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Arterial Infusion Chemotherapy Embolization for Recurrent or Metastatic Soft Tissue Sarcoma: A Retrospective Study of 113 Patients

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ABSTRACT

This investigation assessed the practicality and tolerability of arterial infusion chemotherapy embolization (AICE) for patients with recurrent or metastatic soft tissue sarcoma (STS), and examined prognostic indicators that could support more personalized treatment planning. This retrospective analysis enrolled 113 individuals with recurrent/metastatic STS who underwent AICE at the Fifth Medical Center of the PLA General Hospital. Key endpoints included progression-free survival (PFS) and overall survival (OS). Survival patterns were illustrated using Kaplan–Meier curves, and potential prognostic factors were evaluated via univariate and multivariate Cox proportional hazards models. Treatment-related adverse events (TRAEs) were categorized following Society of Interventional Radiology (SIR) criteria. In the 113-patient cohort, the median OS reached 19.0 months (95% CI: 12.8–25.3), with a 2-year OS of 45.1%. The median PFS was 11.0 months (95% CI: 8.6–13.4), and the 2-year PFS was 25.7%. The objective response rate (ORR) was 37.2% (95% CI: 28.3%–46.8%), while the disease control rate (DCR) was 76.1% (95% CI: 67.1%–83.6%). Univariate testing identified tumor size, distant metastasis, number of post-operative therapies, pathological grade, and the neutrophil-to-lymphocyte ratio (NLR) as significant predictors of both OS and PFS ($P < 0.05$). Multivariate Cox modeling further verified that tumor size, metastasis status, number of post-surgical regimens, pathological differentiation, and short-term therapeutic response served as independent determinants of OS ($P < 0.05$). The most frequent TRAEs included procedure-related pain (23.0%), temporary myelosuppression (15.0%), and post-treatment fever (6.2%). No serious or fatal toxicities, and no treatment-associated deaths, were documented, reflecting excellent tolerability. AICE appears to be a viable and well-tolerated option for recurrent/metastatic STS, providing meaningful disease control and survival benefit in this patient population. Confirmation through larger prospective, multicenter investigations is warranted, along with studies integrating AICE with immune-based or targeted approaches to refine therapeutic strategies for STS.

Keywords: Soft tissue sarcoma, Arterial infusion chemotherapy embolization, Efficacy, Safety, Prognosis

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Introduction

Soft tissue sarcoma (STS) encompasses a diverse collection of malignancies originating from mesenchymal tissues, consisting of more than 100 subtypes and representing under 1% of adult cancers [1]. The combination of rarity and heterogeneity poses major barriers to accurate diagnosis and optimal management [2]. According to the American Cancer Society, ~13,400 new cases and ~5,140 deaths were anticipated in 2023, representing 0.8% of cancer-related mortality [3]. While uncommon overall, its broad spectrum of histologies—such as liposarcoma, leiomyosarcoma, and undifferentiated pleomorphic sarcoma—contributes to highly variable clinical behavior and often unfavorable outcomes [4].

For localized disease, complete surgical excision remains the cornerstone therapy [5] and can cure many early-stage patients. However, even with adequate surgery and frequent incorporation of radiotherapy, local recurrence rates may reach ~40–50%, and distant spread occurs in ~30%, leading to reduced long-term survival. Once metastasis develops, 5-year survival typically falls below 20% [6, 7].

In advanced or unresectable STS, systemic chemotherapy has remained the traditional frontline strategy for decades. Anthracycline-based regimens—most commonly doxorubicin, with or without ifosfamide—form the standard backbone across adult subtypes [8]. Yet the objective response rate is only 20–30%, and median PFS usually does not exceed six months [9]. Historical data show a median OS of roughly 12–18 months for metastatic disease treated with first-line chemotherapy [10]. Despite incremental progress, no regimen has consistently demonstrated clear OS superiority over doxorubicin in randomized trials. These limitations emphasize the urgent need for innovative therapeutic modalities.

