

# Is pneumonectomy still necessary?

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Surgical resection of lung cancer is the mainstay in patients with a curative intent. In centrally located lung cancers, pneumonectomy is indicated in case of clear involvement of different lobes or central broncho-vascular structures. However, a parenchyma-sparing surgical option including sleeve resection of the bronchus, the pulmonary artery or both was proven to be valid in centrally-located nonsmall cell lung cancer (NSCLC) (1). This approach has the advantage to provide complete tumor resection while avoiding pneumonectomy. Initially proposed for cancer patients with poor cardio-pulmonary functions, sleeve lobectomy has progressively gained acceptance and replaced pneumonectomy even in patients with excellent cardiopulmonary function. Functional advantages have been investigated and described by Martin-Ucar showing mean FEV1 loss of 170 (range, 0-500) vs. 600 (range, 200-1,400) mL after sleeve lobectomy and pneumonectomy respectively (2). In addition, the morbidity, mortality and quality of life results have favored parenchymal sparing procedures. It should be noted, however, that some authors, whilst advocating for sleeve lobectomy as a preferred option for overall and disease-free survival reasons, do report that sleeve lobectomy increases the risk of pulmonary complications such as pneumonia, atelectasis requiring bronchoscopy, ARDS, and mechanical ventilation for more than 2 days over pneumonectomy (3-8)

The decision to perform pneumonectomy or sleeve lobectomy is generally based on both oncological and physiological considerations. However, the main concern is the theoretical risk that a central tumor resected by sleeve lobectomy could have a poorer prognosis due to lesser local control than following a resection by pneumonectomy. Hence, the surgeon faces a challenge with the decision of how much lung parenchyma to preserve in patients with centrally located tumor, to be balanced with the long-term quality of life and survival prognosis. Tumor recurrence rates after sleeve lobectomy are comparable to those reported for pneumonectomy (6,9-11). Some caution is required when considering sleeve lobectomy over pneumonectomy in the context of associated nodal disease. It is currently suggested that sleeve lobectomy is safe and superior to pneumonectomy in cases with no nodal disease involvement (N0). In N1 and N2 disease, this statement is less clear cut with studies reporting more recurrences with sleeve lobectomy compared to pneumonectomy (12,13). However, most of these recurrences where distant and the overall survival of patients was not different between sleeve and pneumonectomy groups. Caution should nonetheless be taken when considering results of that nature, since they may include a degree of selection bias (patients with a more advanced disease might not be considered for sleeve lobectomy to begin with) (9,11) and room for interpretation of the N-status of a given disease (3), compounded by a less-than-obvious impact of sparing parenchyma in N2 patients (10).

The impact of neoadjuvant chemotherapy in the context of sleeve lobectomy was also studied by us and others. Sleeve lobectomy for NSCLC could be safely performed after induction chemotherapy and radiochemotherapy. Indeed, the 90-day postoperative mortality and the incidence of airway complications (bronchial stenosis and

#### Journal of Thoracic Disease, Vol 10, No 12 December 2018

6415

bronchopleural fistula) were similar to those observed in patients who did not receive neoadjuvant therapy (14). In addition, further studies have shown a clear pathological downstaging in patients thus favoring lung sparing procedures and improving overall patient prognosis (10).

Whilst sleeve lobectomy has been proven to be oncologically equivalent to pneumonectomy, this surgery is known to be technically more challenging than a pneumonectomy. The recent contribution by Maurizi et al. (15) adds to the knowledge of the sleeve lobectomy technicalities by sharing interesting long-term results on the so-called "Y-sleeve resection", that is the reimplantation of the upper lobe bronchus after a lower sleeve lobectomy or bilobectomy. This is a relatively infrequent surgical approach with technical difficulties related to reconstruction and risks of postoperative complications. These difficulties lie on the fact that the bronchial segments to be anastomosed show size discrepancies making the suture more complicated; the pulmonary artery is near and this proximity may add some difficulty to the operation; the mediastinal side of the anastomotic side is poorly exposed to the surgeon; and the segmental division of the upper lobe is near the operation site. Thus, this report expands the general understanding of the Y-sleeve reconstruction procedure and that if the operation is run with caution, the operation is technically feasible (albeit challenging) including when performed after chemotherapy and the outcomes oncologically adequate. Regarding some of the challenges such as size discrepancy between the two bronchial stumps, Maurizi et al. share technical details on suture placement and technique to circumvent these difficulties, and state a preference for open surgery over VATS for this specific case. They also share interesting contra-indications (infiltration of the fissures and of the pulmonary artery branches for the upper lobe), which would warrant pneumonectomy, and debunk the idea that the angle between the mainstem bronchus and the upper lobe bronchus might represent an undue technical issue. Of their group of 23 patients with NSCLC, they report results that all patients benefitted from complete R0 resections, with one case of peri-operative mortality and three cases of major complications. Complete long-term patency of the reconstructed airway could be documented in all the patients except for one who died in the early postoperative period, with a mean follow-up of 46 (range, 2-117) months and a local and distant recurrence rate at 32% over that period. It is noteworthy that amongst their patients, none developed endobronchial or perianastomotic recurrence. Finally, these authors report a 3- and 5-year overall and disease-free

survival rates of patients who initially had NSCLC at 76.3% and 55.1% (overall survival) and 68.7% and 62.9% (disease-free survival), thus matching figures presented by other authors for this type of surgery. Perhaps more interestingly, they report that N2 staging of the initial tumor might be the main factor affecting survival after broncho-vascular reconstruction, a fact already reported by other studies (1,7,8).

