Abstract. This study examined 45 patients with well-differentiated liposarcoma who were surgically treated at our hospital (initial surgery in 41 patients and reoperation in 4). Only one patient had recurrence among patients who underwent initial surgery, and the recurrence was localized in the retroperitoneal space. For patients who underwent reoperation, the mean time between the initial surgery and the recurrence was 16.5 years. None of the 45 patients developed distant metastasis. It is important to preserve not only neurovascular bundles but also lower limb muscles in order to maintain ambulatory ability in the elderly patients. For well-differentiated liposarcomas of the limbs, it is important to establish a surgical margin beyond the marginal resection border and to perform muscle resection to the extent that would not greatly reduce the muscle strength.

Well-differentiated liposarcoma is a relatively slow-growing tumor that usually occurs in elderly patients. It is difficult to differentiate well-differentiated liposarcoma from a benign lipoma and other lipomatous tumors; Magnetic resonance imaging (MRI) (1-4) and murine double minute 2 (MDM2) gene amplification (5, 6) in tissue samples have been reported to be useful in their differentiation. However, definitive differentiation is often difficult before resection. In many cases, the entire resected specimen is evaluated histopathologically and diagnosis can subsequently be made for the first time. The resection margin of well-differentiated liposarcoma tends to be less than the one performed in conventional extensive resection (7, 8). However, operative procedures from marginal resection to extensive resection vary among institutions. In this study, we examined the outcomes of well-differentiated liposarcomas treated at our hospital and we discuss future treatment strategies.

Patients and Methods

The subjects of this study were 45 patients with well-differentiated liposarcomas who were surgically treated in our hospital between January 1989 and July 2010 and who were followed-up for at least 6 months. The study group consisted of 17 men and 28 women. The procedure was initial surgery in 41 patients and reoperation in four patients who were referred to our hospital due to recurrence. After surgery, these patients revisited our outer patient clinic every four to six months and local recurrences check was performed by magnetic resonance imaging (MRI) and lung metastases were checked by chest computed tomography (CT).

Results

The mean age was 63.4 years (range: 35-80 years) in 41 patients who received the initial surgery at our hospital. Liposarcoma occurred in the lower limbs in 29 patients, in the trunks in 8 patients (including in the retroperitoneal space in 1 patient) and on the upper limbs in 4 patients, indicating a predilection for the lower limbs. The mean tumor size was relatively large at 14.4 cm × 11.5 cm. The mean time between the first notice of the tumor by the patient and the patient’s visit at the hospital was 38.2 months (range: 2 days-30 years). In many cases, the tumor was left untreated for a long period of time. Six patients underwent extensive resection, thirty-two patients underwent marginal resection, and three patients underwent intralesional resection of the microfocal lesion. The mean postoperative follow-up period was 62 months (range: 5-247 months). Recurrence was observed in one patient only. This patient had undergone...
marginal resection and had retroperitoneal recurrence (1/41 patients). The recurrence occurred two years after surgery.

As mentioned previously, four patients were referred to our hospital for resection of the recurrence. The mean age at initial surgery was 53.5 years (range: 45-68 years), and the mean age at reoperation was 70.0 years (range: 67-72 years). The mean time between the initial surgery and recurrence was 16.5 years (range: 4-26 years). A long period of time had passed from the initial surgery to reoperation. Recurrence was seen in the lower limbs in three patients and in the upper limb in one. All four patients underwent marginal resection. In all patients, details of the surgical margin at the initial surgery were unknown due to the long period of time that had passed.

The mean follow-up period after reoperation was 38.8 months (range: 33-47 months), and no patient had another recurrence. In our study, there was no patient among the 45 studied patients who had distant metastasis.

**Discussion**

The National Soft Tissue Tumor Registry is published annually in Japan (10). According to this registry, the number of liposarcoma cases registered in 2009 was approximately twice the number of malignant fibrous histiocytoma (MFH) cases due to revision of pathological criteria for MFH. Liposarcoma was the most prevalent tumor among the registered malignant soft tissue tumors. Well-differentiated liposarcoma accounts for approximately 50% of all liposarcomas, and is a soft tissue tumor that is seen relatively often. Conventionally, well-differentiated liposarcoma is considered to be a soft tissue sarcoma with low malignancy. However, the new 2002 WHO classification categorized well-differentiated liposarcoma in the same group as atypical lipomatous tumors. Atypical lipomatous tumors have similar histopathological features with well-differentiated liposarcoma and occur in superficial locations (10). In this WHO classification, well-differentiated liposarcoma was categorized as an intermediate, locally aggressive tumor and was excluded from the category of malignant tumors (Table I). The number of recent reports regarding the minimization of the resection margin has increased. The basis of minimizing the resection margin is the WHO classification. However, there is still no consensus on the optimal surgical margin. In our study, we examined therapeutic outcomes for well-differentiated liposarcoma over 20 years and we also examined future treatment strategies.

In our study, the mean time between the first notice of the tumor by the patient and treatment was three years for patients who underwent the initial surgery. The tumor was left untreated for 30 years at the longest. The long length of time until treatment, indicated that the tumor was growing slowly, caused no subjective symptoms such as pain, and had predilection for areas such as the thigh, where it was less noticeable by others. For patients who underwent reoperation, the mean time from the initial surgery to the final follow-up was 22 years. There was no distant metastasis in patients who underwent initial surgery or reoperation. This indicates that well-differentiated liposarcoma does not cause, or only rarely causes distant metastasis. When past studies examined the therapeutic outcomes of malignant soft tissue tumors in elderly patients, high-grade MFH was often included in the examination for well-differentiated liposarcoma. However, we believe that tumors such as high-grade MFH should be excluded from the examination of well-differentiated liposarcoma.

