

# Simple Guidelines for Efficient Referral of Soft-Tissue Sarcomas

## A Population-Based Evaluation of Adherence to Guidelines and Referral Patterns

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**Background:** Optimal treatment of soft-tissue sarcoma requires multidisciplinary management at a sarcoma center. However, these rare tumors are often misinterpreted as benign and many are inadequately treated outside a sarcoma center, with an increased risk of local recurrence that often requires further extensive surgical treatment. To improve referral and centralization of soft-tissue sarcoma management in the southern Sweden health care region, an open-access outpatient clinic at our sarcoma center and simple referral guidelines have been established for the past thirty years. The guidelines call for referral of all deep-seated soft-tissue tumors and of all  $\geq 5$ -cm superficial tumors before open biopsy or surgery. We evaluated adherence to these guidelines and characterized referral patterns. We also studied the consequences of our strategy with regard to the relative numbers of benign and malignant diagnoses among referred patients.

**Methods:** Adherence to guidelines, referral pathways, and time to referral to the sarcoma center were analyzed in a population-based series of 100 consecutive patients with soft-tissue sarcoma in the extremities or trunk wall. We also analyzed diagnosis and management of benign and malignant tumors in a second cohort consisting of 464 consecutive patients referred to the sarcoma center because of a soft-tissue tumor.

**Results:** Ninety-seven of the 100 patients with soft-tissue sarcoma were referred to the sarcoma center. All fifty-eight of the deep-seated soft-tissue sarcomas and twenty-eight of the forty-two superficial tumors were referred before open biopsy or surgery. Three-quarters of the patients with soft-tissue sarcoma first presented to a general practitioner. One-quarter of these patients were directly referred to the sarcoma center, which cut the referral time in half compared with patients initially referred to a local hospital. One-quarter of all patients referred to the outpatient clinic were diagnosed with a malignancy, with the majority of the malignancies being soft-tissue sarcoma.

**Conclusions:** Our simple referral guidelines and open-access outpatient clinic resulted in nearly complete referral of patients with soft-tissue sarcoma to the sarcoma center. The “excess work” associated with referral of benign tumors according to our strategy was limited to the diagnosis of three benign tumors for each malignant tumor. We consider this surplus evaluation of benign tumors acceptable and probably necessary to achieve a high referral rate of soft-tissue sarcoma before initial surgery.

**Level of Evidence:** Therapeutic Level III. See Instructions for Authors for a complete description of levels of evidence.

Soft-tissue sarcoma in the extremities or trunk wall typically present as a painless lump with no accompanying loss of function and no influence on the patient's general health. Recognition and diagnosis of soft-tissue sarcoma are challenging because of the rarity of this type of tumor. Benign soft-tissue

tumors, such as lipomas and fibrous and vascular tumors, are more than 100 times as common as malignant tumors<sup>1,2</sup>. There is general agreement that optimal treatment of soft-tissue sarcoma requires referral for management by a multidisciplinary sarcoma team before any surgery or open biopsy<sup>3-6</sup>. Failure to recognize the

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**TABLE I Characteristics of the Cohort of 100 Patients with Soft-Tissue Sarcoma**

Age* (yr)	74 (27-97)
Men/women†	63/37
Size* (cm)	7 (1-25)
Superficial tumors	5 (1-20)
Deep-seated tumors	9 (1-25)
Superficial/deep-seated to the fascia†	42/58
Malignancy grade, high/low†	84/16
Tumor location†	
Trunk wall	4
Upper extremity, proximal	15
Upper extremity, distal	10
Lower extremity, proximal	50
Lower extremity, distal	21
Histopathological subtype†	
Undifferentiated pleomorphic sarcoma/malignant fibrous histiocytoma	30
Myxofibrosarcoma	21
Leiomyosarcoma	20
Liposarcoma	10
Synovial sarcoma	5
Other	14

\*The values are given as the median, with the range in parentheses. †The values are given as the number of patients, which is also equal to the percentage since the cohort consisted of 100 patients.

need for treatment by a sarcoma specialist risks inadequate staging and shelling out of tumors, resulting in insufficient resection margins and an increased risk of local tumor recurrence<sup>7,8</sup>. Because of the high risk of persisting disease after a soft-tissue sarcoma is shelled out, repeat excision is needed if the initial tissue margins remain positive for tumor cells<sup>4,9</sup>. The consequence for the patient may be a final surgery (in some cases even amputation) that is more mutilating than would have been the case if a sarcoma specialist had planned and performed the first operation<sup>2,8,10,11</sup>.

