The Role of Extended Pulmonary Metastasectomy

Monica Casiraghi, MD, Patrick Maisonneuve, Eng,† Daniela Brambilla, Msc,* Francesco Petrella, MD,* Piergiorgio Solli, MD,* Juliana Guarize, MD,* Filippo De Marinis, MD,‡ and Lorenzo Spaggiari, MD, PhD*§*

Background: The role of extended pulmonary resection for lung metastases is still unclear, and little information is available in the literature. This study was performed to analyze the outcomes and prognostic factors of patients who underwent extended resections for pulmonary metastases.

Methods: From 1998 to 2013, 1027 patients underwent lung metastasectomy procedures. Twenty-nine patients had extended pulmonary resections: three resections of the chest wall, one azygos, one diaphragm, four vascular resections/reconstructions, six sleeve resections, and 14 pneumonectomies.

Results: Extended resection was performed for metastatic disease mainly from epithelial (62.1%) and sarcomatous (20.7%) tumors. Complete resection was obtained in all patients. Thirty-day operative morbidity and mortality rates were 38% (11 of 29) and 0%, respectively. Only one patient had a major complication due to a bronchopleural fistula. Mean hospital stay was 6.3 days. After a median follow-up of 27 months, 16 patients (55%) had died. At univariate analysis, survival was determined by primary tumor histology ($p = 0.03$); the number of metastases, nodal status, disease-free interval or extension of surgery (pneumonectomy vs. lobar resection) were not related to survival probably due to the low number of patients. Overall survival after a complete extended metastasectomy was 66% at 2 years, 42% at 5 years, and 36% at 10 years.

Conclusions: Extended resections performed during pulmonary metastasectomies are associated with low mortality and morbidity rates and an acceptable long-term survival when performed in selected patients susceptible to complete resection.

Key Words: Extended surgery, Lung metastasectomy, Morbidity and mortality, Outcome.

(*J Thorac Oncol.* 2015;10: 924–929)

*Division of Thoracic Surgery, European Institute of Oncology, University of Milan, Milan, Italy; †Division of Epidemiology and Biostatistics, ‡Division Clinical Oncology, European Institute of Oncology, Milan, Italy; and §School of Medicine, University of Milan, Milan, Italy.

Disclosure: The authors declare no conflict of interest.

Abstract accepted for oral presentation at 28th EACTS Annual Meeting in Milan, October 11–15, 2014.

Address for correspondence: Monica Casiraghi, MD, Division of Thoracic Surgery, European Institute of Oncology, Via G. Ripamonti, 435 20141 Milan, Italy. E-mail: monica.casiraghi@ieo.it

DOI: 10.1097/JTO.0000000000000547

ISSN: 1556-0864/15/1006-0924

In the past, pulmonary metastases (PM) were considered fatal in less than 2 years,[1,2] and had no indication for surgical treatment. Since 1927, when George Divis described the first intentional lung metastasectomy, many case reports have shown that surgical resection of lung metastases could improve survival in selected patients.[3,4]

Whereas pneumonectomy and lobectomy were the predominant resections performed for PM until the late 1940s, advances in imaging technology in the early 1980s led to the detection of smaller and asymptomatic nodules in the follow-up of cancer patients. This allowed the more conservative lung-sparing resection to become the standard surgical procedure for those patients.[5–12] In 1947, Alexander and Haight[7] reported 42% of pneumonectomies and 50% of lobectomies for lung metastases, compared with rates of 4% and 6% reported in 1984 by Mountain et al. and the Memorial Sloan-Kettering experience, respectively.[11,12]

Even if the recent surgical trend for lung metastasectomy is "lung sparing" surgical resection, major resections could still be reserved for highly selected patients. As already demonstrated in the literature, the completeness of surgery after pulmonary metastasectomy is the most important prognostic factor in terms of survival.[13] Because surgery should be offered with a prospect of cure, it seems obvious to consider extended resection a therapeutic option to achieve long-term survival.

In 1993, Putnam and et al.[14] were the first to establish that resections of multiple PM or PM involving more than lung parenchyma were technically similar to resections for locally advanced non–small-cell lung cancer. They defined extended resection as pneumonectomy or pulmonary resection with en bloc resection of the chest wall or other major structures (diaphragm, pericardium, superior vena cava).

Unfortunately, the role of extended pulmonary resection for lung metastases is still unclear, and little information is available in the literature. This study was performed to analyze the outcomes and feasibility of extended resections for PM.

PATIENTS AND METHODS

From 1998 to 2013, 1027 consecutive patients at the European Institute of Oncology (IEO, Milan, Italy) underwent lung metastasectomy procedures. Patients' individual consent for the use of their clinical data for research purposes was obtained before intervention. Twenty-nine patients (2.8%) had extended pulmonary resections defined as pneumonectomy or pulmonary resection with en bloc resection of the chest wall

or other major structures (diaphragm, pericardium, superior vena cava).

