Wide resection of soft tissue sarcomas after unplanned primary procedures
A long-term follow-up study

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Abstract
Unplanned resection of soft-tissue sarcomas (STS) predispose the patients to recurrences and metastases, secondary wide resection is usually warranted.

To investigate the outcomes of re-excision of STS after unplanned initial resection.

The records of 39 patients undergoing re-excision of STS after unplanned initial resection from January 2006 through December 2015 were retrospectively investigated.

There were 17 males and 22 females, the mean age was 45.7 years. Most initial unplanned resections were performed in rural hospitals by surgeons from general surgery department, dermatology department, plastic surgery department, and orthopedic department. Thirty-five patients underwent secondary wide resections in our department. Histopathological findings indicated positive margins after primary surgeries in 18 patients. Until the conclusion of 37.2-month follow-up, 7 patients developed metastasis, 3 had local recurrence, and 7 were dead. Positive margins were associated with increased metastases and lower survival rates (P < .05). There was no significant difference in recurrences between the 2 groups.

Unplanned initial resection of STS often lead to unfavorable prognosis. Primary wide resections are warranted for this disease entity.

Abbreviations: CT = computed tomography, STS = soft-tissue sarcoma.

Keywords: re-excision, soft tissue sarcoma, survival rate, unplanned initial excision

1. Introduction
Soft-tissue sarcomas (STSs) are primary malignant tumors constituting less than 1% of all malignancies with an incidence of 1 to 2/100000.1-3 Whereas benign soft-tissue tumors are more common with an incidence of 300 times as STS.4 Due to the rarity of STS, superficial masses are usually resected as benign tumors, and pathological examinations are often ignored. Most of these operations are performed by surgeons without specialty training in oncology,5,6 such as general surgeons, plastic surgeons, orthopaedic surgeons and dermatologists from rural hospitals. Despite the ever increasing training program regarding treatment of STS, unplanned resections are still common in China, especially in underdeveloped area.

2. Materials and methods
2.1. Patients
From January 2006 through December 2015, 39 patients with STS who had received unplanned resections were referred to our institution for further treatment. There were 17 male patients and 22 female, the mean age was 45.7 years (range, 18 to 78 years). The tumor locations included the trunk in 12 cases (30.7%), upper extremities in 9 (23.1%), and lower extremities in 18 (46.2%). Histological diagnoses included synovial sarcoma, dermatofibrosarcoma protuberans and undifferentiated pleomorphic sarcoma. More than 85% patients had undergone initial unplanned resections of tumors in village clinics, municipal- and county-level hospitals. Furthermore, most of the unplanned procedures were performed by general surgeons, plastic surgeons, orthopaedic surgeons, and dermatologists. Positive margins were determined by histopathological findings in 18 patients. No patients had received neoadjuvant chemotherapy before the primary surgery. (Tables 1 and 2)
2.2. Treatment Strategy

Treatment algorithm for patients undergoing unplanned resection of STS was as follows: 35 patients received secondary wide resection of tumor. Intraoperative frozen sections indicated negative margins were achieved. Postoperative chemotherapy was applied in 14 patients. Two patients received amputation for unresectable STS. One patient with multiple metastases received chemotherapy without having surgeries. One patient received chemotherapy based on positron emission tomography-computed tomography (CT) and pathological findings.

2.3. Evaluation

The endpoints of the follow-up were deaths. Follow-up was carried out through telephone and out-patient clinic interview. Recurrences were detected with use of ultrasonic examinations and magnetic resonance imaging. Rates of local recurrence, metastasis and 5-year survival were compared between patients with and without positive margins after primary surgery.

2.4. Statistical Analyses

All statistical analysis was performed by using SPSS software (version 13.0, IBM, Armonk, NY), with statistical significance being set at \( P < .05 \).

3. Results

According to the pathologic findings in secondary procedures, 18 patients had positive margins after primary surgeries. Fortunately, negative margins were achieved in all 35 patients after secondary wide resection. One patient had infection after primary procedures, and had vacuum scaling drainage followed by secondary wound closure with use of local flap. No patients had motor/sensory dysfunction. All cases were followed up for at least 10 months (from 10 to 127 months, mean 37.2 months). 7 patients had metastases, 3 had recurrences, and 7 were dead. The 5-year overall survival rate was 80.5% (Table 3, Fig. 1).

3.1. Local recurrence

Two in 18 patients with positive margins had local recurrences, whereas 1 in 21 having negative margins had recurrences. There was no significant difference in recurrence between the 2 groups \( (P = .441; \text{Table 4}) \).