Referral guidelines for patients with a soft-tissue tumor have been established in many countries to improve the management of soft-tissue sarcoma. The referral criteria vary; many guidelines emphasize referral of tumors with a deep location and/or a size of  $\geq 5$  cm, and others also include pain and/or observed tumor growth<sup>4,12-14</sup>. However, the latter two criteria are often not met by a soft-tissue sarcoma<sup>15,16</sup>. Overall, adherence to many of the guidelines has been poor, with an estimated 18% to 85% of patients with soft-tissue sarcoma currently being referred to sarcoma centers. Moreover, many patients are referred to a tertiary sarcoma center only after inadequate initial surgery or after a local recurrence, or they are not referred at all<sup>3-8,10-12,17-23</sup>.

The southern Sweden sarcoma center in Lund was founded in 1970. We initially experienced a poor rate of referral; one-

fourth of patients with soft-tissue sarcoma were not referred at all, and one-third were referred after surgery; thus, less than one-half of patients were referred before open biopsy or local excision<sup>15</sup>. We therefore developed simple referral guidelines for patients with a soft-tissue tumor; these were based on studies of the relative incidences of benign and malignant soft-tissue tumors according to tumor size and depth. This resulted in the recommendation that patients with a  $\geq 5$ -cm soft-tissue tumor and all patients with a deep-seated soft-tissue tumor (regardless of size) be referred directly to the sarcoma center before surgery or open biopsy. There are no requirements for diagnostic investigations before referral<sup>11,2,14</sup>.

To evaluate the efficiency of our simple guidelines, we characterized referral pathways and the time until referral from general practitioners to the sarcoma center in 100 consecutive patients with soft-tissue sarcoma within our health care region. We also evaluated the consequences of our guidelines and open-

**TABLE II Characteristics of the Cohort of 464 Patients with a Soft-Tissue Tumor Evaluated at the Outpatient Clinic in 2004 and 2005**

Age* (yr)	56 (18-98)
Men/women†	222/242 (48/52)
Size* (cm)	5 (1-26)
Superficial tumors	4 (1-26)
Deep-seated tumors	5 (1-25)
Superficial/deep-seated to the fascia†	230/234 (50/50)
Benign/malignant†	351/113 (76/24)
Tumor location†	
Trunk wall	103 (22)
Upper extremity, proximal	75 (16)
Upper extremity, distal	59 (13)
Lower extremity, proximal	116 (25)
Lower extremity, distal	111 (24)
Type of tumor†	
Sarcoma‡	74 (16)
Carcinoma	29 (6)
Lymphoma	10 (2)
Lipoma	118 (25)
Desmoid	12 (3)
Benign OSS§	182 (39)
Benign NOS§	39 (8)

\*The values are given as the median, with the range in parentheses. †The values are given as the number of patients, with the percentages in parentheses. ‡This cohort also included some patients living outside the southern Sweden health care region but referred to the sarcoma center. As a result, the number of cases of soft-tissue sarcoma diagnosed at the outpatient clinic during 2004-2005 was greater than the number identified in the southern Sweden health care region using the population-based Swedish Cancer Registry that was used for the analysis of referral pathways of patients with soft-tissue sarcoma. §OSS = otherwise specified, and NOS = not otherwise specified.