Recent developments in both precision therapeutics and immune-based treatments have expanded the options available for managing STS. Anti-angiogenic agents such as anlotinib and immune checkpoint blockers (ICIs, including pembrolizumab) have been incorporated into certain sarcoma subgroups, producing encouraging activity [11]. In the Phase II SARC028 study, pembrolizumab as monotherapy generated an 18% overall response rate across several histologic categories. Notably, outcomes differed depending on subtype: 4 of 10 individuals with undifferentiated pleomorphic sarcoma responded (40% ORR), whereas none of the 10 patients with leiomyosarcoma demonstrated a response [12]. A few rare variants have shown particularly striking sensitivity. Alveolar soft part sarcoma (ASPS)—a translocation-driven entity—has proven unusually receptive to ICIs. In a Phase II trial evaluating atezolizumab, the reported ORR reached 37%, accompanied by prolonged tumor control in advanced cases [13]. Nevertheless, despite these improvements, the majority of STS patients still gain only limited benefit from available targeted or immune-directed approaches. Common subtypes such as LMS and many liposarcoma categories remain largely ICI-refractory, and even responsive tumors often require combination strategies for deeper and more durable responses. These contrasting patterns support the model of sarcomas existing along an immunologic “hot–cold” spectrum and emphasize how crucial proper patient selection is for immunotherapy. Overall, while progress exists, long-term advantages remain modest and the need for new therapeutic avenues persists.

A technique that may compensate for shortcomings in systemic therapy is Arterial Infusion Chemotherapy and Embolization (AICE), a localized treatment delivered through catheterization. In AICE, concentrated chemotherapy is released directly into the arterial branches supplying the tumor, followed immediately by embolization of those same arteries. This produces substantially higher drug exposure at the tumor site than intravenous dosing while potentially limiting systemic toxicity [14]. The embolization step further generates ischemia, driving tumor cell death through necrosis and apoptosis and amplifying the impact of chemotherapy [15]. Comparable approaches have decades of experience in other cancers—for example, hepatic arterial infusion with embolization is widely utilized for hepatocellular carcinoma or liver metastases and is known to enhance outcomes when integrated with systemic therapy [16]. For STS specifically, related treatments such as isolated limb perfusion and intra-arterial infusion have resulted in strong local responses in advanced extremity disease. Research on AICE itself is still emerging, but early reports are encouraging [17]. A recent systematic review found that combining intra-arterial chemotherapy with embolization may produce high rates of local control in recurrent or metastatic STS, and in some instances can even convert unresectable tumors into candidates for surgery [18]. Compared with other focal treatments—including radiotherapy or radiofrequency ablation—AICE enables very precise drug deposition and substantially alters the local tumor microenvironment, making synergistic combinations with targeted therapies or ICIs plausible [19].

Although systemic therapy has improved incrementally, patients with advanced STS still experience limited benefit: traditional regimens such as doxorubicin or targeted agents like pazopanib typically yield a median PFS of only 4–6 months and relatively low response rates [20]. While various arterial procedures (e.g., transarterial chemoembolization or embolization alone) have demonstrated technical feasibility in small series, contemporary evidence for AICE—especially regarding safety parameters, effectiveness, and appropriate patient selection—remains sparse. To address these gaps, we performed a retrospective exploratory evaluation to describe the practicality, toxicity profile, and clinical outcomes associated with AICE in individuals with recurrent or metastatic STS in routine practice. We additionally assessed tumor- and patient-related characteristics for possible correlations with outcomes to help identify prognostic factors that could guide therapeutic planning and combination strategies. We proposed that AICE would be manageable from a safety standpoint and would offer meaningful disease control in advanced STS, with survival potentially influenced by variables such as tumor load or incorporation of multimodality therapy. Insights from this investigation may clarify where AICE fits into contemporary sarcoma care and support future prospective trials integrating AICE with innovative systemic agents.

Materials and Methods

Study design and eligibility

This was a single-center retrospective study that compiled clinical information from 113 individuals with recurrent or metastatic STS treated with AICE at the Fifth Medical Center of the General Hospital of the Chinese PLA from November 2011 to April 2020. The study objective was to assess outcomes, safety, and prognostic indicators associated with the procedure. Patients were included if they met the following criteria:

(1) age ≥3 years with no sex limitations;
(2) histologic confirmation of STS—or, in previously diagnosed patients, imaging evidence of an unresectable lesion strongly suggestive of STS—consistent with the 2013 WHO classification;
(3) receipt of at least one AICE session;
(4) ECOG ≤3;
(5) estimated survival ≥3 months;
(6) complete follow-up and clinical documentation.

Exclusion criteria were:

(1) significant bleeding risk, platelet count <50×10⁹/L, or uncorrectable coagulopathy;
(2) inability to remain in the procedural position;
(3) poor overall health status—including extensive metastases, serious infection, high fever—plus cachexia, major organ dysfunction, severe anemia, or metabolic disturbance unlikely to improve quickly;
(4) widespread metastases or predicted survival <3 months.

As shown in **Figure 1**, 113 adult patients ultimately fulfilled all criteria and were included.

