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Reconstructive Surgery in Soft Tissue Sarcomas—Long-Term Outcome and Quality of Life

Reiner Wirbel[1], Steffen Weber[2], Angela Olinger[3], Wolf Mutschler[4], Tim Pohlemann[2]

[1]*Department of Trauma, Hand and Reconstructive Surgery, Verbundkrankenhaus Bernkastel-Wittlich, Wittlich, Germany*

[2]*Department of Trauma, Hand and Reconstructive Surgery, University Hospital of Saarland, Homburg-Saar, Germany*

[3]*Department of Orthopedics, Rheumatology, Trauma and Hand Surgery, Mediclin Hospital, Plau am See, Germany*

[4]*Department of Surgery, Ludwig-Maximilians-Universität, München, Germany*

The long-term oncological and functional outcome including quality of life should be evaluated in soft tissue sarcomas (STS). The need for reconstructive surgery with possible influence on the results should also be analyzed. Tumor stage mainly influences the prognosis of STS. Advances in reconstructive surgery mostly allow limb salvage. Limited information exists about functional outcome and life quality. A total of 86 patients (51 men, 35 women, mean age 50.5 years) with a minimum follow-up of 10 years were analyzed. We determined the oncological outcome (local recurrences, metastases, overall survival) of tumors at varying stages: stage I (n = 30), stage II (n = 52), and stage III (n = 4). Functional outcome and quality of life of the survivors were measured using the Musculoskeletal Tumor Society (MSTS) criteria and the EORTC-QLQ-C-30 (European Organisation for Research and Treatment of Cancer-Quality of Life-Questionnaire-Core-30 module) questionnaire. Tumor stage influenced the survival and the development of metastases. Survival rates were 89.5 and 88% after 5 and 10 years in stage I, and 56.5 and 49% in stage II tumors. Surgical margin influenced the development of local recurrence. Reconstructive procedures were necessary in 27 patients. After a median follow-up of 144 months, 36 patients were dead: 29 of their malignancy and 7 of other diseases. Fifty long-term survivors presented good results for MSTS (mean score: 82.4) and EORTC-QLQ-C-30

Corresponding author: Reiner J. Wirbel, MD, Verbundkrankenhaus Bernkastel-Wittlich, Koblenzer Str. 91, D-54516 Wittlich, Germany. Tel.: 0043 6571 1532310; Fax: 0043 6571 1532390; E-mail: reiner.wirbel@web.de

(mean score: 79.8), the results were independent on the need of reconstructive surgery. In stage II STS, the survival drops even after 5 years. The surgical treatment of STS requires the knowledge of different reconstructive techniques; functional results and quality of life are not compromised by the need for reconstructive surgery.

Key words: Reconstructive surgery – Soft tissue sarcoma – Quality of life

Soft tissue sarcomas (STS) represent a heterotopic group of tumors of mesenchymal origin which can be divided into low-grade and high-grade tumors by histomorphologic criteria and clinical course.

The treatment of soft tissue sarcomas has to be valued by the oncological outcome as well as by the achieved clinical and functional results.

Aside from the radiotherapy and the chemotherapy, surgical therapy is the most important part of the multimodal treatment concept. However, considering the prognosis of patients with soft tissue sarcomas, there remains the question of adequate surgical treatment.

Several studies have shown that the functional results are worse after amputation compared with those achieved with limb salvage procedures, but the quality of life is considered to be not dependent upon the surgical technique performed.[1–7] However, there remains the dilemma between the adequate surgery—that is, the oncological and radical extent of the procedure, and the prevention of a serious loss of function, especially in soft tissue sarcomas localized in the extremities.

Most of the studies of patients with soft tissue sarcomas have a limited follow-up of 5 years. Studies with long-term results of functional and oncological outcome and of the obtained quality of life are rare.

We like to focus on the long-term outcome by the presented retrospective study. Therefore, a minimum follow-up of 10 years was selected. At the time of the study, radiation therapy and chemotherapy were performed only in selected cases. Therefore, reliable statements were not possible concerning these treatment modalities.