3.2. Metastasis

Six patients presenting with positive margins had metastases. The metastasis rate in patients with positive margins was significantly higher than that of patients with negative margins (1 of 21 patients; \( P = .027; \text{Table 4} \)).

3.3. Rate of survival

The 5-year survival rates were 64.5% and 95.2% in patients with and without positive margins respectively. There was significant difference between the 2 groups. \( (P = .028; \text{Table 4, Fig. 2}) \).

Table 1

| Histological type of STS          | No. of patients | Gender | Site          |
|----------------------------------|----------------|--------|---------------|
| Synovial sarcoma                 | 10             | 5      | Thunk         |
| Synovial sarcoma                 | 5              | 5      | Upper extremity|
| Synovial sarcoma                 | 1              | 0      | Lower extremity|
| Malignant fibrous histiocytoma   | 8              | 4      | Thunk         |
| Malignant fibrous histiocytoma   | 4              | 4      | Upper extremity|
| Malignant fibrous histiocytoma   | 1              | 1      | Lower extremity|
| Dermatofibrosarcoma protuberans  | 8              | 2      | Thunk         |
| Liposarcoma                      | 5              | 2      | Upper extremity|
| Liposarcoma                      | 3              | 1      | Lower extremity|
| Leiomyosarcoma                   | 2              | 1      | Thunk         |
| Leiomyosarcoma                   | 1              | 0      | Upper extremity|
| Leiomyosarcoma                   | 1              | 0      | Lower extremity|
| Alveolar rhabdomyosarcoma        | 1              | 0      | Thunk         |
| Alveolar rhabdomyosarcoma        | 0              | 0      | Upper extremity|
| Alveolar rhabdomyosarcoma        | 0              | 0      | Lower extremity|
| Pleomorphic rhabdomyosarcoma     | 1              | 0      | Thunk         |
| Pleomorphic rhabdomyosarcoma     | 0              | 0      | Upper extremity|
| Pleomorphic rhabdomyosarcoma     | 0              | 0      | Lower extremity|
| Myxofibrosarcoma                 | 1              | 1      | Thunk         |
| Myxofibrosarcoma                 | 0              | 0      | Upper extremity|
| Myxofibrosarcoma                 | 0              | 0      | Lower extremity|
| Clear cell sarcoma               | 1              | 1      | Thunk         |
| Clear cell sarcoma               | 0              | 0      | Upper extremity|
| Clear cell sarcoma               | 0              | 0      | Lower extremity|
| Epithelioid fibrosarcoma         | 1              | 0      | Thunk         |
| Epithelioid fibrosarcoma         | 0              | 0      | Upper extremity|
| Epithelioid fibrosarcoma         | 0              | 0      | Lower extremity|
| Primitive neuroectodermal tumors | 1              | 0      | Thunk         |
| Primitive neuroectodermal tumors | 0              | 0      | Upper extremity|
| Primitive neuroectodermal tumors | 0              | 0      | Lower extremity|

Table 2

| Level of hospitals | No. of patients | Without residual tumor | With residual tumor |
|--------------------|----------------|------------------------|---------------------|
| Provincial-level   | 5              | 4                      | 1                   |
| Municipal-level    | 10             | 6                      | 4                   |
| County-level       | 21             | 10                     | 11                  |
| Village clinics    | 3              | 1                      | 2                   |

Table 3

| Index                              | Values          |
|------------------------------------|-----------------|
| Age, yr: range, mean               | 18–78, 45.7     |
| Gender                             | Gender          |
| Male                               | 17              |
| Female                             | 22              |
| Residual diseases                  | Residual diseases |
| Positive                           | 18              |
| Negative                           | 21              |
| Re-resections                      | Re-resections   |
| Yes                                | 35              |
| No                                 | 4               |
| Chemotherapy after re-resections   | Chemotherapy after re-resections |
| Yes                                | 14              |
| No                                 | 25              |
| Follow-up time, mo: range, mean    | Follow-up time, mo: range, mean |
| 10–127                             | 37.2            |
| Total 5-yr survival rates          | 80.5%           |
4. Discussion

In clinical practice, patients with STS often have improperly designed procedures due to misdiagnosis. In the present study, of the 39 STS patients undergoing unplanned initial procedures, only 5 patients were operated on in provincial-level hospitals, no procedures were performed by specialized oncological surgeon. Some of the primary procedures were carried out by general surgeons, plastic surgeons, orthopaedic surgeons, and dermatologists. No cases had biopsy and intraoperative frozen section. According to pathological findings, 16 patients had positive margins after primary procedures. Studies investigating the outcome of unplanned primary surgeries for STS are sparse. Kang et al suggested the recurrence rate was significantly lower in patients referred to tertiary hospitals than in those from other medical institutes.\(^{[7]}\) In this study, we did not compare the outcomes of treatment among hospitals of different levels because only 5 patients underwent unplanned primary procedures in provincial-level hospital. However, we found the rates of positive margin was higher in lower-level hospitals than in provincial-level hospital.