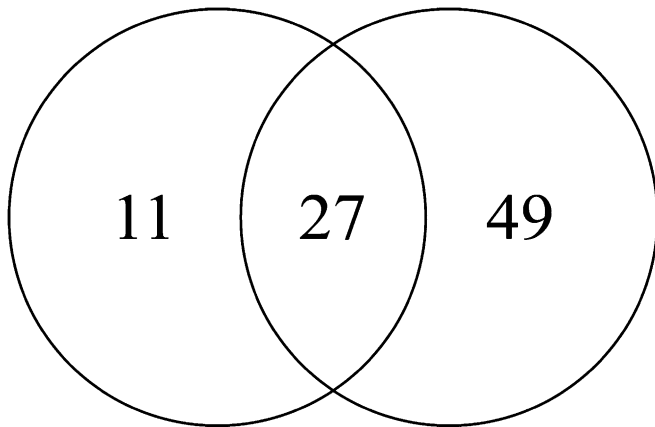


Fig. 1-A

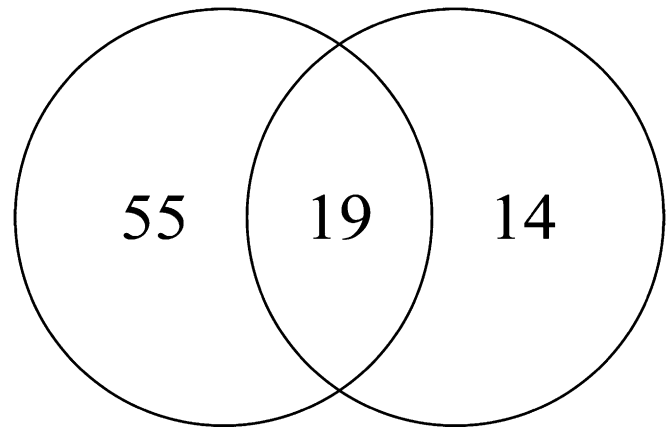


Fig. 1-B

**Fig. 1-A** Location and timing of fine needle aspiration. Left circle: before referral to the sarcoma center. Right circle: at the sarcoma center. Overlap: before referral but repeated at the sarcoma center. **Fig. 1-B** Location and timing of patient evaluation by imaging techniques. Left circle: before referral to the sarcoma center. (Forty-one of the fifty-five patients evaluated before referral had superficial tumors, which do not always require imaging evaluations.) Right circle: at the sarcoma center. Overlap: both before referral and at the sarcoma center.

access outpatient clinic with regard to the possible unnecessary referral of benign tumors by studying the ratio of benign to malignant diagnoses in a second cohort consisting of consecutive patients referred to our outpatient clinic.

### Materials and Methods

In the first portion of the study, adherence to the guidelines, referral time, and referral patterns were studied in a cohort of 100 consecutive adult patients (at least eighteen years old) with primary soft-tissue sarcoma in the extremities or trunk wall diagnosed in the southern Sweden health care region (population, 1.6 million in 2006) between January 2002 and April 2006 (Table I). The patients were identified with use of the population-based Swedish Cancer Registry, which has 96% coverage of patients with malignant tumors<sup>24</sup>. Eight patients who had a strictly cutaneous tumor were excluded. Clinical data were collected from primary health care centers, local hospitals, and the sarcoma center. The referral time was defined as the number of days from the first visit to a physician until referral to the sarcoma center.

The median age at diagnosis was seventy-four years (range, twenty-seven to ninety-seven years). One-half of the tumors were located in the thigh. The median tumor size was 7 cm (range, 1 to 25 cm); the median size was 5 cm for superficial tumors and 9 cm for deep-seated tumors. The predominant histological subtypes were undifferentiated pleomorphic sarcoma/malignant fibrous histiocytoma, myxofibrosarcoma, leiomyosarcoma, and liposarcoma, and eighty-four of the 100 tumors were of high histological malignancy grade (Table I).

In the second portion of the study, the impact of our organization, with its simple referral guidelines and open-access outpatient clinic, was assessed with regard to the ratio between benign and malignant tumors in a cohort of consecutive patients evaluated at the clinic.

The second cohort consisted of all 464 patients referred to the sarcoma center outpatient clinic because of a suspected malignant soft-tissue tumor during two consecutive years (2004 and 2005). Since this time period fell within the time period for the first cohort, the second cohort included some of the patients with soft-tissue sarcoma in the first cohort. The tumor locations differed from those in the soft-tissue sarcoma cohort; one-quarter of the tumors was located in the thigh or groin, and one-half of the tumors were deep-seated. The median tumor size was 5 cm (range, 1 to 26 cm) (Table II).