The presented study has 2 primary goals: (1) to analyze and define the significance of surgery, especially the need for reconstructive procedures that may compromise the functional outcome; and (2) to show the long-term (*i.e.*, more than 10 years) oncological and functional results that can be expected in patients with soft tissue sarcomas.

Patients and Methods

Patients

A total of 203 patients with soft tissue sarcoma located at the trunk or the extremities were treated surgically in our department from January 1993 to December 2009. To get information about the long-term prognosis, patients with a minimum follow-up of 10 years were selected. Thus, only patients treated between 1993 and 2000 were included in this study.

There were 86 patients (51 men, 35 women) with an average age of 50.5 years (range, 16–86 years) at the date of surgery. The most frequent tumors were the malignant fibrous histiocytoma (n = 26, 30.2%), liposarcoma (n = 19; 22%), and leiomyosarcoma (n = 12; 13.9%). Fibrosarcomas were seen in 8 cases (9.3%), rhabdomyosarcomas in 7 cases (8.1%), and synovial sarcomas in 6 cases (6.9%). There were 2 angiosarcomas, two malignant schwannomas, and 4 other tumor entities.

Concerning to the classification of Enneking,[8] there were 30 (34.8%) low-grade (stage I) and 52 (60.4%) high-grade (stage II) tumors. In 4 cases, distant metastases had to be observed (stage III).

In 51.1% of the cases, the tumor was localized in the lower extremity (n = 44). In 26 cases (30.2%), the tumor originates from the upper extremity and in 16 cases (18.7%), from the trunk.

In 35 (40.2%) of the patients, the tumor was primarily resected under the suspicion of a benign soft tissue tumor; in 31 of these cases, the tumor was localized extra-compartmentally. The histopathologic examination revealed a sarcoma with an intralesional resection. These patients were admitted for further surgery to achieve a wide resection. The median duration between previous intralesional surgery and admission was 5.2 weeks (range, 2–16 weeks). There were 19 stage I tumors and 16 stage II tumors in this group.

Fifteen patients (17.4%) were presented with local recurrence with a median interval of 23.6 months (range, 1–132 months) to the primary surgical procedure. In this group, there were 4 stage I tumors and 11 stage-II tumors. It was the first local

recurrence in 7 cases, 2 patients were admitted with a second local recurrence, 3 with the third, and 3 even with additional local recurrences, respectively.

All patients were informed that their data would be submitted for publication, and gave their consent.

Methods

Oncological follow-up care

All patients were regularly seen at postoperative follow-up care. The demographic data were collected. The complications and the adjuvant therapies were also analyzed. The survival rate and the occurrence of local recurrence and metastases were determined. The survival probability was estimated by the method of Kaplan and Meier.[9] The achieved surgical margin,[10] the tumor stage, and the tumor volume were analyzed as prognostic factors for the incidence of local recurrence or metastases.

Analyzing the oncological outcome, a special focus was laid on the group of patients that underwent previous intralesional surgery and on the group of patients with local recurrences.

Function and quality of life

The performed surgical procedures (limb salvage procedure versus amputation) and the need for plastic reconstructive surgical techniques were analyzed and correlated with the achieved function and quality of life.

All survivors were examined at the last clinical follow-up in January 2010. The functional results were rated according to the MSTS criteria.[11] The system includes the 6 following categories: 3 general: pain, function of the affected joint, emotional acceptance; and 3 specific depending on the extremity affected: supports, walking ability, and gait analysis (for the lower extremity), hand positioning, manual dexterity, and lifting ability (for the upper extremity). A maximum of 5 points for each factor produces a maximum score of 30 points. The total score is divided by 30, resulting in the functional evaluation rate. The rating was considered excellent if 5 of the 6 factors scored 5 points, independent of the score of the sixth factor. A good rating was recorded if 5 factors scored 3 points or more, and the sixth factor 2 points or less. A fair rating was regarded if 5 of the 6 factors scored 1 point or more, and the sixth factor 0 points. If 2 or more factors scored 0 points, the rating was considered poor.

