Feasibility and Long-Term Outcomes of Surgery for Primary Thoracic Synovial Sarcoma

Sara Pieropan¹, Olaf Mercier¹, Delphine Mitilian¹, Pauline Pradère¹, Dominique Fabre¹, Daniela Iolanda Ion², Olivier Mir³, Barbara Galbardi⁴, Vincent Thomas De Montpreville⁵, Elie Fadel¹

1. Department of Thoracic and Vascular Surgery and Heart-Lung Transplantation, Marie Lannelongue Hospital-GHPSJ, Paris-Saclay University, 133 avenue de la Resistance, 92350 Le Plessis-Robinson, France
2. Department of Anesthesiology, Marie Lannelongue Hospital-GHPSJ, Paris-Saclay University, 133 avenue de la Resistance, 92350 Le Plessis-Robinson, France
3. Department of Medical Oncology, Gustave Roussy Institute, 114 Rue Edouard Vaillant, 94805 Villejuif, France
4. Department of Medical Oncology, IRCCS San Raffaele Hospital, Via Olgettina, 60, 20132 Milan, Italy
5. Department of Pathology, Marie Lannelongue Hospital-GHPSJ, Paris-Saclay University, 133 avenue de la Resistance, 92350 Le Plessis-Robinson, France

Classification: original article

Word count: 4999

Corresponding author: Sara PIEROPAN

Department of Thoracic Surgery, CHU Amiens-Picardie, 1 Rond-Point du Professeur Christian Cabrol, 80054, Amiens, France; Phone: +33 03 22 08 73 54; E-mail: Pieropan.Sara@chu-amiens.fr
GRAPHICAL ABSTRACT

Key question: Is surgery for primary thoracic synovial sarcoma feasible and does it provide good survival?

Key findings: Surgery might achieve a good survival, provided R0 resection is obtained, with low postoperative morbidity and mortality

Take-home message: In selected patients and for resectable disease, surgery should always be proposed as part of a multimodal strategy

CENTRAL IMAGE

Legend: overall survival after diagnosis in patients undergoing surgery for primary thoracic synovial sarcoma: tumor-free resection margins (R0) versus contaminated resection margins (R+).
ABSTRACT

Objectives: Primary thoracic synovial sarcoma is a rare, high-grade, malignancy. Involvement of vital organs is frequent and may decrease the benefits of surgical resection. We reviewed our practice at a highly experienced thoracic-surgery center to assess early and long-term outcomes after surgery.

Methods: We conducted a retrospective, observational, single-center study of patients undergoing curative-intent surgery for primary thoracic synovial sarcoma between January 1, 2000, and January 31, 2021, as part of multidisciplinary management. We assessed demographics, medical history, histopathology, and follow-up information.

Results: We enrolled 20 patients (13 males) with a median age of 40 years and a median tumor size of 11 cm. Neoadjuvant chemotherapy was administered to 13 patients. Surgery consisted in extrapleural pneumonectomy (n=7), extrapleural lobectomy (n=5), chest-wall resection (n=4), or tumor resection (n=4). R0 resection was achieved in 16 (80%) patients. Adjuvant therapy was given to 13 patients. Postoperative complications developed in six patients. Median hospital stay was 11.5 days. Overall survival at 2 and 5 years was 51% and 22%, respectively; median overall survival was 25 months and median disease-free survival was 8.5 months. Relapses occurred in 15 patients. By univariate analysis, incomplete resection was the only significant predictor of survival (P=0.01).

Conclusions: Primary thoracic synovial sarcoma is an aggressive disease. Surgery included in a multimodal treatment may contribute to achieving a good outcome, providing that an R0 resection is obtained. Given the considerable technical challenges of surgery, patient selection and referral to an experienced center are crucial to minimize morbidity and mortality.

