Editorial

Uniportal video-assisted thoracic surgery segmentectomy: a promising new development for thoracic surgery

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The recent development of novel therapies such as immunotherapy and targeted therapies has breathed a gust of hope on the management of non-small cell lung cancer (NSCLC). Yet, this disease does remain a leading cause of cancer death worldwide (1). Since the prospective randomized controlled study published by Ginsberg in 1995, pulmonary lobectomy is considered the standard surgical procedure for early-stage NSCLC, showing a lower local recurrence rate and a better long-term overall survival rate when compared to sub-lobar resection (2). Nowadays, screening programs and radiological improvements allow detection of solid NSCLCs at an earlier stage as well as of those with ground glass components (3). Thus, thoracic surgeons perform an ever-increasing number of pulmonary resections for small nodules, a trend with no end in sight. As NSCLCs can be detected early in their oncological course, the question of whether sub-lobar resections might be sufficient to preserve lung parenchyma as compared to the standard lobectomy is still open.

Pulmonary segmentectomy may represent an interesting alternative to lobectomy, by potentially offering lower postoperative morbidity and better quality of life (4). Moreover, since this technique preserves lung parenchyma, frail patients or those with poor pulmonary functions that exclude them from lobectomy might receive an oncologically satisfying surgical resection (4,5). In addition, in case of recurrence or newly diagnosed NSCLC, pulmonary segmentectomy increases the possibility for the patient to undergo a subsequent surgical resection.

Recently, two randomized controlled trials (RCT) compared lobectomy and sub-lobar resection for NSCLC ≤2 cm (6,7). The first study found a significantly better overall survival in patients undergoing segmentectomy as compared to lobectomy, in spite of a higher rate of local relapse (6). The second RCT showed similar disease-free and overall survival rates after sub-lobar (wedge, segmentectomy) or lobar resection during a median follow-up of 7 years (7). In light of these promising results, one might expect that the number of parenchyma-sparing, sub-lobar resections for carefully selected patients with peripheral stage IA NSCLC will increase in the coming years, not only for compromised patients with poor pulmonary functions, but also for fit patients who might have potentially tolerated lobectomy.

Compared with non-anatomical wedge resection, pulmonary segmentectomy theoretically allows better safety margins and more extensive hilar lymph node dissection. Hence, oncological outcomes such as local tumor recurrence or long-term survival might be improved. We previously reported on the safety and feasibility of video-assisted thoracic surgery (VATS) segmentectomy for oncological or benign disease indications. Our results demonstrated better peri-operative outcomes in patients undergoing VATS segmentectomy (n=240) compared to

lobectomy (n=450) (4).

However, compared to wedge resection or lobectomy, pulmonary segmentectomy is a technically more challenging procedure and specific steps and obstacles need to be overcome during the learning curve: proper identification of the patient's anatomy, correct delineation of the intersegmental plane and definition of sufficient surgical margins between pulmonary lesion and intersegmental plane. All these steps need to be addressed before surgery. Perioperative localization of the pulmonary nodule might be difficult, particularly in patients presenting ground glass opacities. Several techniques have been described to help the surgeon to intra-operatively detect the lesion and facilitate identification of the distance between the lesion and subsequent intersegmental plane. For example, the use of preoperative computed tomography (CT)-guided hook-wire devices, fiducials or dyes allows nodule identification in more than 95% of cases (8). Pulmonary segmentectomy involves an individual division of segmental broncho-vascular structures localized deep in the pulmonary parenchyma. This dissection can increase the risk of bleeding complication, which might be technically difficult to overcome. Finally, intersegmental plane delimitation might also be tricky but easily facilitated using systemic injection of indocyanine green or inflation technique (9,10). Three-dimensional reconstruction softwares were recently developed to better clarify pulmonary anatomy to plan surgery (11,12). With the help of theses technological novelties, VATS segmentectomy can be safely and efficiently performed even for complex cases.