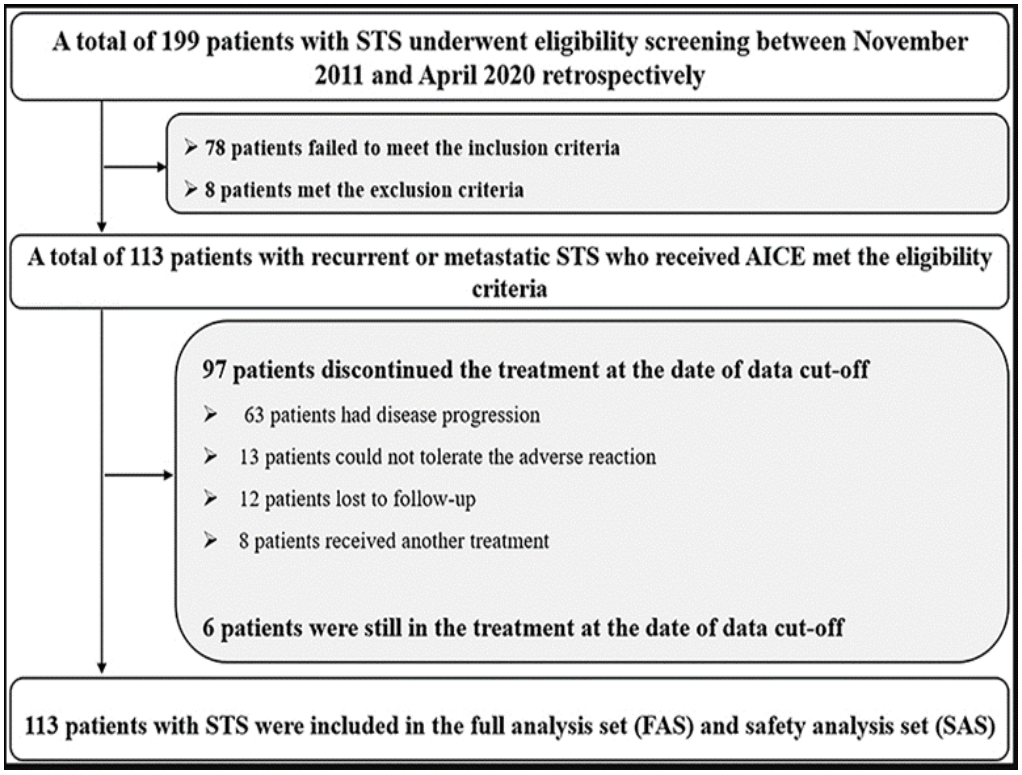

Figure 1. depicts the procedural outline of this retrospective investigation examining arterial infusion chemotherapy combined with embolization (AICE) in patients with recurrent or metastatic soft tissue sarcoma.

The Ethics Committee of the Fifth Medical Center of the PLA General Hospital approved the study protocol. Because the analysis relied on previously collected clinical information, individual informed consent was not requested. All steps conformed to the ethical directives of the Declaration of Helsinki.

AICE treatment procedure

Before AICE was undertaken, each participant received updated imaging—CT, MRI, or PET-CT—to document the tumor's extent, anatomical site, and the presence or absence of distant spread. Baseline blood analyses, including hematologic indices, liver and renal biochemistry, and coagulation parameters, were carried out to ensure that the patient could safely undergo locoregional therapy.

An experienced interventional radiologist performed all AICE procedures using fluoroscopic visualization. Access to the femoral artery was obtained with the modified Seldinger approach, and the catheter was advanced to the arterial segment supplying the tumor. Angiography was used both to verify accurate catheter placement and to evaluate the tumor's vascular characteristics. Embolization was incorporated only when the lesion exhibited strong arterial perfusion; otherwise, arterial drug infusion alone was performed. When embolization was indicated, a microcatheter was advanced into the dominant feeding branch, and embolic materials (lipiodol or microspheres) were administered until near-stasis was achieved.

Chemotherapy selection—cisplatin with epirubicin—was tailored to the tumor's pathology, the patient's prior therapies, and organ function. After embolization, continuous intra-arterial cisplatin (70–80 mg/m²) was infused for 4 hours, followed by intravenous epirubicin (50–70 mg/m²) on days 3 and 4. Each therapeutic course was repeated every 3–4 weeks. Cisplatin dose was lowered to 50–70 mg/m² in individuals with impaired renal clearance (creatinine clearance <60 mL/min) or earlier treatment-related nephrotoxicity. When tumor vascularity was minimal, only catheter-based arterial infusion was carried out using the same chemotherapy schedule. AICE was used either to facilitate subsequent procedures, such as surgery or radiotherapy, or to provide palliative management for metastatic disease.

