

# Soft Tissue Sarcoma: Can a Rescue Procedure be Performed when the First Surgery was Unsuccessful?

J. Duart-Clemente<sup>a</sup>, M. San-Julián<sup>a</sup>, R. Martínez-Monge<sup>b</sup> and S. Martín-Algarra<sup>b</sup>

<sup>a</sup>Department of Orthopedic and Trauma Surgery. Navarre University Clinic. University of Navarre. Pamplona. <sup>b</sup>Department of Oncology. University Clinic. University of Navarre.

**Purpose.** The purpose of this paper is to review the experience of our hospital in treating patients diagnosed with a soft-tissue sarcoma (STS) in one of their limbs who sought consultation further to inappropriate surgical resections or a local relapse.

**Materials and methods.** This is a retrospective study of 64 patients treated for STS in another hospital; the patients were divided into 2 groups: group A, comprised 27 patients where the initial excision proved to be inappropriate («whoops procedure»); group B was made up of 37 patients that had a local recurrence of a STS. The disease-free and accumulated (Kaplan-Meier) survivorship rates were calculated.

**Results.** Group A: all 27 patients were reoperated and in 12 cases a residual tumoral disease was detected (44%). Twenty-three patients received associated radiotherapy (intraoperatively, brachytherapy and/or external beam radiotherapy). Mean follow up was 67 months (24-216). Three had a local recurrence, two of them requiring amputation. Eleven percent of patients had died at the time of examination. The disease-free survivorship rate at 216 months was 85%.

Group B: 35 of the 37 patients were reoperated (94%). Chemotherapy was used in 21 cases and in four cases isolated limb perfusion was used with TNF and melphalan (10.8%). Twenty-seven patients received radiotherapy (external beam, intraoperative and/or brachytherapy) (72%), 19 of them had received radiotherapy after the first one (70%). In 20 cases (10%) both chemotherapy and radiotherapy were used. Mean follow-up was 80 months (range: 12-264). Sixteen patients had metastasis further to treatment and nineteen had major complications. Forty-three percent of patients had died at the time of this review. Disease-free survivorship at 264 months was 16%.

**Conclusions.** After a «whoops procedure» it is possible to obtain a high disease-free survivorship rate in patients referred immediately to specialized units. Nevertheless, when local recurrence occurs, the disease-free survivorship rate decreases sharply.

**Key words:** *soft tissue sarcoma, «whoops procedure», local recurrence.*

## Sarcoma de partes blandas: ¿existe posibilidad de rescate cuando la primera cirugía no fue resolutive?

**Objetivo.** El objetivo de este trabajo es revisar la experiencia de nuestro centro en el tratamiento de pacientes diagnosticados de sarcoma de partes blandas (SPB) en una extremidad que consultan tras resecciones quirúrgicas inadecuadas o recidiva local.

**Material y método.** Se trata de un estudio retrospectivo de 64 pacientes remitidos tras el tratamiento de un SPB en otro centro, divididos en 2 grupos: el grupo A, compuesto por 27 pacientes a quienes se realizó una escisión inadecuada inicial (*whoops procedure*) y el grupo B, con 37 pacientes afectados de una recidiva local de un SPB. Se calculó la tasa de supervivencia libre de enfermedad y la tasa de supervivencia acumulada (Kaplan-Meier).

**Resultados.** Grupo A: la totalidad de los 27 pacientes fueron reintervenidos y en 12 casos se detectó enfermedad tumoral residual (un 44%). Veintitrés pacientes recibieron radioterapia asociada (intraoperatoria, braquiterapia y/o externa). El seguimiento medio ha sido de 67 meses (24-216). Tres pacientes presentaron recidiva local, uno de los cuales precisó amputación. El 11% de los pacientes habían fallecido en el momento de la revisión. La tasa de supervivencia libre de enfermedad a los 216 meses ha sido del 85%.