To determine the quality of life, the QoL-C30 (quality of life–core module 30) questionnaire was used.[12,13] Tumor-specific symptoms and functional impairments are considered in this questionnaire. The 30 questionnaire-items concern 3 different categories: global health status; functional scales (physical, role, emotional, cognitive, and social functioning); and different symptom scales (fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties).

The answers are valued using a special formula.[12] The results represent each scale and subscale by a percentage score. A high score in the functional scales and in the global health status means a good quality of life, whereas a high score in the symptom scales indicates a poor result.

ANOVA was used for statistical analysis of the oncological long-term results. To compare subgroups T test and Wilcoxon-test were applied. A value of $P < 0.05$ was considered significant.

Results

Surgical treatment

In the 30 low-grade tumors, the surgical margins achieved were wide in 21 cases, and marginal in 9 cases. In the 52 high-grade tumors, the margins were radical in 7, wide in 21, marginal in 19, and intralesional in 5 cases. In the 4 stage III tumors, the margins were marginal in 2 cases, wide in 1, and intralesional in 1 case.

In 27 patients (31%), 28 different plastic-reconstructive surgical procedures were necessary to close the soft tissue or bony defect produced by the resection of the tumor. In 8 cases, simple mesh graft was sufficient; in 14 cases, different local or free fasciocutaneous or muscle-flaps (Fig. 1) were needed. In 1 case, tendon transfer was necessary; vascular grafts (Fig. 2) had to be performed in 3 cases. In 2 cases, bony reconstructions had to be used.

Reconstructive procedures were necessary in 9 of the 26 tumors (34.6%) located in the upper extremity and in 18 of the 44 tumors (40.9%) originating from the lower extremity. As expected, there were larger tumor volumes in these cases requiring reconstructive surgery, measuring 620 mL on average (range, 250–4800 mL).

Amputations had to be performed in 9 patients (10.4%): hemipelvectomy (n = 3), the lower extremity (n = 3), and the upper extremity (n = 3).

Thirty-five out of the 86 patients had a previous intralesional surgery under the suspicion of a benign tumor. In 20 of these cases, no tumor tissue

Fig. 1 Latissimus free flap to close a defect at the left medial ankle in a synovial sarcoma.

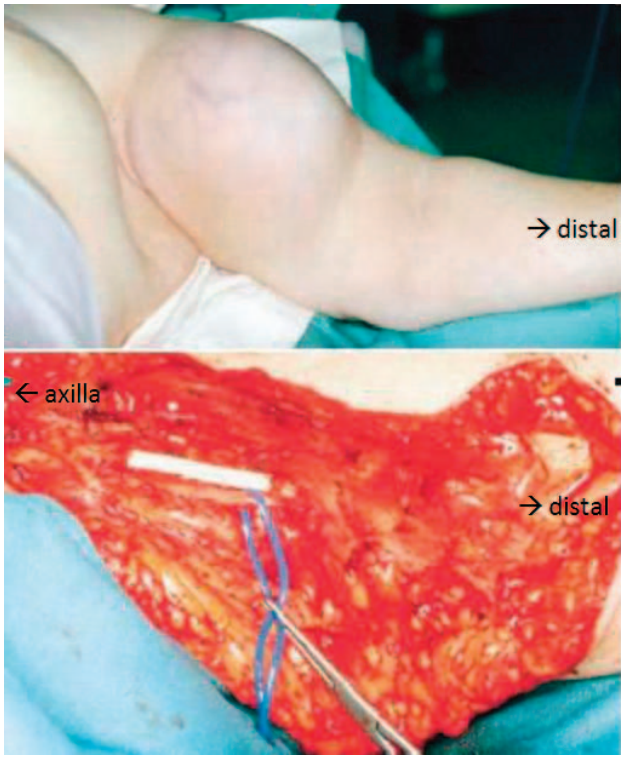

Fig. 2 Vascular graft of the brachial artery after resection of a leiomyosarcoma at the left-sided medial upper arm.

could be found histologically after the performed wide resection. The median tumor volume of the remaining 66 specimens was 451 mL (range, 3–4800 mL). The stage I tumors were smaller (386 mL) than the stage II tumors (442 mL), but the difference was not significant.

