

Surgical Complexity of Pulmonary Resections Performed for Oligometastatic NSCLC



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ABSTRACT

Introduction: Pulmonary resection has been established as an important component of local consolidative therapy (LCT) for oligometastatic NSCLC. However, technical aspects of such surgical procedures have not been well characterized. We sought to review the complexity of operations performed within a large cohort of patients with oligometastatic NSCLC.

Methods: We identified patients treated at a single institution between 2000 and 2017 with stage IV NSCLC, with three or fewer synchronous metastases, and who underwent surgical resection of the primary tumor. Medical records were reviewed, and aspects of surgical complexity were recorded. Descriptive analyses were performed.

Results: Among 194 patients with oligometastatic NSCLC, 173 (89%) received LCT and 30 (15%) underwent resection of the primary tumor. Thoracotomy was performed in 25 patients (83%), and procedures included 25 (83%) lobectomies, three (10%) pneumonectomies, and two (7%) sublobar resections. Mean blood loss was 200 (50–600) mL, and operative time was 200 (72–492) minutes. Proximal pulmonary artery control was needed in four (15%). Sleeve resection was needed in four (15%). Unplanned procedural change was required in two patients (7%). Chest wall resection occurred in three patients (11%). Lymph nodes were characterized as hard or densely adherent in nine (33%), and operations were described as more difficult than usual in 16 cases (59%).

Conclusions: Surgery has emerged as a key strategy for LCT among patients with oligometastatic NSCLC. These operations can be performed safely, yet frequently require advanced techniques and complex resection strategies. As

such, health care teams must be prepared for the technical challenges of these cases.

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Keywords: Oligometastatic; Non-small cell lung cancer; Surgery; Complexity

Introduction

The management of oligometastatic NSCLC has rapidly evolved in recent years, with heightened emphasis on the benefits derived from local consolidative therapy (LCT). Prior to undergoing LCT, individuals with stage IV NSCLC typically undergo systemic therapy consisting of chemotherapy, targeted

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therapy, immunotherapy, or a combination thereof. Following systemic therapy, LCT may be offered in the form of radiation, surgery, or a hybrid approach. Pulmonary resection has been established as an important component of LCT. It has been previously shown by our group to be both feasible and associated with long-term benefits for oligometastatic NSCLC, offering improved disease-free and overall survival in carefully selected patients.^{1,2} As such, we believe that surgery should remain part of LCT for operable oligometastatic patients with NSCLC.³

However, despite the promising evidence supporting the growing application of surgical resection for LCT in metastatic NSCLC, the technical aspects of such surgical procedures have not been well characterized. For patients undergoing treatment with novel systemic agents in the neoadjuvant setting for earlier staged disease, surgeons have subjectively reported more difficult cases, and a greater frequency of conversion to open procedures has been noted.^{4–6} Data regarding surgical challenges for the oligometastatic NSCLC population remain lacking. In this study, we sought to review the technical complexity of operations performed within a large cohort of patients with oligometastatic NSCLC.

Materials and Methods

After obtaining institutional review board approval with waiver of informed consent, we conducted a retrospective review of patients treated at a single institution between 2000 and 2017 with stage IV NSCLC and three or fewer synchronous metastases at the time of diagnosis.² This cohort was initially curated through the use of a novel natural language processing algorithm to identify patients with NSCLC and whose medical records included the non-negated use of keywords related to oligometastatic disease prior to manual review of flagged records to determine eligibility for study inclusion.² The definition of oligometastatic as three or fewer metastatic sites was selected according to criteria established in a previous phase 2 trial of LCT for oligometastatic NSCLC out of our institution.^{1,7}

Patients were eligible for inclusion in the present analysis of surgical complexity only if they underwent pulmonary resection of the primary lung tumor. No restriction was placed on the receipt of, or response to, systemic and/or other therapies before surgical resection of the primary tumor.

