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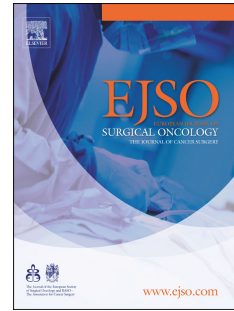
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Improved diagnosis and treatment of soft tissue sarcoma patients after implementation of national guidelines: a population based study

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ABSTRACT

Aim

The majority of clinicians, radiologists and pathologists have limited experience with soft tissue sarcomas. In 2004, national guidelines were established in the Netherlands to improve the quality of diagnosis and treatment of these rare tumours. This study evaluates the compliance with the guidelines over time.

Patients

Population based series of 119 operated patients with a soft tissue sarcoma (STS) diagnosed in 1998-1999 (79 before implementation of new guidelines) and in 2006 (40 after implementation)

Methods

Coded information regarding patient and tumour characteristics as well as (the results of) pathology review was collected from the medical patient file by two experienced data-managers.

Results

Diagnostic imaging of the tumour was performed according to the guidelines in 75-100% depending on the site of the tumour (abdominal versus non-abdominal) as well as the time of diagnosis.

Adherence to the guidelines with respect to invasive diagnostic procedures in patients with non-abdominal STS improved over time. A pre-operative histological diagnosis was obtained in 42% of the patients in 1998-1999 and in 72% of the patients in 2006 ($p < 0.001$). The guidelines for reporting on pathology were increasingly adhered to. In 2006, (nearly) all pathology reports mentioned tumour size, morphology, tumour grade, resection margins and radicality. This represents a major improvement compared to the pathology reports in 1998-1999, where these aspects were not mentioned in 14% to 40% of the cases. The proportion of prospective pathology reviews by (a member of) the expert panel increased from 60% in 1998-1999 to 90% in 2006 ($p = 0.001$).

Discussion

The compliance with the guidelines has been optimised by the increased attention to this group of patients. Most important factors have been the reporting of the results of the first evaluation and the (discussions about) the centralisation of treatment. Further improvements could be reached by the prospective web based registry monitoring logistic aspects as well as parameters useful for the evaluation of the quality of care.

INTRODUCTION

Soft tissue sarcomas (STS) are a rare and heterogenous group of tumours with a variable biology and clinical behaviour.¹⁻³ Subsequently, the majority of clinicians and pathologists have limited experience with the extensive variability in clinical and histopathological presentation of these tumours and their complex multimodality treatment. In the Netherlands a national guideline has been available since 1993.^{4-6*} In 1997 the guideline was regionally updated for the western part of the country.^{7*}

Pre-operative multidisciplinary discussion of the results of diagnosis and staging is considered as an essential element of the treatment strategy since the chosen surgical approach depends on the size of the tumour and its relation to surrounding structures, as well as the histological type of the tumour, the histological grade and the presence of metastases at the time of diagnosis. It is the aim of the multidisciplinary meeting to define the optimal therapeutic approach, which usually consists of resection of the tumour followed by radiotherapy if indicated.

In 2004 a new, national, evidence-based guideline was published.^{8,9} This guideline recommends the review of all available histological material by a regional expert panel. In the region of the Comprehensive Cancer Centre West (CCCW) such a panel has been available for a much longer time which enables the evaluation of the impact of pathologic review.

Compliance with guidelines is important for various reasons. Experience from clinical trials indicates that diagnosis and treatment according to strict rules affects clinical outcome and patient survival.¹⁰

Similarly, explicit guidelines improve clinical practice because appropriate preoperative investigations and accurate staging are essential for planning of appropriate treatment.¹¹

This study intends to evaluate the adherence to guidelines in the CCCW region over time (between 1998 and 2006) with the ultimate goal to further improve the quality of oncological care for patients with a soft tissue sarcoma.

* Of the 1993 and 1997 guidelines an English version is not available. Since the aspects of the guidelines studied were roughly unchanged during the years an appendix was added to the manuscript consisting of a flowchart concerning the diagnosis and treatment of soft tissue tumours.