As in a previous reports (11), our study showed that well-differentiated liposarcoma has a predilection for the lower limbs in elderly patients. In many cases, the tumor size was large. If a simple extensive resection was performed including the surrounding muscle tissue, then muscle strength would have been greatly reduced after surgery in many cases (Figure 1A and B). The results of our study revealed the following: (i) Well-differentiated liposarcoma

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**Table I. WHO classification of liposarcomas (revised 2002) (10).**

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<thead>
<tr>
<th>Benign</th>
<th>Intermediate (locally aggressive)</th>
<th>Malignant</th>
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<tr>
<td>Lipoma</td>
<td>Atypical lipomatous tumor/well differentiated liposarcoma</td>
<td>Dedifferentiated liposarcoma</td>
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<td>Lipomatosis</td>
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<td>Myxoid liposarcoma</td>
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<td>Lipomatosis of nerve</td>
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<td>Round cell liposarcoma</td>
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<td>Lipoblastoma/lipoblastomatosis</td>
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<td>Pleomorphic liposarcoma</td>
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<td>Angiolipoma</td>
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<td>Mixed-type liposarcoma</td>
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<td>Myelolipoma</td>
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<td>Liposarcoma, not otherwise specified</td>
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<td>Chondroid lipoma</td>
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<td>External angiomyelolipoma</td>
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<td>Extra-adrenal myelolipoma</td>
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usually occurred in relatively elderly patients. (ii) No distant metastasis occurred in any patient. (iii) The mean time to recurrence was approximately 16 years. Based on these results, we concluded that resection can be performed with reduced resection margins instead of a conventional, simple extensive resection for well-differentiated liposarcoma of the limbs. Specifically, marginal resection is considered appropriate for well-differentiated liposarcoma with a well defined border (such as inside the muscle tissue) as well as for the preservation of neurovascular bundles. If the tumor border with the surrounding normal tissue is ill-defined, extensive resection is considered appropriate. Such resection includes excision of some normal tissue in order to prevent there being left any amount of residual tumor.

In recent years, the importance of locomotive syndrome has begun to be recognized (12, 13). From the standpoint of this syndrome, it is important to perform resection only to the extent necessary and in order to prevent dramatic decrease in the muscle strength. According to the 2010 Comprehensive Survey of Living Conditions of People on Health and Welfare, Japan, joint diseases and bone fractures/falls accounted for approximately 25% of the causes for the elderly aged 75 years or older to require primary nursing care (Figure 2) (14). This suggests that motor disorders of the limbs is the cause, in approximately one quarter of the patients, for requiring primary nursing care. Such motor disorders are the most common causes for primary nursing care in the elderly. These elderly patients are often already enduring conditions such as dementia, cerebrovascular disease, and asthenia.

Muscle strength decreases approximately 2% each year due to aging. In particular, muscle mass decreases predominantly in the lower limbs. Some patients in their early old age might not have ambulatory problems in the early stages after surgery in which muscle strength is preserved. However, the muscle mass of the lower limbs can decrease with aging if excessive resection of muscles is performed. In such cases, a great risk for gait disorder could arise in the postoperative course. Thus, it is important to preserve as much muscle as possible in order to prevent future locomotive syndrome and to maintain a patient’s activity of daily living (ADL).

Dedifferentiation occurs in 6% of well-differentiated liposarcomas of the limbs. Dedifferentiation has been reported to occur approximately three times more often for liposarcomas
in the retroperitoneal space compared to those of the limbs (11). There has been a report of death after dedifferentiation of well-differentiated liposarcoma during follow-up. In a well-differentiated liposarcoma of the limb, the tumor can have an invasion-like growth pattern in parts of muscles and the tumor border with the surrounding normal tissues can be ill-defined. In such a case, resection of muscle tissue might be unavoidable, for prevention of recurrence, to the extent that it does not greatly impair the function of the affected limb. Retroperitoneal well-differentiated liposarcomas have been reported to have poor therapeutic outcomes (15-17). When difficulty of reoperation is a factor, it is important to perform resection as extensively as possible at the initial surgery.

It is important to note that our study retrospectively examined therapeutic outcomes of patients whose final pathological diagnosis was well-differentiated liposarcoma. As in patients with retroperitoneal well-differentiated liposarcoma, MRI can reveal septum or components other than fatty components in patients with well-differentiated liposarcoma of the limb. If a patient is suspected to have a high-grade tumor, extensive resection should be performed, as is conventionally carried out.

In conclusion, well-differentiated liposarcoma has a predilection for the lower limbs in relatively elderly patients. In our study, the mean time between the first notice of the tumor by the patient and the initial examination was approximately three years. In patients with recurrence of well-differentiated liposarcoma, the mean time between the initial surgery and recurrence was long, approximately 16 years. There was no distant metastasis detected in patients with well-differentiated liposarcoma at our hospital. If the tumor border between the normal tissue and the well-differentiated liposarcoma of the limb is ill-defined, sub-extensive resection is performed including the surrounding soft tissue, such as parts of muscle tissue. If the border is well-defined between such a tumor and its surroundings or areas adjacent to neurovascular bundles, marginal resection and sub-extensive resection are desirable.
Conflicts of Interest

The Authors have no conflicts of interest to disclose.

References


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