

Sublobar resection for stage IA non-small cell lung cancer

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Abstract: Advancements in the diagnosis, staging and management of lung cancer have all led to improvements in outcomes associated with sublobar resection. Lobectomy, for early stage lung cancers has been the treatment of choice for many years. However, there is mounting evidence that sublobar resection when applied to the appropriate patient population can provide not only excellent oncologic results but also equivalent survival to lobectomy. Therefore, it is time that we reevaluate the management of peripheral stage IA lung cancers.

Keywords: Lung cancer; sublobar resection; lobectomy; stage IA lung cancer

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Introduction

Thoracic oncology has changed significantly in the last few decades, however, surgical resection remains the mainstay of therapy for early stage lung cancers in patients without prohibitive surgical risk. Based on the work of the Lung Cancer Study Group, lobar resection has been favored due their findings of improved overall survival (OS) and lower risk of recurrence with lobectomy when compared to sublobar resection (1). However, since the publication of the LCSG's randomized trial in 1995, many advances in the diagnosis and management of lung cancer have been made. Notable changes include: the wider use and higher resolution of computed tomography (CT) scans resulting in the discovery of smaller and non-solid lung nodules, improved clinical staging and diagnosis due to the use of PET CT, EBUS and mediastinoscopy, an aging population with more comorbidities and a higher proportion of dedicated, thoracic surgeons.

The extent of appropriate resection for stage IA lung cancers remains an area of debate and there are many salient arguments both for and against lobectomy and sublobar resection. The purported benefits associated

with lobectomy are: decreased local recurrence, better parenchymal margins, better lymphatic clearance and sampling and improved overall and disease free survival (DFS). The potential benefits of segmentectomy or wedge resection include sparing lung parenchyma particularly in patients with poor pulmonary reserve or for patients likely to require additional resection in the future.

Many primarily retrospective reviews have evaluated the utility of sublobar resection and results have been varied (2). Notably, these studies have not specifically looked at the use of intentional sublobar resection in patients otherwise eligible for lobectomy. Inherent in the majority of prior studies were selection biases wherein patients undergoing sublobar resection were older, had worse cardiopulmonary reserve, other associated comorbidity, or lesions were under staged. Additionally, bias in technique with inadequate margins, resections being performed by non-specialized surgeons and inconsistent or incomplete lymph node sampling have also confounded the results. Recent enthusiasm for major database mining, even with attempts to correct for selection bias with propensity matching give an aura of credible comparison, but remain flawed due to unmeasured variables that impact outcomes. However,

recent studies have demonstrated improved outcomes with sublobar resection for stage IA lung cancer by excluding patients with comorbidity who would be candidates for either lobectomy or sublobar resection. These offer compelling evidence for broader utilization of both segmentectomy and wedge resection for early stage lung cancers.

Sublobar resection vs. lobectomy

Yendamuri *et al.* using the SEER database, evaluated outcomes following sublobar and lobar resections for <2 cm non-small cell lung cancers (NSCLC) from 1987–2008 and they were able to demonstrate improved outcomes over this time period for sublobar resection when compared to lobectomy (3). Their analysis divided cases by time period, 1987–1997, 1998–2004 and 2005–2008 and demonstrated a trend toward more favorable OS and DFS for sublobar resection compared to lobectomy over time. Specifically, they demonstrated that by 2005–2008 there was no difference in survival between lobectomy and sublobar resection. These findings led them to conclude that due to the improvement in diagnostic and staging technologies, contemporary early stage lung cancer is an inherently different entity than early stage cancers studied by the LCSG in the 1980s. The meta-analysis by Cao *et al.* offers further support for sublobar resection and addressed the issue of patient selection and the intentional use of sublobar resection in patients otherwise eligible for lobectomy (4). Twelve studies were included in their meta-analysis, in which 1,078 patients underwent sublobar resection and 1,667 patients underwent lobectomy and they found no significant difference in OS or DSF. Similar results have been reported by both Okada *et al.* and Altorki *et al.* (5,6). Notably, Altorki *et al.* further reported no significant differences in pathologic upstaging, cancer related death, all cause death or local recurrence in their propensity matched evaluation of stage IA lung cancers (solid nodules only) detected by screening CT scan using I-ELCAP's database from 1993–2011 (6).

