PERSPECTIVE ARTICLE

Operability versus Resectability in Non-Small Cell Lung Cancer: A Multidisciplinary Perspective

Operabilidade versus Ressecabilidade no Cancro do Pulmão de Não Pequenas Células: Uma Perspetiva Multidisciplinar

João Maciel

Thoracic Surgery Department, Hospital Santa Marta, ULS São José, Lisbon, Portugal

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Autor Correspondente/Corresponding Author:

João Maciel

ORCID ID: 0000-0002-7363-2784

Thoracic Surgery Department, Hospital Santa Marta, ULS São José, R. de Santa Marta 50, 1169-024 Lisboa, Portugal

Email: jsmaciel@gmail.com

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Operability and resectability are crucial concepts in managing non-small cell lung cancer (NSCLC). Operability refers to a patient's ability to safely undergo surgery, considering factors such as pulmonary function, cardiovascular status, comorbidities, and overall performance status. Resectability pertains to the technical feasibility of completely removing the tumor surgically, based on size, location, invasion into adjacent structures, and lymph node involvement. Curative surgery is possible only when both operability and resectability are favorable. Evaluating resectability begins with comprehensive staging to determine the extent of disease and plan treatment. Imaging modalities like positron emission tomography-computed tomography (PET-CT) provide metabolic and anatomical information to detect metastases and assess regional lymph nodes.[1] Magnetic resonance imaging (MRI) of the brain is used to exclude central nervous system metastases, especially in patients with neurological symptoms or advanced disease.[2] Mediastinal staging is vital due to its prognostic implications in NSCLC. Techniques such as endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) enhance mediastinal assessment by allowing minimally invasive

sampling of lymph nodes with high sensitivity and specificity.[3] Accurate staging determines resectability and guides treatment decisions, distinguishing patients who may benefit from surgery from those better served by nonsurgical therapies. In early-stage NSCLC (stages I and II), surgical resection remains the gold standard for long-term survival.[4] Lobectomy with systematic lymph node dissection is the standard procedure, aiming for complete tumor removal and accurate pathological staging.[5] However, managing stage IIIA and IIIB disease is challenging due to the heterogeneous nature of these stages, which often involve mediastinal lymph node metastases (N2 disease) or invasion into adjacent vital structures (T3-T4 tumors). The critical question is whether surgery should be performed in these cases and, if so, when. Defining resectability in advanced NSCLC lacks a universal standard and depends on multiple factors, including tumor characteristics, patient physiology, and surgical expertise. Guidelines from the European Society for Medical Oncology (ESMO) provide resectability criteria, emphasizing the importance of achieving negative surgical margins (R0 resection).[6] Patients with single-station N2 disease or T4N0 tumors may be considered for surgery if R0 resection is feasible. Additionally, patients who respond to preoperative systemic therapy may become surgical candidates, provided that a pneumonectomy is not required.[7] Advances in surgical techniques have expanded the possibilities for resectability, even in complex cases. Technologies like extracorporeal membrane oxygenation (ECMO) enable surgeons to perform intricate procedures without traditional cardiopulmonary bypass, reducing perioperative risks.[8] This innovation has allowed successful resections in cases previously deemed unresectable due to tumor invasion into critical structures. Less invasive techniques are also being adopted for operable patients considered high-risk due to comorbidities or limited pulmonary function. Segmentectomy and wedge resection are lung-sparing procedures that can be curative in select patients with small, peripheral tumors (≤2 cm).[9] Initially explored in patients considered inoperable, these approaches are now recognized as viable options for certain early-stage cancers. The JCOG0802/WJOG4607L randomized trial demonstrated that segmentectomy can achieve outcomes comparable to lobectomy in appropriately selected patients.[10] When extensive surgical intervention is necessary to achieve an R0 resection, meticulous planning and advanced techniques are imperative. Tumors invading adjacent structures like the chest wall, mediastinum, or great vessels present significant challenges. Procedures such as intrapericardial lobectomy involve removing the affected lobe while preserving surrounding structures, improving postoperative pulmonary function. These demand high surgical expertise and may involve reconstructive techniques or ECMO support. The limits of resectability are often defined by the involvement of critical structures. Certain anatomical boundaries, such as the esophagus and heart, represent “red lines” beyond which resection may not be feasible due to unacceptable risks. Conversely, structures like the trachea and major vessels may be considered “yellow lines,” where resection is possible but requires specialized skills and multidisciplinary collaboration. Ethical considerations must guide clinical decisions, balancing potential surgical benefits against morbidity risks and impact on quality of life. Patient preferences and goals should be central to the decision-making process. Shared decision-making involves discussing expected outcomes, potential complications, and alternative treatments. In some cases, palliative care may be the most appropriate approach to manage symptoms and maintain quality of life. A multidisciplinary approach is essential in managing complex NSCLC cases. Decisions regarding operability and resectability should involve thoracic surgeons, medical oncologists, radiation oncologists, pulmonologists, radiologists, and pathologists. This collaboration ensures that all therapeutic options are considered and that treatment plans are tailored to the patient’s circumstances. Advances in minimally invasive techniques like video-assisted thoracoscopic surgery (VATS) and robotic-assisted thoracic surgery (RATS) offer advantages such as reduced postoperative pain, shorter hospitalizations and faster recovery compared to traditional open surgery.[9] They are particularly beneficial for high-risk patients who may not tolerate extensive surgery. However, their application in complex resections is still evolving and requires specialized training and experience. The integration of immunotherapy into neoadjuvant and adjuvant treatment regimens is an emerging area of interest. Immune checkpoint inhibitors have shown promise in improving survival outcomes in advanced NSCLC. Clinical trials are evaluating the efficacy of combining immunotherapy with surgery and other modalities in earlier stages of the disease. The NADIM trial demonstrated that neoadjuvant chemotherapy combined with nivolumab resulted in high rates of pathological complete response in patients with stage IIIA NSCLC, suggesting a potential paradigm shift. Personalized medicine is becoming increasingly relevant in NSCLC management. Molecular profiling of tumors can identify specific genetic mutations and biomarkers that may predict response to targeted therapies and immunotherapies. This approach allows for more individualized treatment plans, potentially improving outcomes and reducing unnecessary toxicity. Ultimately, the limits of surgical resection are defined by the combination of tumor biology, patient physiology, and the technical capabilities of the surgical team. The goal is to achieve

an R0 resection while minimizing operative risk and preserving quality of life. Continuous multidisciplinary collaboration ensures that decisions are evidence-based and aligned with best practices.

Ongoing research and clinical trials will continue to refine strategies for managing this challenging disease, aiming to improve survival rates and enhance the quality of life for patients with NSCLC.

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