KEYWORDS Primary Thoracic Synovial Sarcoma, Surgical treatment, Feasibility
ABBREVIATIONS AND ACRONYMS

CT: Computed Tomography
DFS: Disease-Free Survival
EPP: Extrapleural Pneumonectomy
ICU: Intensive Care Unit
MDT: Multidisciplinary Team
OS: Overall Survival
PTSS: Primary Thoracic Synovial Sarcoma
SS: Synovial Sarcoma
INTRODUCTION

Synovial sarcoma (SS) accounts for only 5% to 10% of all soft tissue sarcomas[1] and usually develops in the extremities. SS is a high-grade malignancy classified as a mesenchymal spindle-cell tumor of uncertain differentiation[2] and is characterized in over 90% of the cases by a t(X;18) (p11;q11) translocation, which is pathognomonic.[3, 4] Primary thoracic SS (PTSS) is extremely rare, contributing to 4%–14% of all SSs, and mostly affects adults in the third and fourth decade.[5]

The treatment of SS is frequently multimodal.—Neoadjuvant chemotherapy is recommended for non-resectable disease, while adjuvant chemotherapy may be administered to high-risk patients.[6, 7] Surgical resection should be considered in all patients with localized SS.[8] However, because of the potential involvement of vital organs and need for extensive resection, surgery can be very demanding and may be followed by major complications.[9] If resection is incomplete, adjuvant radiotherapy should be given to improve local control.[8]

Five-year overall survival (OS) of patients with SS arising from any site ranges from 52% to 66%.[10] However, location within the thorax is associated with a far poorer prognosis, with only 30% of patients being alive 5 years after surgery.[3, 11]

As PTSS is rare, experience on treatment, notably surgery, is limited. Only case reports and small cohort studies are available[9, 12], and data on early and long-term outcomes are particularly scarce.

The primary aim of our study was to evaluate OS in patients undergoing curative-intent surgery for PTSS. The secondary aims were to assess the feasibility of surgery based on hospital-stay duration, postoperative complications, and 30-day mortality and to determine disease-free survival (DFS).
PATIENTS AND METHODS

We conducted a retrospective, single-center study of consecutive patients who underwent curative-intent surgery for PTSS between January 1, 2000, and January 31, 2021, at our Thoracic Surgery department. Patients were identified by searching the histopathology laboratory database. We excluded patients with thoracic metastasis of a primary SS of another site, patients who underwent only diagnostic procedures, or first surgical treatment at another institution.

We collected demographics, preoperative data (risk factors, comorbidities, clinical and radiological presentation, preoperative histological diagnosis, neoadjuvant therapy, and functional preoperative evaluation), details on the surgical procedure, postoperative data (intensive-care-unit [ICU] admission, mechanical ventilation duration, postoperative complications classified according to Clavien-Dindo,[13] and hospital stay length), and follow-up data (relapses and subsequent treatments, vital status at last follow-up, and cause of death).

As our center is exclusively surgical, follow-up was not performed in our hospital. For the purpose of the study, we collected information on follow-up by a combination of contact with patients or primary physicians and oncologists, and data linkage to a national death register. We did not have any missing data.

R software version 4.1.0 was used for the statistical analysis (http://www.cran.r-project.org/doc/FAQ/R-FAQ.html#Citing-R). Data were described as the median [interquartile range] or absolute frequency (percentage). Kaplan-Meier plots were used to describe OS and DFS. Cox regression was chosen for the univariate analysis to identify factors associated with outcomes. Comparing the results with the log-rank test, we did not find any difference between the two methods. As the sample size is small, we did not perform a competing risk analysis nor a multivariable analysis as they would not have a statistical power. P values smaller than 0.05 were considered statistically significant.
The study protocol was approved by the ethics committee of the French society for cardiovascular and thoracic surgery (Société Française de Chirurgie Thoracique et Cardio-Vasculaire, CERC-SFCTCV-2021-02-22). In keeping with French law about retrospective studies of anonymized patient data, informed consent was not required.

RESULTS

Through the histopathology database we identified 65 patients. Twenty patients met our selection criteria (figure 1), In 17 cases the diagnosis was confirmed by identification of the t(X;18) translocation. In the remaining three patients, tissue alterations by the fixative precluded Fluorescence In Situ Hybridization (FISH), but the diagnosis was confirmed by retrospective review of the slides by expert histopathologists.

13 patients were males and seven females, and median age was 40 [28–54] years old, 16 had no history of major comorbidities at the diagnosis. One patient had atrial fibrillation, one chronic obstructive pulmonary disease, one diabetes, and one a history of breast cancer treated by radiotherapy on the same side of the PTSS. Nine (45%) patients had a history of smoking.

