

## Surgery Remains the Best Solution for Patients With Soft-Tissue Sarcomas

**A** new retrospective analysis finds that prolonged survival from metastatic sarcoma can be achieved for selected patients with repeated resections of metastases (*J Surg Oncol.* 2018;118:167-176).

Study co-author Hans-Georg Kopp, MD, from the department of medical oncology, hematology, immunology, rheumatology, and pulmonology at the University of Tübingen in Germany, says that to the authors' knowledge, only a small number of retrospective studies have reported a survival benefit for patients with soft-tissue sarcoma after complete resection of pulmonary metastases. "While our study does not break new ground, it does confirm what others have found previously: surgical removal of metastases may be beneficial in sarcoma patients, especially if they have been carefully selected. Indeed, clinical characteristics such as resectability of metastases, time of recurrence, and number

of metastases are helpful biomarkers when it comes to the consideration of metastasectomy in individual cases."

### Study Details

Patients selected for inclusion in the study were identified from the database of patients from the University Hospital Tübingen who were diagnosed with sarcoma between October 1982 and October 2015. Each patient was aged 18 years or older and underwent surgical resection of regional and/or distant metastases.

The researchers characterized a series of variables that could influence the overall survival (OS) of patients with metastatic sarcoma (OS was the primary endpoint of the analysis). These independent variables included:

- Patient sex and age at diagnosis.
- Histological type and grade of the primary tumor, anatomical site, size, resection of the primary

### KEY POINTS

- Surgery remains the primary option for patients with metastatic soft-tissue sarcoma who are candidates for intervention.
- Repeated resections of metastases from different localizations are a strong predictor of prolonged survival.
- Long-term survival of at least 10 years was achieved in a significant percentage of the patients studied.
- The PFI after prior treatments should be considered as a decisional support for repeated resection of metastases.

tumor, and cancer center in which the primary histological diagnosis was made.

- Time of occurrence of metastases, their location, and the number of metastases.
- Treatment of metastases, including resection at first recognition of metastases, number of metastasectomies, surgeries according to the number of metastases resected during each operation, number of pulmonary resections performed for metastases, the surgical technique used for pulmonary metastasectomies, and the type of lung resection performed.

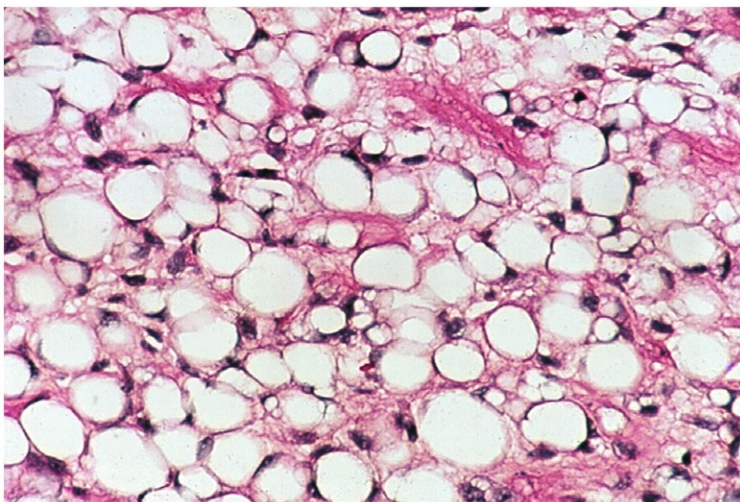


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- Disease outcomes, including whether a local recurrence occurred before metastases and the progression-free interval (PFI).
- Whether the first-line therapy was surgery only or surgery combined with radiotherapy, chemotherapy, or radiochemotherapy.

A total of 102 patients (42 men and 60 women) who underwent at least 1 metastasectomy were included in the study. The age range of the patients at the time of primary diagnosis was 19 to 85 years with a median age of 47 years.

Because pathology specimens that were over 10 years old were routinely disposed of, central pathology review from 26 patients (25.5%) could not be performed. Of the 76 tumor samples available for central review, the reference pathologist revised the histological type or grade of 9 cases and 14 cases, respectively; for 3 cases, both type and grade were revised.

## Main Findings

Of the 102 patients, researchers were able to document the histological grade for 87.3% (89 patients). These included 37 patients with metastatic sarcoma with initially low-grade (grade 1 or 2) disease. High-grade disease (grade 3) was reported for 52 patients.

Tumor size at the time of the primary diagnosis was recorded in 50 patients. In 4 patients, the primary lesion measured less than 5 cm. In 46 cases, it measured 5 cm or more.

The researchers found that there were 24 patients with synchronous metastases at the time of the primary diagnosis, and 69 patients who subsequently developed metachronous metastatic disease.

Metastases in 72 patients were limited to 1 site, whereas 30 patients had metastases in 2 or more sites. Not surprisingly, there were 44 patients (43.1%) in whom the initial single site of metastasis was the lungs.

A total of 80 patients underwent resection of the metastases at the first indication of metastatic disease, and 22 patients underwent surgery at a later time. There were 53 patients who underwent more than 1 metastasectomy, including those who underwent 2 (28 patients; 27.5%), 3 (17 patients; 16.7%), 4 (3 patients; 2.9%), 5 (3 patients; 2.9%), 6 (1 patient; 0.1%), and even 7 (1 patient; 0.1%) resections of metastatic disease.

A total of 44 patients (43.1%) did not undergo any surgery for lung metastases because their pulmonary metastases were unresectable or because unresectable metastases occurred at 1 or multiple sites.

There were 12 patients who developed a local relapse prior to distant metastases and 90 patients who demonstrated solely metastatic relapses. Information regarding PFI was available for 96 patients, with 44 individuals having a PFI of less than 12 months and 52 patients with a PFI of 12 months or longer.

The researchers reported that with an average observation time of 118 months, the median OS of the 102 patients with soft-tissue sarcoma was 64 months. Survival rates at 3, 5, 10, and 20 years were 70.7%, 50.3%, 24.7%, and 14.8%, respectively. These results, Dr. Kopp says, are consistent with earlier studies, most notably a study by the French Sarcoma Group of 1024 patients who had synchronous metastatic soft-tissue sarcoma (*Cancer*. 2011;117:1049-1054).

## Study Strengths and Weaknesses

Dr. Kopp says that although there were no real surprises uncovered, “the strength of our study was the comparatively high number of patients and the long follow-up.” In their conclusion, the researchers state that in patients with operable disease, especially if metastases occurred after a significant PFI, “resection of metastases is an effective therapeutic option with a significant survival benefit at the time of primary diagnosis, as well as for recurrent occurrence. Notably, long-term survival of at least 10 years was achieved in a significant proportion of patients.”

“The utility of this study is purely confirmatory,” says Keith A. Delman, MD, vice chairman of education and professor of surgery in the division of surgical oncology at Emory University School of Medicine in Atlanta, Georgia. Dr. Delman agrees that because there is no effective systemic therapy for most types of metastatic sarcomas, surgery should be considered when an option. “Surgery remains the primary option for patients who are candidates for intervention—even aggressive surgery.”

Dr. Kopp says the next step should be to correlate their findings with a new, deeper understanding of the molecular pathology. “For example, if we knew that subgroups of soft-tissue sarcoma with certain mutations would (or would never) benefit from rather aggressive surgical removal of metastases, we could better advise our patients.”

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