All patients included in the analysis had a controlled or controllable primary tumor, and no extrapulmonary metastases. Suspected pulmonary metastatic lesions were evaluated during pretreatment and tumor staging or during regular follow-up after resection of primary tumors. All patients were studied with contrast-enhanced total body computed tomography (CT) scan; positron emission tomography/CT (PET/CT) with fluorodeoxyglucose has been routinely used since 2001, and performed in 22 patients showing no evidence of extra thoracic metastases. Five patients underwent preoperatory CT-guided fine needle aspiration biopsy with a positive result in four cases, negative in one. Bronchoscopy was performed in seven patients with lesions situated near the tracheobronchial tree, and in six cases it was diagnostic. All 19 patients who did not have a preoperative diagnosis underwent an intraoperative frozen section of the tumor to confirm the diagnosis of metastasis and the planned surgery; we usually performed an intraoperative biopsy of the tumor using a trucut procedure to reduce possible intracavity dissemination.

Thoracic surgeons, radiotherapists, and oncologists confirmed patients' resectability during a multidisciplinary meeting based on the following selection criteria: primary tumor controlled, disease-free interval (DFI), absence of extra thoracic metastases highlighted by modern staging system, such as CT scan and PET scan, technical feasibility of the pulmonary resection, adequate preoperative cardiac and respiratory function evaluated with forced expiratory volume in the 1st second, diffusing capacity of the lung for carbon monoxide, and perfusion lung scan in case of pneumonectomy. Besides these selection criteria, every patient was evaluated case by case analyzing the previous medical treatments performed, and considering the surgery as the best therapeutic option for these patients.

All lung nodules were identified visually or by palpation depending to the site of resection and histopathologically analyzed/confirmed during surgery. Extended resection was performed by means of open surgery in all cases. Lymph node dissection or sampling was performed in 25 cases.

Based on the oncologist's evaluation, 18 patients (62.1%) received chemotherapy before surgical resection of the lung nodules, and five patients (17.2%) received it afterwards.

DFI was defined as the time between treatment of the primary tumor and diagnosis of metastases.

Operative mortality was defined as death occurring within 30 days of extended resection, and all deaths beyond 30 days but during the same hospital stay. Postoperative complications were classified as minor or major.[15,16]

Statistical Methods

Overall survival was defined from the date of metastasectomy to the date of last contact or death. Overall survival curves were plotted using the Kaplan–Meier method and the log-rank test was used to assess differences in survival between groups. Univariate and multivariate Cox proportional hazard regression was used to assess the association between clinical characteristics and overall survival rates. Analyses were performed with SAS software version 8.2 (Cary, NC). All p values were two-sided.

RESULTS

Ten were men and 19 were women. Mean age was 56 years (range 18–81 years). Primary tumors were classified in four histological categories: epithelial, sarcoma, melanoma, and germ cell tumors. Eighteen patients (62.1%) developed metastases from epithelial tumor, six (20.7%) from sarcoma, four (13.8%) from melanoma, and one (3.4%) from germ cell tumor. Besides the histology of the primary tumor according to the completeness of resection (epithelial, sarcoma, melanoma, and germ cell tumors), we specified in detail the anatomical site of the epithelial tumors in Table 1.

Complete resection was obtained in all patients.

DFI was 0 to 12 months in three patients (10.3%), 12 to 36 months in eight patients (27.6%), and 36 months or more in 18 patients (62.1%). Nineteen patients had a single lung metastasis and 10 had multiple lesions.

Fourteen patients underwent pneumonectomies, whereas lobectomies and sublobar resections were performed on 11 and four patients, respectively. Pulmonary resection was associated with chest wall resection in three patients, pulmonary artery resection in three (two resection and reconstruction and one vascular sleeve), bronchial sleeve resections in six, azygos vein resection in one, diaphragm resection in one, and pericardium resection, and reconstruction in one. Pulmonary artery and pericardium were reconstructed with bovine pericardium patch, and chest wall with methacrylate prosthesis. Diaphragm was resected with no need of reconstruction.

Data on the indications for extended resection, such as histological primary tumor types, number of PM, preoperative respiratory function, such as forced expiratory volume in the 1st second and diffusing capacity of the lung for carbon monoxide, presence or absence of nodal metastases, surgical approach, DFI, and relapses are described in detail in Table 1.

Only one patient underwent pneumonectomy had a major complication due to bronchopleural fistula treated by thoracostomy after 30 days. Minor complications occurred in 10 patients (34.4%): atrial fibrillation was the most frequent complication (6 of 10), followed by anemia and atelectasis necessitating aspiration of bronchial secretions. More details regarding postoperative complication are presented in Table 2.

Median intensive care unit stay was 1.3 days (range 1–3 days) and the median length of total hospital stay was 6.3 days (range 3–10 days). No intraoperative mortality was observed. Thirty-day operative morbidity and mortality rates were 38% (11 of 29) and 0%, respectively.

Postoperative treatments, such as chemotherapy or radiotherapy were administered to seven patients (24.1%) based on multidisciplinary evaluation. Seventeen patients had recurrent pulmonary disease, and subsequent metastasectomy was performed on four patients: in three patients, metastasectomy was performed contra laterally, and one patient had a redo-metastasectomy (on the same side). Seven patients out of 15 patients who received en bloc resection had systemic recurrence whereas none had locoregional recurrence.