Predictors of survival after resection of retroperitoneal sarcoma, the pathologist point of view.

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Adult soft tissue sarcomas are rare heterogeneous and aggressive mesenchymal tumours in terms of location, histology, molecular profile and prognosis. It should be noted that the World Health Organization recognizes over 100 different subtypes of soft tissue lesions, each with specific presentation and biologic behaviour. Accurate diagnosis by a dedicated experienced (soft tissue) pathologist is essential to define patient prognosis. Retroperitoneal soft tissue sarcomas (RPS), excluding visceral sarcomas, account for 0,15% of all malignancies and about 15% of soft tissue sarcomas. Their tendency for locally advanced disease at presentation, difficulty to resect with widely clear margins, and predilection for local recurrences contribute to the complexity of their clinical management. Therefore, diagnostic work-up and treatment of RPS in specialized centres are recommended. In the retroperitoneum, the most common histologic subtypes include well-differentiated and dedifferentiated liposarcoma, which often recurs only in the retroperitoneum, and leiomyosarcoma, which is associated with high rates of distant metastases in addition to local recurrences. Solitary fibrous tumours, gastrointestinal stroma cell tumours (GIST) and desmoids are also relatively not uncommon in the retroperitoneum. Surgery remains the primary treatment modality, with complete resection the only chance for cure. The roles of radiation therapy and chemotherapy remain controversial. Current American Joint Committee on Cancer (AJCC) soft tissue sarcoma staging is derived from data examining prognostic factors in patients with extremity STS. Because of essential differences in disease characteristics, its applicability in staging RPS is limited. This is why the development of reliable prognostic tools is needed. In an attempt to improve the predictive capacity of sarcoma-specific risks of death in general and/or in RPS contexts, several soft tissue sarcomas nomograms have been proposed. It is now recognized that histological (sub) type and histological grade are the most important prognostic factor for adult soft tissue sarcomas. As the best predictor of metastasis development and tumour mortality, histological grade is a key parameter of the currently used TNM clinicopathological staging system. Two histological grading systems are used in daily practice, the National Cancer Institute (NCI) and the French Federation of Cancer Centres Sarcoma Group (FNCLCC) systems. They have been devised by combining histological parameters: number of mitoses per high-power field, the presence of necrosis, cellular and nuclear morphology and the degree of cellularity for the NCI grading; and tumor differentiation, mitotic index and extent of necrosis for the French system. Histolological grading is a cheap, quick and easy method for identifying sarcomas with high metastatic potential, and should be used in daily practice for most soft tissue sarcomas. However, its limitations should be kept in mind: no current grading system performs well for every type of sarcoma, and grading is less informative than histotype for some of them. Furthermore, its moderate reproducibility and the existence of an intermediate grade representing almost half of cases and corresponding to undetermined prognosis, should not be forgotten. The current universal use of core needle biopsies is also a limitation for grading. The development of molecular grading in addition to histological grading probably represents the next step. Molecular signatures based on quantities evaluation of chromosomal complexity such as CINSARC (complexity index in sarcomas) appear as a strong independent predictive factor for metastasis in several types of sarcoma (including leiomyosarcomas, high-grade undifferentiated sarcomas, synovial sarcomas and GISTs). When they can be instituted in daily practice on formalin fixed, paraffin embedded material, molecular signatures will not only provide information on risk of metastasis, but also better understanding of cancer development, response or resistance to evaluated drugs, and potential targets for future treatments.