In 15 patients (17.4%), 16 complications were observed. Of these complications, 13 were wound healing problems, 9 of which required surgical revision. All of these local complications could be cured. Further complications included an osteonecrosis as the result of radiotherapy, a deep vein thrombosis, and a cerebrospinal fluid fistula requiring surgical closure, each in one case, respectively.

Adjuvant therapies

Adjuvant therapies were performed in 43 patients. Adjuvant radiotherapy was used in 23 cases, chemotherapy in 9 cases, and combined radiochemotherapy in 11 cases. At the time of the study, adjuvant therapy was performed only in selected cases and in clinical trials. The indication for radiotherapy was usually seen in high-grade tumors and in large (*i.e.*, >5 cm) low-grade tumors. The indication for chemotherapy was proved only in clinical trials and studies without general guidelines or recommendations.

Because of the restricted number of cases, and because of the individual indication for the adjuvant therapies in our series, reliable statistical evaluation of a potential benefit concerning the overall survival or the incidence of local recurrence was not feasible.

Oncological results

At the date of evaluation, 29 patients died of their malignancy and 7 patients died of other causes. The median survival time was 58 months (range, 26–74 months). The patients presenting with stage III tumors had a median survival time of 15.25 months. Local recurrences were observed in 13 patients (15.1%) after an average of 14.3 months (range, 4–47 months). Distant metastases were seen in 23 patients (26.7%) after an average of 11.7 months (range, 3–21 months). In most cases (n = 21), there was pulmonary metastases.

The incidence of local recurrence significantly depended upon the achieved surgical margin. The tumor volume had no influence. Concerning all tumor stages, local recurrences were significantly more frequent in cases of achieved marginal margin compared with those of wide or radical margin. These findings could be stated in both subgroups, (*i.e.*, in the low-grade as well as the high-grade

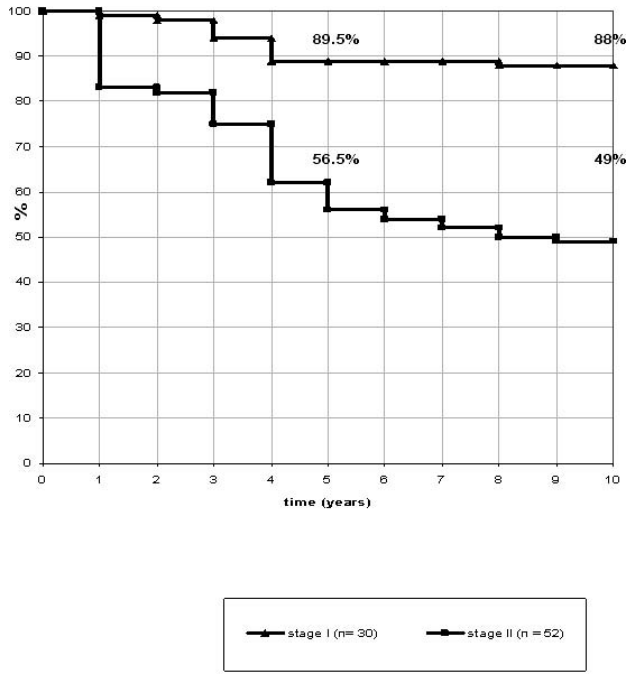

Fig. 3 Five- and 10-year survival probability in relation to tumor stage (stage III-tumors were excluded).