Thirty-five patients received secondary wide resections in our department. However, the procedures were associated with some drawbacks, such as extensive tissue removal, prolonged operation time, functional loss and increased risk of local recurrence.\(^{[8]}\) Of the 35 patients, it is difficult to determine the surgical safety margin before the re-resection due to the interference of the post-operative reactive changes on CT or magnetic resonance imaging.\(^{[9,10]}\) Therefore, we had to perform more extensive resection than standard procedures. Furthermore, intraoperative frozen section was mandatory. Skin grafting was used in 1 patient due to significant tissue defect. Therefore, the length of hospital stay was prolonged and the medical expenses raised.

Some authors suggested unplanned resection is not an independent risk factor for unfavorable oncological outcome in terms of local recurrences, metastases, and overall survival.\(^{[4,11]}\) However, disputes remains about this clinical issue.\(^{[12,13]}\) The inconsistency of previous findings in the literature might be related to failure of including positive margins as a risk factor for the prognosis. Sixteen patients did not obtain negative margins according to the pathological findings after primary procedures and 2 patients had positive margins in the first resection according to the second wide resection in our department. Similarly, previous studies reported a positive margin rate of 35% to 37%.

| Table 4 | Comparison between patients with and without residual tumor. |
|--------|-------------------------------------------------------------|
|         | With residual tumor | Without residual tumor | P value |
| Local recurrence |                        |                        |         |
| Yes     | 2 (11.1%)           | 1 (4.8%)               | .441    |
| No      | 16 (88.9%)          | 20 (95.2%)             |         |
| Time, mo | 10.50±0.50          | 8                      |         |
| Metastasis |                        |                        | .027    |
| Yes     | 6 (33.3%)           | 1 (4.8%)               |         |
| No      | 12 (66.7%)          | 20 (95.2%)             |         |
| Time, mo | 8.50±2.87           | 8                      |         |
| 5-yr Survival rate | 64.5%              | 95.2%                 | .028    |

Figure 1. Overall 5-year survival rate of 39 patients.
to 56% after unplanned resections. As for local recurrences, our findings demonstrated residual tumor after unplanned resections was not an independent risk factor for patients undergoing unplanned primary procedures. However, the rate of metastases in patients with positive margins after initial primary procedures was significantly higher and the overall survival rates was lower than that of patients with negative margins. Our findings are contrary to that of previous literature. We deduce such inconsistent results might be attribute to different time and resection magnitudes. Extensive resection and intraoperative frozen section might explain the low rate of local recurrence in this study. Otherwise, unplanned primary resection with positive margins destroyed the capsule of the tumor, and longer interval between unplanned resection and re-resection might increase the possibility of metastasis. On the other hand, secondary procedures for the cases of positive margins may activate tumorogenic mechanisms, this could exert negative impacts on survival.

Adjuvant radiotherapy or chemotherapy are necessary for STS, especially for patients with positive margins after unplanned primary procedures. Kepka et al. reported adjuvant radiotherapy was an effective treatment for patients undergoing re-resection, the 10-year local and distant control rates were 86% and 80% respectively. Adjuvant chemotherapy is used for certain types of chemo-sensitive sarcomas, but the literature showed no significant effects on distant metastases and survival. Furthermore, neoadjuvant chemotherapy is usually used in locally advanced sarcomas to decrease the recurrence and metastasis rates of initial excision with negative surgical margins. In this study, due to the heterogeneity of pathological diagnoses, it would be of no clinical significance to investigate the relationship between survival and chemotherapy.

5. Conclusions
Unplanned primary resection of STS is common. Wide resection is mandatory for favorable outcomes. Furthermore, patients with positive and uncertain margins after primary surgery should have secondary resection as soon as possible. Extensive resection and intraoperative pathological determination are important to improve the outcome of secondary procedures. If the demerits of unplanned resection and the knowledge of soft tissue tumor had been well recognized by the surgeon of lower level hospitals, unplanned resection of soft tissue tumor would be less and more patients with soft tissue tumor would receive professional treatment. For this purpose, our department have organized about 20 lectures about bone and soft tissue sarcoma in different cities of Shandong Province of China in the past 3 years. We believe that the diagnosis and treatment of soft tissue sarcoma in Shandong Province would be improved in the near future.

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