Editorial Commentary

Anatomical partial lobectomy: implications in the light of JCOG0802/WJOG4607L and CALGB140503 (Alliance) trials

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Lung cancer is still a major public health problem, burdened with a significant death rate. However, the spread of large-scale screening programs with low-dose computed tomography (LDCT) has increased in recent years the number of high-risk subjects diagnosed with early-stage lung cancer, resulting in a significant reduction in the mortality rate linked to this disease (1). In the Nederlands–Leuvens Longkanker Screenings Onderzoek (NELSON) study, almost 60% of all patients with lung cancer were affected by stage I disease, leading to 24% mortality reduction in the male population and 39% in females (1).

Surgery still remains the mainstay of the treatment of early-stage lung cancer. In 1995, the results of the North America Lung Cancer Study Group (LCSG) randomized trial discouraged a conservative approach to T1N0 disease by means of sublobar resection compared with pulmonary lobectomy in virtue of supposed higher recurrence and mortality rates (2). Despite the well-described potential flaws of this underpowered study, lobectomy remained the gold-standard for the treatment of localized lung cancer for many years. Recently, the JCOG0802/WJOG4607L and CALGB140503 (Alliance) non-inferiority randomized trials demonstrated that sublobar resection (anatomical segmentectomy only in the former, both anatomical segmentectomy and wedge resection in the latter) can offer comparable long-term survival and improved respiratory function preservation compared to lobectomy for patients with tumors smaller than 2 cm (T1a and T1b) (3,4). In light of these results, limited resection may become the treatment of choice for early-stage disease in patients without contraindications for surgery.

Despite the optimal survival results, it is important to highlight that higher loco-regional disease recurrence rate was evident in patients who underwent sublobar resection compared to those randomized in the lobectomy groups in both JCOG0802/WJOG4607L and CALGB140503 (Alliance) trials. Considering that negative lymph nodal status is always assessed intraoperatively, the risk of recurrence in case of sublobar resection versus lobectomy can be attributed to the inability to obtain an adequate dissection of intraparenchymal lymph node stations (i.e., stations 11-12-13) or a sufficient resection margin free from the tumor. In the search for possible alternative approaches, Qiu and colleagues reported their experience in a large cohort of patients affected by early-stage non-small cell lung cancer (NSCLC) treated by anatomical partial lobectomy (APL), defined as a tumor-centered anatomical resection ranging from single segmentectomy to multiple combined subsegmentectomies or complex segmentectomies, based both on the position of the lesion and the regional vascular anatomy in order to guarantee a safe 2-cm-free resection margin (5). Over 3,300 patients were operated in a 6-year period; surgeries were conducted by minimally invasive approach by means of uniportal

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or multiportal video-assisted thoracic surgery (VATS) with negligible risk of thoracotomic conversion. A major limitation of this study is the lack of long-term oncological results; nevertheless, interesting data about perioperative planning and postoperative results were reported.

The authors have emphasized the importance of the use of a 3D-reconstruction software for the identification of the surgical margin based on preoperative CT scan, in order to assist the surgeon in the planning of the most appropriate type of lesion-centered resection. In this series, no APL was converted into a major resection, and only 2 patients required reintervention because of insufficient resection margin at final pathology. This is an important result, considering that, while the proportion of patients in the sublobar resection arm found with positive resection margin at final pathologic review was low in both JCOG0802/WJOG4607L (3 out of 552 cases) and CALGB140503 (Alliance) (2 out of 340 cases) studies, 4 additional cases in the former trial and 10 in the latter required further parenchymal resection on the basis of margin invasion found at intraoperative frozen section evaluation (3,6). These data leave space for discussion to establish potential indications for performing an APL rather than another type of sublobar resection based on precise preoperative targeted imaging assessment. In fact, it has been demonstrated that routine preoperative 3D-CT scan reconstruction allows timely change of planned resection and it is a valuable tool to significantly lower the amount of cases with inadequate margin distance in patients undergoing sublobar resections (7).

In their study, Qiu *et al.* analyzed the surgical outcomes of patients undergoing APL; the most common postoperative complication was the occurrence of prolonged air leaks (PAL) over 5 days after surgery reported in more than 45% of cases. Among the others, complex cases and operator's experience were identified as independent predictors of complications (5). Consistently with this study, a safety-analysis of the JCOG0802/WJOG4607L trial showed a significant higher rate of PAL in the group of patients who underwent anatomical segmentectomy; among them, complex segmentectomies, i.e., involving the division of 2 or more intersegmental planes, were identified as predictors of increased rate of respiratory complications (8). Well experienced surgeons also reported a longer learning curve for complex segmentectomy than lobectomy to reduce the risk of PAL and to achieve adequate tumor-free surgical margins (9).

As an alternative to VATS, the robotic approach has gained progressively greater consensus among thoracic surgeons. In 3 years, from 2015 until 2018, the rate of robotic minimally invasive sublobar resections increased from 7.3% to 22% overall (10). The intrinsic characteristics of the robotic system (improved dexterity, tremor filtration, 3D-enhanced vision, and built-in infrared technology) were demonstrated to be major determinants of the adoption of this technique both among open and VATS surgeons. A large retrospective analysis by Zhou and colleagues compared the outcomes of robotic, VATS and open segmentectomies in a single center. Despite a higher proportion of complex segmentectomies (45% *vs.* 15% in the VATS group), robotic operations were boasted by lower open conversion rate (0 to 7.5%, respectively), reduced incidence of PAL (3.9% to 12.5%, respectively), lower blood loss and increased margin/tumor ratio. Additionally, patients undergoing robotic surgery have benefited from the assessment of a greater number of lymph node stations than patients getting VATS (11).

The JCOG0802/WJOG4607L and CALGB140503 (Alliance) studies gave definitive answer to the oncological value of sublobar resection for the treatment of stage I lung cancer. Yet, the choice of the best resection approach is still under discussion. If validated accurately designed studies, APL tumor-centered resection could represent an alternative option aiming to obtain adequate tumor-free margins and to reduce the possibility of local recurrence. In this subset, the robotic technique could offer at this time more advantages than VATS. Other factors, such as the introduction of new platforms in the market, the spread of associated techniques [indocyanine green (ICG)-aided intersegmental plane dissection and preoperative 3D-reconstruction], will certainly have a major impact in the definition of the actual role of robotic thoracic surgery for pulmonary sublobar resection.

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