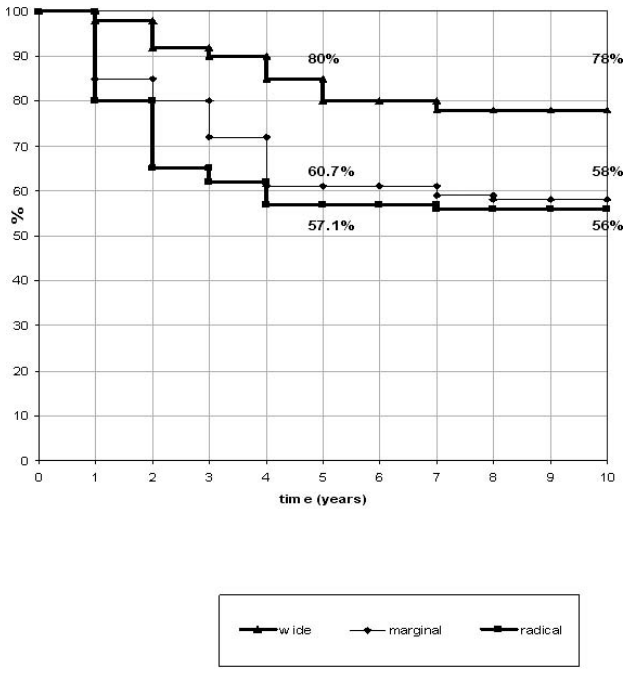

Fig. 4 Five- and 10-year survival probability in relation to the surgical margin (stage III tumors and intralesional resections were excluded).

tumors). The incidence of distant metastases was higher in high-grade tumors than in low-grade-tumors; but in both tumor subgroups, the incidence of distant metastases did not depend upon the surgical margin.

Excluding the 4 patients presenting with stage III tumors, 2 different groups were also analyzed, the one (n = 35) with previous intralesional surgery, and the other (n = 47) without previous intralesional surgery. We found even less local recurrences and less distant metastases in the patients with previous intralesional surgery compared with those patients without previous surgery, but the difference was not significant. However, the achieved surgical margin was valued as wide in 20 cases of the 35 patients with previous intralesional surgery, where no tumor could be found at the histological examination.

In the 15 cases presented primarily with a local recurrence, there were no worse oncological results. Most tumors (n = 11) were high-grade tumors. The local recurrence could be cured in 10 out of 15 patients.

Thirteen patients developed local recurrences. Ten of these cases occurred within the first 2 postoperative years. The local recurrences could be cured in 4 cases, twice by amputation, and twice by a renewed resection.

Distant metastases developed in 23 patients; 6 of them were treated surgically. Only 2 patients could be cured, 1 by resection of a peripheral soft tissue metastasis, the other patient is considered a complete responder after chemotherapy for 148 months up to the date of evaluation. All other patients with distant metastases died of their disease.

The Kaplan-Meier survival analyses in relation to tumor stage and the achieved surgical margin are shown in Figs. 3 and 4.

The overall survival was significantly dependent on the tumor stage after 5 years and after 10 years. The survival probability of 56.5% after 5 years decreased in patients with high-grade sarcomas to 49% after 10 years, whereas the reduction of the survival probability during this period was insignificant in patients with low-grade sarcomas (89.5–88%). Stage III tumors and intralesional resections were not considered.

Patients underwent wide resection showed a better prognosis than patients with marginal resection, but the difference was not significant. In both groups, there was a similar reduction of the survival probability in the period of 5 to 10 years postoperatively. The worse prognosis after radical resections can be explained by the fact that there were only high-grade tumors in this group.

Table 1 Scores of MSTS of the different categories in 50 long-term survivors in relation to necessity of plastic-reconstructive procedures

Categories	Without RP (n = 37) Score, %	With RP (n = 13) Score, %
General		
Pain	72.3	72.5
Function	90.4	88.5
Emotional acceptance	73.4	74.1
Specific upper extremity (n = 15)	(n = 9)	(n = 6)
Hand positioning	92.3	90.4
Manual dexterity	93.4	93.8
Lifting ability	77.8	76.4
Specific lower extremity (n = 27)	(n = 20)	(n = 7)
Support	80.2	80.5
Walking ability	85.4	84.1
Gait	80.2	80.1

RP, reconstructive procedure.

There were also no differences in the 5- and 10-year survival rate concerning the tumor volume, previous intralesional surgery, the primary presentation with a local recurrence, or chemotherapy in high-grade sarcomas.