In our practice, patients with metastatic disease have been considered for surgery when they have Eastern Cooperative Oncology Group performance status 0 to 1, adequate pulmonary reserve to tolerate the anticipated extent of resection, and absence of any substantial comorbidities that would render them to be considered

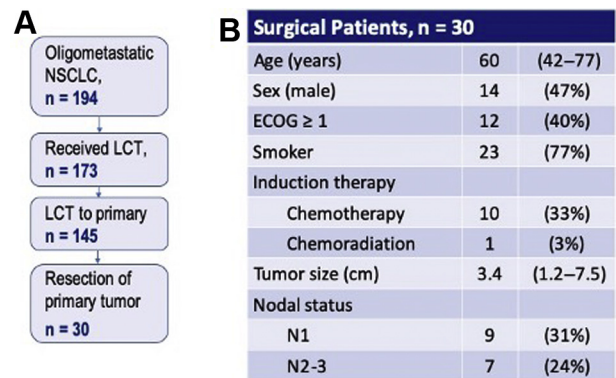


Figure 1. Patient cohort. (A) A total of 194 patients presented with oligometastatic NSCLC, among whom 173 (89%) received LCT, with 30 (15%) specifically undergoing resection of the primary tumor. (B) Characteristics of the patient cohort, with categorical variables described as n (%) and continuous variables described as mean (range). ECOG, Eastern Cooperative Oncology Group; LCT, local consolidative therapy.

inoperable. Presence of pleural metastases as well as preoperative expectation of pneumonectomy have been considered contraindications for operating on patients with oligometastatic NSCLC.

Individual patient records were reviewed in detail, and aspects of surgical procedures were recorded, including standard metrics, such as approach, blood loss, operative time, and markers of case complexity such as need for proximal pulmonary arterial control, unplanned change in extent of resection, and presence of hilar fibrosis. Descriptive analyses were performed.

Results

Our patient cohort was derived from 194 patients with oligometastatic NSCLC, among whom 30 (15%) underwent resection of the primary tumor (Fig. 1A). For those surgical patients, the mean age at the time of their operation was 60 years, and just under half were men (Fig. 1B). Eastern Cooperative Oncology Group status was 1 or greater for 40% of these patients, and just over three-quarters were previous or current smokers. A total of 37% underwent induction therapy preoperatively, most of whom had chemotherapy alone, though one patient had undergone chemoradiation. The mean tumor size at surgery was 3.4 cm and nodal disease was present in most cases, with approximately one-third having N1 disease and another one-quarter having N2 or 3 disease.

With regard to intraoperative details, thoracotomy was needed in 25 of these patients (83%), despite the frequent use of minimally invasive strategies at our institution during these years. Most of these operations (24, 80%) were initiated via thoracotomy due to the

Table 1. Surgical Complexities

Intraoperative Finding	n	%
Intraoperative change in extent of resection	2	7
Proximal pulmonary artery control	4	15
Sleeve resection	4	15
Fibrotic/densely adherent nodes	9	33
Chest wall resection	3	11
Required reconstruction with mesh	2	7
Required soft tissue/muscle flap transfer	3	11
Reported as complex/challenging	16	59
Intraoperative consultation required	4	15

Note: Intraoperative challenges for those patients among whom operative notes were available, N = 27.

anticipated extent of adhesions and hilar fibrosis. Six cases were begun minimally invasively, among which one (16.7%) required conversion, owing to extensive fibrosis of the hilar structures. The majority of resections performed were lobectomies (25, 83%), though 10% (3 of 30) of these patients required pneumonectomies, and sublobar resections were much less common (2 of 30, 7%). Operative notes were available for 90% (27 of 30) of the cohort, who had mean blood loss of 200 mL (range: 50–600 mL) and mean operative time of 3 hours and 20 minutes (range: 72–492 minutes).

To summarize the intraoperative challenges encountered, proximal pulmonary artery control was needed in 15% (Table 1). Sleeve resection was indicated in 15%, including one bronchial sleeve, one pulmonary arterial sleeve, and two double sleeves. Unplanned procedural changes were required in 7%, including one unexpected pneumonectomy. Chest wall resection, including ribs and/or sternum, was needed in more than 10%. Reconstruction with mesh was needed in 7%, and with soft tissue or muscle flap transfer in 11%. Lymph nodes were characterized by surgeons in their operative notes as hard and densely adherent in one-third of procedures, and terms noting “difficult” or “challenging” operations were found in the majority of operative reports (59%). Surgeons relied on intraoperative consultation with other surgeons or the patients’ family members in 15% of the cases for intraoperative decision making.

