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ScienceDirect
EJSO xx (2014) 1–5
EJSO the Journal of Cancer Surgery
www.ejso.com

Intra-muscular location in soft tissue sarcomas: Impact on oncologic outcome

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Accepted 26 January 2014
Available online ■ ■ ■

Abstract

Background: Soft tissue sarcoma (STS) of intra-muscular location is confined within well-defined barrier, amenable to easier surgical resection. It is generally assumed that STS of intra-muscular location would have favorable outcomes compared to those of inter-muscular location. However, no clear evidence on this assumption can be found. This study examined if intra-muscular location of STS would have favorable effect on oncologic outcomes.

Methods: Among the 161 patients treated for previously untreated, non-metastatic and deep-seated STS, extra-compartmental tumors (65) or tumors that spread beyond the muscle of origin (23) were excluded. Remaining 73 patients were classified into two groups according to tumor location; intra-muscular group (confined within muscle of origin, $n = 32$) and inter-muscular group (located between muscles, $n = 41$).

Results: Two patients (6.3%) in intra-muscular group developed local recurrence whereas 10 patients (24.3%) developed local recurrence in inter-muscular group ($p = 0.056$). Patients in intra-muscular group showed significantly better local recurrence-free survival than those in inter-muscular group ($p = 0.029$). However, there was no significant difference in development of metastasis ($p = 0.143$) nor disease-specific survival ($p = 0.106$).

Conclusions: Our study indicates that STS of intra-muscular location is associated with better local control. Whether this advantage is due to its biological property or surgical resectability remains to be elucidated.
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Keywords: Intra-muscular; Soft tissue sarcoma; Outcome; Barrier; Compartment

Introduction

Whether or not the tumor is located within a well-defined anatomic barrier dictates the feasibility of surgical procedure and possibly patient prognosis in soft tissue sarcoma (STS) of the extremities. This concept is reflected in the Surgical Staging System (SSS) of the Musculoskeletal Tumor Society as this system is based on compartmental status of the tumor along with the histologic grade of the tumor.[1]

STS of intra-muscular location are confined within the well-defined fascial barrier, amenable to easier surgical resection.[2] It is generally assumed that STS of intra-muscular location may have favorable patient outcomes compared to those of inter-muscular location. However, the role of muscle as an anatomic barrier in STS has not been defined in SSS.[3] Moreover, no clear evidence on this assumption can be found in the literature.

We therefore investigated if intra-muscular location compared to those of inter-muscular location would have favorable effect on oncologic outcomes in patients with extremity STS.

Patients and methods

567 extremity STS that underwent surgery from 1996 to 2010 at Seoul National University Hospital ($n = 447$) or National Cancer Center (120) were reviewed. Our institutional review board approved this study and the informed consent was waived. For the purpose of analysis, previously untreated cases with non-metastatic and deep-seated tumors were selected (Fig. 1). Thus, patients with metastasis at diagnosis ($n = 41$), superficial tumors (55), recurrent

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http://dx.doi.org/10.1016/j.ejso.2014.01.015

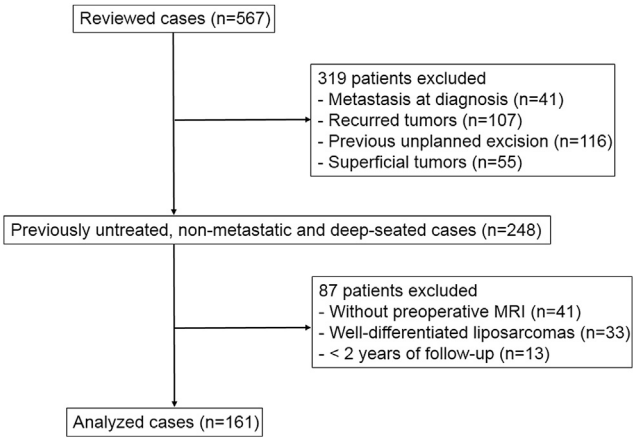

Figure 1. Flow-chart showing the selection process of patients.

tumors (107) or who were referred after an unplanned excision (116) were excluded. Well-differentiated liposarcomas (33) were also excluded because of their benign nature. Patients without preoperative MRI (41) and less than 2 years of follow-up (13) were also excluded.

The remaining 161 patients were classified according to the tumor location on MRI; compartmental status based on Surgical Staging System (SSS) and tumor location with regard to the muscle of origin (Fig. 2). Of the 161 patients, extra-compartmental tumors on MRI based on SSS ($n = 65$) were excluded. Among the 96 intra-compartmental tumors, those that spread beyond the muscle of origin ($n = 23$) were excluded as these tumors were thought to represent aggressive tumors. The remaining 73 patients were classified into two groups according to tumor location with regard to the muscle of origin; tumors were considered as intra-muscular if they were confined within the muscle of origin on MRI scans ($n = 32$, Fig. 3A and B) and tumors were defined as inter-muscular if they were located between the muscles ($n = 41$, Fig. 3C and D). Review of postoperative pathology reports confirmed the classification.