Statistical evaluation was performed with use of the two-sample Wilcoxon rank sum test. Ethical approval for the study was obtained from the Lund University ethics committee.

### Source of Funding

Financial support was received from the Swedish Cancer Fund, the Swedish Research Council, the Maggie Stephens Fund, and the Region Skåne. These funding sources had no influence on the planning or performance of the study or on the analysis of the results.

### Referral Pattern

In the first cohort, consisting of the 100 consecutive patients with soft-tissue sarcoma identified with use of the Swedish Cancer Registry, ninety-seven patients were referred to the sarcoma center for definitive treatment. The three patients who were not referred had superficial tumors, and two of the three were elderly patients with comorbidities. Among the ninety-seven patients with soft-tissue sarcoma who were referred, all fifty-eight with a deep-seated tumor and twenty-eight of the thirty-nine with a superficial tumor were referred before any surgical procedure. The remaining eleven patients with a superficial tumor underwent an initial surgical shelling out procedure performed in a local hospital or by a general practitioner before referral to the sarcoma center; seven of these eleven tumors were <5 cm in size. No open biopsies were performed outside the sarcoma center, and no patient was referred to the sarcoma center because of a local recurrence.

Diagnostic investigations were performed before referral in many cases, but many of these investigations either needed to be repeated at the sarcoma center or were not necessary (e.g., magnetic resonance imaging [MRI] of a small superficial tumor) (Figs. 1-A and 1-B). Although the guidelines emphasize that a ≥5-cm superficial tumor requires referral, nineteen patients with a smaller superficial soft-tissue sarcoma were also referred. In seventeen of these patients, the referral occurred after prior investigations (in seven patients, after local excision; in eight, after fine needle aspiration biopsy with results suggestive of sarcoma; and in two, after computed tomography or MRI indicating a non-lipomatous tumor).

Three-quarters (seventy-five) of the patients initially sought health care through their general practitioner, nine sought emergency care at their local hospital, and twelve were referred through other routes; the initial health care contact for the remaining four patients could not be determined. The median referral time in the cohort, based on complete clinical data for seventy-eight patients, was fifty days. Although the referral time could not be determined for the remaining twenty-two patients, all of these patients were initially referred to a local hospital rather than directly to the sarcoma center. No difference in referral time according to characteristics such as patient sex, patient age, tumor size, or tumor depth could be identified. The median time until referral to the

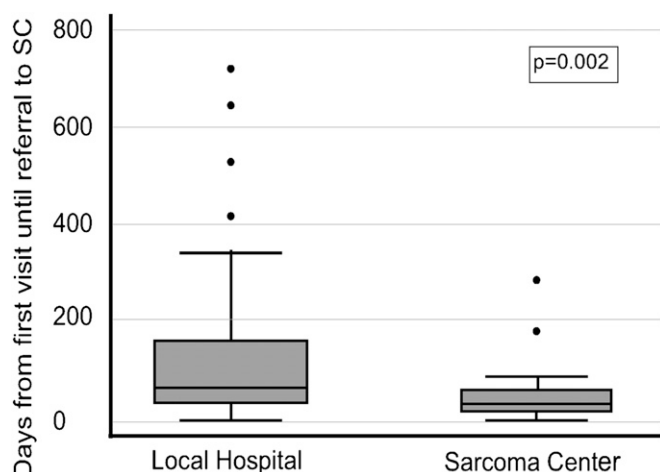


Fig. 2  
Referral time (days from the first visit to a physician until referral to the sarcoma center) according to whether the referral pathway was through the local hospital or directly to the sarcoma center (SC).

sarcoma center was sixty-four days for patients referred initially to a local hospital by their physician (based on data for fifty of the seventy-two patients), whereas the median time was thirty days for the twenty-eight patients referred directly to the sarcoma center ( $p = 0.002$ ). Hence, direct referral shortened the time to evaluation at the sarcoma center by one month (Fig. 2).

### Diagnosis at the Outpatient Clinic

In the second cohort, the tumor was diagnosed as malignant in 113 (24%) of the 464 patients examined at the sarcoma center outpatient clinic. Seventy-four of the malignant tumors were diagnosed as a sarcoma, twenty-nine as a carcinoma, and ten as a lymphoma. A benign soft-tissue tumor was diagnosed in the remaining 351 patients (Table II).

