy, but would he benefit from a limited pulmonary resection?’ In a thorough systematic review of the literature, clinical data from 16 good quality studies on this subject were scrutinized. The evaluation suggested that limited (sublobar) resections were associated with higher cancer-related death rates, overall death rates, and locoregional recurrence rates compared to conventional lobectomy for lung cancer. However, limited resection carries a decreased rate of complications and shorter hospital stays, and survival begins to approximate that of lobectomy for tumours ≤ 2 cm in size and after adjusting for variables such as

older age and limited node sampling in patients having limited resections. The conclusion is that lobectomy remains the most reliable surgical treatment for early-stage lung cancer, but in selected patients who unable to undergo lobectomy, sublobar resection is a viable alternative.

Point/Counterpoint: are limited resections appropriate in non-small cell lung cancer? Yes/No

Authors: Donington JS and Detterbeck FC.

Reference: Chest 2012; 141:588-592.

URL: <http://chestjournal.chestpubs.org/content/141/3/588.full.html>

Comments: Two expert thoracic surgeons present eloquent and powerful arguments for and against performing sublobar resections for lung cancer in a highly interesting editorial debate. The current clinical evidence surrounding sublobar resections is very well summarized. It is made very clear that despite the recent resurgence of interest in sublobar resection, considerable controversy remains and its role in management algorithms for lung cancer has not yet been fully defined.

2. Minimally invasive surgery and immuno-surveillance

Morphological analysis of circulating tumour cells in patients undergoing surgery for non-small cell lung carcinoma using the isolation by size of epithelial tumour cell (ISET) method

Authors: Hofman V, et al.

Reference: Cytopathology 2012, 23, 30–38.

URL: <http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2303.2010.00835.x/full>

Comments: It is a frequently asked question in surgery exactly why patients with supposedly localized tumor should have distant metastases after complete curative resection. Some surgeons believe that cancer cells may be 'shed' from the primary tumor into the circulation on manipulation of the lung during surgery, sowing the seeds of future distant metastases. This paper reports a multi-center European study of 250 patients with resectable NSCLC and 59 healthy controls. In the cancer patients, malignant cells were identified in peripheral blood samples of 41% of patients, and possibly malignant cells in a further 6%. No circulating non-haematological cells – benign or malignant – were detected in the blood of healthy subjects. This study reconfirms some earlier papers reporting the phenomenon of 'shedding' from lung cancer tumors.

Recurrence dynamics for non-small-cell lung cancer: effect of surgery on the development of metastases

Authors: Demicheli R, *et al.*

Reference: J Thorac Oncol 2012; 7:723–730.

URL: http://journals.lww.com/jto/Abstract/2012/04000/Recurrence_Dynamics_for_Non_Small_Cell_Lung.13.aspx

Comments: This recent paper presents an event dynamics study using a database of 1506 patients undergoing initial surgery for NSCLC. Distinct peaks of recurrence occurred at specific times after surgery, with the pattern dominated by distant metastasis events. This result suggests a transient phase of acceleration of metastatic growth following surgical excision of the primary tumor, and at the very least demonstrates the existence of a clear temporal relationship between surgery and distant metastasis. This paper may be construed as circumstantial evidence for the concept of increased tumor cells shed into the circulation in the immediate post-operative period.

Patterns of recurrence and incidence of second primary tumors after lobectomy by means of video-assisted thoracoscopic surgery (VATS) versus thoracotomy for lung cancer

Authors: Flores RM, *et al.*

Reference: J Thorac Cardiovasc Surg 2011; 141:59-64.

URL: <http://jtcs.ctsnetjournals.org/cgi/content/full/141/1/59>

Comments: Following from the above tumor 'shedding' hypothesis, previous studies in abdominal surgery have suggested that the immune system may partly regulate whether such shed cells ultimately give rise to distant metastases. The fact that minimally invasive surgical (MIS) techniques disrupt the immune system less than open surgery has therefore led to speculation that MIS for cancer surgery may be associated with better recurrence-free survival. In this paper, 520 patients undergoing lobectomy by means of video-assisted thoracoscopic surgery (VATS) were compared with 652 underwent lobectomy by means of thoracotomy. Logistic regression demonstrated a lower risk (odds ratio, 0.65; P = 0.01) of recurrent disease in patients undergoing video-assisted thoracoscopic surgery after adjusting for age, stage, sex, histology, tumor location, and synchronous primary tumors. This appears to be predominantly secondary to a higher rate of distant recurrence in the thoracotomy group (11% vs 6%, P<.0001). More importantly, the rate of locoregional recurrence between the 2 groups was

identical. This noteworthy study corroborates the hypothesis that MIS may cause less disruption to the immuno-surveillance of circulating cancer cells in the peri-operative period.

3. Proceeding to surgery with no pre-operative tissue diagnosis

Lung cancer screening and video-assisted thoracic surgery

Authors: Petersen RH, *et al.*

Reference: J Thorac Oncol. 2012;7: 1026–1031.

URL: http://journals.lww.com/jto/Abstract/2012/06000/Lung_Cancer_Screening_and_Video_Assisted_Thoracic.11.aspx

Comments: This paper reports the results of the Danish Lung Cancer Screening Trial which randomized 4104 smokers and previous smokers to either screening with five annual low-dose CT scans or no screening. As expected, more patients were found to have lung cancer in the screening group. More importantly, 75% of the patients in the screening group had early stage, operable disease compared to only 33% in the control group. Of the patients receiving surgery, 81% in the screening group received VATS compared to only 50% in the control group. This study exemplifies the modern paradox resulting from the increased availability of imaging and screening services today. On the one hand, more patients are potentially identified with early stage, curable disease. But on the other hand, there is a resulting surge in demand for diagnostic services to investigate the incidentally found lesions. As the authors discuss, these lesions are more likely to be small and hence less accessible for conventional diagnostic procedures such as bronchoscopy or fine-needle aspiration. There is thus an increasing trend to rely on VATS for diagnosis as well as resection.