In the same spirit of preserving lung parenchyma, the question of performing this surgery using a less invasive technique, such as a single small incision [uniportal video-assisted thoracic surgery (UVATS)], arises (13,14). The main theoretical advantage of the UVATS approach is the reduction of intercostal nerve injury compared with traditional multiport surgery. Thus, postoperative pain decreases due to reduced compression on the intercostal nerves and patients present significantly less subsequent paresthesia (15). Several meta-analyses and propensity-matched studies reported favorable postoperative outcomes after UVATS anatomical pulmonary resections when compared with multiportal approach (5,15,16). Harris *et al.* reviewed 8 studies including 1,850 patients undergoing VATS lobectomy for NSCLC. They found a significant reduction in overall complication rate (12.0% *vs.* 13.7%, P=0.009), length of hospital stay (6.2±2.6 *vs.* 6.7±3.4 days, P<0.0001) and duration of drainage (4.5±2.2 *vs.* 5.4±2.9 days, P=0.0006) in the UVATS group (16). However, none of these differences was statistically significant after propensity-matched analysis. Another group performed a meta-analysis on eight studies including 1,546 patients undergoing VATS segmentectomy for NSCLC. They found a significant reduction of the postoperative length of stay [mean difference (MD): –0.40 days, P=0.01], length of drainage (MD: –0.47 days, P=0.004) and postoperative pain on day 3 (MD: –0.90, P<0.00001) and day 7 (MD: –0.33, P=0.02) in the uniportal group (15). However, they did not find any difference between approaches in terms of postoperative morbidity, number of resected lymph nodes or conversion to open thoracotomy (15). Regarding oncological outcomes (overall survival, local control), both approaches seem to be equivalent (5,15). Xie *et al.* performed a propensity-matched study including 1,056 patients of whom 325 presented an invasive adenocarcinoma with a median follow-up of 52 months and found similar recurrence (HR 1.62, 95% CI: 0.715–3.666, P=0.247) and 5-year overall survival (HR 1.105, 95% CI: 0.337–3.624, P=0.87) rates between uniportal and multiportal VATS segmentectomy (5).

There is little doubt that UVATS is a safe approach for lobectomy. However, for segmentectomy, additional technical difficulties should be addressed before UVATS can be considered the standard of care. These include the specific angle of vision through the single incision with the use of coaxial devices; the need of dedicated instruments and the proper introduction of instruments for bronchovascular structure and intersegmental plane resection (13,14).

Due to these technical specificities, the learning curve of UVATS segmentectomy has been evaluated by various centers (17-19). Chen *et al.* reviewed 124 UVATS segmentectomy cases for lesions of <2 cm performed by the same surgeon with previous UVATS lobectomy experience and found that learning curve was completed after 57 cases (17). Similar results were reported by another group (19). Another study described that UVATS segmentectomy can be completely performed after 20–29 cases but mastered only after 58–63 cases without increased rate of conversion thoracotomy (18). Indeed, in our own experience, we feel that simple UVATS segmentectomy can be achieved quite soon in the learning process (generally after 25 cases), but more complex cases should be introduced progressively depending on the surgeon's skills (14). Moreover, as mentioned by the International VATS Lobectomy Consensus Group in 2014, surgeons need to perform at least 20 VATS lobectomy cases per year to maintain their operative skills (20). Thus, UVATS segmentectomy

should preferentially be introduced in high volume centers. Other options are available for surgeons to become more familiar with this technique, such as webinars, videos, and observation visits in specialized centers.

Zhou *et al.* performed an interesting propensity-matched study including 2,630 patients undergoing uniportal (n=400) or multiportal (n=2,230) VATS segmentectomy for stage IA NSCLC (21). They found no difference in terms of postoperative morbidity (4.3% *vs.* 4.7%, P=0.84), 5-year overall survival (97.7% *vs.* 99.4%, P=0.78) or progression-free survival (99.7% *vs.* 98.2%, P=0.18) between uniportal and multiportal approach. However, they noticed a difference in the number of lymph nodes stations harvested, with a significantly lower number in the UVATS group (4.43 *vs.* 4.68, P=0.02). This could be explained by the more difficult vision through the single incision of the entire mediastinum. However, total number of lymph nodes harvested were similar between groups and survival or recurrence were not affected. Another difference identified in the study of Zhou *et al.* was the higher hospitalization costs (7.58 *vs.* 7.24 kUSD, P<0.001) and the longer operative time (107 *vs.* 98 minutes, P<0.001) in the UVATS group. As previously mentioned, UVATS approach requires specific instruments that could increase total hospitalization costs. Of course, instruments can be amortized and in the long run, costs would not be impacted in a major way. Regarding operative time, these authors identified a decreasing duration of surgery in the UVATS group over the 6 years of patients' inclusion.

Interestingly, they observe similar post-operative outcomes and conversion rate between simple and complex (requiring transection of at least two intersegmental planes) segmentectomy. Learning curve was thus completed during the study and the length of operative time tended to converge in the last years of inclusion. Interestingly, as in prior retrospective studies, the choice of surgical modality (uni- *vs.* triportal) was driven by unreported variables. Surgeons would preferably choose a triportal approach in case of anatomical variations, complex cases, comorbidities, etc. Thus, study groups are not completely comparable and further randomized controlled trials would be necessary to overcome this bias.

In conclusion, even if the clinical benefits of uniportal over multiportal VATS are modest, we do believe that UVATS segmentectomy can be safely performed by surgeons who are highly specialized in UVATS anatomical pulmonary resections. Indeed, UVATS segmentectomy is a technically feasible procedure, with a reasonable learning curve, favorable postoperative outcomes and a low rate of conversion to multiportal VATS or open procedure.

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