The clinical reasoning behind combining arterial and intravenous delivery was threefold:

(1) regional administration raises intratumoral drug levels far above those achievable with systemic therapy alone while reducing systemic exposure;
(2) intravenous chemotherapy complements locoregional infusion by treating microscopic disease not visible on imaging;
(3) experience from other solid tumors shows that pairing intra-arterial and systemic regimens can improve response and survival outcomes with acceptable toxicity [21].

After the session, patients underwent vital-sign surveillance and symptom management. Pain medicines, prophylactic antibiotics, and general supportive care were given when needed. Follow-up imaging was ordered at scheduled intervals to document therapeutic response.

Evaluation of efficacy and safety

The primary endpoints for this study were overall survival (OS)—measured from the start of AICE until death—and progression-free survival (PFS)—the interval from first AICE exposure until radiologic progression or death [22]. Tumor status was reassessed by CT or MRI every 1–2 treatment cycles and throughout follow-up. Secondary endpoints included radiologic response according to RECIST 1.1, classifying outcomes as complete response (CR), partial response (PR), stable disease (SD), or progressive disease (PD). Objective response rate (ORR) was defined as CR + PR, whereas disease control rate (DCR) was calculated as CR + PR + SD [23].

Treatment-related adverse events (TRAEs) were recorded at each AICE treatment and during follow-up, and were categorized following the Society of Interventional Radiology (SIR) complication scale:

A: no treatment, no consequences;
B: minimal management without sequelae;
C: hospitalization ≤48 hours;
D: major intervention or hospitalization >48 hours;
E: permanent impairment;
F: death [24].

TRAEs were tabulated both per procedure and per patient and included catheter-associated complications, bleeding events, and chemotherapy-related toxicities (hematologic and non-hematologic). Any delays in planned therapy or hospital admissions due to AICE toxicity were also documented.

Follow-up

All subjects were enrolled in a uniform follow-up schedule and were reassessed every three months until death or the end of the study period. Surveillance consisted of repeated CT or MRI scans to track tumor evolution, laboratory analyses (blood counts, renal and hepatic function, and tumor markers), and ongoing documentation of clinical status. Survival information—including progression, treatment-related events, and mortality—was collected through clinic visits, phone contact, and review of inpatient or outpatient records. The cutoff date for data collection was November 15, 2023, with a median monitoring duration of 23.5 months (range 1.0–112.5 months).

Statistical analysis

All computations were carried out in SPSS 25.0. Continuous measurements were summarized as x±s, and differences between two independent samples were examined with t-tests. Categorical variables were assessed through the χ^2 test. Survival assessments were completed in Stata 14, where Kaplan–Meier curves were produced; group contrasts relied on the Log-rank test, with medians and 95% CIs reported. Any variable reaching significance in the univariate stage was subsequently examined using a Cox proportional hazards regression, from which HRs and 95% CIs were obtained to determine factors influencing OS and PFS. For subgroup analyses, chi-square or Fisher's exact tests were used for categorical measures, and t-tests or Mann–Whitney U-tests were applied for continuous measures. A $P<0.05$ threshold defined statistical significance.

Results and Discussion

Baseline characteristics

A total of 113 individuals diagnosed with recurrent or metastatic STS were evaluated. Their baseline information **(Table 1)** shows 68 (60.2%) were male and 45 (39.8%) female. The cohort's median age was 35 years (range 3–83). Primary tumor sites included: abdominal cavity (33.6%), limbs/hips (29.2%), pelvic cavity (20.4%), pleural cavity (9.7%), and head/neck (7.1%). The largest tumor diameter had a median of 10.7 cm (range 1.5–25.3 cm), with 58 (51.3%) having lesions ≥10 cm. At enrollment, 94 (83.2%) already demonstrated distant dissemination. Pathologic grades consisted of G1: 5 (4.4%), G2: 49 (43.4%), and G3: 59 (52.2%). Clinically, 11 (9.7%) were stage III and 102 (90.3%) were stage IV. The NLR distribution was ≤3 in 57 (50.4%) and >3 in 56 (49.6%). The mGPS was 0–1 in 78 (69.0%) and 2 in 35 (31.0%). Regarding treatment mode, 32 (28.3%) received infusion alone, whereas 81 (71.7%) underwent infusion plus embolization. Treatment frequency showed 62 (54.9%) completed one cycle, and 51 (45.1%) received at least two cycles.

Table 1. Baseline characteristics of 113 patients with recurrent/metastatic soft tissue sarcoma.