Surgical resection of highly suspicious pulmonary nodules without a tissue diagnosis

Authors: Heo EY, *et al.*

Reference: Jpn J Clin Oncol 2011; 41:1017–1022.

URL: <http://jjco.oxfordjournals.org/content/41/8/1017.full>

Comments: The point above raises the question: in the era of increasing numbers of indeterminate lung nodules being found, do we run the risk of performing excessive numbers of 'unnecessary' operations for lesions that ultimately turn out to be benign? In this study from Korea, 113 patients with pulmonary nodules suspicious for lung cancer underwent operation without prior tissue diagnosis. Benign nodules were found in 15% of patients, but it was suggested that surgery without tissue diagnosis decreased total costs, hospital stay and waiting time.

Operating on a suspicious lung mass without a preoperative tissue diagnosis: pros and cons

Authors: Sihoe ADL, *et al.*

Reference: Eur J Cardio-Thorac Surg 2013 (in press).

URL: <http://ejcts.oxfordjournals.org/content/early/recent>

Comments: This study from Hong Kong is the most recent and most thorough investigation of the impact of operating with a pre-operative tissue diagnosis. Of 443 consecutive patients receiving surgery for confirmed or suspected NSCLC, 206 (46.5%) had no diagnosis confirmed preoperatively. These included 97 (47.1%) for whom it was decided to proceed to surgery without attempts at obtaining preoperative diagnosis. After surgery, benign disease was found in only 16 (7.8%) patients without preoperative diagnosis, and none of these patients experienced mortality or significant morbidity. In return, a significantly lower proportion of patients without preoperative diagnosis experienced prolonged waiting times between presentation and being accepted for thoracic surgery. This did not result in higher rates of Stage I disease or better recurrence-free survival on survival analysis. Nonetheless, this study gives the clearest indication to date that proceeding to surgery without preoperative diagnosis in selected patients is safe and can potentially reduce the interval between presentation and surgical management. This approach may potentially help alleviate the growing burden on diagnostic services as increasing numbers of patients present with incidentally found lung nodules in future.

4. Expanding candidacy for lung cancer surgery

Improved outcomes associated with higher surgery rates for older patients with early stage non-small cell lung cancer

Authors: Gray SW, *et al.*

Reference: Cancer 2012; 118:1404–11.

URL: <http://onlinelibrary.wiley.com/doi/10.1002/cncr.26363/pdf>

Comments: In this study, the authors identified 17,638 patients aged 66 years or older who were diagnosed with stage I or II NSCLC. Geographical areas with high and low rates of curative surgery for early stage lung cancer were compared to estimate the effectiveness of surgery in older and sicker patients. It was found that higher rates of surgery for stage I/II NSCLC were associated with improved survival, even when older patients and sicker patients underwent resection. This paper offers a fine example of the ever increasing numbers of studies showing the benefits of modern surgery in patients traditionally deemed to be 'high-risk' for major lung resections. Old age alone is no longer considered a contra-indication for lung cancer surgery by most thoracic surgeons today.

Is it safe to include octogenarians at the start of a video-assisted thoracic surgery lobectomy programme?

Authors: Amer K, *et al.*

Reference: Eur J Cardio-Thorac Surg 2012; 41:346–352.

URL: <http://ejcts.oxfordjournals.org/content/41/2/346.full>

Comments: This study goes even further to explore surgery for elderly lung cancer patients by comparing outcomes of patients aged below or above 80 years. Considering only patients who received VATS for lung cancer surgery, rates of admission to the intensive care unit and of atrial fibrillation were higher in octogenarians, but there were otherwise no differences in relation to morbidity, mortality and the 3-year survival rate. This study emphasizes the contemporary belief of many thoracic surgeons that VATS so effectively reduces the morbidity of surgery that it can now be performed as safely in elderly patients as in younger patients. The effective 'reach' of curative lung cancer surgery can now be extended to patients hitherto considered 'inoperable'.

Lobectomy in octogenarians with non-small cell lung cancer: ramifications of increasing life expectancy and the benefits of minimally invasive surgery

Authors: Port JL, *et al.*

Reference: Ann Thorac Surg 2011; 92:1951–57.

URL: <http://ats.ctsnetjournals.org/cgi/content/full/92/6/1951>

Comments: This American study looked at 121 octogenarians who underwent lobectomy: 40 VATS and 81 through open thoracotomy. Compared with thoracotomy, VATS patients had fewer complications, shorter length of stay, and were less likely to require admission to the intensive care unit or rehabilitation after discharge. Survival comparisons demonstrated no significant difference between the two techniques. This paper further corroborates the view that VATS has allowed curative surgery to be more safely extended to patient previously deemed 'too old' for major lung resection. In addition, the authors argue that the life expectancy trends have significant ramifications for the evaluation and treatment of octogenarian patients. With the benefits of modern VATS meeting the challenge of patients living for longer than even before, lung cancer patients of any chronologic age should nowadays be evaluated on an individual basis in the context of a multidisciplinary approach in order to confer optimal treatment.

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