Referral patterns, prognostic models and treatment in soft tissue sarcomas

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Chapter 2

Diagnosis and the referral pattern of soft tissue sarcoma patients

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There is a general trend towards centralization of health care. The debate about centralization has been accelerated by studies that show a correlation between volume of surgery and better outcome, which relates particularly to complex oncology health care. [1-3] For sarcoma patients, improved outcome when treated at a high volume hospital has been recognized and recommendations about referral to a specialized sarcoma centre have been promoted worldwide. [4,5]

Soft tissue sarcomas are rare and largely outnumbered by benign soft tissue tumors – e.g. lipomas, fibrous and vascular tumors – by at least 100 to 1 [6], what makes clinical suspicion and recognition of soft tissue sarcomas difficult. This is further complicated by the fact that two-thirds of the tumors are located in the extremities or in the trunk wall and typically present as painless lumps without loss of function or influence on the patients general health. Frequently, patients accidentally observe a mass, or refer to a trauma to the affected area that called their attention to a pre-existing lesion. At diagnosis, the majority of soft tissue sarcomas have reached a size of more than 5 cm [7-10] A soft tissue tumor in the thigh may grow to 10-15 cm in diameter before it becomes apparent and retroperitoneal tumors can grow to 25-30 cm before causing any symptoms. Therefore, any large and/or deep, undefined tumor mass should be evaluated using radiological imaging (contrast enhanced MRI or CT) to assess tumor size, tumor structure, and for tumor staging. An experienced radiologist at the sarcoma centre can differentiate between benign and malignant soft tissue lesions, define the anatomical origin, and in some cases define the nature of the tissue.

For complete diagnosis, histological assessment of the tumor is mandatory by means of biopsy. Because soft tissue sarcomas comprise some 50 subtypes with heterogeneity within, tumors biopsy should be performed at a sarcoma centre to avoid unrepresentative tissue sampling and misdiagnosis. Furthermore, obtained tissue can be stored in tissue banking for future diagnostic and/or research purposes.

Failure to recognize soft tissue sarcomas may lead to shelling out of tumors, so called ‘whoops’ procedures, which have considerable consequences. It may

preclude later staging and excision with proper margins, relevant adjuvant treatment, and as a consequence a high risk of local recurrence. Furthermore, patients managed in a sarcoma centre are intensively followed according to the sarcoma guidelines for early detection of recurrence, which varies from 10-15% locally to over 30% of distant recurrences. [10,11] At the sarcoma centre patients could participate in clinical trials and metastatectomy is increasingly offered in case of single or multiple (lung) metastases. These improvements in multidisciplinary management of soft tissue sarcoma ought to lead to a substantial decrease in morbidity and mortality rates.

There is general agreement that soft tissue sarcoma patients should be referred to a sarcoma centre, and now focus has turned on delay in the diagnosis and treatment of sarcoma patients. [12,13] Due to the subtle presentation and lack of experience, both a patient delay and doctor delay is common, allowing the soft tissue tumor to grow a considerable size, which complicates surgical resection, and increases the risk for development of metastasis. As size is a strong prognostic factor [5, 14] and one of the few that can be influenced, early recognition of sarcomas and prompt referral to a sarcoma centre should be promoted in order to further improve outcome. To ensure adequate referral, simple guidelines are required. Based on epidemiological data showing that 99% of benign soft tissue tumors are superficial and 95% are less than 5 cm in diameter [15], the southern Sweden sarcoma centre in Lund has established simple referral guidelines that recommend referring of all patients with soft tissue tumors larger than 5 cm and all deep-seated tumors, irrespective of size [16]. Depth is defined in relation to the deep fascia, and all tumors below the deep fascia are considered deep-seated tumors. Other countries also included pain or observed tumor growth in the referral guidelines. [17] Although, nationwide guidelines exist for the diagnosis, treatment and follow up of soft tissue sarcoma patients in the Netherlands, and referral to a sarcoma centre is promoted, no official referral guidelines are recorded. [11,12] A recent study conducted at the sarcoma centre in Lund reported a nearly 100% referral rate of patients with sarcoma of the extremities before biopsy or local excision. [4] The successful implementation of referral guidelines is the result of many years of education for medical students and specialists in-training in general surgery and orthopaedics with continuous feedback regarding outcome for patients referred. Nevertheless, the same study did observe a median doctors delay of longer than 1.5 months. Other studies have reported even longer doctors delays of around 6 months. [7,18]

Additionally, the diagnostic work up of soft tissue sarcomas can extend the delay between presentation and treatment when performed inefficient and inadequate. On that account, guidelines for diagnosis and treatment were designed to ensure appropriate pre-operative investigations, accurate staging and evidence based decision making. In the region of the Comprehensive Cancer Centre North-Netherlands (CCCN), the first guidelines for the diagnosis and treatment of patients with STS were developed in February 1983 by a cooperative group for rare tumors. [12] After realization of the first Dutch nationwide accepted guidelines in 1993, the guidelines have been revised several times. Since the latest revision in 2011 (Richtlijn diagnostiek weke delen tumoren (versie 2.0 herziening 2011)) of the Netherlands Comprehensive Cancer Organisation (IKNL), the guidelines recommend to perform conventional X-ray, a MRI scan for sarcomas of the extremities and trunk, and a CT scan for sarcomas of the intra-thoracic and intra-abdominal cavity. Additional imaging like a bone scintigraphy or Positron-emission tomography (PET) scans are not included in the routine diagnostic work-up. For histological diagnosis, a histological core needle biopsy is required. In case of a heterogeneous tumor it is recommended to perform an ultrasound or CT scan guided biopsy.