PATIENTS

Patients with a STS diagnosed in the period 1998-1999 (before implementation of new guidelines) and in 2006 (after implementation) were included in the study. Patients were selected from the population-based Leiden Cancer Registry of the CCCW. Selected STS were located in the head and neck area, (retro)peritoneum, extremities, thorax and trunk. Patients younger than 16 years at diagnosis and patients with STS from gynaecological or urological origin were excluded. Inclusion was restricted to operated patients. Non-operated patients were not selected, because in these cases the choice of treatment was individualised which hampered the evaluation of the compliance to the guidelines.

METHODS

Datacollection and definitions

Information regarding patient and tumour characteristics as well as (the results of) pathology review was collected from the medical patient file. Items on the registration form were based on studies of the Swedish Sarcoma Group Register.¹² The data were collected and coded by two data-managers of the CCCW.

A pre-operative diagnosis STS was assumed to be *considered* if this was explicitly recorded in the medical files or if histological material had been evaluated preoperatively and/or adequate imaging had been performed.

Content of the guidelines

The guidelines^{8,9} for diagnostic work-up require physical examination and imaging techniques indicating the size of the tumour and its extension in surrounding tissues (see flowchart in the appendix). In general magnetic resonance imaging (MRI) is the imaging method of choice, followed by computed tomography (CT) and conventional X-ray. In case of intra abdominal or intra thoracal tumours a CT is preferred to MRI. Distant metastases were excluded by pulmonary X-ray and an additional CT-scan in specific cases (patients with a T2/N1 tumour with a negative pulmonary X-ray). For definitive histological diagnosis, a true-cut biopsy is advocated. Only in patients with small (≤ 3 cm), unsuspecting and superficial (above the superficial fascia) tumours a radical excisional biopsy could be performed. In patients with large (> 3 cm), suspicious or deep tumours (beneath the superficial fascia), incisional biopsy was required before surgical treatment if true-cut biopsy provided

insufficient diagnostic evidence. Referral to a centre was recommended for patients with large and complex tumours.

Surgery and pathology

Surgical treatment consisted of a wide resection of the tumour, which is defined as 'en bloc' resection of the tumour (including the biopsy tract) with at least 2 cms of normal tissue in its surroundings.

State of the art diagnostic pathology is regarded to include statements about the radicality of resection¹³⁻¹⁵, grading¹⁶ and if appropriate expression of specific markers and assessment of chromosomal translocations and/or mutations in tumour specific genes. These elements have all been taken care of in our approach although not all findings are reported explicitly.

Pathology review (prospectively or retrospectively) was performed by the regional expert panel.

The regional expert panel is made up of at least five pathologists from the regional hospitals with a special interest in soft tissue tumours. The panel is chaired by a pathologist with qualified expertise in this area and who is also a referent pathologist of the EORTC soft tissue and bone sarcoma group.

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RESULTS

In total, 119 patients with an operated STS were included in the study. Of these patients, 79 were diagnosed in the years 1998 and 1999 (before the implementation of the evidence-based national guidelines), and 40 were diagnosed in 2006 (after implementation). The patients in the two periods did not differ with respect to patient and tumour characteristics (Table 1). About half of the patients were male and the majority of the patients was younger than 70 years. Eighteen percent of the STS were intra-abdominal tumours, and 82% of the STS were located in the extremities, trunk or head and neck region. In 1998-1999, more small and superficial STS were included than in 2006: 18 versus 4. More than 60% of the STS were myogenic sarcomas, myxofibrosarcomas and liposarcomas, but various other types of STS within the WHO-categories were also found. The patients received their primary treatment in 11 district hospitals and/or one university hospital in the CCCW. The annual number of patients per hospital varied from 1 to 10 in the years 1998-1999 and from 1 to 15 in 2006.

Diagnostic procedures (Table 2)

For patients with a tumour in the extremities, trunk or head and neck region, the diagnosis STS was considered pre-operatively in 46 of the 66 patients in 1998-1999 and in 25 of the 32 patients in 2006 ($p=0.47$). For the remaining patients with a non-abdominal tumour, the diagnosis STS was made only after surgery (whoops surgery). These cases concerned a tumour smaller than 3 cm and located above the superficial fascia in 11 of 20 patients in 1998-1999 and in 2 of 7 patients in 2006.

In both periods the guidelines for diagnostic imaging for non-abdominal tumours (i.e. MRI) were adhered to in 75% of the patients in whom STS was considered pre-operatively. Of the non-abdominal STS without MRI, 4 of the 12 tumours in 1998-1999 and 2 of the 6 tumours in 2006 were smaller than 3 cm and located above the superficial fascia.