Functional results and quality of life

Evaluations of function and quality of life after an average follow-up of 12 years [range, 10–16 years; i.e., 144 months (range, 120–192 months)] were possible in 50 long-term survivors. There were 15 women and 35 men with a median age of 51.6 years (range, 28–81 years) at the date of evaluation. In 27 patients of the long-term survivors, the tumor was localized in the lower extremity, in 15 cases in the upper extremity, and in 8 cases at the trunk.

The median MSTS-score was 82.4 % (range, 62–100%). There were no significant differences concerning the patient's age or sex and the localization of the tumor. Thirty-eight of the 50 patients (76%) were free of pain.

The 4 long-term surviving amputees showed marginally lower, but not significant different scores (median score: 79.8%). The median scores of the categories pain, function, and emotional acceptance, as well as the specific scores for the upper and for the lower extremities are summarized in Table 1. The specific scores showed marginally better values for the upper extremity, but there were no significant differences concerning the localization.

The best results were found in the category of function, and in the category of walking ability for the patients who underwent tumor resection of the lower extremity. Only 3 of the 27 patients in the lower extremity group needed walking frames.

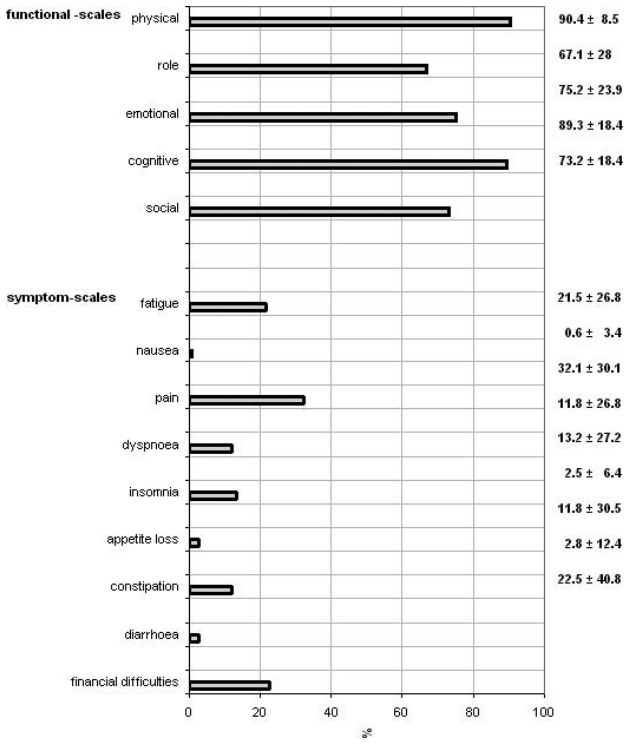

Fig. 5 Results of the Qol-C30 questionnaire in 50 long-term survivors.

The scores of MSTS in the patients underwent reconstructive surgical procedures did not differ from the scores of the patients who did not require such procedures. The survivors treated primarily with adjuvant radiotherapy also did not present with inferior functional results.

The results of the QoL-C30 questionnaire are shown in Fig. 5. There were no significant differences concerning patient's age, sex, or localization of the tumor. The amputees also did not present with worse values. The best results were seen in the categories physical and cognitive functioning. Thirty-two patients are retired, but only 4 of them (8%) were unable to work due to the tumor disease. Fourteen patients (28%) stated a moderate or severe restriction of their daily activities. Six patients (12%) felt compromised in the category of social functioning, and 8 patients (16%) felt compromised in the category of emotional-functioning.

Considering the symptoms scales, the highest values were seen in the pain category, followed by the fatigue and financial difficulties categories.

Moderate pains were stated by 12 patients (24%); increased fatigue was reported by 11 patients (22%).

Ten patients (20%) admitted financial problems due to their physical status, and due to their tumor treatment, respectively.

The symptoms scales also revealed no differences concerning patient's age, sex, or localization of the tumor. The amputated patients presented values that were no worse.

The global quality of life revealed a mean score of 72.8 (±22.3%) without significant differences concerning localization of the tumor, patient's age or sex, and concerning the performed surgical procedure (limb salving versus amputation).