Characteristic	n	%
Age (years)		
≤35	37	32.7%
>35	76	67.3%
ECOG performance status		
0–1	4	3.7%
2–3	109	96.3%
Gender		
Male	68	60.2%
Female	45	39.8%
Primary tumor location		
Head and neck	8	7.1%
Pleural cavity	11	9.7%
Abdominal cavity	38	33.6%
Pelvic cavity	23	20.4%
Limbs and hips	33	29.2%

Maximum tumor diameter (cm)		
Median (range)	10.7 (1.5–25.3)	–
<10 cm	55	48.7%
≥10 cm	58	51.3%
Distant metastasis		
No	19	16.8%
Yes	94	83.2%
Pathological grade		
G1	5	4.4%
G2	49	43.4%
G3	59	52.2%
Clinical stage		
III	11	9.7%
IV	102	90.3%
Neutrophil-to-lymphocyte ratio (NLR)		
≤3	57	50.4%
>3	56	49.6%
Modified Glasgow Prognostic Score (mGPS)		
0–1	78	69.0%
2	35	31.0%
Treatment modality		
Arterial infusion only	32	28.3%
Arterial infusion + embolization	81	71.7%
Lines of previous systemic therapy		
0	19	16.8%
≥1	94	83.2%
Number of AICE treatment cycles		
1	62	54.9%
≥2	51	45.1%

Note: “Infusion” = intra-arterial chemotherapy without embolization; “Infusion + embolization” = intra-arterial chemotherapy with lipiodol or microsphere embolization.

Among all 113 participants, 51 (45.1%) proceeded to subsequent therapy, 17 (15.1%) did not receive further treatment, and information was unavailable for 45 (39.8%). For those who continued treatment (n=51):

- 23 (20.4%) underwent systemic chemotherapy
- 13 (11.5%) received targeted agents
- 9 (8.0%) were given immunotherapy
- 6 (5.3%) used traditional Chinese medicine

Pathological subtypes

As detailed in **Table 2**, distribution of histologic types included liposarcoma (17, 15.0%), leiomyosarcoma (14, 12.4%), malignant fibrous histiocytoma (10, 8.9%), fibrosarcoma (9, 8.0%), interstitialoma (8, 7.1%), and rhabdomyosarcoma (8, 7.1%). Additional categories comprised:

- synovial sarcoma (7, 6.2%)
- aggressive fibromatosis (5, 4.4%)

- myofibroblastoma (4, 3.5%)
- PNET (4, 3.5%)
- ASPS (4, 3.5%)
- undifferentiated sarcoma (4, 3.5%)
- malignant neurinoma (4, 3.5%)

Less frequent diagnoses were SFT (3, 2.7%), hemangiosarcoma (3, 2.7%), spindle cell sarcoma (3, 2.7%), epithelioid sarcoma (2, 1.8%), and other subtypes (5, 4.4%).

Table 2. Pathological subtypes of the 113 patients with recurrent/metastatic soft tissue sarcoma.

Pathological Type	n (%)
Liposarcoma	17 (15.0%)
Leiomyosarcoma	14 (12.4%)
Malignant fibrous histiocytoma	10 (8.9%)
Fibrosarcoma	9 (8.0%)
Interstitialoma	8 (7.1%)
Rhabdomyosarcoma	8 (7.1%)
Synovial sarcoma	7 (6.2%)
Aggressive fibromatosis	5 (4.4%)
Primitive neuroectodermal tumor (PNET)	4 (3.5%)
Alveolar soft part sarcoma (ASPS)	4 (3.5%)
Undifferentiated sarcoma	4 (3.5%)
Malignant peripheral nerve sheath tumor (malignant neurinoma)	4 (3.5%)
Myofibroblastoma	4 (3.5%)
Solitary fibrous tumor (SFT)	3 (2.7%)
Hemangiosarcoma	3 (2.7%)
Spindle cell sarcoma	3 (2.7%)
Epithelioid sarcoma	2 (1.8%)
Others	5 (4.4%)

Survival outcomes

According to **Figure 2**, patients treated with AICE had a median PFS of 11.0 months (95% CI: 8.6–13.4). The PFS rates at 1 year and 2 years were 45.1% (95% CI: 35.8%–54.0%) and 25.7% (95% CI: 18.0%–34.0%), respectively.

As displayed in **Figure 3**, the median OS for the whole cohort was 19.0 months (95% CI: 12.8–25.3). The 2-year OS reached 45.1% (95% CI: 35.8%–54.0%), and the 3-year OS was 41.7% (95% CI: 19.6%–35.9%).