The tumor was symptomatic in 18 patients, causing chest pain (n=11), dyspnea (n=5), hemoptysis (n=3), cough (n=3), dysphagia (n=2), thoracic bulge (n=1), and/or arm swelling (n=1). In two cases, the diagnosis was incidental.

The initial tumor was pleuropulmonary in 11 patients (55%), some of which had a chest wall infiltration. Other locations were the mediastinum (n=4), chest wall (n=4), and trachea (n=1). The median tumor diameter was 11 [8–15] cm.

Preoperative diagnosis was obtained in 18 patients, by computed tomography (CT)-guided percutaneous biopsy (n=10) or surgical biopsy (n=8). The histopathological diagnosis was SS in 12 patients, sarcoma other than SS in four patients, and undetermined malignancy in two patients.

Neoadjuvant treatment, consisting in four to six cycles of chemotherapy was given to 13 patients. Surgery consisted in extrapleural pneumonectomy (EPP) (n=7), extrapleural
lobectomy (n=5), chest-wall resection (n=4), and tumor-mass resection (n=4). Surgery was performed by excising the tumor en bloc with all the structures and/or tissues macroscopically infiltrated. In case of chest wall resection, a macroscopical margin of at least 3 cm was considered safe for complete resection. If a preoperative biopsy was performed, the biopsy tract and the scar were safely removed.

All patients underwent surgery by an open approach. EPP, extrapleural lobectomies and posterior mediastinum resections were performed by a posterolateral thoracotomy. EPP were systematically associated with a diaphragm resection and reconstruction with a Goretex mesh as well as a pericardium resection and reconstruction with a Vycril mesh (figure 2). In extrapleural lobectomy, as the tumor was adherent to the chest wall, the parietal pleura was excised en bloc.

An anterior transclavicular approach was preferred for tumors involving the apex, as it allowed optimal control of the vascular and nervous structures of the thoracic inlet. Because of the number of resected ribs (maximum 4 ribs) and the location of the chest wall defect, chest wall resections did not need reconstruction. The only case requiring osteosynthesis was a sternal resection. Reconstruction was made with 3 Titanium bars and a Goretex mesh.

Histopathological examination showed a complete resection (R0) in 16 patients, R1 was found in 3 patients:

- in a right EPP with chest wall resection, R1 was detected on a chest wall nodule and on the superior pulmonary vein
- in a right EPP, the resection appeared to be R1 on the pulmonary artery
- in the resection of a posterior mediastinal tumor, R1 was found on the aortic and the oesophageal adventitia.

A macroscopic incomplete resection (R2) was found in a patient who underwent a resection of a posterior mediastinal mass. R2 was confirmed on the specimen in multiple intra-pericardiac zones.
Seven patients required ICU admission with a median ICU stay of four days. Only one patient required postoperative mechanical ventilation. Median hospital stay was 11.5 [8–14] days.

Postoperative complications occurred in six patients, some of whom experienced more than one complication. They are summarized in table 1. No patient died within 30 days after surgery.

Adjuvant treatment was given to 13 patients: 11 received radiotherapy and two received chemotherapy. Globally, 11 patients received both neoadjuvant chemotherapy and adjuvant radiotherapy, two only neoadjuvant chemotherapy, two only adjuvant chemotherapy, and five only surgical treatment.

A local recurrence was diagnosed in 15 patients, of whom only one also had a distant metastasis (liver). Recurrences were treated by chemotherapy in 7 patients, and pazopanib in two patients. Three patients received palliative care. Surgery was performed in 2 patients. Unfortunately, in both cases, the resection was incomplete (R1). One patient received second-line chemotherapy and died 1 year after the second surgery, the other received chemotherapy and radiotherapy and died 2.5 years after.

2-years and 5-years OS was 51% and 22%, respectively (Figure 3). Median OS was 25 months. 2-years DFS was 24% (Figure 4), with a median of 8.5 months. All patients presenting a recurrence died from the disease. In the 16 patients with R0 resection margins, 5-years OS and DFS were both 29%. 5 patients were still alive at the time of last follow-up with no evidence of disease. Three of them had long follow-ups of 10, 11, and 18 years, with a median follow up of 127 months.