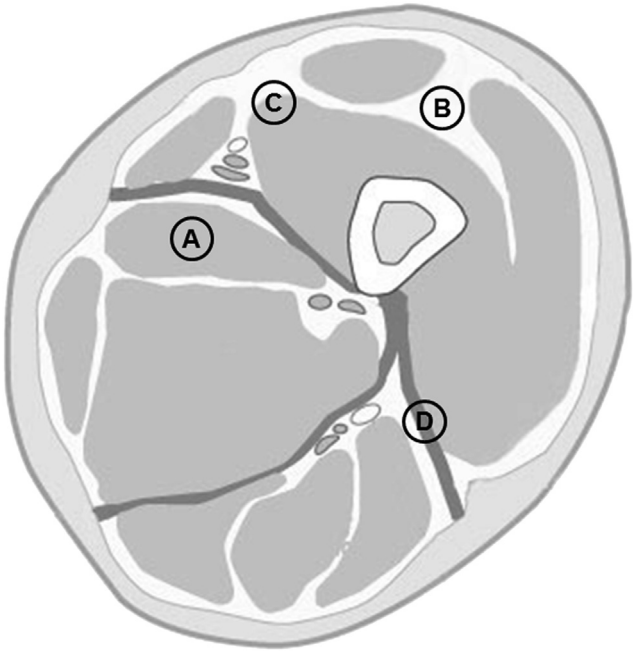

Figure 2. Diagram showing the classification of STS location in relation to the muscle of origin. (A) Intra-muscular tumors were defined as those confined within the muscle of origin (B) Inter-muscular tumors were defined as those located between the muscles (C) Extramuscular tumors were defined as intra-compartmental tumors that spread beyond the muscle of origin (D) Extra-compartmental tumors were defined as those that spread beyond septum, deep fascia or space sarcomas.

The most common histologic subtypes were undifferentiated pleomorphic sarcoma (21%), liposarcoma (18%), synovial sarcoma (11%), myxofibrosarcoma (7%), and leiomyosarcoma (7%). Anterior thigh (23%), medial thigh (16%), posterior thigh (15%), and buttock (10%) were the most common compartmental locations. Overall 16 different muscles were involved in the intra-muscular group, with vastus lateralis ($n = 5$), rectus femoris (3), vastus intermedius (3) deltoid (3) and gluteus maxmius (3) muscles most commonly involved.

Histologic grading was performed using the Federation Nationale des Centres de Lutte Contre le Cancer (FNCLCC).[4] There were 11 low grade (grade 1) tumors (15%) and 62 high grade (grade 2 or 3) tumors (75%). The tumor size was defined as the largest diameter described in the pathology report or the largest diameter measured in the radiographs. The median tumor size was 8.0 cm (range, 1.1–20.0 cm) and this value was used to categorize the patients into 2 groups for analysis. Tumors were resected with a wide margin in 55 patients (73%) and marginal margin in 17 (27%). For intra-muscular tumors surrounded by normal cuff of muscle confined within fascia on preoperative MRI, the muscle was removed without removing any additional tissues. For intra-muscular tumors with regions close to the muscle fascia, additional tissues surrounding the muscle were removed to achieve adequate margin ($n = 20$). Inter-muscular tumors were removed with surrounding muscles to achieve wide margin. Amputation was not performed in any of the patients. Radiation therapy was administered in 57 patients (78%), all post-operatively. Thirty-five of 37 FNCLCC grade 3 (95%) and 22 of 25 grade 2 tumors (88%) were treated with radiation therapy. All patients received external beam radiation and the median dose was 60 Gy (range, 50–65 Gy). Postoperative chemotherapy was administered in 17 patients (23%). Chemotherapy was administered in patients with histologic diagnoses regarded as more chemo-sensitive, such as synovial sarcoma ($n = 6$), rhabdomyosarcoma (2) and extraskeletal Ewing's sarcoma (2). Patients with high risk of recurrence, based on clinical information such as histological grade and tumor size, were also considered for chemotherapy. Among 17 patients, 11 patients received chemotherapy after completing radiation therapy.

The two groups showed similar patient and disease characteristics, such as histological grade, tumor size and

Please cite this article in press as: Kim H-S, et al., Intra-muscular location in soft tissue sarcomas: Impact on oncologic outcome, Eur J Surg Oncol (2014), http://dx.doi.org/10.1016/j.ejso.2014.01.015

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