Grupo B: 35 de los 37 pacientes fueron reintervenidos (94%). En 21 casos se asoció quimioterapia y en 4 perfusión aislada de la extremidad con factor de necrosis tumoral (TNF) y melfalan (10,8%). Veintisiete pacientes recibieron

Corresponding author:

M. San Julián.  
Avda. Pío XII 36.  
31008 Pamplona.  
E-mail: msjulian@unav.es

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radioterapia (externa, intraoperatoria y/o braquiterapia) (72%), 19 de ellos habían recibido ya radioterapia después de la primera (70%). En 20 casos (10%) se asoció quimioterapia y radioterapia. La media de seguimiento ha sido de 80 meses (12-264). Dieciséis pacientes presentaron metástasis después del tratamiento y diecinueve tuvieron complicaciones mayores. El 43% de los pacientes había fallecido en el momento de la revisión. La tasa de supervivencia libre de enfermedad a los 264 meses ha sido del 16%.

**Conclusiones.** Después de una escisión inadecuada inicial se puede obtener una alta tasa de supervivencia libre de enfermedad en pacientes remitidos inmediatamente a centros especializados. Sin embargo, cuando aparece la recidiva local, las posibilidades de supervivencia libre de enfermedad disminuyen drásticamente.

**Palabras clave:** *sarcoma partes blandas, whoops procedure, recidiva local.*

Soft tissue sarcomas (STS) are a heterogeneous group of malignant neoplasms derived from the extraskeletal connective tissue originating in the mesoderm<sup>1</sup>. They are classified into different groups on the basis of their similarities in terms of clinical presentation, pathological appearance and biological behavior<sup>2</sup>.

STSs account for around 1% of adult malignant tumors<sup>3</sup>. A general practitioner may see a new case every 24 years<sup>4</sup>. Given their low incidence, it is recommended that they should be referred to a specialized center so that they can be assessed by multidisciplinary teams before performing a biopsy or administering treatment<sup>5</sup>. We should suspect an STS when the patient is over 50 and the tumor is over 5 cm in length, deep-lying and causes pain; or if it has increased in size in the last few months<sup>6,7</sup>.

Accurate diagnosis and staging of STSs require an experienced physician. Furthermore, they required a multidisciplinary therapeutic approach combining an accurate surgical resection with radiation therapy and/or chemotherapy<sup>8</sup>. Nonetheless, in our environment they are sometimes treated by inexperienced surgeons, who tend to make an erroneous initial excision (EIE), due either to an error in the pre-op presumptive diagnosis or to the fact that the surgeon did not consider the possibility of an STS and made his diagnosis only based on the pathological study of the resected sample without an oncological criterion. This is what has been called a *whoops procedure*, since the STS diagnosis is made «by surprise»<sup>9</sup>.

On the other hand, in spite of appropriate current treatment of primary STS, recurrence rates remain high (10-20%) according to several prospective randomized studies<sup>10,11</sup>. These figures are likely to be considerably higher when patients are treated in non-specialized centers, and it

is also very likely that the people who performed the EIE are not cognizant of the patient's final outcome.

The purpose of this paper is to present the long-term results of the treatment of patients that underwent a *whoops procedure* or an STS relapse and who came to the Navarre University Clinic after being treated elsewhere.

## MATERIALS AND METHODS

Between the years 1984 and 2004, 64 patients diagnosed with STS and previously treated at other institutions came to the Department of Orthopedic and Trauma Surgery of the Navarre University Clinic to be therapeutically assessed. Thirty-nine were male and 25 women, with a mean age of 43 years (10-82).

Two groups of patients were identified: group A was made up of patients consulting following an EIE (or a *whoops procedure*) for an STS and group B was made up of patients who had had previous STS treatment and who at the time of consultation already have a relapsing local disease.

A full clinical record was created for every patient including time of first diagnosis, time elapsed between first diagnosis and consultation in our center, anatomical location of the tumor, pathological diagnosis, previous treatment and presence of long-distance metastasis. The clinical record also included treatment used at our institution and post-treatment evolution: disease-free period, persistence of residual disease, local recurrence, presence of long-distance metastasis, as well as toxicity of treatment and, if applicable, data on the patient's death.

