Editorial

# Sleeve lobectomy or pneumonectomy for non-small cell lung cancer? Searching for an optimal balance between oncological, surgical and functional results

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The main objective in surgery for non-small cell lung cancer (NSCLC) is to achieve good oncologic safety, which includes R0 resection of the tumor and radical lymphadenectomy. Patients with centrally-located NSCLC should undergo pneumonectomy (PN) but, considering the not negligible morbidity and mortality related to this technique, they could benefit from a lung tissue-preserving resection, especially when cardio-pulmonary reserve is limited. Since Thomas (1) firstly applied this procedure for therapeutic option, "sleeve" pulmonary resection was designed to conserve as much pulmonary tissue as possible.

Currently, sleeve lobectomy (SL) has an almost definite role in the surgical management of NSCLC patients whose pulmonary reserve is considered inadequate to permit PN.

On the other hand, there is an ongoing, large debate concerning the role of sleeve resection in those patients judged as "clinically-fit" for PN. Indeed, although many recent reports (2,3) have suggested that sleeve resection may achieve adequate curability rates, different opinions still emerge on the surgical completeness and early/long-term results after pulmonary sleeve resection.

In this setting, the study performed by Andersson and co-workers (4), which analysed the post-op outcomes and long-term survival results of 107 NSCLC patients who underwent SL or PN, adds very interesting information to such debate. Their results have great potential impact on the clinical decision-making process in locally-advanced NSCLC. Focusing on post-op outcomes, long-term survival and QoL results, the authors comprehensively compared these two techniques (SL *vs*. PN) using a propensity-matched analysis in a retrospective monocentric cohort of locally-advanced NSCLC cases. In line with other authors (5-20) (see also *Table 1*), they observed as PN-group was associated with higher incidence of major complications (29.9%) when compared with SL-group (P=0.027) with a remarkably different rates of re-operation (25.4% in PN-group *vs*. 7.5% in SL-group). Regards of the 90-day mortality rate, they observed different results between the two groups (7.5% for PN-patient *vs*. 5% in SL-patient) but this difference was not statistical significant. However, these results are substantially in line with data coming from a large meta-analysis focused on this topic (21). In details, the meta-analysis (including a total of 19 trials with 3,878 subjects) showed that the pooled postoperative mortality in patients undergoing SL was 2.91% (38/1,306) as compared with 5.86% (149/2,542) in patients receiving PN. Such difference resulted to be statistically significant (OR, 0.50; 95% CI, 0.34–0.72) in favour of SL-group.

Concerning long-term survival, no difference was noted by Andersson and colleague (4). The 5-year survival rate

**Table 1** Comparative results between sleeve lobectomy and pneumonectomy: an overview on pertinent literature

| Study | Year | No. of patients | | Post-op mortality (%) | | Anastomotic or stump complications (%) | | Arterial sleeve-lobectomy | Induction therapy (%) | | 5-year LTS (%) | | Local relapse (%) | | QoL | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | SL | PN | SL | PN | SL | PN | | SL | PN | SL | PN | SL | PN | SL | PN |
| Gaissert | 1996 | 72 | 56 | 4.0 | 9.0 | 1.3 | 1.7 | – | 4.2 | – | 42.0 | 44.0 | 14.0 | – | – | – |
| Yoshino | 1997 | 29 | 29 | 0 | 6.9 | 0 | 10.3 | 0 | – | – | 65.7 (3-year) | 58.8 (3-year) | 10.3 | 20.6 | – | – |
| Suen | 1999 | 58 | 142 | 5.2 | 4.9 | 3.4 | 0.7 | 0 | 5.1 | – | 37.5 | 35.8 | – | – | – | – |
| Lausberg | 2000 | 81 | 40 | 1.2 | 7.5 | 0 | 7.5 | 35.8 | – | – | 45.0 | 30.4 | – | – | – | – |
| Okada | 2000 | 151 | 60 | 0 | 2.0 | 6.6 | 0 | 13.9 | – | – | 48.0 | 28.0 | 8.0 | 10.0 | – | – |
| Martin-Ucar | 2002 | 38 | 81 | 10.5 | 9.9 | 5.0 | 2.4 | 16.0 | – | – | 64.0 (1-year) | 73.0 (1-year) | – | – | – | – |
| Ghiribelli | 2002 | 38 | 127 | 5.2 | 3.9 | 23.6 (all complications) | 23.2 (all complications) | – | 0 | 0 | 38.0 | 25.0 | 5.2 | 4.8 | – | – |
| Deslauriers | 2004 | 184 | 1,046 | 1.3 | 5.3 | 3.2 | – | 0 | – | – | 52.0 | 33.0 | 22.0 | 35.0 | – | – |
| Ludwig | 2005 | 116 | 194 | 4.3 | 4.6 | 6.9 | 3.6 | 26.0 | – | – | 39.0 | 27.0 | – | – | – | – |
| Bagan | 2005 | 66 | 151 | 4.5 | – | 28.8 (all complications) | 29.9 (all complications) | 13.0 | – | | 72.5 | 53.2 | 4.5 | 7.6 | – | – |
| Kim | 2005 | 49 | 200 | 6.1 | 4.1 | 2.0 | 1.0 | 0 | 12.0 | 0 | 53.7 | 59.5 | 32.6 | 8.5 | – | – |
| Takeda | 2006 | 62 | 110 | 1.6 | 1.8 | 3.2 | 3.6 | – | 25.8 | 16.8 | 53.4 | 32.9 | 9.7 | 10.9 | – | – |
| Parissis | 2009 | 79 | 29 | 2.5 | 8.5 | 16.4 (all complications) | 21.6 (all complications) | 0 | 0 | 0 | 46.8 | 37.1 | 17.7 | 19.4 | – | – |
| Park | 2010 | 105 | 105 | 1.0 | 3.6 | 3.1 | 1.8 | 17.8 | 17.1 | 15.2 | 58.4 | 32.1 | 14.3 | 16.2 | – | – |
| Gómez-Caro | 2011 | 55 | 21 | 3.6 | 5.0 | 1.8 | 14.0 | 27.0 | 20.0 | 9.5 | 61.0 | 31.0 | 1.8 | 9.5 | – | – |
| Berry | 2014 | 35 | 52 | 3.9 | 5.7 | 2.8 | 3.8 | 0 | 0 | 0 | 46.8 (3-year) | 65.2 (3-year) | 10.0 | 26.0 | – | – |
| Cusumano* | 2014 | 51 | 68 | 3.9 | 2.9 | 3.9 | 4.4 | – | 100.0 | 100.0 | 42.8 | 47.0 | 22.4 | 12.1 | – | – |
| Andersson | 2015 | 40 | 67 | 2.5 | 6.0 | 5.0 | 0 | – | 27.5 | 20.9 | 40.0 | 38.4 | 2.5 | 4.5 | No difference | |