All soft-tissue sarcomas were treated at the center, as were 122 of the 351 benign tumors when the experience of a sarcoma surgeon was considered beneficial. Sixty-six of the benign tumors treated at the center (including twenty-five lipomas, ten neurilemmomas, four hemangiomas and two desmoid tumors) were deep-seated. Of the remaining 229 patients with a benign tumor, four patients with a desmoid tumor were treated with interferon, fifty-seven were referred to their local hospital for surgery, and 168 required no intervention after confirmation of a benign diagnosis.

### Discussion

Poor management of soft-tissue sarcoma is still a reality. Because of insufficient experience, surgery performed outside of a sarcoma center may result in misdiagnosis, inadequate surgical margins, and failure to consider relevant adjuvant treatment. Previous studies have shown that tumor tissue often persists following a primary operation that is not performed by a sarcoma specialist, leading to an increased frequency of local recurrence<sup>2,4,8,9,11</sup>. Surgery required to treat a local recurrence is often more extensive than surgery performed on an untouched primary tumor at a sarcoma center<sup>7,8,10</sup>. The extent of the problem is not clear since many of the reported sarcoma series are hospital-based and do not take non-referred patients into account<sup>3-8,10-12,17-23,25</sup>. The Lund sarcoma center, which serves the southern Sweden health care region with 1.6 million inhabitants, initially also experienced a poor rate of referral. Because of this, we developed simple referral guidelines that

recommend direct referral of patients with a  $\geq 5$ -cm superficial tumor and patients with a deep-seated tumor regardless of size. The guidelines were based on epidemiological studies on the size and depth of benign compared with malignant soft-tissue tumors<sup>15,26</sup>. Since implementation of these guidelines in the early 1980s, the referral rate has improved over time (Fig. 3)<sup>10,15</sup>. The guidelines were later adopted by the Scandinavian Sarcoma Group, which also noted improvement in their referral rate<sup>7,14,27</sup>.

Our guidelines are easy to apply since they neither require investigations before referral nor include pain or observed tumor growth. Most soft-tissue sarcomas are painless and are noted incidentally by the patient<sup>15</sup>; in such cases, tumor growth cannot be assessed when the patient consults a physician immediately after finding the tumor accidentally. We therefore deliberately omitted these criteria from our guidelines since they risk misleading physicians who are inexperienced with soft-tissue sarcoma. Internationally, however, many guidelines for referral include pain and observed tumor growth in addition to tumor size and depth<sup>4,12-14</sup>.

To minimize the problems associated with the performance of open biopsy and/or misdiagnosis outside the sarcoma center, no investigations or diagnosis are required before referral to our sarcoma center. An open biopsy performed by a surgeon and evaluated by a pathologist who are both inexperienced with sarcoma is associated with a considerable risk of a wrong diagnosis, local spread of sarcoma, or a misplaced incision that makes limb-sparing definitive surgery difficult. This has been reported by Mankin et al., who also demonstrated that the performance of open biopsy outside sarcoma centers was common in the U.S.<sup>19,20</sup>. The main reason to perform an open biopsy is to exclude a malignancy; however, our data and experience strongly suggest that the patient should instead be referred immediately to a sarcoma center with the tumor untouched.

None of the patients in the present study underwent an open biopsy before referral to the sarcoma center, and no deep-seated

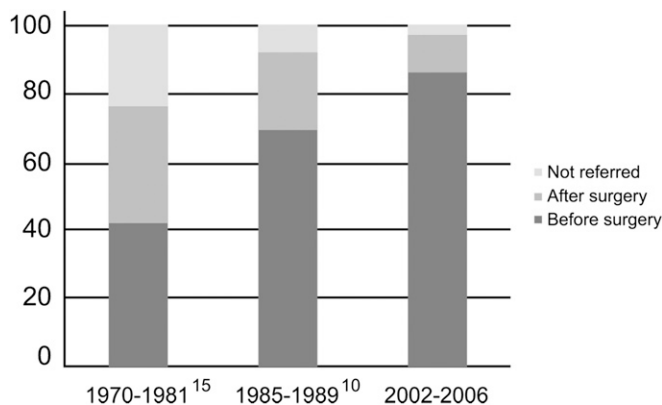


Fig. 3  
The referral pattern over time in the southern Sweden health care region, showing the percentage of patients who were referred to the sarcoma center with the tumor untouched, referred after surgery, or not referred at all. The data were obtained from the present study and previous studies by Gustafson et al.<sup>10</sup> and Rydholm<sup>15</sup>.