The requested CT in case of an abdominal STS was performed in 10 of 13 patients in 1998-1999 and in all 8 patients in 2006 ($p=0.26$).

The use of diagnostic imaging for distant metastases did not change over time.

Adherence to the guidelines with respect to invasive diagnostic procedures in patients with non-abdominal STS improved over time. A pre-operative histological diagnosis was obtained in 42% of the patients in 1998-1999 and in 72% of the patients in 2006 ($p<0.001$). An excisional biopsy was performed in 25 of the 66 patients with non-abdominal STS in 1998-1999 compared to 8 of 32 patients

in 2006. In 11 and 1 of these patients, respectively, the excisional biopsy concerned a tumour that was smaller than 3 cm and located above the superficial fascia.

Most patients in 1998-1999 (72%) and in 2006 (75%) were discussed multidisciplinary ($p=0.83$). For the remaining patients, it was not documented whether or not a multidisciplinary discussion had taken place.

Treatment (Table 3)

Less than half of the (primary) resections were performed in a university hospital: 37% in 1998-1999 and 50% in 2006 ($p=0.17$). The proportion of patients who underwent a re-resection was constant over time: 24% of the patients diagnosed in 1998-1999 and 18% of the patients diagnosed in 2006 ($p=0.41$). Re-resection was performed more often if STS was not suspected pre-operatively (67% versus 11%, $p<0.001$).

The outcome of surgery (including re-resection) for patients with a non-abdominal STS in 2006 was less favourable than in 1998-1999: the proportion of patients whose tumour was not radically removed was 19% in 2006 compared to 6% in 1998-1999 ($p=0.02$). However, in 1998-1999 there were proportionally more small and superficial tumours than in 2006. Most of these patients received additional radiotherapy. This was not the case for 9 out of 66 patients in 1998-1999 and for 1 out of 32 patients in 2006, for whom radiotherapy may not have been feasible.

Pathology reports (Table 4)

The guidelines for reporting on pathology were increasingly adhered to. In 2006, (nearly) all pathology reports mentioned tumour size, morphology, tumour grade, resection margins and radicality. This represents a major improvement compared to the pathology reports in 1998-1999, where these aspects were not mentioned in 14% to 40% of the cases. The proportion of prospective pathology reviews by (a member of) the expert panel increased from 60% in 1998-1999 to 90% in 2006 ($p=0.001$).

DISCUSSION

Guidelines on diagnosis and treatment of soft tissue sarcomas have been available in the region for many years and updates were distributed to all involved clinicians by the regional multidisciplinary working group Bone and Soft Tissue Sarcomas. It could therefore be assumed that all clinicians were informed about the most recent version of the guideline during the study period. Through this forum continuous awareness is propagated and clinicians are in some way accounted for their decision making in patients with soft tissue sarcomas.

Increasing awareness among medical specialists

Since the majority of patients are admitted through the out-patient ward of the surgical departments (not necessarily specialised in oncology) the primary awareness at this first intake is crucial. Apart from the introduction and implementation of the revised soft tissue sarcoma guideline a shift in approach amongst the surgical oncologists in the CCW region was evolving. This shift concerned the joint regional approach in the diagnosis and treatment of so called low-volume complex solid cancers, i.e. esophageal, pancreatic, locally advanced rectal cancer and liver metastases. Through centralised data collection and frequent reporting and discussions on the volumes and outcomes of these tumours clinicians were confronted with their own results, compared to others. By this approach an increasing awareness arose with respect to the benefits of centralised treatment. This shift undoubtedly also had an effect on the diagnosis and treatment of soft tissue sarcomas, perhaps not that much on centralisation but clearly on adherence to the guidelines.

Improving the implementation of guidelines

The current evaluation gave insight in the way soft tissue sarcomas were diagnosed and treated within the region of the CCCW over time, although the number of patients is small. In many aspects the guidelines were increasingly adhered to. The most remarkable changes were found in the percentage of pre-operative histological diagnosis in patients with a non-abdominal tumour and in the percentage of patients in whom pathology review was performed prospectively. The continuous and repetitive referral to the national guidelines can be accounted for this effect since more awareness for the standardised work-up is created amongst the first clinicians in line, not always the most experienced ones, therefore having highly valuable educational impact. A secondary but important effect of this

guideline-based and multidisciplinary approach is the phenomenon that doctors better adhere to guidelines because of public confrontation and accountability.