By univariate analysis, incomplete resection was the only variable significantly associated with lower OS ($P=0.01$) (Figure 5). Age, tumor size, additional treatment (either neoadjuvant or adjuvant or both), and type of surgery did not appear to influence survival (Table 4.2).
DISCUSSION

PTSS is a very rare malignancy, and surgically resectable patients represent an even smaller subgroup of PTSS patients. In the current study, we found that in highly selected patients, surgery included in a multimodal strategy might contribute to achieve a good survival. The main determinant to obtain this result was complete resection without perioperative mortality, underlining the importance of performing these procedures in expert thoracic surgical centers.

The median age of 40 years in our population is consistent with earlier reports, while the predominance of males in our study contrasts with the usually more even sex distribution in previous works.[14, 15] Also in keeping with published data, the symptoms were not specific and consisted chiefly of chest pain, dyspnea, cough or hemoptysis.[16, 17] PTSS is typically diagnosed as a large mass, with a median diameter of 11 cm in our cohort and up to 13 cm in earlier studies.[18]

As indicated in the ESMO-EURACAN guidelines, clinical staging should be completed by a CT scan of the abdomen and pelvis. Imaging of the brain is not standard for SS and should be performed based on the clinical presentation. 18F-FDG (fluorodeoxyglucose) PET (Positron Emission Tomography) scan may be reserved for characterizing equivocal CT findings such as lymph node involvement.[8] In our series, the clinical staging was achieved by performing either an 18F-FDG-PET scan or a total body CT scan. Further exams, such as a flexible bronchoscopy, a thoracic magnetic resonance imaging, or a gastroscopy were performed in specific cases.

Preoperative histopathological diagnosis should be sought routinely to guide treatment decisions.[19] In our cohort, the presence of a malignancy was established in 90% of patients, but the diagnosis of SS was made in only 67%, illustrating the challenges raised by the differential diagnosis. Difficult cases must therefore be referred to specialized centers to ensure correct diagnosis. In our study, 3 cases needed confirmation of the diagnosis by our expert pathologists, who belong to the French soft tissue and visceral sarcoma pathology review network (RRePS).
The variability in treatment strategies in our cohort reflects the absence of consensus regarding the optimal management of PTSS. Induction chemotherapy was proposed when the tumor was not eligible for R0 resection, with the aim of obtaining a tumor shrinkage. However, the topic of neoadjuvant chemotherapy in soft tissue sarcoma remains controversial. Several ongoing trials are trying to address this question (NCT04307277 and NCT03805022).

Adjuvant chemotherapy was considered in patients aged < 40 years old and able to tolerate doxorubicin and/or ifosfamide and those with R1 resection[20].

In our series, 5 patients had a resectable disease at diagnosis and did not have the criteria for adjuvant therapy, therefore the received an exclusive surgical treatment. It is important to underline that every decision of the treatment process was taken through a multidisciplinary team (MDT) dedicated to sarcoma, and discussed with the patients.

The importance of (MDT) management has been widely established, notably for rare malignancies.[21] Recently, He et al. published a study on the impact of MDT management for PTSS. Although MDT discussion was not independently associated with outcomes, the median OS of patients managed by an MDT was longer than that of patients who were not (46.0 vs. 18.0 months).[11] At our institution, the MDT included experts from national referral centers for sarcoma and thoracic surgery.

Surgery should be considered as part of the multimodal treatment of PTSS. However, due to the aggressiveness of PTSS and possible infiltration of vital organs, surgery is often very demanding. Morbidity and mortality in nowadays oncological thoracic surgery have been widely investigated. The 30-day mortality rates and the postoperative complication rates for pneumonectomy range from 4% to 7% and 20% to 40%, respectively.[22] Turbendian et al. described a morbidity of 37% and a mortality of 6% in patients undergoing surgery for mediastinal sarcomas.[23] The only previous study detailing postoperative complications for PTSS had 15 patients, of whom one (6.6%) died postoperatively, three had major complications requiring reoperation, and five had minor complications.[9] The lower
complication rates in our cohort may be explained by the high selection of patients and the expertise of the surgical team.