This article emphasises the technical progresses of sleeve lobectomy and the extended criteria for sleeve lobectomy indications. Recent advances by our group and others have allowed to enable lung sparing surgery by the use of extrathoracic muscle flaps as airway substitutes in challenging centrally located tumors involving the trachea or carina (16,17). This approach had reasonable 90 mortality (8.2%), 11.1% of airway complications with 94% of the surviving patients that had intact airways with no endobronchial/ tracheal appliances. This experience is particularly relevant for patients presenting the complex clinical combination of a centrally localized NSCLC lesion extending to the carina and lateral trachea, a concomitant induction therapy and who may require, in addition to pneumonectomy or sleeve lobectomy, a partial or complete carinal resection to obtain tumor-free resection margins (16). As a matter of fact, mechanical tension is the largest contributor to failure at the site of anastomosis and it may be due to various elements (differential diameter between the two bronchi; natural tendency of the bronchi to remain open, sometimes compounded by increased rigidity due to a prior chemotherapy; length of the resection; multiple operations). Such situations warrant a restoration of airway integrity that might be difficult to achieve without using a muscle flap patched into the defect, thus sparing the surgeon the necessity to join the resection margins into an anastomosis. Our observations demonstrate that these reconstructions are not only mechanically stable, but, will in time be entirely reepithelized with respiratory epithelium (17).

It is noteworthy that, in case of classical sleeve lobectomy, protection of the bronchial anastomosis by muscular flap may not be necessarily mandatory. Indeed, other authors report very convincing results after sleeve lobectomies without wrapping the bronchial anastomoses with a tissue flap, including in patients who underwent neoadjuvant chemo- or chemoradiotherapy (18). In spite of the good results reported by this group, many centers still consider that coverage of the anastomosis should be routinely performed to decrease the rate of broncho-pleural fistula. Recently, extended sleeve resection (more than one lobe) have been proposed to avoid pneumonectomy. Hong *et al.* reported a study on 63 patients with anastomosis between right main and lower bronchi (n=14), right main and upper bronchi (n=37), left main and basal segment (n=4) and left main and upper divisional bronchis (n=8) (19). They observed 10 (16%) anastomosis-related complications with no significant difference in term of mortality, anastomotic complication and loco-regional recurrence compared to a standard sleeve lobectomy. In a similar approach, Hishida *et al.* also reported extended sleeve lobectomies combining left lower lobectomy with lingulectomy in 10 patients with acceptable morbidity and no loco-regional recurrence during a median follow-up of 31 months (20).

The vicinity of the pulmonary artery (PA) to the operation site is indeed a difficult aspect. It is however acceptable to envision that one could perform an arterial resection followed by its reconstruction and observe convincing results. Different techniques are available for PA reconstruction depending mainly on the size of the defect and the surgeon's experience (21): direct reconstruction with tangential vascular reconstruction with direct suture, transverse suture, end-to-end anastomosis and/or graft reconstruction with different autologous tissues. Whilst the various technical possibilities to achieve this surgical procedure might be seen as acceptable options, one should not obfuscate the difficulty associated with this surgical procedure.

The future will be the adaptation of these different techniques by VATS (22-24) or RATS (25), a development which is already underway, albeit with small numbers for the time being. Some centers are nowadays capable of performing VATS or RATS sleeve lobectomy or even double sleeve. Given the current developments of instrumentation and surgical skills, it is not unrealistic to imagine that both might contribute to reducing the technical difficulties of this operation, thus further mainstreaming it.

In conclusion, we can state that on the one hand, sleeve lobectomy has gained much wider acceptance than initially envisioned, including for patients with uncompromised cardio-pulmonary function. This is not to say that pneumonectomy is not performed any more, just that it became less frequent as the techniques for sleeve lobectomy allowed more and more difficult resections to be performed. In that sense, the contribution by Maurizi *et al.* (15) is a prime example of a contribution towards pushing the limits of what surgeons can achieve with sleeve lobectomy.

Cases will always remain when the only option is

pneumonectomy, and these include for instance the cases when lobes are infiltrated. The question might still be open of whether nodal involvement has an impact on this decision. Yet, as techniques and research progress, sleeve lobectomy allows for resections and reconstructions of increasing complexity, and we do not doubt that further technical improvements (including VATS and RATS) might fuel that momentum. To the extent that sleeve lobectomy allows complete resections and results either similar (recurrences, survival) or superior (quality of life) to pneumonectomy, this latter surgical procedure might continue to decrease in frequency until it is limited to some indications only, for which no other, less radical option, might be available to the surgeon.

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## Footnote

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

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