Lung metastases from Soft Tissue Sarcoma

Impact paragraph

Lung metastases (LM) are the most frequent consequence of Soft Tissue Sarcoma (STS) but, while a lot of research has been focused on the primary tumor, less is known about the diagnosis and the treatment of LM that represent a challenge for clinicians, since LM represent an advanced stage of the disease and are the most frequent cause of death.

This Thesis was aimed at getting more insights into diagnosis, treatments, and prognostic factors of LM secondary to soft tissue sarcoma with a glance to future perspectives.

Important messages came across from our data that can influence clinical decision making.

First, the discrimination between benign and malignant PNs, particularly in small nodules, is challenging. Early detection of pulmonary LM in these patients is critical for choosing the best treatment option (surgical resection, chemotherapy, radiotherapy, etc.) that significantly influences prognosis. CT imaging represents the gold standard for detecting PNs. With the introduction of last-generation CT scanners, the number of detected nodules has dramatically increased. Therefore, a non-negligible number of suspicious lung nodules may be negative for malignancy on histological examination. On the other hand, false-negative CT findings are not infrequent with small nodules identified at lung surgical palpation. Therefore, CT screening of suspicious nodules is still an area of active research.

We have demonstrated that lung nodules > 5.6 mm, well-defined margin nodules, increased size from baseline CT, and a new onset nodule, increase the risk of malignancy up to 28 times when associated with synovial sarcoma histology. However, our data have highlighted that without the support of clinical data, many CT features lose their specificity.

For instance, we found that 30% of malignant nodules did not increase in size and 52.4% of them showed ill-defined margins. In addition, to further complicate the matter, a well-defined nodule is also typical of a benign lesion and the other significant CT features are shared with many other neoplasms.

The question arises as what to do when detecting very small nodules at CT scan that do not increase in size and have no defined margins. The key message is that, in case of STS grade ≥ II, residual primary tumor ≥ R1, and when the primary tumor is a leiomyosarcoma, referral to surgery is, in our opinion, mandatory.

Surgical resection is well accepted as a standard approach to treat metastases from STS isolated in the lungs.

Synovial sarcoma and myxofibrosarcoma increased the risk of disease-specific death by 2.5 times after lung metastasectomy (LMTS). The overall survival of synovial sarcoma has not significantly changed across the last three decades, and this can be attributed to the age-shift of patients towards older age, the reduction of localized forms of the tumor and the higher percentage of cases in the trunk, lung, and pleura, all factors negatively influencing the prognosis.

In our clinical practice, we have observed that very often, the number of recurrent metastases is very high with synovial sarcoma making these lesions poorly or not suitable to surgery.

Moreover, myxofibrosarcoma is one of the most common type of STS in patients over 60 years, and it is one of the most aggressive type of these neoplasms. Its clinical diagnosis, as well as its histopathologic identification, can be challenging. In our cohort, most of the myxofibrosarcomas were > 5 cm, and more often, the tumor was located distally. All these features have been correlated with a worse prognosis.

Our analysis showed that, in case of malignant peripheral nerve sheath tumor (MPNST) histotype, a disease-free interval (DFI) up to 68 months and a lung nodule size ≥ 4 mm predicted lung recurrence after the first metastasectomy.

In addition, our high-performance machine learning-based model demonstrated that older age at the primary tumor diagnosis was the strongest feature (100%) related to recurrence of STS lung metastasis after the first lung metastasectomy.

Despite the limitation of the small number of patients in our cohort, this research gives insights that can have an important impact on clinicians dealing with STS.

Our thesis strongly supports a multidisciplinary STS team involving radiologists, radiotherapists, oncologists, surgeons, and pathologists for clinical decision-making bearing in mind that professional reduced awareness of STSs as well as the non-specific nature of many symptoms of these rare neoplasms may lead to delays in diagnosis.