In group A, in addition to what is mentioned above, we analyzed the presence of residual tumoral disease in the resected sample. In group B, we recorded the time elapsed between the first treatment and the local recurrence diagnosis.

Treatment comprised a combination of limb-preserving surgery, radiation therapy (external, intraoperative, brachytherapy) and chemotherapy (systemic, endovenous, associated or not to hyperthermia with tumor necrosis factor [TNF] and melphalan).

Survivorship was calculated by means of the Kaplan-Meier method.

## RESULTS

Location and pathological diagnosis are summarized in tables 1 and 2.

### Group A (27 patients)

All 27 patients in group A came to our institution a mean of 38 days (9-90) after the first surgery, with the sus-

**Table 1.** Anatomical location of tumors in our series

Location	Number of patients
Upper limb	22
Clavicle	1
Scapula	3
Shoulder	3
Armpit	2
Arm	6
Elbow	3
Forearm	3
Hand	1
Lower limb	42
Groin	1
Gluteus	7
Thigh	24
Knee	6
Leg	1
Ankle	1
Foot	2

**Table 2.** Pathological diagnosis of the tumors in this study

Pathological diagnosis	Number of patients
Malignant fibrous histiocytoma	18
Liposarcoma	17
Synovial sarcoma	11
Leiomyosarcoma	5
Other	13

picion of an EIE of an unidentified tumor (fig. 1). All patients were treated by means of a re-excision widening the surgical margins. A pathological analysis was made of the sample taken during surgery, tumoral cells being detected in 12 patients (44% of cases). In 23 cases radiation treatment

was applied: 18 patients were subjected to external radiation therapy, 15 to intraoperative radiation therapy and 6 were implanted a brachytherapy catheter during surgery and were later given radiation therapy. On 9 occasions, systemic chemotherapy was prescribed. Minimum follow-up of these patients was 24 months and maximum 216 (mean: 67 months). During follow-up 3 patients had a local recurrence of the disease, one of whom required an amputation. Three patients developed a metastasis and all three of them died. Disease-free survivorship was 85%.

### Group B (37 patients)

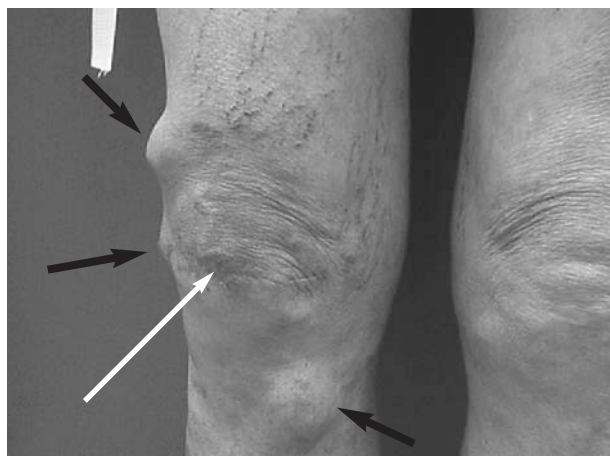
These patients came to our center after a mean 26 months from their first treatment, after being diagnosed with a recurrence (figs. 2 and 3). Time elapsed between first treatment and relapse was a minimum of 2 months and a maximum of 216 (median value: 12 months). Five patients presented with metastasis at the time of primary diagnosis (three pulmonary and two with ganglion involvement). The first relapse after the first treatment occurred after a mean 26 months (median: 12 months). Before coming to our center, all patients had been subjected to surgery and given chemotherapy in 11 cases and radiation therapy in 19. In our hospital 35 patients were given surgical treatment followed by chemotherapy in 21 cases, 4 of which were treated by means of hyperthermia and TNF and melphalan-based isolated limb perfusion. Minimum follow-up from diagnosis was 12 months and maximum 264 (median: 80 months). During evolution and after the salvage protocol introduced in our center, 16 patients showed a progression of their disease with metastatic involvement (pulmonary in 11 cases, musculoskeletal in 6, ganglion-related in one case, cerebral in one and ovarian in one). Twenty patients suffered a new recurrence, 5 of whom were treated with radical



**Figure 1.** Patient operated in another center for a subcutaneous groin tumor 3 cm in diameter (B). Pathological diagnosis was a malignant fibrous histiocytoma with positive surgical margins. A transverse scar with a skin island that had a further perpendicular scar together with the drain out-flow hoses (A) greatly complicated the «rescue» procedure.