soft-tissue sarcoma was operated on outside the sarcoma center. The main reason for this is that our center is now well known in the health care region, and physicians within the region are aware that soft-tissue sarcoma should be referred to the sarcoma center for treatment before any surgery is performed. Also, the physician can telephone the sarcoma center directly for a consultation. Direct referral to a sarcoma center rather than primary referral to a local hospital shortens the time to see a sarcoma specialist. Thus, an open-access outpatient clinic accepting referrals from all physicians is preferable. Furthermore, the publicly funded nature of the Swedish health care system means that the decision to refer a patient does not involve economic considerations.

Although we do not require any diagnostic investigations before referral, several patients had undergone MRI and/or needle biopsy. Many of these investigations were repeated at the sarcoma center because the MRI was of suboptimal quality or the needle biopsy did not include sufficient cytogenetic and molecular genetic studies for pretreatment diagnostic testing<sup>28</sup>. It may be argued that MRI would be diagnostic for a lipoma and would thus spare the patient a visit to the sarcoma center; however, in clinical practice a large number of patients with a deep-seated lipoma are referred because of uncertainty about the diagnostic precision of MRI. If MRI has been performed before referral, it may help to distinguish between benign and malignant tumors. However, this investigation must not interfere with prompt referral to a sarcoma center. For example, if the suspicion of a malignancy is not noted when the MRI is requested, the investigation may be assigned a low priority, resulting in delayed referral.

Our population-based series differed from many hospital-based studies of soft-tissue sarcoma<sup>4,6,29</sup>: the patient age at our sarcoma center was higher, the tumor size was smaller, and the fraction of superficial sarcomas was higher. This may be explained by selection bias—i.e., a tendency for older patients and patients with small and superficial tumors to be treated outside of a sarcoma center. Nijhuis et al. showed that older patients were not referred to a sarcoma center as often as younger patients<sup>21,30</sup>. The smaller median tumor size in the present study might be related to the high referral rate of soft-tissue sarcoma that was achieved, which implies high awareness of the existence of sarcoma and of where it should be referred.

The findings of this population-based study demonstrated that our strategy involving simple guidelines and an open-access outpatient clinic allowed ninety-seven of 100 consecutive patients with soft-tissue sarcoma to be referred to our sarcoma center for treatment. Importantly, all of the deep-seated soft-

tissue sarcomas and two-thirds of the superficial ones were referred before incisional biopsy or surgery.

Concerns have been raised about an undesirable “crowding” effect in the clinic resulting from referral guidelines that are too liberal—i.e., a situation in which patients with a benign tumor outnumber those with a malignant tumor to such an extent that they delay the management of the patients who do have soft-tissue sarcoma<sup>31,32</sup>. Therefore, data on all patients examined at the outpatient clinic during two consecutive years were analyzed to determine the final diagnosis and treatment. In our consecutive series, three benign soft-tissue tumors were evaluated for each malignant tumor, and more than one-half of the latter were soft-tissue sarcoma. Furthermore, one-third of the benign tumors underwent surgery at our center without delaying the management of the malignant tumors. Thus, we find this surplus referral of benign tumors manageable and probably necessary to achieve a high referral rate of untouched soft-tissue sarcoma.

The simple referral guidelines were publicized through extensive outreach activities, lectures on sarcoma at medical schools and local hospitals, targeted education on sarcoma for residents in orthopaedic surgery, and continuous feedback to physicians regarding the outcomes of the patients who were referred. The beneficial referral pattern that we observed is encouraging, and it demonstrates that nearly complete referral of soft-tissue sarcoma is feasible. To further improve the referral pattern, the guidelines should be publicized more among general practitioners, and physicians should be encouraged to refer patients directly to a sarcoma center since this reduces the time to diagnosis. ■

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