Discussion

Soft tissue sarcomas are very rare tumors, accounting for less than 1% of all malignancies in adults.[5,14,15] They can be divided into low- and high-grade tumors by the means of histopathological criteria resulting in the surgical classification according to Enneking.[8,10]

The multimodal treatment concept includes surgery, radiotherapy, and chemotherapy. The two basic treatment goals are local tumor control (*i.e.*, prevention of local recurrence) and systemic tumor control (*i.e.*, prevention of distant metastases).

The significance of chemotherapy is seen in childhood soft tissue sarcomas, there exist no clear guidelines in the adult population. A possible benefit for the overall-survival has to be valued in further clinical trials and studies.

The significance of radiotherapy is meanwhile well defined for local tumor control.[16,17] In high-grade and in large (*i.e.*, >5 cm) low-grade tumors, the recurrence rate is significantly reduced. We cannot make any reliable statement about these adjuvant treatment modalities in our study. At the time of our study period, the indication for radio- or chemotherapy was seen only in selected cases.

The predominant role of surgery in the treatment concept of soft tissue sarcomas is generally acknowledged.[14,15] But the extent of the surgical procedure is still a matter of discussion, considering the prognosis of the different tumor stages and the possible loss of function. Wide resection has to be achieved for local tumor control.[2,4,14–16,18] As shown in our series, the incidence of local recurrence is increased if only a marginal margin was achieved. The treatment of local recurrence is much more difficult, resulting in the loss of primarily preserved function in most of the cases.

By review of the literature, primary amputation is necessary in about 10% of the cases.[2,4,7,14] These reports agree with our findings (10.4%).

To close the defect after adequate resection, different reconstructive surgical procedures can be necessary. Reconstructive surgery is reported to be indicated in up to 50 to 80% of cases.[19] In our series, reconstructive surgical procedures were necessary in 27 of 86 patients (31%). The indication depends on the localization of the tumor. To preserve the function and to avoid an amputation, reconstructive surgical procedures are more frequently indicated if the tumor is located peripherally.[19] The palette of the procedures can range from simple mesh grafting to local, free muscle or fasciocutaneous flaps to vascular grafting to tendon transfers to extensive bony reconstructions. As expected and confirmed by our series, the need for plastic-reconstructive procedures increases in large tumors, but we could not find any restriction in the long-term functional results.

The complication rate after resection of soft tissue sarcomas is reported to range from 25 to 30%,[14–17] in most of the cases related to wound healing problems due to seromas or hematomas. The complication rate was 17.8% in our series. The large cavitations resulting from tumor resection can facilitate the occurrence of seromas. The indication for different muscle flaps can be seen in these cases. Planned vacuum sealing and second look procedures may help to minimize this problem.

In most cases, the long-term functional results after the resection of soft tissue sarcomas are described as good. In our series, the mean MSTS-score revealed even 82.4 points. These findings correspond with the data of the literature.[1–4,16,18,20] Our results did not depend on the patient's age or sex, tumor volume, or the localization of the tumor.[21] These findings disagree with the observations of Davis *et al*,[1] who reported a negative impact on function caused by the patient's age by tumor volume. In our series, the functional results were also not compromised neither by the need for reconstructive surgical procedures nor by the fact of adjuvant radiotherapy. However, a reliable statement concerning both of these factors possibly influencing the functional results is not feasible because of the limited number of patients.

The score of MSTS is the most common measuring instrument[11] of the function in patients who underwent resection of a soft tissue sarcoma; but the function is not the only factor that determines quality of life.[2,5–7,12,18,22]

The quality of life core–30 questionnaire has been established during the last decade to determine the quality of life in tumor patients.[12,13] As confirmed by our findings, approximately 10 to 30% of the patients report a restriction of daily activities, or social functioning.[3,5–7,12,20,22]

Using the MSTS criteria, many studies report a poorer functional result in amputees compared with those who underwent limb salving procedures.[4,14,16,20] In our series, the MSTS-score was also lower in amputated patients, but not significantly. The results of the QoL-C30-questionnaire showed comparable values, in amputations and in limb salvage procedures, respectively. These findings were confirmed by other authors,[5–7,16,20,22] demonstrating that quality of life is not solely defined by the achieved function. As described by a recent study[22] the quality of life in tumor patients is mostly affected by social integration and by participation of life roles.

