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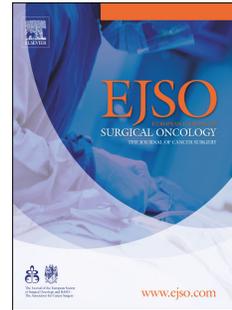
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CURRENT PATHOLOGY WORK-UP OF EXTREMITY SOFT TISSUE SARCOMAS, EVALUATION
OF THE VALIDITY OF DIFFERENT TECHNIQUES

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Abstract

Objective: In patients with extremity soft tissue sarcomas (STS) a correct histopathological diagnosis is considered important before surgical treatment. We evaluated the preoperative use and sensitivity of the various pathology techniques.

Methods: In a population based study in patients operated for a newly diagnosed extremity STS between January 2000 and December 2003 the preoperative pathology work-up was evaluated. Data were retrieved from a national pathology database (PALGA). The sensitivity of the three techniques was assessed considering an examination affirmative when the conclusion of the pathology report stated the presence of mesenchymal malignancy.

Results: The pathology reports of 573 patients were identified in the database. In 177 patients (31%) no pathology examination was done before resection of the tumour. In the remaining 396 patients the pathology procedure of first choice had been an incisional biopsy (IB) in 195 patients (49 percent), a core needle biopsy (CNB) in 90 patients (23 percent) and a fine needle aspiration (FNA) in 111 patients (28 percent). An affirmative diagnosis was established in 95% of the patients following an IB, in 78% after a CNB and in 38% following FNA. After an initial CNB an additional IB was performed in 18 of the 90 patients improving the yield to 89%. After an initial FNA a subsequent histological biopsy was done in 53 of the 111 patients, increasing the sensitivity to 71%.

Conclusions: In this population based study in patients treated for extremity STS, the proportion of patients operated without preoperative pathology evaluation was high. In the remaining patients an incisional biopsy was still the most commonly performed technique with the highest yield.

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Key words:

Soft tissue sarcoma, extremity, pathology, biopsy

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Introduction

The advocated work-up of extremity soft tissue tumours consists of magnetic resonance imaging (MRI) followed by a histological biopsy. An open incisional biopsy (IB) has traditionally been the golden standard for establishing a preoperative histopathological diagnosis. Although the sensitivity of an IB is high, the technique has disadvantages. General or regional anesthesia is usually needed while wound complications are common and affecting the treatment plan in up to one fifth of patients who had an IB. [1]

Several studies have documented good results with less invasive diagnostic procedures like large core needle biopsy (CNB), reporting a sensitivity of core needle biopsies of approximately 95 percent. [2-5] Therefore core needle biopsies has become equally acceptable in the last 15 years. Some authors even advocate the use of fine needle aspiration (FNA).[6] CNB and FNA are less invasive procedures and since the diagnostic yield in expert hands is high, [7,8] these procedures might displace IB as the routine pathology examination of extremity soft tissue tumours.

Most of the reported data originate from specialised cancer centers, thereby potentially introducing selection bias. In patients with soft tissue masses, who are referred to such hospitals, the level of clinical suspicion is usually high as well as the expertise of the examining pathologist .

We conducted a population-based study by selecting patients from a Dutch national pathology database. The current use and yield in everyday practice of the various pathology techniques in the work-up of extremity STS was evaluated.

Patients and Methods

Study design

Population based data were retrieved from the Dutch Network and National Database of Pathology (PALGA). PALGA is a computerized database that receives its information from all pathology laboratories in the Netherlands. Standardized abstracts from local data are coded by local pathologists according to the SNOMED classification [9] and then submitted to PALGA. The PALGA database contains standardized abstracts with items about the anatomic localization of the tumour, the type of biopsy or cytology, the SNOMED code of the diagnosis and an abstract of the pathology report with further pathological aspects of the diagnosis. The information in the database is limited: it does not provide demographic data of the patient, nor information about tumour size and it does not allow patient identification (for patient privacy reasons).

A search was directed to all records filed in the PALGA database regarding patients operated for a newly diagnosed extremity soft tissue sarcoma (STS). Skin lesions and desmoid tumors were not included. All standardized abstracts of patients operated between January 2000 and December 2003 were selected. In addition, records of these patients regarding the preoperative pathology examinations were retrieved from the same database.

The pathology work-up was studied by evaluating the preoperative use of an open IB, a large CNB and a FNA. Secondly, the sensitivity of these three techniques was assessed by reviewing the conclusions of the PALGA abstracts for an affirmative diagnosis. When the abstract of the preoperative examination stated the presence of a 'mesenchymal malignancy' the examination was considered affirmative. In addition to the analysis of the separate techniques, we evaluated the yield of the strategies as determined by the initially performed pathology technique, e.g. the yield of all performed pathology examinations in the group of patients that initially had a FNA.

Finally, the abstracts were reviewed for histomorphological sarcoma type. The preoperative histomorphological diagnosis was compared to the definitive diagnosis of the operative specimen, which

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was considered the “gold standard”.

Statistical analysis

Associations between proportions of affirmative diagnoses of the various techniques and various clinicopathological factors were explored using Chi-square analysis.

