Editorial

Comparison of pulmonary metastasectomy and stereotactic body radiation therapy for the treatment of lung metastases

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Lung metastasectomy is one of the most frequently performed procedures by thoracic surgeons worldwide whose goal is to resect all pulmonary metastases from primary neoplasms without leaving residual disease (1). In order to accomplish an effective procedure, basic oncologic principles need to be respected when performing lung metastasectomy: the primary tumor must be controlled or controllable; no further extrathoracic uncontrollable metastatic spread exists; lung procedure need to be radical without major impairment of respiratory function; no effective alternative treatments with lower morbidity should be available (2).

More than 75% of patients suffering from lung metastases present also metastases to extra-thoracic organs; in fact, only 15% to 25% of patients presenting lesions limited to the lungs can be considerate as appropriate candidates for pulmonary metastasectomy (3).

Metastatic involvement of intrathoracic lymph nodes is associated with reduced survival after lung metastasectomy but does not represent by itself a formal contraindication to surgical resection, although the role of lymph node dissection in pulmonary metastasectomy and the prognostic impact of nodal involvement are still debated (4).

In our past experience we found that affected lymph nodes found during sampling or radical lymphadenectomy during pulmonary metastasectomy had a negative impact on survival, thus being the nodal status and number of resected pulmonary metastases independent prognostic factors (5); on the contrary, other reports showed no effect of nodal status on survival of operated patients (6,7).

Cardiopulmonary function testing is a crucial aspect of the preoperative assessment of patients' candidate to metastasectomy: in fact, although sublobar resections are most often used, global pulmonary tissue loss need to be predicted in the setting of multiple lesions (8-10). We have previously showed, in fact, that spirometric modifications following lung metastasectomy are conditioned by total volume lung parenchyma resected within the first 90 days; moreover, functional loss after three or more sub-anatomical resections is comparable with that observed after lobectomy (11).

Although the Pulmonary Metastasectomy Working Group of the European Society of Thoracic Surgeons showed that atypical segmentectomies were the most common used procedures to resect pulmonary metastases (12), extended resections may play an effective role in selected patients with deeply located nodules or lesions infiltrating closer structures like pericardium, diaphragm, chest wall and superior vena cava to obtain a radical resection improving survival (13).

From the initial experience of the International Registry of Lung Metastases established in the early '90s until the more recent series, the idea that lung metastasectomy is potentially curative-based on complete resectability, disease-

free interval and number of metastases as independent prognostic factors—has constantly strengthened (14-17).

However, the major limit of the evaluation of the clinical efficacy of pulmonary metastasectomy is the lack of data on the clinical outcome of patients who could potentially benefit from surgical resection but who are not offered the procedure, as operable patients are almost always submitted to surgical resection (18).

We will probably be able to focus on this aspect thanks to the results of the ongoing PulMiCC trial, randomizing lung metastasectomy with active monitoring for pulmonary metastases in patients with successfully treated for colorectal cancer (19,20) although these results will not be known for at least ten years and will not be extended to different cancers (21).

Stereotactic body radiotherapy (SBRT) is the treatment of choice for elderly patients affected by early-stage primary NSCLC who are ineligible to surgical resection due to comorbidities or impaired respiratory function (22). Based on these experiences in lung cancer, SBRT has also been advocated for treating pulmonary metastatic lesions from several primary tumors and some prospective trials investigating the role of SBRT in metastatic disease was recently started (23,24), although results of these trials are only expected within the next years. Rieber *et al.* retrospectively analyzed 700 patients receiving SBRT for lung metastases and identified several prognostic factors for better selecting patients who might be successfully treated by SBRT: patients with a reduced performance status presented a significantly worse survival and local control; moreover overall survival (OS) was significantly affected by primary tumor histology and number of metastases; finally patients with a longer interval between primary tumor diagnosis and SBRT treatment disclosed significantly better survival (22).

Lee *et al.* retrospectively compared the treatment outcomes of SBRT and metastasectomy in patients with pulmonary metastases: twenty-one patients received SBRT for 29 pulmonary metastatic lesions and—on the other hand—30 patients underwent pulmonary metastasectomy for 30 metastatic lesions, the vast majority receiving wedge resection while only 2 patients (3.9%) underwent lobectomy (25). Although no differences were observed between the two groups in terms of age, gender, ECOG PS, smoking history, pulmonary function, comorbidities and interval between diagnosis of primary tumors and detection of pulmonary metastases, the median tumor size was larger in the SBRT than in the metastasectomy group.

As a result, progression free survival (PFS) was significantly longer in patients receiving metastasectomy than in those undergoing SBRT. There were no significant differences in local control or OS between the two groups. Moreover, PFS rates were significantly affected by the presence or absence of synchronous metastases.

Multivariate analysis disclosed that the presence of synchronous metastases significantly and negatively influenced PFS (25).

In conclusion, both pulmonary metastasectomy and SBRT can be successfully indicated for the treatment of lung metastases, although SBRT is commonly reserved—in daily clinical practice—to elderly patients unfit for surgery or those refusing metastasectomy; both surgical resections and SBRT offer the best results in terms of PFS and OS in patients with good performance status, with small and single pulmonary metastases and a preferably long time interval between primary tumor diagnosis and treatments, while patients with synchronous metastases are only likely to obtain a small benefit from local treatment, whether via SBRT or surgery.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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