Thereby it is confirmed once more that oncological and not functional aspects have to influence the choice of the adequate surgical procedure (amputation versus limb salvage).

Beside the attained functional result every tumor therapy has to be measured primarily by the achieved oncological outcome. The overall survival mostly depends upon the tumor stage. The 5-year survival probabilities range from 50 to 60% in stage II tumors, up to 80 to 90% in stage I tumors.[14,15,20] These reports are confirmed by our findings presenting survival rates of 89.5% in stage I tumors and 56.5% in stage II tumors. Most studies reported an oncological follow-up of 5 years.[2,15–18,22] However, we could demonstrate in our series that the survival probability will decrease further; low-grade sarcomas showed an insignificant decrease of survival probability from 89.5% after 5 years to 88% after 10 years, but high-grade sarcomas from 56.5% after 5 years to 49% after 10 years, respectively.

There are some other prognostic factors in soft tissue sarcomas reported in the literature, such as tumor type, tumor volume, and localization.[9,17] We could not confirm these observations, maybe due to the limited number of patients.

The overall survival in our series only depended on the tumor stage. Low-grade sarcomas were on average smaller than the high-grade sarcomas (386 mL versus 442 mL), but the difference was not significant. It has been suggested that low-grade sarcomas were smaller in our series and therefore resectable more frequently with a wide margin. However, we could not find a statistical significance. The 5-year survival rate was 60.7% when a marginal margin was achieved and 80% when a wide margin was feasible; the 10-year survival rate was 58% and 78%, respectively.

However, we agree with other authors:[14,15] the achieved surgical margin is the most important prognostic factor for local tumor control. The incidence of a local recurrence was significantly higher in tumors resected with a marginal margin compared with those resected with a wide margin. We observed significantly more local recurrences, when only a marginal margin was feasible.

Some studies demonstrated that the occurrence of local recurrence promotes the development of distant metastases resulting in a poor overall survival.[2,20] In our series, we saw 15 patients presented with a local recurrence without concomitant distant metastases. Ten of them could be cured, and we could not find a worse oncological outcome. But the small number of cases may not allow any statistical predication.

When distant metastases are detected, the treatment approach is palliative in most cases. There are predominantly pulmonary metastases. In our series only 2 of 23 patients with metastases are still alive.

Another common problem in the surgical management of soft tissue sarcomas is the fact of a previous unplanned surgery with intralesional margin possible. The histological examination of the tumor resected under the suspicion of a benign process reveals surprisingly a sarcoma. This problem is extensively described by Rougraff *et al*.[23] They report a series of 106 patients with a primary inadequate surgical procedure. The renewed resection revealed no residual tumor tissue in 32% of patients. In our series, residual tumor tissue was not detectable in 20 of 35 cases (57%). The thesis of Rougraff *et al*[23] that patients who underwent previous intralesional surgery have a worse prognosis cannot be confirmed by our results. We found even better oncological results. This may be the consequence of the large amount of small tumors in this subgroup, and of the wide resections feasible in our series. The specimens where tumor tissue could not be found after the renewed resection (57%) were classified as wide resections.

In conclusion, different reconstructive surgical procedures may be necessary to close the defect after adequate resection of a soft tissue sarcoma. Long-term functional results and the quality of life are not influenced by the surgical procedure performed. The quality of life is not solely influ-

enced by the archived function. Therefore, oncological and not functional aspects determine the extent of the surgical procedure. The surgical margin achieved is the most important factor in local tumor control and overall survival is mainly depended on tumor stage. In high-grade sarcomas, the survival rate drops even after 5 years. Long-term studies with prolonged follow-up will be helpful to define the exact oncological outcome. Additional studies will be necessary in the future to determine the possible benefit of adjuvant therapies for systemic tumor control.

Acknowledgments

The authors declare that they have no conflict of interest.

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