Minimally invasive segmentectomy for early stage lung cancer gains momentum

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The extent of surgical resection for peripheral clinical T1N0M0 non-small cell lung cancer (NSCLC) ≤2 cm continues to be a matter of debate. In 1995, results from 'The lung cancer study group' trial established lobectomy as the standard of care. Since then, an extensive body of literature mainly composed of retrospective studies supports the use of radical anatomical segmentectomy, certainly for older patients with limited cardiopulmonary function. In a select group of patients, segmentectomy has been shown to be oncologically equivalent to lobectomy and it offers better preservation of pulmonary function (1,2). Paralleled with advancements in various diagnostic modalities, the understanding of segmental anatomy of pulmonary arteries, veins and bronchi continues to improve. Moreover, the risk of developing metachronous, recurrent or second primary lung cancer after therapeutic lung cancer resection surgery remains significant. Hence, patients with preserved lung function are more likely to withstand further therapeutic lung cancer surgery.

In comparison with lobectomy via thoracotomy, thoracoscopic lobectomy has been associated with lower morbidity, decreased pain, shorter chest tube duration, shorter length of hospital stay, and faster return to activities of daily living. Similar advantages apply to thoracoscopic segmentectomy (3). However, segmentectomy is usually considered a more technically challenging operation than lobectomy. Segmentectomies are broadly classified into typical and atypical. Typical segmentectomies include trisegmentectomy (left S^{1-3}), lingulectomy (S^{4-5}), superior segmentectomy (S^6) and basilar segmentectomy (S^{7-10}). Atypical segmentectomies entail surgical resection of individual segments of the right and left upper, middle or lower lobes. Typical segmentectomies are technically feasible and widely adopted by minimally invasive thoracoscopic approaches, however the widespread utilization of atypical segmentectomies remains challenging and literature describing operative techniques is still limited.

Zhu and colleagues nicely describe and present a video of their experience with a single direction strategy in thoracoscopic stapler-based left S^3 segmentectomy (4). The surgical principle behind single direction strategy is based on minimizing the manipulation of lung parenchyma which potentially overcomes the difficult exposure of incomplete fissures frequently encountered during the conduct of segmentectomies. The authors describe ligating the intrasegmental venous tributaries of the S^3 (V^3b+c), while preserving the intersegmental vein (V^3a) that lies between the subsegments S^3a and S^3b. This is followed by exposure and ligation of anterior segmental artery (A^3). Then, the trisegmental bronchus behind the venous tributaries is dissected, and the anterior segmental bronchus (B^3) is divided, while preserving the apicoposterior bronchus (B^{1+2}). After gentle reventilation, the intersegmental plane is demarcated and the left anterior segment (S^3) is divided with endostaplers. In this case, the ligation and division of the vascular structures was performed using a combination of suture ties and an energy device. It is frequently difficult to accommodate a stapler to divide segmental vessels of small caliber with resultant risk of prohibitive tension and possible avulsion. White *et al.* have reported safety of energy-based ligation of pulmonary vessels over a 6-year experience in video-assisted thoracoscopic lobectomy and segmentectomy (5).

Demarcation of the intersegmental plane in this case was obtained by gentle reventilation. Sometimes collateral ventilation to adjacent segments may obscure the intersegmental plane. Other groups of thoracic surgeons performing segmentectomies advocate for the use of indocyanine green fluorescence (ICG) dye to demarcate the intersegmental plane (6). An alternative mode of demarcation involves using jet ventilation via the segmental bronchi to be divided or injecting air using a 25-gauge needle via the divided segmental bronchial stump. Once developed, the intersegmental planes can be divided with electrocautery or staplers. The benefit of electrocautery is complete expansion of the adjacent segments, hence maximizing residual pulmonary function. The disadvantage is a higher propensity for air-leak. Fibrin sealants and polyglycolic acid-based felts can be used to cover the raw surfaces to minimize air-leaks (7). Stapler-based segmentectomy have the potential advantage of providing better sealing of the lung parenchyma and reducing post-operative air leak and associated bronchopleural fistula and empyema. The success of stapler-based segmentectomy lies in obtaining adequate negative surgical margins. The distance from the tumor to the parenchymal staple line should be at least 2 cm or equivalent to the size of the tumor (8). However, it is sometimes challenging to manipulate the lung to provide adequate orientation to place the stapler in the intersegmental plane. Patients with interstitial lung disease or severe emphysema may particularly benefit from using staplers to divide the intersegmental planes.