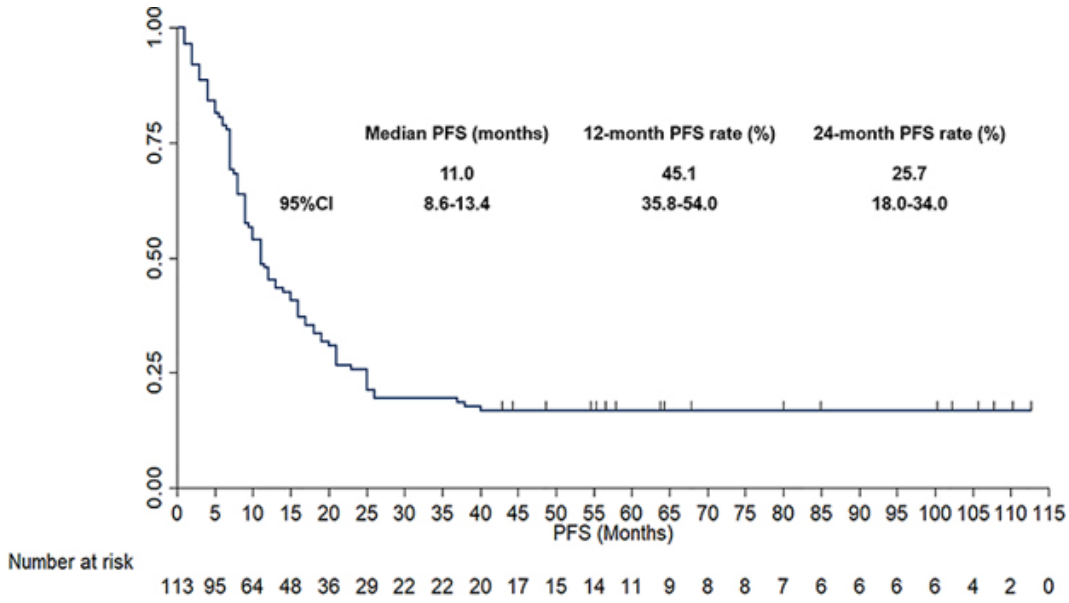

Figure 2. Kaplan–Meier curve for progression-free survival.

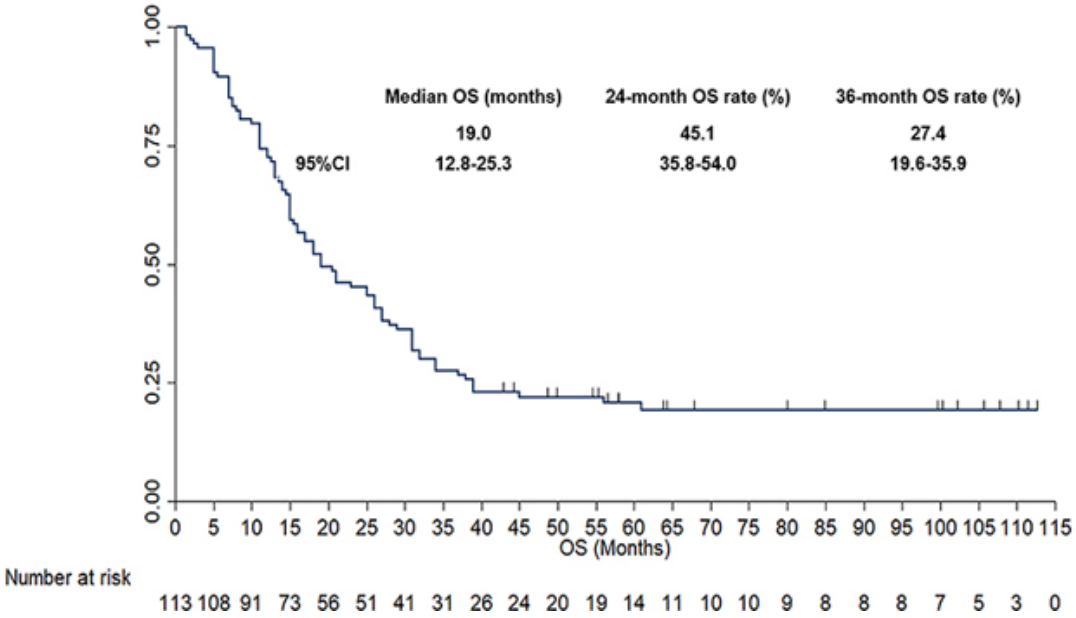

Figure 3. Kaplan–Meier curve for overall survival.