Relation to comparable studies

In the Netherlands a similar study was performed and published earlier.²⁹ This study was performed in the Northern part of the Netherlands between 1989 and 1996. Guidelines were significantly better adhered to in specialised centres²⁹. The benefit of centralised treatment of soft tissue sarcomas was also described in other publications.³⁰⁻³³ The additional value was expected to be due to an increased familiarity with alarm signals and with the existing guidelines as well as more experience with the complex treatment which results in appropriate preoperative investigations and accurate staging, essential for planning of appropriate treatment.¹¹ This association was not found in the CCCW region possibly because the study population was too small.

How a better adherence to guidelines was and can be achieved

The increased adherence to the guidelines, however, can be explained by a few factors in addition to the process that was already described. First, the results of the first study have been communicated with all involved clinicians within the region in order to encourage the use of the available guidelines. Second, pathologic material was increasingly reviewed by a regional expert panel. These factors combined with the strong regional intention to further improve the quality of surgical oncological care have resulted in the intended centralisation of treatment in which patients with a tumour > 3 cm, located subfascially or tumours with an aberrant course in a specialised centre. The second evaluation was performed during the process of centralisation. This explains why patients were still operated on in several district hospitals. Moreover, in 2004, the national evidence-based guideline⁸ was published. Both have contributed to a higher awareness and attention for the diagnosis and treatment of patients with soft tissue sarcomas. Further improvements could be reached by the prospective webbased registry which was started in 2005 and which is used for monitoring logistic aspects as well as indicators of the quality of care.

Table 1: Patient and tumour characteristics by period of diagnosis

	1998-1999 N	2006 N	P value
Total no. of patients	79	40	
Gender			0.85
Male	37	20	
Female	42	20	
Age at diagnosis			0.41
< 50	29	12	
50-69	21	15	
70-79	19	6	
80 +	10	7	
Tumour site			0.20
Extremities	45	16	
Trunk / head / neck	21	16	
Abdomen	13	8	
Tumour size and location *			0.24
Small / superficial	18	4	
Large / deep	48	28	
Abdominal	13	8	
Morphology			0.16
Myogenic sarcoma	17	10	
Myxofibrosarcoma	18	10	
Liposarcoma	10	8	
Synoviosarcoma	4	2	
Nerve sheath sarcoma	2	4	
Sarcoma other / NOS	28	6	

* Small/superficial tumours are located in extremities/trunk/head/neck, less than 3 cm in greatest dimension, and located above the superficial fascia.

Large/deep tumours are located in extremities/trunk/head/neck, and more than 3 cm in greatest dimension or located beneath the superficial fascia.

Table 2: Adherence to the diagnostic guidelines by period of diagnosis

	1998-1999 N	2006 N	P value
Non-abdominal STS	66	32	
STS considered pre-operatively			0.47
Yes	46	25	
No	20	7	
MRI *			1.00
Yes	34/46	19/25	
No	12/46	6/25	
Invasive diagnostic procedures			<0.001
Cytology	13	1	
True cut biopsy	6	17	
Incisional biopsy	22	6	
Not performed (excisional biopsy)	25	8	
Abdominal STS	13	8	
CT scan			0.26
Yes	10	8	
No	3	0	
All STS	79	40	
Diagnostic imaging for distant metastasis			0.32
Yes	61	28	
No	16	12	
Unknown	2	0	
Discussed in multidisciplinary meeting			0.83
Yes	57	30	
No/Not recorded	22	10	

* for patients in whom STS was considered pre-operatively.

Table 3: Treatment by period of diagnosis

	1998-1999 N	2006 N	P value
All STS	79	40	
Primary resection in university hospital			0.17
Yes	29	20	
No	50	20	
Re-resection performed			0.41
Yes	19	7	
No	60	33	
Non-abdominal STS	66	32	
Resection margins			0.10
Wide	41	14	
Marginal	9	10	
Intra-lesional	4	4	
Unknown	12	4	
Optimal treatment *			0.23
Yes	49	28	
No	9	1	
Unknown	8	3	

* Treatment was considered optimal if resection margins were free or if the patient received post-operative radiotherapy after irradical surgery.