Wedge resection vs. segmentectomy

The appropriate method of sublobar resection is also a topic of debate and the question of whether segmentectomy or wedge resection has shown superiority also warrants discussion. Wedge resection, particularly for small, peripherally located stage IA cancers can provide adequate

oncologic margins, be performed quickly and minimally invasively. Segmentectomy is technically more challenging but offers improved lymphatic clearance over wedge resection while also sparing lung parenchyma. In a prospective study Tsutani *et al.* compared segmentectomy (n=56) and wedge resection (n=93) to lobectomy (n=90) for ground glass opacity predominate stage I adenocarcinoma and found no statistically significant difference in recurrence free survival or overall survival across the three groups for stage IA disease (7). In their study, wedge resection was performed for T1a lung cancers more frequently than segmentectomy and no lymph node involvement was found with T1a cancers compared to 2.4% of T1b cancers. Although this was not statistically significant they did recommend that for T1b cancers segmentectomy was preferred due to better lymph node sampling inherent with the procedure, while wedge resection remains adequate for T1a cancers. Similar results were recently published by Hou *et al.* in their meta-analysis which included 9 studies, wherein they also found no significant difference in DFS between segmentectomy and wedge resection in high risk patients with stage IA disease. However, they did find that OS and cancer specific survival favored segmentectomy when compared with wedge resection for stage I and stage IA lung cancer. Similar to Tsutani *et al.* subgroup analysis demonstrated no statistically significant difference in outcomes for T1a NSCLC (8).

Discussion

When patients are evaluated by a dedicated thoracic surgeon and selected appropriately, sublobar resection can be performed successfully and with excellent oncologic outcomes. Keys to success, much like any resection for lung cancer start with patient selection and a full assessment of the patient's functional status, comorbidities and anatomic considerations. Given the shift toward improved clinical staging and diagnosis of lung cancer, sublobar resection in the setting of small, peripheral stage IA lung cancer should be considered a reasonable alternative to lobectomy and in some cases may be preferred. Evidence to support the use of either segmentectomy or wedge resection for stage IA lung cancer is well founded and numerous, contemporary studies have demonstrated equivalent OS and DFS for sublobar resection when compared to lobectomy in properly selected patients. The benefits of sublobar resection are many and include preservation of lung function, decreased perioperative morbidity and mortality, and preservation of

lung parenchyma that may allow subsequent resections in the era of increasingly identified multifocal ground glass opacities.

The National Comprehensive Cancer Network (NCCN) guidelines in non-small cell lung cancer lay out clear principles for surgical management, including the consideration of sublobar resection (9). The guidelines note that an anatomic pulmonary resection is preferred for the majority of patients undergoing surgery for lung cancer. A segmentectomy or wedge resection is considered appropriate in patients with poor pulmonary reserve or other major comorbidity if a complete resection with adequate margins and lymph node sampling/dissection can be performed. However, sublobar resection is also considered appropriate for patients with a peripheral lung nodule ≤ 2 cm, particularly if the nodule is $\geq 50\%$ non-solid, has pure adenoma-in-situ histology, or has demonstrated a radiologic doubling time of ≥ 400 days. Surgical principles recommended by the NCCN are parenchymal resection margins > 2 cm or \geq the size of the nodule, as well as standard sampling or dissection of appropriate N1 and N2 lymph nodes.

These guidelines underscore that sublobar resections are applicable to both high and low risk surgical candidates. Some cases may warrant an open surgical resection rather than a minimally invasive approach in order to ensure both appropriate margins and sound staple lines. None of the studies reviewed specifically addressed the issue of lymph node assessment in early stage lung cancers. In the United States, formal pre-resection mediastinal lymph node assessment is recommended for all stage IB lung cancer and higher, and on a case-by-case basis for stage IA disease. The question of appropriate lymph node staging is beyond the scope of this review. However, a clear association between lymph node status and prognosis following lung cancer diagnosis exists and therefore formal lymph node sampling or dissection is a key component to pathologic staging and when performed concomitantly with resection should not impose undue risk to the patient.

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Footnote

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

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