Despite such frequent intraoperative challenges, R0 resection was achieved in 97% (29 of 30) of these procedures, and morbidity was acceptable, with average length of stay of 5.9 days (range: 2–29 d). Postoperative adverse events are characterized in Table 2, demonstrating that the most frequent complications were atrial fibrillation (7 of 30, 23%) and prolonged air leak (3 of 30, 10%), as might be expected.

Among this surgical cohort, 18 of 30 patients (60%) were alive at 5 years, with one patient lost to follow-up

Table 2. Early Postoperative Outcomes

Clinical Outcome	n	%
Initial admission ICU	2	7
Prolonged air leak	3	10
Pneumonia	1	3
Atelectasis requiring bronchoscopy	1	3
Pleural effusion requiring drainage	1	3
Reintubation	1	3
Respiratory failure, tracheostomy	1	3
Atrial fibrillation	7	23
Urinary tract infection	2	7
Wound infection	1	3
Postoperative transfusion	1	3
Discharged with chest tube	2	7
Discharged on home oxygen	2	7

Note: Postoperative morbidities for patients after resection of primary tumor in oligometastatic disease, N = 30. ICU, intensive care unit.

at 20.7 months. Median survival for this group was 58.6 months (range: 8.8–210.2 mo).

Discussion

This study is the first to describe the advanced surgical maneuvers that are frequently required in these often technically challenging cases. By identifying the deviations from a more typical resection, providers will be able to better plan and more safely execute resections for advanced NSCLC. While this cohort is limited in size, and this may affect the generalizability of our findings, we hope that the results described herein can be useful for health care teams as the population of patients who may be offered surgical resection continues to expand.

In general, these patients tend to have more extensive adhesions, increased frequency of dense fibrotic tissue involving the hilar structures, and greater prevalence of firm lymph nodes, often adherent to the pulmonary arterial branches and airways. We hypothesize that the nodes were firm and indurated due to the extent of disease at diagnosis, with many of the patients having extensive nodal involvement, as well as due to their treatment response. We have previously revealed that extent of nodal reduction during neoadjuvant therapy is associated with case complexity,⁸ which supports this hypothesis; however, this is an important area of future investigation.

As surgery has emerged as an important aspect of LCT in patients with oligometastatic NSCLC, we continue to demonstrate that operative resection can prolong survival. While this is an exciting new area of innovation for surgeons as we continue to evolve our care for patients with advanced disease, we must recognize, as highlighted herein, that health care teams should be prepared for the technical challenges of such cases.

We have found that these operations can be performed safely, yet they require frequent advanced techniques and complex resection strategies. Putting patient safety first, surgical teams should ensure that resources including time, equipment, and expertise are allocated properly in operative planning.

CRediT Authorship Contribution Statement

Mara B. Antonoff: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision, Validation, Writing - review & editing, Resources, Software, Visualization.

Ahsan Farooqi, Ethan B. Ludmir: Data curation, Formal analysis, Investigation, Methodology, Validation.

Hope A. Feldman: Data curation, Formal analysis, Investigation, Validation, Writing - review & editing, Resources, Software.

Saumil Gandhi: Formal analysis, Investigation, Methodology, Supervision, Writing - review & editing, Resources.

Daniel R. Gomez: Conceptualization, Methodology, Supervision, Validation; Writing - review & editing.

Wayne L. Hofstetter, Reza J. Mehran, David C. Rice, Boris Sepesi, Stephen G. Swisher, Garrett L. Walsh: Investigation, Methodology, Writing - review & editing, Resources.

Kyle G. Mitchell: Conceptualization, Data curation, Formal analysis, Investigation, Software, Methodology, Validation, Writing - review & editing.

Ravi Rajaram: Investigation, Methodology, Writing - review & editing.

Ara A. Vaporciyan: Conceptualization, Investigation, Methodology, Writing - review & editing, Project administration, Software, Resources, Supervision.

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