Abstract: Metastatic breast cancer has been defined as a systemic disease. Although resection of pulmonary metastases is a common treatment in other primary malignancies, the role of breast cancer metastasectomy is more contentious. Solitary or fewer numbers of pulmonary metastases and longer disease-free interval are, as in other cancers where pulmonary metastasectomy is performed, significant prognostic factors. For proven pulmonary metastases, the level of evidence for a curative approach is low, but some patients might benefit from a metastasectomy followed by an elective and appropriate complementary oncological treatment.

Key Words: Breast cancer, Pulmonary metastasectomy.

In the more recent article, Singletary et al. present the results of eight retrospective studies that examined the survival outcomes in the patients with breast cancer with isolated metastases to the lung treated with surgery with or without postsurgical systemic therapy. Median survival times ranged from 42 months to 79 months, with 5-year actuarial survival rates ranging from 35 to 80% and 10-year actuarial survival rates ranging from 8 to 60%.

An analysis was performed in 467 female patients from International Registry of Lung Metastases (IRLM). The survival rates associated with complete resection of pulmonary metastases are 38, 22, and 20% after 5, 10, and 15 years, respectively. Median survival was 37 months. Incomplete resections were associated with a 5-year survival of 18% with median survival being 25 months. The difference in the log-rank test was significant.

Among 13,502 patients with breast cancer at the Mayo Clinic, there were 60 patients (0.4%) with isolated pulmonary metastases. Actuarial 5-year survival was 35.6% in those with apparent complete resections and 42.1% with incomplete resections. This study did not address the factors of possible prognostic significance. The authors could not demonstrate improved survival after complete pulmonary resection of metastatic breast carcinoma in this highly selected group of patients.

Generally in pulmonary metastasectomy, a long disease-free interval (DFI) after treatment of primary tumor is a prognostic factor associated with positive survival outcomes. In lung metastases from breast cancer with or without chemotherapy, this has been shown. In complete resections and DFI of ≥36 months, the analysis of this factor shows a 5-, 10-, and 15-year survival of 45, 26, and 21%, respectively. When DFI was <36 months, survival rates at same times were 28, 16, and 16%, respectively (P = 0.0001). In incomplete resections, patients with a DFI ≥ 36 months also have a more favorable prognosis.

Various perioperative variables were investigated retrospectively in 41 patients by Chen et al., after lung metastasectomy from breast cancer, to confirm the role of metastasectomy and to analyze the prognostic factors for overall survival. These authors considered that pulmonary metastasectomy in patients with previous breast cancer might be justified when fewer than four pulmonary metastases were present or there was a DFI of more than 3 years.

Adjuvant therapies are the norm in breast cancer, and additional chemotherapy before, after, or before and after metastasectomy is likely to have an effect making interpretation of the effect of surgery difficult. In a study by Staren et al., the mean survival time was 55 months in the group receiving surgery compared with 33 months in the group receiving medical treatment only. Murabito et al. reported a mean survival time of 79 months.
in patients receiving surgery versus 9 months in patient receiving medical treatment. In the International Registry of Lung Metastases (IRLM), 5-year survival after complete resection and without further therapy was 39%, with chemotherapy after resection 44%, and with prior chemotherapy 20%.

Welter et al. retrospectively analyzed the role of breast cancer metastasectomy in 47 patients with histologically proven pulmonary metastases from breast cancer. The main prognostic factor was the estrogen receptor status, with a 5-year survival for receptor positive patients of 76% and 12.1% for receptor negative ones.

**DISCUSSION**

The widely varying outcomes in the eight series summarized by Singletary et al. exemplified by quoted 10-year survival ranging from 8 to 60% is clearly a problem in drawing firm conclusions from these reports. This variation is more likely to be attributable to the patients and their selection than to the quality or effectiveness of the surgery they received.

Selection is extreme. Two articles provide a denominator and are summarized in Table 1. Few patients with breast cancer have solitary isolated lung metastases, and only some of them are operated on. When the denominator is available, a similar number (approximately 1/200) have surgery, and the outcomes are identical for the highly selected patients with operated solitary lung metastasis.

In assessing the effectiveness of metastasectomy, it is usual to compare the results for those in whom complete resection was achieved and in those in whom it was not. In the IRLM data, there was twice the 5-year survival (38% versus 16%) and a longer median survival. The difference (albeit not significant) was in the other direction in the Mayo clinic report (36% versus 42%).

Other factors associated with longer survival are the number of metastases and the interval since the initial presentation, the diagnosis or first resection, and the pulmonary metastasectomy, rather loosely referred to as the DFI. These apply in breast cancer data, but as with other cancers, it is a general prognostic feature irrespective of metastasectomy.

Given that breast cancer is treated as a systemic disease and chemotherapy is the norm, separating the effects of surgery from chemotherapy is difficult. Similarly, estrogen receptor status is a general factor in the prognosis of breast cancer. Welter et al. concluded that the evidence for a curative approach is low and that gains in life expectancy for patients with breast cancer with pulmonary metastases are attributable to chemotherapy and antihormone treatment.

**CONCLUSION**

Although resection of pulmonary metastases is a common treatment in other primary malignancies, the role of breast cancer metastasectomy is controversial. It should be noted that the majority of solitary nodules in these patients are not breast cancer metastases, so resection of solitary nodules in these women who may otherwise have a good prognosis is appropriate for diagnosis and guide management. The level of evidence for a curative approach for resection of proven pulmonary metastases is low, but the evidence does not preclude the possibility that some patients might benefit from a metastasectomy preceded or followed by appropriate oncological treatment.

**REFERENCES**