Similar technical descriptions of segmentectomies have been published using different platforms for video-assisted minimally invasive thoracic surgery (9,10). The robotic platform offers the advantage of a 3D high definition camera and wristed instruments with seven degrees of motion. A particular challenge for small ground glass nodules (GGN) or deeper nodules is the difficulty of palpating during minimally invasive operations. In addition to evolving platforms and surgical techniques for thoracoscopic segmentectomy, there is increasing interest in developing tools to facilitate tumor localization. Images of the segmental pulmonary bronchovascular structures can be individually reconstructed in three dimensions and subsequently merged (11,12). Methods for tumor localization include CT and/or fluoroscopy-guided placement of fiducial markers and hook wires, or injections of methylene blue, radioactive colloids, or ICG. Tumor localization can be further enhanced by using various lung mapping and three-dimensional navigation techniques based on contrast enhanced multi-detector CT scans. Virtual navigational bronchoscopy has made bronchoscopy-mediated lung marking possible without real time CT imaging (13). Lung mapping provides ‘geographic information’ on the lung surface which facilitates placing multiple dye markings via navigational bronchoscopy, not only around the tumor, but also on oncologically appropriate resection lines in the intersegmental planes.

Numerous retrospective studies have compared the long-term oncologic outcomes between segmentectomy and lobectomy, comprised of single institutional as well as various national databases (1,14,15). Unfortunately, most of the studies have grouped together segmentectomy and wedge resections as sub-lobar resections (16). Hence, not surprisingly the sublobar resections have a higher propensity for locoregional recurrence. These results, along with technical challenges in performing an anatomical segmentectomy has marred their ‘true’ potential for oncologic success as well as widespread adoption. Kodama *et al.* compared lobectomy with segmentectomy performed for cT1a NSCLC detected as part-solid or pure solid nodules (17). Similar locoregional recurrence was observed in both groups (lobectomy: 6.5%, segmentectomy: 3.7%) for a median follow-up period of 76 and 82 months, respectively. Similarly, no significant 5-year survival difference was observed in propensity matched cohorts. A recent meta-analysis showed similar oncologic outcomes for segmentectomy as compared to lobectomy for tumor size 2 cm or smaller, but not for tumors between 2 and 3 cm. Another meta-analysis of pooled studies with published locoregional recurrence data, showed equivalent local and distant recurrences between lobectomy and segmentectomy for stage IA tumors (15,16). However, for a definite recommendation at this time, these results need to be confirmed in randomized controlled trials.

The two much awaited clinical trials in North America and Asia, Cancer and Leukemia Group B 140503 and Japan Clinical Oncology Group 0802/West Japan Oncology Group 4607L, are comparing the utility of sublobar pulmonary resections over lobectomy for early stage lung cancer. In particular, besides comparing survival both studies evaluate post-resection pulmonary function as an essential end-point. Hence, the dictum of lobectomy for early stage lung cancer might very well be questioned as the results of these important trials come forth. Additionally, there has been a paradigm shift in outcomes studies with added emphasis on postoperative functional quality of life and pulmonary function after lung cancer resection surgery.

Node-positivity is an important point of contention for intra-operative decision making between segmentectomy and lobectomy. Current guidelines recommend converting to lobectomy for any positive lymph nodes diagnosed intraoperatively (N1 or N2). However, it is hard to submit all dissected lymph nodes for intraoperative frozen section. Hence, for an unsuspected lymph node metastases diagnosed on final pathology, no clear guidelines exist in terms of deciding between completion lobectomy, or adjuvant systemic chemotherapy without additional surgery. Yang *et al.* studied the long-term outcomes after lobectomy for non-small lung cancer with unsuspected pN2 disease, comparing the survival outcomes with patients who received induction chemotherapy + radiation followed by lobectomy (17). Though the 5-year survival of unsuspected pN2 cohort was worse than the group receiving induction treatment (30% *vs.* 40%), after matched-pair analysis, no significant survival differences was found between the two groups (37% *vs.* 37%). In their sub-group analysis, patients receiving adjuvant chemotherapy after detection of unsuspected pN2 disease had significantly improved 5-year survival (40%) compared to the group that did not. It is possible that adjuvant systemic therapy plays a more essential role than the extent of surgical resection in node-positive disease.

Despite gaining popularity and momentum, widespread adoption and oncological indication for segmentectomy remains a matter of debate, and further validation in long-term clinical trials is required. Additionally, the recognition of early stage lung cancer as a heterogeneous group of diseases with variable ratios of solid/non-solid component and a variable range of biologic behavior has further complicated the selection of patients to match the extent of lung resection. Nevertheless, the advent of newer modalities of localization and advancements in surgical platforms has certainly brought complex segmentectomies within the realm of minimally invasive thoracic surgery. In time, as the data from prospective trials mature, the true potential of segmentectomy will come to fore and a perfect balance between long term oncologic outcomes and parenchymal sparing lung cancer surgery may be achieved.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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