**Figure 2.** Patient diagnosed with multiple local recurrences of a superficial soft tissue sarcoma operated in a different institution one year before with incomplete resection of the primary tumor.



**Figure 3.** Transverse pre-patellar incision (white arrow) in a patient operated on the basis of a suspicion of bursitis. A soft tissue sarcoma was diagnosed and several months later multiple local recurrences appeared (black arrows).

surgery. Nineteen patients developed some major complication, especially the ones who were reirradiated: 8 infections, 6 problems with closure of suture or dehiscence thereof, 2 post-radiation therapy fractures and one cerebrospinal fluid fistula, deep venous thrombosis and post-radiation therapy paresis. Sixteen patients died (mean survivorship: 18 months (10-48)). Disease free survivorship was 16%.

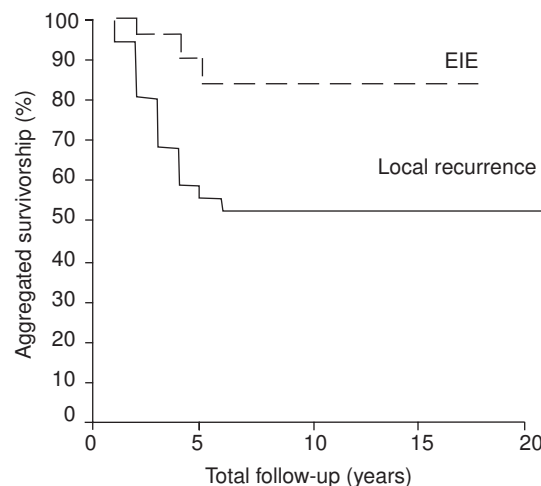
Figure 4 shows the aggregated survivorship of the 2 series (calculated with the Kaplan Meier method).

## DISCUSSION

STS are a rare entity; they account for only 1% of all tumors<sup>3</sup>. Consequently there are few centers that have experience of STSs. Given their infrequency and shrouded and unspecific symptoms, STSs often go undiagnosed and are therefore ineffectively treated.

In some countries, it is advisable to refer patients to specialized centers when a high suspicion of STS exists<sup>7</sup>, since it has been shown that survivorship and functionality results tend to improve significantly<sup>5</sup>. The most sensitive parameter as regards a tumor's tendency to malignancy/benignity is its growth pattern, followed by age over 53 and tumor size<sup>12</sup>.

Conventional treatment for limb sarcomas includes the association of surgery to radiation therapy. This multidisciplinary approach has replaced amputation as the treatment of choice and has also led to lower rates of local recurrence<sup>8</sup>. Moreover, when a relapse had already occurred, amputation does not contribute significantly to survivorship when compared to limb-preservation treatment. However, for some authors amputation may reduce the risk of developing a further local recurrence<sup>13,14</sup>, even if it does not increase survivorship.



**Figure 4.** Aggregated survivorship data for patients treated in our center for a soft tissue sarcoma after being treated in another institution. EIE: erroneous initial excision.

Most recurrences occur in the first two years, but late recurrences (after 5 years) should not be ruled out<sup>15</sup>. Factors related to local recurrence are: tumor size, histological grade, quality of surgical margin, tumor depth and previous recurrence<sup>16</sup>.