Referral of patients to tertiary-care centers with high thoracic-surgery volumes and considerable experience in performing complex procedures is crucial to minimize morbidity and mortality. An extensive body of literature has emphasized the impact of institutional and surgeon experience on outcomes. However, studies about lung resection surgery have shown conflicting results. An analysis of a large database found that lung-cancer-resection volume did not predict mortality.[24] Nevertheless, when analyzing more complex procedures such as pneumonectomies, surgery performed in high volume centers seems to be associated to reduced odds of mortality and lower rates of failure-to-rescue after postoperative complications.[25]

The poor prognosis of PTSS is well documented. A literature review of 15 clinical trials on chemotherapy as first-line treatment for locally advanced and metastatic synovial sarcoma showed an OS of 15 months and a progression-free survival of 6.3 months[26]. In our cohort, median OS was 25 months, and OS at two and five years was 51% and 22%, respectively. Comparisons with earlier studies are difficult due to the variability in data-reporting methods, incomplete follow-up information, and probable differences in patient selection for surgery[27, 28]. Table 3, summarizing previously reported long-term outcomes, shows similar OS to ours in some studies[9, 29] and better OS in others.[3, 18] The high frequency of recurrence shortly after surgery in our cohort is consistent with earlier data[30].

Nonetheless, long survivals have been achieved.—In our series, three patients were alive 10, 11, and 18 years after initial surgery. Similarly, in his series of 25 patients Zeren et al. reported 3 long survivors, with an OS between 12 and 16 years.[17]

However, no factors associated with long-term survival have been identified.[4, 5, 18] Age, sex, tumor size, preoperative and postoperative treatments, histological subtype, SSX-SS18 fusion type, Ki-67 expression, and mitotic rate were prognostic factors for survival in some studies but not in others. In our study, the only factor significantly associated with OS by univariate analysis was incomplete resection, which was also consistently significant in
other studies.[9, 14] More specifically, when analyzing the R0 patients' subgroup, we found the same 5-year OS and DFS of 29%, which supports the conclusion that we should strive for an R0 resection, even if it can be very demanding, as it is the only factor that seems to make a difference in the outcome of these patients.

A major limitation of our study is the retrospective design and the absence of a control group. Moreover, the high patients selection and the single center recruitment may have induced selection bias. As our institution is a purely surgical center and doesn't have an oncological department, we did not have a group of patients undergoing medical treatment or palliative care to compare to our series.

Another major limitation is represented by the small sample size, which mainly depends on the rarity of this disease, thus precluding a multivariable analysis and limiting difference detection and results' interpretation. Randomized trials comparing surgery to other treatments would be unethical, and multicenter observational studies in larger populations are therefore needed to provide more reliable results for diagnosis and treatment of PTSS. Molecular targeted therapies and immunological strategies are under investigation, and trials evaluating genomic features as potential predictive markers are ongoing and may improve outcomes in the near future.

In conclusion, in patients with resectable PTSS, surgery as part of a multimodal strategy may contribute to achieving a good survival, provided R0 resection is obtained. Given the considerable technical challenges raised by complete PTSS resection, it is of utmost importance that patients are carefully selected and treated in experienced tertiary referral centers to minimize morbidity and mortality.
FIGURE LEGENDS

Figure 1. Patients’ selection flow chart

Figure 2. Example of a patient with a pulmonary and pleural tumor
(a and b) 26-year-old female with a 10·12·12-cm right intrathoracic mass, pleural lesions, and a pleural effusion.
(c) She had a partial response to five chemotherapy cycles then underwent a right EPP. The postoperative course was uneventful.
(d) Operative specimen: histology showed an R0 resection of a biphasic synovial sarcoma that measured 10.5·7.5·3 cm and partially infiltrated the diaphragm; the tumor contained a necrotic hemorrhagic component, cystic areas, and microcalcifications.