Subgroup evaluation revealed that individuals whose tumors measured ≥10 cm survived a median of 15.0 months (95% CI: 12.0–18.0), markedly below the 27.0 months (95% CI: 22.4–31.6) observed in those with tumors <10 cm (P = 0.006). A similar disparity appeared for PFS: the ≥10 cm cohort showed 9.0 months (95% CI: 7.1–10.8) versus 16.0 months (95% CI: 11.9–20.1, P = 0.011) in the ≤10 cm group. When distant metastasis was present, median OS reached only 16.0 months (95% CI: 13.7–18.7), compared with 39.0 months (95% CI: 6.3–71.7, P<0.001) among patients lacking metastatic disease. Their PFS values were 9.5 months (95% CI: 7.7–11.3) and 23.0 months (95% CI: 11.7–34.3), respectively (P = 0.001). Moreover, receiving ≥2 postoperative therapies corresponded to a median OS of 27.0 months (95% CI: 23.3–30.8), clearly surpassing the 13.0 months (95% CI: 10.9–15.1) reported for those with 0–1 therapy (P<0.001). The PFS comparison followed the same pattern: 11.0 months (95% CI: 13.7–20.3) for those treated with ≥2 therapies versus 7.0 months (95% CI: 6.6–7.4) in the 0–1 therapy category (P<0.001). Pathological grade, stage, number of treatment cycles, and early treatment outcome also demonstrated significant univariate associations with OS and PFS (P<0.05).

All variables identified above were tested in a multivariate Cox model. As displayed in **Table 3**, several parameters independently influenced OS among patients treated with AICE for recurrent or metastatic STS.

Having a tumor exceeding 10 cm increased the probability of death (HR = 1.7; 95% CI: 1.1–2.7; P = 0.014) compared with tumors ≤10 cm. Baseline distant metastasis exerted the strongest detrimental impact, raising the mortality hazard 4.4-fold (HR = 4.4; 95% CI: 2.3–8.7; P<0.001). Patients limited to 0–1 therapeutic approaches also fared worse (HR = 2.3; 95% CI: 1.4–3.6; P = 0.001), highlighting the benefits of multimodal strategies. High-grade tumors (G3 vs G1+G2) predicted inferior OS (HR = 1.6; 95% CI: 1.0–2.6; P = 0.043), and stage IV status versus stage III carried an elevated mortality risk (HR = 2.1; 95% CI: 1.3–3.2; P = 0.005). In addition, failing to achieve PR after AICE independently indicated poorer outcomes (HR = 1.7; 95% CI: 1.0–2.8; P = 0.049). Conversely, the distinction between one AICE cycle and ≥2 cycles did not significantly influence OS (HR = 1.3; 95% CI: 0.6–2.8; P = 0.560).

Table 3. Multivariate Analysis of OS

Characteristic	β	HR	95% CI	P-value
Maximum tumor diameter (cm)				
>10 vs ≤10	0.551	1.7	1.1–2.7	0.014
Distant metastasis				
Yes vs No	1.513	4.4	2.3–8.7	<0.001
Number of previous postoperative systemic therapies				
0–1 vs ≥2	0.823	2.3	1.4–3.6	0.001
Pathological grade				
G3 vs G1+G2	0.482	1.6	1.0–2.6	0.043
Clinical stage				
IV vs III	0.73	2.1	1.3–3.2	0.005
Number of AICE treatment cycles				
1 vs ≥2	0.23	1.3	0.6–2.8	0.560
Short-term efficacy				
SD+PD vs PR	0.51	1.7	1.0–2.8	0.049

The multivariate assessment for PFS **(Table 4)** produced similar observations. Patients with NLR > 3 displayed a heightened risk of progression (HR = 1.6; 95% CI: 1.0–2.5; P = 0.046) relative to those with NLR ≤ 3. Tumors >10 cm continued to behave unfavorably, with a 1.7-fold greater risk of progression (HR = 1.7; 95% CI: 1.1–2.6; P = 0.013). Distant metastasis again represented a major negative determinant (HR = 3.1; 95% CI: 1.7–5.8; P<0.001). Limiting therapy to 0–1 modalities significantly worsened PFS (HR = 3.2; 95% CI: 2.0–5.1; P<0.001). High-grade histology (G3 vs G1+G2) likewise predicted shorter PFS (HR = 1.6; 95% CI: 1.1–2.5; P = 0.032), and stage IV disease carried a 2.3-fold greater likelihood of progression (HR = 2.3; 95% CI: 1.7–3.2; P = 0.007). Meanwhile, neither AICE cycle number (1 vs ≥2; P = 0.600) nor immediate radiologic outcome (SD+PD vs PR; P = 0.150) reached significance for PFS.

