



# Limited-anatomic resection for ground-glass like lung cancer—simplicity does not mean inefficacy

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In the past, lung cancer has usually been diagnosed at an advanced stage with most disease presenting as a solid nodule or mass on chest computed tomography (CT). As such, in early studies evaluating the efficacy of surgical resections, lobectomy offered improved local control and overall survival compared to sublobar resection (1), and has been well-established as the gold standard in the treatment of lung cancer. However, as screening for lung cancer becomes more prevalent, the spectrum of diagnosed lung cancers has now undergone significant changes. Recently, there has been a growing incidence of pulmonary ground glass nodules (GGNs), which is a new entity representing early-stage lung adenocarcinoma and is especially prevalent among Asian females (2). The exceptionally good outcomes associated with the treatment of GGN-appearing adenocarcinoma (3) with nearly 100% 5- and 10-year postoperative survival have rekindled an interest in sublobar resections.

While not all GGNs require immediate surgical resection (4), for those requiring surgery, early results have confirmed the efficacy of sublobar resection as a definitive treatment option if the nodule is small ( $\leq 2$  cm), peripheral, and presents with limited invasiveness (5). A recent multicentric prospective trial even suggested an equally good prognosis for wedge resection and segmentectomy in a select subset of GGN-predominant lung cancers (6). Given the growing data, it seems reasonable to assert that for a GGN with a minimal risk of spread, the key principle is to ensure an adequate resection margin. As such, for more centrally located GGNs that may be difficult to approach by wedge resection, a non-standard, limited-anatomic

resection, which selectively divide vessels and bronchi of the target region, may be sufficient (7). The anatomy is limited to an extent with just enough room for the stapler to complete a resection margin similar to a segmentectomy. In this way, strict dissection and division of every segmental vein are not mandatory and often spared. However, as thoracic surgeons, we tend to be resistant to change and adapt our practice, like transitioning from lobectomies to sublobar resections. In China, proponents of full-anatomic resections continue to perform sub-segmentectomies for GGNs that could have otherwise been treated with wedge resections.

From a historical point of view, the case for a full-anatomic resection for GGNs focuses on three main aspects: first, full-anatomic resection ensures dissection of segmental or subsegmental lymph nodes which in turn minimizes the risk of tumor recurrence in cases of occult lymph node metastasis; second, it is believed to maintain an optimal ventilation-perfusion ratio without probable dead space or shunting post-resection; third, by isolating management of vessels and bronchi, the risk of staple line failure may be better controlled.

To date, however, few of the above-mentioned benefits have been confirmed. On the other hand, given the excellent prognosis of GGN-predominant lung cancers, there is growing evidence to indicate that limited-anatomic resections may achieve similar outcomes to full anatomic resections with less tissue resected. Lymph node metastasis is rare, if any, and lymph node dissection may be unnecessary in these tumors (8). The latter, however, can be conveniently identified with a preoperative chest CT.

Consolidation tumor ratio (CTR), defined as the ratio of size of solid component to the maximum tumor dimension, is measured on CT and has been shown to correlate well with lung cancer prognosis (9). It has also proven useful in the prediction of pathological subtypes of invasive adenocarcinoma (10), with ground-glass predominant lung cancer presenting a small CTR frequently corresponding to adenocarcinoma in situ or minimally invasive adenocarcinoma.

In terms of postoperative lung function, the existing literature has also demonstrated discrepant results with what has previously been thought. Specifically, lung function after a wedge resection is generally preserved whereas a standard segmentectomy results in a reduction in lung function up to twice as much as that after lobectomy per segment resected (11). It seems that much is still unknown about the mechanisms of pathophysiological change after lung resection, and that the ability of the human body to compensate for ventilation-perfusion mismatch as a result of surgery is underestimated.

With the ongoing development of new surgical instrumentation, there are now an assortment of cartridges to choose from, and staple line failure is no longer a major threat in routine lung resections. Therefore, we believe that the anatomic dissection for a low-risk GGN should end at a point where a safe margin can be ensured when firing staples. Any excessive dissection could translate into additional tissue damage and monetary costs but with little gain in return. This is especially true for subsegmentectomy, in which the resection margin is no more than that of a wedge resection, but the amount of dissection work is multiplied. Understandably, it is the surgeon's nature to push the boundaries of surgical expertise, and it is a feat that such a subsegmentectomy can only be accomplished by the most technically-skilled of hands. However, one should always bear in mind that a patient's benefit always comes first and that technical feasibility should never be placed on top of therapeutic necessity. As such, the indications for full-anatomic resection should be carefully examined so as not to include low-risk GGNs. Moreover, our experience suggests that limited dissection in a previous sub-lobar resection does facilitate a future completion lobectomy for a second primary lung cancer if it were to arise.

However, as small subpleural GGN were hardly visible or palpable, it might be difficult to identify resection lines with a safe margin intraoperatively for limited-anatomic resection, as with other types of sublobar resection. Fortunately, with the guidance of evolving lung marking and imaging

techniques, such as indocyanine green dye (12), microcoil marking (13) and virtual-assisted lung mapping (14), a surgeon can be better informed of the nodule location so that a reasonable decision can be made on how far the anatomy should go to ensure an adequate margin.

In summary, for ground-glass predominant lung cancer with limited invasiveness, resection margin can be considered the only determining factor for operational success. Non-anatomic or limited-anatomic sublobar resection, although technically simpler than a standard full anatomic resection, does not necessarily mean inferiority in treatment efficacy. As we continue to improve treatment outcomes for patients with lung cancer, we propose a shift in the treatment paradigm to the former in the optimal management of GGNs moving forward.

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