Extra-Thoracic Solitary Fibrous Tumours: Outcomes and Prognosis

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Abstract

Introduction: Solitary fbrous tumours (SFTs) are rare spindle cell neoplasms and have been described according to location as intra-thoracic and extra-thoracic. The World Health Organization classifes SFT as having intermediate malignant potential with low risk of metastasis. Initially extra-thoracic SFTs (ESFT) were considered to be benign with lower rates of mortality when compared to their thoracic counterpart. However, more recent series have found that ESFT behave more aggressively than previously thought. Our tertiary referral ag ,
classifed as malignant (MSFT) and 71% tumours were classifed as benign (ESFT) after resection. We noted that 50% for patients with MSFT were initially benign ESFT on initial biopsy.

Conclusion: Our study showed that 50% of biopsies for patients with MSFT were initially benign and we feel this has important surgical considerations. Certain prognostic factors are important to help risk stratify these patients. We would recommend that patients with ESFT should be kept under surveillance in a manner similar to patients with malignant soft tissue sarcomas.

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A review of all patients with a pathological diagnosis of ESFT was carried out between 2006 and 2019. Ninety-five patients were identified during this 13-year time period; the relevant biopsy and resection histopathology data was reviewed using the hospital electronic patient record system. A database was created to record patient demographics, diagnosis, tumour size, tumour site, tumour depth and surgical resection margins. Clinic notes were reviewed to record follow up data including adjuvant therapy, local recurrence, metastases and survival months for cases with at least two-year follow up data.

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The aim of all analyses was to examine the association between patient and tumour characteristics in relation to three outcomes: recurrence, metastasis and survival. As there were several factors of interest, the analyses were performed using regression methods. The specific method was dependent on the nature of outcome variable.

For each outcome, the analyses were performed in two stages. Initially, a series of univariable analyses examined the association between each factor and the outcome. The second stage of the analysis examined the joint association between the factors and the outcome in a single multivariable analysis. To restrict the number of variables in this second stage in the analysis, only variables showing some association with the outcome in the univariable analyses ($p<0.2$) were considered. To retain only the statistically significant variables in the final model, a backwards selection procedure was used. This involves omitting non-significant variables, one at a time, until only significant variables remained.

Both recurrence and metastasis were binary (yes/no) outcomes. Due to this characteristic, the analysis for these outcomes was performed using logistic regression. The exception to the above method of analysis was when there were no recurrences in one category of a variable. In such a situation, logistic regression cannot be used, and the analysis was instead performed using Fisher's exact test. Survival analysis methods were used to analyse patients over survival; by using a time to death or time last known to be alive. Due to the survival nature of the outcome, the analysis was performed using Cox regression.

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A total of 95 patients had a diagnosis of ESFT on biopsy or resection histology between 2006 and 2019. Of these 75 were eligible for the study. 20 patients met the exclusion criteria. Five patients were excluded because of thoracic SFT location. 12 patients only had biopsy data and no resection data. Two patients had myxoid spindle cell lipoma as the diagnosis and one patient had atypical lipomatous tumour as the diagnosis. The remaining 75 patients who were used for analysis in the study had biopsy and resection data. 14 of these patients were diagnosed between 2017-2019 and therefore follow up data (recurrence, metastasis, survival) was not analysed for these cases.

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The results suggested that histological diagnosis, tumour location and mitotic count were statistically significant with regards to metastasis when examined individually. However, there was no significant association with margins, tumour size or tumour depth. Metastasis was more common in MSFT patients, where it occurred in over 40% patients, than benign ESFT patients (2%). The odds of metastasis were 30 times greater in MSFT patients than in benign ESFT patients. The pelvis/trunk location had the highest occurrence of metastasis with half of all patients with this tumour location having developing metastatic disease, compared to less than 10% of patients in the other outcomes. The odds of metastasis were 11 times higher in the pelvis/trunk location compared to the lower limb. Additionally, 80% of the tumours in the pelvis/trunk location were malignant ESFT. A higher mitotic count was also associated with a greater chance of metastasis. Those in the ≥ 4/10 had odds of metastasis that were over 12 times higher than those with a lower count.

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Initially the survival of the group as a whole was examined. The data suggested that the median survival time for all patients was 8.0 years. When examining individual factors, only histological diagnosis was found to be significantly associated with patient survival (p 0.005). Survival was shorter in the MSFT who had a median survival time of 5 years, contrasting with a median survival of 11 years for the SFT group. The risk of death at any time in the MSFT group was 6.5 times greater than in the benign ESFT group. A graphical illustration of the survival times for the two diagnosis groups are shown in Figure 1. None of margins, tumour location, mitotic count, tumour size and tumour depth were significantly associated with survival times Table 2.

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Complete resection was achieved in 73/75 cases, two cases had fragmented tumour specimen. Adjuvant therapy data and treatment regimens were reviewed for patients who presented between 2006–2016 (52 cases). 10/52 cases had malignant features on tumour resection data and were treated with neoadjuvant therapy. Specifically,

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SFT were initially described as intra-thoracic however these tumours have been subsequently discovered in extra-thoracic locations including head and neck, abdomen, pelvis, retroperitoneum, breast and extremities [14]. Initially, ESFT were reported to be benign with lower rates of recurrence of 6% and 1% mortality when compared to their thoracic counterpart [11] however, since extra-thoracic SFTs have been considered separately, there have been studies which show that ESFT may have increased rates of malignancy [12,13, 15]. There are very few studies that have analysed clinical outcomes of recurrence, metastasis and death in patients with extra-thoracic tumours.

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Our study showed 22 MSFT out of a total 75 cases (29%) from 2006 to 2019 which is correlates with the most recent literature review reporting a range of 11 to 33% malignant ESFT [13]. We were able to collect data on recurrence, metastasis and survival for cases with adequate follow up (n=61). Our overall rate of recurrence and metastasis for benign and malignant ESFT was 11% and 13% respectively with an

recurrence, metastasise and malignancy than previously thought. Many studies have reviewed the histological data of ESFT however few have analysed the clinical outcomes and follow up data. Certain prognostic factors such as histological diagnosis, tumour location, presence of high mitotic count are important to help risk stratify and help identify those at risk of recurrence, metastasis and death. It is evident that there is a need for close surveillance as these tumours can behave aggressively and may have poor outcomes late on. In addition, we suggest that all ESFT should be resected in a similar way to high grade soft tissue