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Original Article

Effect on Survival of Local Ablative Treatment of Metastases from Sarcomas: A Study of the French Sarcoma Group

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Abstract

Aims: Recent data suggest that patients with pulmonary metastases from sarcomas might benefit from ablation of their metastases. Some data are available regarding osteosarcomas/angiosarcomas and lung metastases. The purpose of this study was to assess the efficacy of local ablative treatment on the survival of patients with oligometastases (one to five lesions, any metastatic site, any grade/histology) from sarcomas.
Materials and Methods: A multicentric retrospective study of the French Sarcoma Group was conducted in sarcoma patients with oligometastases who were treated between 2000 and 2012. Survival was analysed using multivariate sensitivity analyses with propensity scores to limit bias.
Results: Of the 281 patients evaluated, 164 patients received local treatment for oligometastases between 2000 and 2012. The groups' characteristics were similar in terms of tumour size and remission of the primary tumours. The median follow-up was 25.7 months; 129 (45.9%) patients had died at this point. The median overall survivals were 45.3 (95% confidence interval = 34–73) months for the local treatment group and 12.6 for the other group (95% confidence interval = 9.33–22.9). Survival was better among patients who received local treatment (hazard ratio = 0.47; 95% confidence interval = 0.29–0.78; $P < 0.001$). Subgroup analyses revealed similar findings in the patients with single oligometastases (hazard ratio = 0.48; 95% confidence interval = 0.28–0.82; $P = 0.007$); a significant benefit was observed for grade 3, and a trend was observed for grade 2.
Conclusion: Local ablative treatment seemed to improve the overall survival of the patients who presented with oligometastatic sarcomas, including soft tissue and bone sarcomas. The survival benefit remained after repeated local treatments for several oligometastatic events. Surgery yielded the most relevant results,

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but alternative approaches (i.e. radiofrequency ablation and radiotherapy) seemed to be promising. The relevance of these results is strengthened by our analysis, which avoided biases by restricting the population to patients with oligometastatic disease and used propensity scores.

Key words: Local treatment; metastectomy; oligometastases; radiofrequency; radiotherapy; sarcoma

Introduction

Metastases of solid tumours have been considered to be non-curable diseases. However, oligometastases and oligorecurrence, which correspond to limited numbers of typically non-bulky metastases, seem to have different natural histories and better prognoses than polymetastatic disease [1,2]. This entity might thus be proposed to be an intermediate stage between non-metastatic and metastatic diseases [3]. The benefit of the aggressive treatment of metastases was shown in colorectal cancer with pauci-metastatic liver or lung dissemination in the 1980s [4]. Local treatments, which often consist of surgery, have been carried out sequentially after systemic treatment and have primarily included chemotherapy. This approach has since been extended to other cancer types; here, we contribute to the paradigm shift in the treatment of oligometastatic disease.

The incidence of sarcomas is estimated to be about 1–3 per 100 000 persons per year; i.e. about 2000 patients in France. About 50% of patients with sarcoma will experience metastases during the course of the disease. The median overall survival for metastatic sarcomas went from 12 months in the 1990s [5] to 18–24 months in recent studies [6,7]. Local treatments have increasingly been used in recent years for cases of sarcoma. This aggressive surgical attitude has been assessed retrospectively in several sarcoma subtypes, and such investigations have yielded the best evidential foundation for the ablative techniques. Historically, surgical ablations of metastases have primarily been studied in young patients [8] and osteosarcomas result in 5 year survival rates of 20–40%, regardless of systemic treatments, according to several clinical international studies. There are also suggestions of the benefit of surgery for the metastases of soft tissue sarcomas [9,10], which result in long survival times in selected cases [11]. Currently, surgery has the highest level of evidential support regarding the ablation of limited metastases due to reports of cured patients with lung [12], hepatic [13], adrenal [14] and brain [15] metastases; thus, fewer, less-invasive, non-surgical ablative modalities, including radiotherapy [16] and radiofrequency ablation (RFA), have been developed over the last 20 years [17].

The choice between these local strategies has been highly dependent on institutional preferences and, thus, any attempts to conduct randomised trials have been precluded. Systemic treatments are often limited by tolerance and are typically carried out with palliative intent after second-line therapies. Local treatment might be carried out sequentially with chemotherapy or targeted therapy. The patterns of local treatment care over the course of metastatic sarcomas are scarcely described.

Our objective was to assess the effects of local treatment on the overall survival of patients with oligometastatic bone and soft tissue sarcomas, including different histological subtypes and metastatic sites, using propensity scores to avoid selection biases.

Materials and Methods

Patients

Sarcoma patients were selected for this board-approved multicentric retrospective study of the French Sarcoma Group if they had oligometastases that were diagnosed and treated between 2000 and 2012. Oligometastases could occur at any time from disease onset to follow-up regardless of polymetastatic events. Oligometastases were defined as the occurrence of one to five simultaneous metastases regardless of the sites and histologies of those metastases. The World Health Organization tumour classification system was used [18]. The classification of the histology subtypes is presented in Supplementary Data. For clinically relevant statistical purposes, a 'histology grade' was created to account for the 'non-gradable' histologies (e.g. Ewing sarcomas, rhabdomyosarcomas and non-graded synovialosarcomas were included in the grade 3 group). Local treatment was defined as ablative if the aim was to remove all metastases either by means of surgery, RFA or radiotherapy. For subgroup analyses, the irradiated patients were defined by the receipt of an ablative dose of at least 50 Gy in a 2 Gy equivalent dose. The patients were included if they had received a local ablative treatment for metastases before inclusion in 2000, but were not included in the local treatment group in our analysis.

Statistical Analyses

The differences between groups were evaluated using chi-squared or Fisher's exact tests for categorical variables and Student's or Mann–Whitney tests for continuous variables. Overall survival (the main end point) was defined as the time from the diagnosis of oligometastases (at inclusion in the study) until death (all causes). Surviving patients were censored at the last follow-up date. Two-way sensitivity analyses were carried out using propensity scores. A propensity score was incorporated into the model to control for potential selection biases. Indeed, in contrast to randomised trials, observational retrospective studies, although representative of clinical practice, are intrinsically biased by patient selection. The propensity scores (defined as the probability of a case subject receiving a local treatment for