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# Pulmonary Metastasectomy for Melanoma: Beyond the Standard of Care

Stephen C. Yang, MD

Division of Thoracic Surgery, Department of Surgery, The Johns Hopkins Medical Institutions, 600 N. Wolfe St., Blalock 240, Baltimore, MD 21287, USA

In recent years, the controversial role of pulmonary metastasectomy for melanoma has been re-addressed by several authors with the intent to show that surgical resection of these lesions is associated with better survival when compared with medical therapy. In addition, prognostic factors have been put forth to show that surgery is associated with better results in carefully selected patients with resectable pulmonary metastases.

Although at best these data represent years of prospectively gathered information from respected institutions, validation of results from large randomized trials will never be achieved due to poor accrual.

In ''Stage IV Melanoma and Pulmonary Metastases: Factors Predictive of Survival'', Neuman and colleagues[1] present results collected prospectively at Memorial Sloan Kettering Cancer Center since 1995 from a series of 122 patients. This is a rather contemporary and ''pure'' cohort, consisting of patients they have followed since the initial diagnosis of melanoma with subsequent development of pulmonary metastasis, or of those who already had stage-IV disease with the lungs representing the only site of distant metastasis at the time of referral (M1b). As one can surmise, these are rather special and infrequent circumstances, with their study population representing less than 2% of the 7500+ melanoma cases in their databank, and only 0.5% getting resection for pulmonary metastases. Another unique characteristic of this study was the absence of thoracic surgery collaboration and possible additional study patients. Presumably, this was done, in part, to exclude referral bias at a tertiary center, where patients may have been referred directly to the thoracic surgery service that was better equipped for pulmonary resection and/or wanted a more aggressive and ''non-traditional'' approach to their metastasis. However, it cannot be overlooked that patients with less than ideal performance status (as a result of other therapies) and who have failed other treatments are also referred for pulmonary metastasectomy. Although Neuman et al. do not present novel data or selection criteria for pulmonary metastasectomy, they do present the longest median survival (40 months) and one of the higher 5-year survival rates (29%) published to date. Interestingly, nearly 80% of their cohort did not undergo metastasectomy; although some generalization was made (such as the presence of extrathoracic disease), it was not totally apparent why those patients with even solitary pulmonary nodules were not offered surgery.

The authors are to be commended for their unique objectives of presenting this ''pure'' population, extensive work, and reporting unbiased pulmonary surgical data from their viewpoint as opposed to that traditionally published by thoracic surgeons. The post-resectional data represents only 26 patients and, thus, undergoes the scrutiny of a comparatively small study with respect to other published reports in the last 10 years[2–4]. One of the landmark articles regarding pulmonary metastases came in 1997 from Pastorino and the International Registry of Pulmonary Metastases (IRPM)[5]. This database of 5208

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Address correspondence and reprint requests to: Stephen C. Yang, MD; E-mail: syang@jhmi.edu

patients defined a simple classification and favorable factors for resection, which included a disease-free interval (DFI) greater than 36 months and only one metastasis; there were 328 cases with a median survival of 19 months, and 5-year survival was 21%. Comparatively, the results of Neuman et al. are consistent, but median DFI in the surgical group fell short (21 months) of the IRPM data. Nevertheless, 5-year survival rates of 21–33% have been consistent among recent publications over the past 10 years, and have trended toward being higher than in previously published series from the 1970s and 1980s. Many possibilities can account for the better survival rates in the current era. These explanations, common to other surgical therapies, include: better operative selection criteria; use of updated radiological modalities to detect earlier resectable disease (such as PET scanning) and exclude those patients with occult extrathoracic disease who would have previously been operated on; and improvements in surgical techniques and perioperative care.

The data are in. Patients with resectable isolated pulmonary metastases should be treated aggressively and offered resection. The National Comprehensive Cancer Network guidelines for patients with resectable melanoma metastases support this notion[6] and, therefore, this should be the standard of care. Until recently, distant metastasis of any cancer was regarded as systemic disease and surgery would be questioned. This is clear for metastasis to other organs such as liver, brain and occasionally bone, in all of which surgical resection of the lesions can lead to long-term survival in carefully selected patients. In addition, although there are few data, the possibility exists that these solitary nodules may represent a new primary lung cancer, and pulmonary resection should be performed to exclude this, as therapy and prognosis would be impacted greatly.

One final paradigm beyond pulmonary metastasectomy is the use of chemotherapy or biological agents in a neoadjuvant or adjuvant setting, with the understanding that pulmonary involvement represents systemic disease, and knowing the relatively low outcomes with unfavorable pulmonary metastatic characteristics. This has been applied with some success for colorectal cancer. The rationale is to address systemically the patients at high risk of micrometastatic disease elsewhere and select out those most likely to benefit from surgical intervention, sparing those who may be unresponsive to chemotherapy. In this era of developing genomics, molecular markers and biological therapy, obtaining fresh tumor especially different from the primary lesion is essential to advance translational research and hopefully develop novel therapies that someday may lead to personalized cancer care for the individual patient.

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