Figure 3. Kaplan-Meier estimate of overall survival (OS) after the diagnosis of primary thoracic synovial sarcoma

Figure 4. Kaplan-Meier estimate of disease-free survival (DFS) after the diagnosis of primary thoracic synovial sarcoma

Figure 5. Kaplan-Meier estimate of overall survival (OS) after the diagnosis in the groups with tumor-free resection margins (R0) versus contaminated resection margins (R+)
Table 1. Postoperative complications, according to the Clavien-Dindo classification

<table>
<thead>
<tr>
<th>Grade of complication</th>
<th>Number of events and type of complication</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>II</td>
<td>- Pleural or pericardial bleeding in 2 patients - Acute pulmonary edema and gastric ulcer in 1 patient</td>
<td>- Blood cell transfusion - Medical treatment</td>
</tr>
<tr>
<td>IIIa</td>
<td>- Delayed pneumothorax in 1 patient, prolonged air leak in 1 patient - Bronchial obstruction by secretions in 1 patient - Hemothorax in 1 patient</td>
<td>- Chest drainage - Bronchoscopy - Surgery</td>
</tr>
<tr>
<td>IIIb</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>V</td>
<td>0</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 2. Univariate analysis to identify factors associated with overall survival (OS)

<table>
<thead>
<tr>
<th>Factors</th>
<th>N (%)</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>not applicable</td>
<td>1.02</td>
<td>0.99–1.06</td>
<td>0.07</td>
</tr>
<tr>
<td>Tumor size</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;11 cm</td>
<td>10 (50%)</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;11 cm</td>
<td>10 (50%)</td>
<td>0.44</td>
<td>0.28–2.68</td>
<td>0.16</td>
</tr>
<tr>
<td>Neoadjuvant treatment:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>7 (35%)</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>13 (65%)</td>
<td>0.86</td>
<td>0.39–0.56</td>
<td>0.80</td>
</tr>
<tr>
<td>Adjuvant treatment:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>7 (35%)</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>13 (65%)</td>
<td>1.17</td>
<td>0.39–3.56</td>
<td>0.77</td>
</tr>
<tr>
<td>Type of surgery:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other than EPP</td>
<td>13 (65%)</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EPP</td>
<td>7 (35%)</td>
<td>1.53</td>
<td>0.47–4.92</td>
<td>0.48</td>
</tr>
<tr>
<td>Resection margins:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R0</td>
<td>16 (80%)</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R1 and R2</td>
<td>4 (20%)</td>
<td>0.14</td>
<td>0.03–0.62</td>
<td>0.01</td>
</tr>
</tbody>
</table>

95% CI: 95% confidence interval; Ref: reference value; EPP: extrapleural pneumonectomy
Table 3. Cohort studies on the treatment and long-term outcomes of primary thoracic synovial sarcoma (PTSS)