*, all patients undergone neadjuvant therapy; –, data not available. SL, sleeve lobectomy; PN, pneumonectomy.

was similar in both groups (PN: 41.8% *vs*. SL: 37.5%, P=0.665), this suggesting comparable oncologic results. These findings are consistent with other studies published on this topic; indeed when analysing the data coming from recent literature (see *Table 1*), it emerges long-term survival rates ranging from 37% to 61% after SL and from 25% and 59% after PN. In this regards, the meta-analysis performed by Shi and colleague (21) showed better long-term survival results in SL-group when compared with PN-group; in detail, the estimated combined hazard ratio (HR) for overall survival in 13 comparative studies was 0.63 (95% CI, 0.56–0.71) in favor of SL-group, and there was a statistically significant difference also.

An additional major concern when comparing SL *vs*. PN is the incidence of loco-regional recurrence. Andersson and co-workers (4) did not report significant differences when comparing the rates of distant metastasis or loco-regional recurrence between SL- and PN-group (P=0.798). In particular, the rates of loco-regional relapse (2.5% in SL-group *vs*. 7.5% in matched PN-group) were noticeably lower than those observed in literature (see *Table 1*) and reported in the meta-analysis (14.4% in SL patients *vs*. 26.1% in PN patients). The rate of loco-regional relapse is a crucial factor in evaluating the "oncological safety" of sleeve pulmonary resection as compared with PN. Such a low rate of loco-regional relapse reported by Andersson (4) is almost hard to be interpreted due to the absence of data concerning the surgical completeness, that represents an additional relevant "outcome indicator" of this surgical technique.

Indeed, in the line of extreme simplification, when comparing sleeve-resection with PN, there are several "outcome indicators" that we need to take into account. The "ideal" technique should provide for an optimal balance between oncological, surgical and functional results. In this setting, the surgical completeness stays as one of the main "outcome indicators" among with post-operative outcome, long-term survival and QoL result.

Finally, when analysing the long-term QoL results, Andersson and co-workers (4) didn't observe any significant difference between groups in the total score. The only difference is seen for moving and breathing (better results in SL-group), but this was not statistical significant. Looking at the pertinent literature on this topic, only few studies have been reported (22,23) and results are almost preliminary. The best evidences come from a prospective analysis performed by Balduyck and colleague (22) evaluating QoL modification after SL and PN with the European Organisation for Research and Treatment of Cancer (EORTC) QoL questionnaire-C30 and LC-13. The authors prospectively enrolled 10 sleeve lobectomies and 20 pneumonectomies and questionnaires were administered before surgery and 1, 3, 6, and 12 months postoperatively. A significant higher burden of dyspnea, general pain, thoracic pain and shoulder dysfunction was observed after PN when compared with QoL data after SL. Based on these results, the authors (22) concluded that in patients with anatomically appropriate early-stage lung cancer, SL offers better quality of life than does PN. In our opinion, the recovery of a satisfactory QoL after surgery should have greater weight among the various "outcome indicators" reported above. We recently performed a detailed analysis of QoL results (questionnaires: SF-12) in a large cohort of patients after PN (23). Although we observed an overall rewarding preservation of mental and (partially) physical health, physical score (Phy-Sc) significantly decreased after PN, especially in patients with symptoms prior to surgery and with low preoperative FEV1 values. In this context, a better comprehension of the QoL evolution (before and after surgery) is needed in large prospective clinical series comparing SL and PN.

In conclusion, the advances in patient selection criteria and surgical techniques have allowed SL to evolve from a compromise to PN to "first-line" intervention for centrally located lesions of all grades. Moreover, as promising short- and long-term results were demonstrated, SL was accepted as an alternative surgical procedure to PN. Although there isn't yet a high level of evidence, peri-operative outcomes (morbidity and mortality) favour SL. Long-term survival results did not substantially differ between SL and PN while, supposedly, QoL could be better preserved after SL as compared with PN. Recent literature has also shown evidence supporting the use of neoadjuvant treatment (24) and minimally invasive techniques (25) when performing a sleeve-resection.

Therefore, despite PN still retains a significant role in locally-advanced NSCLC, sleeve resections could be performed for centrally located tumor whenever technically, anatomically and oncologically possible.

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