In conclusion, it is important to acknowledge that centralization *per se* is not sufficient and that delays should be investigated, recognized and addressed. In the next chapter, the referral pattern of a distinct group of soft tissue sarcomas – retroperitoneal sarcomas – is discussed.

References

1. Borrowski DW, Bradburn DM, Mills SJ, Bharathan B et al. Volume-outcome analysis of colorectal cancer-related outcomes. Br J Surg. 2010 Sep;97(9):1416-30
2. Vrijens F, Stordeur S, Beirens K, Devriese S et al. Effect of hospital volume on processes of care and 5-year survival after breast cancer: a population-based study on 25000 women. Breast 2012 Jun;21(3):261-6.
3. Markar SR, Karthikesalingam A, Thrumurthy S, Low DE. Volume-outcome relationship in surgery for esophageal malignancy: systematic review and meta-analysis 2000-2011. J Gastrointest Surg. 2012 May;16(5):1055-63.
1. Styring E, Billing V, Hartman L, Nilbert M et al. Simple guidelines for efficient referral of soft-tissue sarcomas: a population-based evaluation of adherence to guidelines and referral patterns. J Bone Joint Surg Am. 2012 Jul 18;94(14):1291-6.
2. Nakamura T, Matsumine A Matsubara T, Asanuma K et al. The symptom-to-diagnosis delay in soft tissue sarcoma influence the overall survival and the development of distant metastasis. J Surg Oncol. 2011 Dec;104(7):771-5.
3. Weiss SW, Goldblum JR, Enzinger FM. (2013) Enzinger and Weiss's soft tissue tumors (4th edition). Philadelphia : Mosby Elsevier.
4. Johnson GD, Smith G, Dramis A, Grimer RJ. Delays in referral of soft tissue sarcomas. Sarcoma. 2008;2008:378574.
5. Glencross J, Balasubramanian SP, Bacon J, Robinson MH et al. An audit of the management of soft tissue sarcoma within a health region in the UK. Eur J Surg Oncol. 2003 Oct;29(8):670-5.
6. Bauer HC, Trovik CS, Alvergard TA, Berlin O et al. Monitoring referral and treatment in soft tissue sarcoma: study based on 1,851 patients from the Scandinavian Sarcoma Group Register. Acta Orthop Scand. 2001 Apr;72(2):150-9.
7. Rydholm A. Improving the management of soft tissue sarcoma. Diagnosis and treatment should be given in specialist centres. BMJ. 1998 Jul 11;317(7151):93-4.
8. Hoekstra HJ, Haas RLM, Verhoef C, Suurmeijer AJH. Adherence to Guidelines for Adult (Non-GIST) Soft Tissue Sarcoma in the Netherlands: A Plea for Dedicated Sarcoma Centers. Ann Surg Oncol. 2017 Oct;24(11):3279-3288.
4. Nijhuis PH, Schaapveld M, Otter R, Hoekstra HJ. Soft tissue sarcoma – compliance with guidelines. Cancer. 2001 Jun 1;91(11):2186-95.
5. Jansen-Landheer ML, Krijnen P, Oostindier MJ, Kloosterman-Boele WM. Improved diagnosis and treatment of soft tissue sarcoma patients after implementation of national guidelines: a population-based study. Eur J Surg Ocol. 2009 Dec;35(12):1326-32.
6. Gustafson P, Akerman M, Alvegard TA, Coindre JM. Prognostic information in soft tissue sarcoma using tumour size, vascular invasion and microscopic tumour necrosis-the SIN-system. Eur J Cancer. 2003 Jul;39(11):1568-76.
7. Myrthe-Jensen O. A consecutive 7-year series of 1331 benign soft tissue tumours. Clinicopathologic data. Comparison with sarcomas. Acta Orthop Scand. 1981 Jun;52(3):287-93.
8. Rydholm A. Management of patients with soft-tissue tumors. Strategy developed at a regional oncology center. Acta Orthop Scand Suppl. 1983;203:13-77.
9. George A, Grimer R. Early symptoms of bone and soft tissue sarcomas: could they be diagnosed earlier? Ann R Coll Surg Engl. 2012 May;94(4):261-6
10. Brouns F, Stas M, De Wever I. Delay in diagnosis of soft tissue sarcomas. Eur J Surg Oncol. 2003 Jun;29(5):440-5.