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Results

In the PALGA database 573 records were identified of patients surgically treated for a primary extremity STS during the study period. The median age of the patients was 56 years (range 0-98 years), gender was equally distributed. The baseline characteristics and the final histomorphological sarcoma subtypes are listed in table 1.

Use of the various pathology techniques

Preoperative pathology examination was done in 396 patients. In these patients an IB was most often done, and the initial and only pathology investigation in 49 percent of the patients (Figure 1). Following an initial CNB a subsequent IB was done in 20 percent of the patients, while an initial FNA was followed by an additional histological biopsy procedure in 47 percent.

In one third of the patients the sarcoma was excised without any preoperative pathology investigation. There was no relation was between gender and age on the one hand, and performing preoperative pathology investigations on the other. Patients with tumours of the leg more often had preoperative pathology examinations than patients with tumours of the upper extremity (72 vs 59%; $p=0.004$) and a number of sarcoma subtypes (liposarcoma and sarcomas NOS) were more often biopsied than leiomyosarcomas (75 vs 58%; $p=0.01$). (Table 1.)

False positive results

With only 2 patients a false positive result was found. Both cases were incisional biopsies. In 1 case a myxoma of the right upper arm had been preoperatively diagnosed as a myxoid liposarcoma and in 1 case a fibromatosis of the left calve had been diagnosed as a leiomyosarcoma.

Yield of the various pathology techniques and workup strategies

An IB resulted in an affirmative diagnosis in 95 percent of the procedures, compared to 78 percent following a CNB and 38 percent after FNA ($P<0.001$; Table 2). When reviewing the pathology reports of the 20 negative core needle biopsies, 9 of the reports concluded that there was some kind if suspicion for malignancy, prompting additional incisional biopsy. In the other cases there was too little material,

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biopsies showed only necrosis, or biopsies did not seem to be representative for the tumour. One biopsy showed mesenchymal malignancy when evaluated in retrospect. IBs following CNBs increased the proportion of affirmative diagnoses from 78 to 89%. (Table 3). Similarly, histological biopsies following initial FNA, increased the proportion of patients in whom an affirmative diagnosis was established preoperatively from 38 to 71 percent.

The sarcoma histomorphology type of the preoperative pathology examination was consistent with the final pathology in 80 percent of the IBs, 56 percent of the CNBs and 10 percent of the FNAs ($p < 0.001$). For IB and CNB, no influence of tumour localization or sarcoma subtype was observed on the proportion of affirmative diagnoses (data not presented).

Discussion

In this population-based study the current use and yield of the various pathology techniques in the preoperative work-up of patients with extremity soft tissue sarcomas was evaluated.

In everyday practice an open incisional biopsy was the investigation of first choice and had the highest yield. Furthermore, still one third of the patients underwent tumour resection without any preceding pathology examination.

Limitations and strength of the study design

Inherent to its design, the study has a number of limitations. The pathology database consists of structured abstracts and therefore contains limited information. Data about the size of the tumour, and the superficial or deep localization of the mass are not available. In addition, the anonymised character of the PALGA database precludes retrieval of clinical data so information about the clinical outcome of the patient is not present either.

Then again, the population based nature of the study is its major strength too. The data do not come from selected centers, where patients are referred to with an already proven or a probably malignant soft tissue tumour. Instead, the information originates from all hospitals in the Netherlands, much in accordance with the referral pattern of patients presenting with soft tissue “lumps”. The present study therefore provides insight into the current “everyday-practice” pathology work-up of patients referred for an extremity tumour that ultimately turns out to be a soft tissue sarcoma..

Use and yield of the various pathology techniques

The main object of our study was the evaluation of the various preoperative pathology techniques. We more or less expected that core needle biopsies would have replaced incisional biopsies as the pathology procedure of first choice. In that respect, the results of our study appear disappointing at first sight. Recent studies have reported excellent results of large core needle biopsies with a reported sensitivity ranging between 90-95% [2,3,5,8], but in the present study large core needle biopsies were still less often used

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than open incisional biopsy, and the sensitivity was “only” 78%, which was substantially lower than the yield of open incisional biopsies. The aforementioned good results of core needle biopsies come from referral centers [2, 12-14], where there is vast experience with sarcoma treatment and hence with the diagnostic work-up too. The limited sensitivity of needle biopsies in the present population based cohort is most likely explained by less experience with the collection of specimens, and less experience with the evaluation of the retrieved material. Nevertheless, the difference between the diagnostic yield of incisional biopsies and core needle biopsies was substantial, as was the difference in obtaining a correct histomorphological diagnosis.

Notwithstanding the observed limited sensitivity of core needle biopsies, it would be premature to conclude that the yield of core needle biopsies is inferior to open biopsies. In 9 percent of the negative cases there was at least some suspicion for malignancy. We observed that the subsequent use of incisional biopsies in one fifth of these patients who initially had a core needle biopsy increased the overall yield of the preoperative pathology work-up in the present study to almost 90%. This “assisted” yield is comparable to the good results of core-needle biopsies in the aforementioned studies, and by doing so 80% of these patients (the cases where the core needle biopsy confirmed the presence of a sarcoma) were not exposed to the disadvantages of open biopsies. [1,15] The yield is not as high as in the group with an initial incisional biopsy, since we have defined the “assisted” yield as the results for the whole group of patients who started with a core biopsy. With some of these patients the level of suspicion must have been too low to add a subsequent incisional biopsy to the diagnostic process.