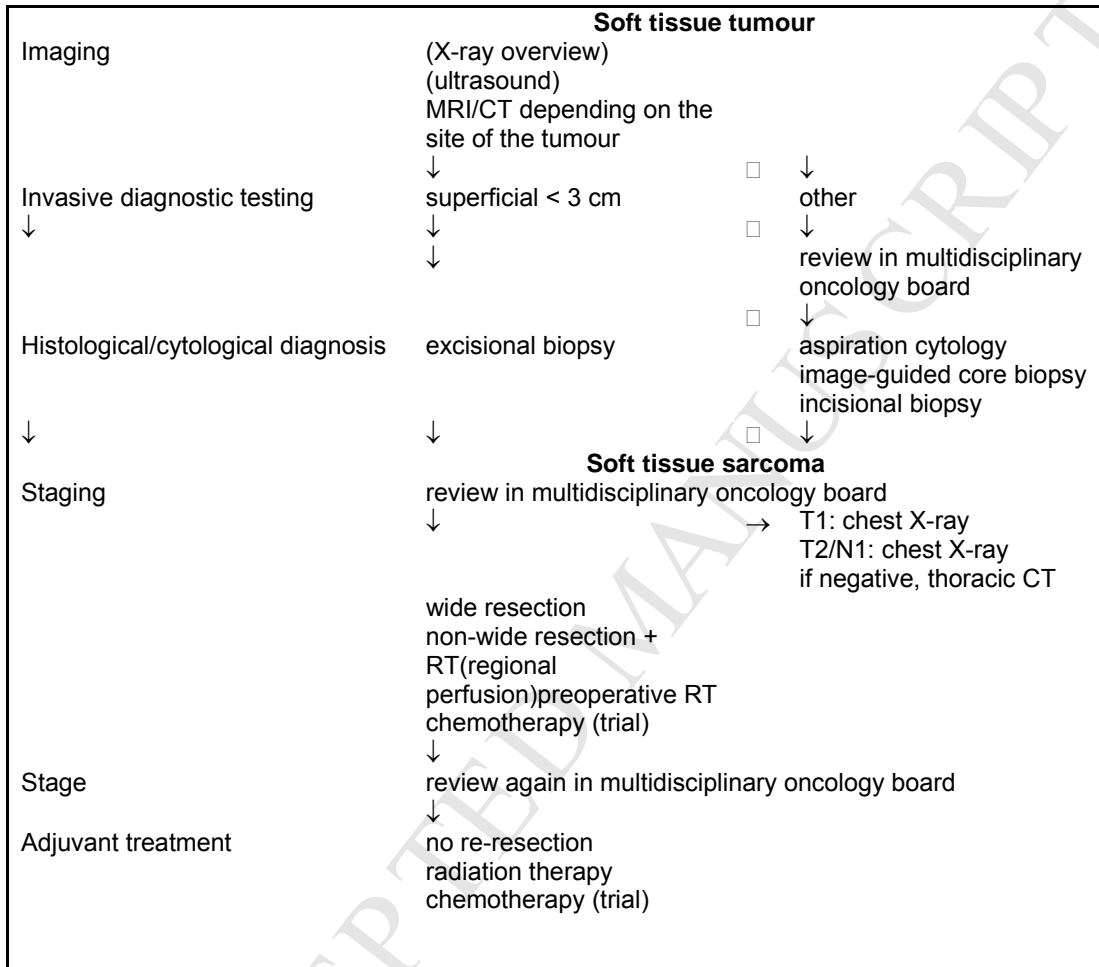
Table 4: Adherence to the guidelines for reporting on pathology by period of diagnosis

	1998-1999 N	2006 N	P value
All STS	79	40	
Pathological reports mentioning:			
Tumour size			<0.001
Yes	55	39	
No	24	1	
Morphology			0.02
Yes	68	40	
No	11	0	
Grade			0.10
Yes	69	39	
No	10	1	
Resection margins			0.004
Yes	61	39	
No	18	1	
Radicality			<0.001
Yes	47	40	
No	32	0	
Pathology reviewed by expert panel			0.001
Yes	47	36	
No	32	4	

Appendix to the guideline on soft tissue tumours, diagnosis chapter

Version: 1.0, Responsible party: Dutch working group on soft tissue tumours, Date: 01 January 2004

FLOWCHART



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