<table>
<thead>
<tr>
<th>Author, year of publication</th>
<th>Sample size</th>
<th>Treatment</th>
<th>R0</th>
<th>FU available information (% of patients)</th>
<th>OS</th>
<th>DFS and information on recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zeren et al., 1995</td>
<td>25</td>
<td>100% surgery</td>
<td>NR</td>
<td>72%</td>
<td>40% died of disease within 1–7 years, 16% died of unrelated causes</td>
<td>16% alive with disease, 16% alive without disease after 2–20 years</td>
</tr>
<tr>
<td>Gartner et al., 1996</td>
<td>5</td>
<td>100% surgery</td>
<td>NR</td>
<td>100%</td>
<td>80% died within 3 years</td>
<td>NR</td>
</tr>
<tr>
<td>Aubry M.C. et al., 2001</td>
<td>5</td>
<td>100% surgery</td>
<td>100%</td>
<td>80%</td>
<td>100% (median FU 9 months)</td>
<td>100%</td>
</tr>
<tr>
<td>Essary et al., 2001</td>
<td>12</td>
<td>8% NR, 92% surgery</td>
<td>NR</td>
<td>100%</td>
<td>2.5-year OS 58%</td>
<td>2-year DFS 25%</td>
</tr>
<tr>
<td>Duran-Mendicuti et al., 2003</td>
<td>5</td>
<td>100% surgery</td>
<td>100%</td>
<td>100%</td>
<td>median OS 22 months</td>
<td>80% recurrence at 2–14 months</td>
</tr>
<tr>
<td>Okamoto et al., 2004</td>
<td>11</td>
<td>10% NR, 90% surgery</td>
<td>NR</td>
<td>91%</td>
<td>50% died of disease within 1–9 years</td>
<td>60% recurrence</td>
</tr>
<tr>
<td>Begueret et al., 2005</td>
<td>40</td>
<td>10% NR, 82% surgery, 8% CT ± RT</td>
<td>NR</td>
<td>83%</td>
<td>2-year DSS 65.3%, 5-year DSS 31.6%</td>
<td>Median DFS 43 months</td>
</tr>
<tr>
<td>Suster et al., 2005</td>
<td>15</td>
<td>80% surgery, 20% RT</td>
<td>83%</td>
<td>40%</td>
<td>NR</td>
<td>80% had recurrence 1–3 years after diagnosis</td>
</tr>
<tr>
<td>Hartel et al., 2007</td>
<td>60</td>
<td>8% NR, 68% surgery, 23% other treatment</td>
<td>NR</td>
<td>90% (63% information on recurrence)</td>
<td>48% died at a mean of 23 months, 46% died within 5 years</td>
<td>18% had local recurrence mean DFS 17 months</td>
</tr>
<tr>
<td>Galetta et al., 2013</td>
<td>15</td>
<td>100% surgery</td>
<td>60%</td>
<td>100%</td>
<td>Median OS 27 months, 10-year OS 33.5%</td>
<td>75% recurrence 5-year DFS 30%, median 15 months</td>
</tr>
<tr>
<td>Kim et al., 2015</td>
<td>14</td>
<td>7% NR, 64% surgery, 28% CT ± RT</td>
<td>NR</td>
<td>93%</td>
<td>21.4% died</td>
<td>57% recurrence 2-year DFS 35.7%</td>
</tr>
<tr>
<td>Lan et al., 2016</td>
<td>26</td>
<td>77% surgery, 12% CT, 13% supportive</td>
<td>NR</td>
<td>73%</td>
<td>Median DSS 14.5 months, 2-year DSS 27.7%</td>
<td>Median DFS in surgical patients 8.5 months</td>
</tr>
<tr>
<td>Study</td>
<td>No.</td>
<td>Treatment</td>
<td>Follow-up</td>
<td>OS 2-years</td>
<td>OS 5-years</td>
<td>DFS Median</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----</td>
<td>-----------</td>
<td>-----------</td>
<td>------------</td>
<td>------------</td>
<td>-------------</td>
</tr>
<tr>
<td>Terra et al., 2018</td>
<td>21</td>
<td>52% NR, 43% surgery, 5% CT+RT</td>
<td>NR</td>
<td>74%</td>
<td>69% died of disease within 5–32 months, 24% alive with disease at 6–45 months</td>
<td>88% recurrence</td>
</tr>
<tr>
<td>He et al., 2021</td>
<td>13</td>
<td>77% surgery, 23% CT + RT</td>
<td>NR</td>
<td>100%</td>
<td>2-year OS 58.3%, 5-year OS 30%</td>
<td>Median DFS 13 months</td>
</tr>
<tr>
<td>Present study</td>
<td>20</td>
<td>100% surgery</td>
<td>80%</td>
<td>100%</td>
<td>Median OS 25 months, 2-year OS 51%, 5-year OS 22%</td>
<td>Median DFS 8.5 months, 2-year OS 24%</td>
</tr>
</tbody>
</table>

R0: complete resection; FU: follow up; NR: not reported; DSS: disease-specific survival; RT: radiotherapy; CT: chemotherapy
**Funding statement:** The authors received no financial support for the research, authorship, and/or publication of this article.

**Conflicts of interest:** None.

**Data availability statement:** The data underlying this article will be shared on reasonable request to the corresponding author.
REFERENCES


States 1996;20:36–45.

Patients with intrathoracic synovial sarcomas (n=65)

Excluded:
- Metastasis from synovial sarcomas arising from other sites (n=28)
- CT-scan or surgical biopsy (n=8)
- Diagnosis not confirmed by FISH analysis (n=5)
- Incomplete data (relapse of a PTSS initially treated in another hospital) (n=4)

Final sample (n=20)