The same cannot be said about fine needle aspirations. Although the latter technique was used as an initial pathology technique as often as a core needle biopsy, the yield was much lower, even after subsequent histological biopsies. Since there are no real advantages of FNA over core needle biopsies, in combination with a very low diagnostic yield, clinicians should be dissuaded from using FNA in patients with extremity soft tissue tumours.

Resection without previous pathology

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While we observed a modest role of core needle biopsies in current everyday practice, an unexpected and worrisome finding of our study was the substantial proportion of patients that underwent resection of their malignancy without any previous pathology investigation. There may be reasons for not performing a biopsy on soft tissue tumours. Some argue that a histological diagnosis is not always necessary, e.g. lipotumours may sometimes be resected without a preoperative histological diagnosis based on the particular MRI-characteristics only. [16] However, the overpresentation of liposarcomas in the group who did have a preoperative biopsy suggests that this reason for not biopsying did not play a role. Another “legitimate” explanation for not biopsying would be the when the tumours were small superficial (subcutaneous) sarcomas, but we have no data to support this. Hence, unawareness of the malignant nature of the mass is the remaining, inconvenient but most probable, explanation. Few papers report on the frequency of these so-called “Oops” operations, one study finding a proportion of 15 %. [17] Our study suggests that the frequency of “Oops”-resections may be much higher than that. This is presently evaluated in a prospective population based clinical study in the central Netherlands.

While centralisation of sarcoma treatment is beyond dispute, centralization is not the solution to improve the work-up of soft tissue tumours. A condition that is not recognized in 30 percent of the patients cannot be referred. The referral pattern of patients with the whole range of extremity “lumps” to community hospitals and the high frequency of malignant tumours that initially go unrecognized, demonstrate the necessity for guidelines that are applicable and valid in everyday practice. The average patient with an extremity mass is referred to the community hospital. In that respect, improving acquaintance with the possibility of a soft tissue sarcoma should still be the top priority for guideline developers. Secondly, notion of a lower sensitivity of a diagnostic technique in other than expert hands should be met by pointing out this limitation of core needle biopsies to the general surgeon evaluating patients with extremity tumours.

Conclusion

In conclusion, in this contemporary population based cohort study evaluating current everyday

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preoperative pathology practice in patients with extremity STS, core needle biopsies were used in a minority of patients as an initial pathology examination. The diagnostic yield of core needle biopsies was low in comparison to other studies, but subsequent incisional biopsies improved the sensitivity in the group of patients who initially had core needle biopsies. An unexpected high proportion of patients underwent tumour resection without preoperative any pathology examination.

Conflict of interest

The authors state that they have no conflict of interest.

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Tables

Table 1. Baseline characteristics and factors affecting the chance of a preoperative biopsy being performed

	N	%	Preoperative pathology Yes (%)	Preoperative pathology No (%)
All patients	573	100	69	31
Gender				
Male	287	50	69	31
Female	286	50	69	31
Age				
0-20 yrs	32	6	66	34
20-40 yrs	119	21	66	34
40-60 yrs	172	30	73	27
60-80 yrs	194	34	66	34
80+	56	10	77	23
Localization				
Arm	136	24	59	41
Leg	437	76	72	28
Histomorphology				
Liposarcoma	172	30	75	25
Leiomyosarcoma	72	13	58	42
Malignant Fibrous Histiocytoma	72	13	74	26
Sarcoma NOS	71	12	75	25
Fibrosarcoma	64	11	67	33
Other	122	22	69	31

Table 2. The yield of the separate pathology techniques in patients with extremity STS (n=573);

2a. Percentage of patients with a conclusion of the preoperative pathology examination:

“mesenchymal malignancy”.

<i>pathology technique</i>	n	“mesenchymal malignancy”	(%)
incisional biopsy	249	237	(95)
core needle biopsy	116	90	(78)
Fine needle aspiration	111	42	(38)

2b. Percentage of patients with a correct preoperative diagnosis regarding histomorphology (preoperative diagnosis = final histomorphology)

<i>pathology technique</i>	n	Correct preoperative histomorphology	(%)
incisional biopsy	249	199	(80)
core needle biopsy	116	65	(56)
Fine needle aspiration	111	11	(10)

Table 3. “Assisted yield” of the various preoperative pathology examination strategies determined by the initially used pathology technique

Initial pathology examination	preoperative pathology examination: “mesenchymal malignancy”	preoperative histomorphology = final histomorphology
FNA (n=111) additional CNB (n=26), IB (n=36)	71%	36%
CNB (n=90) additional IB (n=18)	89%	57%
IB (n=195) None	95%	77%

Figure caption

Figure 1.

Preoperative pathology examinations in patients operated for extremity STS (n=573)

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Figure 1.