The factor that most significantly determines the outcome of patients afflicted with an STS is the quality of the resection of their primary tumor<sup>17</sup>. Therefore surgical planning is crucial to increase survivorship and to achieve optimal local control<sup>18</sup>. The primary surgery is the one offering the greatest chances of healing. For that reason it is of essence that patients be referred to some center with experience of this type of pathology. In this respect, there are 3 potential groups of patients: the first is made up of patients that are referred to an experienced institution when their disease sets in; the second is made up of those patients re-



ferred when a diagnosis is made by chance (EIE) and the third is the group of patients referred once the tumor has metastasized and/or recurred following more or less appropriate treatment. The possibilities of healing for this last group are much lower than those for the first two (15% vs. 85%).

Resection of an STS with an inadequate margin is considered the most negative prognostic factor for local recurrence. For Trovik local recurrence may be twice as high for patients subjected to an ill-performed resection<sup>19</sup>, whereas for Noria this figure could be three times as high<sup>20</sup>. Surgical excision remains the main therapeutic approach to STS. Most factors influencing the patients' evolution (histological grade, size, depth, etc) cannot be altered at the time of diagnosis. Only the quality of the resection carried out in the first surgery can be influenced by the surgeon<sup>21</sup>.

EIEs should be given special consideration. Re-resection is the treatment of choice in cases of EIE<sup>21</sup>. Unlike Siebenrock<sup>22</sup>, we obtained Wide margins preserving all of our patients' limbs. That is to say, an immediate wide resection after an EIE achieves as good a result as a wide resection of the primary tumor<sup>23</sup>. The fact that these *whoops procedures* occur more often in small superficial lesions may well be a factor contributing to this result. In our series, we found that in 44% of patients subjected to an EIE tumor cells could be seen in the re-excised specimen, a rate comparable to that of other studies (35- 77%)<sup>20-22,24,25</sup>. In any event, the fact that no residual disease was detected does not mean that no tumor cells were left over in the surgical bed. This explains that, as regards local control, re-excision has better long-term results than not performing any surgery, regardless of whether tumor cells are actually present in the scar.

When a previously operated patient arrives in a referral center, radiation therapy or chemotherapy can be administered in order to gain better local and systemic control of the disease<sup>11</sup>. In our EIE group, 85% of patients were given adjuvant treatment, in contrast to the series by Siebenrock, where only 33% of patients received such treatment<sup>22</sup>, and we achieved 86% disease-free survivorship during follow-up. Only 11% of *whoops procedures* that came to our center presented with a local recurrence, a rate lower than the 18% reported by Goodlab et al<sup>24</sup>. On the other hand, in recurrences reirradiation led to an increased complications rate, did not improve disease-free survivorship and achieved local control only in half the patients re-irradiated (one could infer that, if the tumor had relapsed in the previous institution prior to radiation therapy, that happened because it was radio-resistant). In patients that came already with a relapse we used all our therapeutic arsenal, including techniques such as TNF and melphalan-based isolated limb perfusion<sup>26</sup> and reirradiation with high-dose brachytherapy<sup>27,28</sup>. However, healing results in this subgroup of patients with local recurrence have been poor. It should be mentioned, however,

that even if in most cases we managed to preserve the limb and avoid amputations the long-term survivorship rate was rather low.

Unlike bone sarcomas, the evolution of STSs tends to be slow. But this does not mean that it cannot become a deadly disease if not treated. However, before undertaking the excision of «a lump», we should consider the possible consequences of our actions for the evolution of these patients since performing an EIE, with no oncological criterion, could lead to the local recurrence of an STS. On some occasions, when initial treatment is inappropriate, these patients present with consecutive local recurrences and metastasis that cause them to die. It is impossible to act upon most of the prognostic factors of STS at its initial presentation; the surgeon can only make a difference in the quality of the first surgical resection<sup>21</sup>. To obtain as good a prognosis as possible, every patient clinically suspected of having an STS should be referred to an experienced center.

Salvage surgical treatment combined with radiation therapy and/or chemotherapy for local STS recurrence leads to low survivorship rates. Nonetheless, when EIE cases are immediately referred to experienced institutions, salvage treatment produces healing rates that are similar to those of tumors treated for the first time in an experienced center.

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#### Conflict of interests

The authors have declared to have no conflict of interests.