Table 4. Multivariate Analysis of PFS

Characteristic	β	HR	95% CI	P-value
Neutrophil-to-lymphocyte ratio (NLR)				
>3 vs ≤3	0.461	1.6	1.0–2.5	0.046
Maximum tumor diameter (cm)				
>10 vs ≤10	0.541	1.7	1.1–2.6	0.013
Distant metastasis				
Yes vs No	1.142	3.1	1.7–5.8	<0.001
Number of previous postoperative systemic therapies				
0–1 vs ≥2	1.172	3.2	2.0–5.1	<0.001

Pathological grade				
G3 vs G1+G2	0.473	1.6	1.1–2.5	0.032
Clinical stage				
IV vs III	0.661	2.3	1.7–3.2	0.007
Number of AICE treatment cycles				
1 vs ≥2	0.191	1.2	0.6–2.4	0.600
Short-term efficacy				
SD+PD vs PR	0.372	1.4	0.9–2.4	0.150

Radiologic outcomes

RECIST 1.1 evaluation revealed no complete responses. Partial responses occurred in 42 patients (37.2%), stable disease in 44 (38.9%), and progression in 27 (23.9%). These figures corresponded to an ORR of 37.2% (95% CI: 28.3%–46.8%) and a DCR of 76.1% (95% CI: 67.1%–83.6%). Notably, a 32-year-old man with fibrosarcoma achieved PR after two AICE cycles; MRI imaging **(Figure 4)** showed a marked decrease in tumor volume, substantial improvement in thoracic symptoms, and clear clinical benefit from treatment.

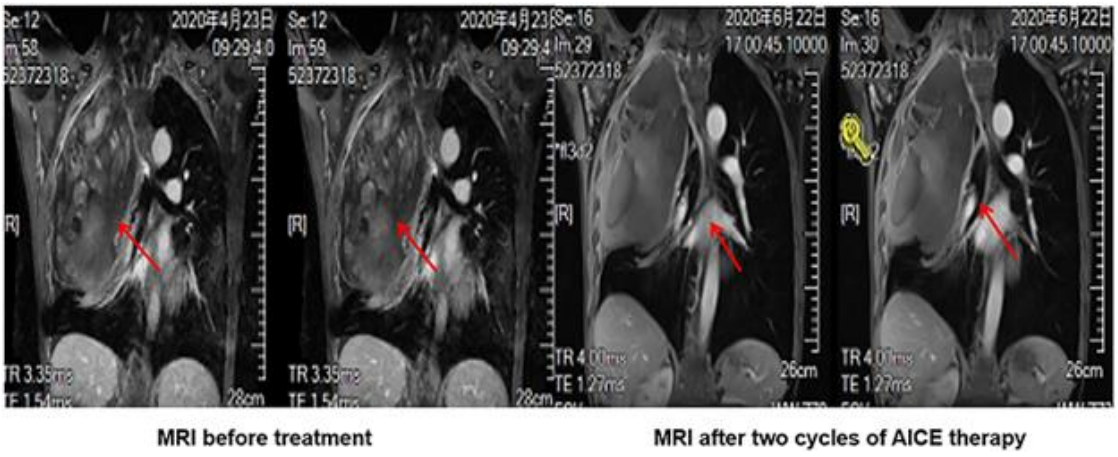

Figure 4. MRI images illustrating how thoracic target lesions changed in a male patient with fibrosarcoma before and after arterial infusion chemotherapy and embolization (AICE). Red arrows highlight the treated hepatic site in both MRI scans.

Safety profile

AICE demonstrated an acceptable safety pattern, and no patient experienced fatal treatment-related toxicity (Grade F). In this analysis, 216 procedures carried out in 113 cases were reviewed to assess immediate adverse effects and technical complications. As presented in **Table 5**, the most common treatment-associated reaction was pain at the treatment site (23.0%). This discomfort was usually mild to moderate (Grade A/B), typical of post-embolization effects, responsive to analgesics, and resolved within a short period. Bone marrow suppression emerged in some procedures as a consequence of concentrated local chemotherapy (15.0%). No Grade E or F hematologic injuries occurred, and all blood count reductions improved with routine supportive management. Fever after embolization—generally low-grade (<38.5°C)—was documented in 7 patients (6.2%). One patient undergoing therapy for liver metastasis developed raised liver enzymes (0.8%, Grade C), though none progressed to liver failure. Impaired renal function of Grade B severity occurred in 2 patients (1.8%). Based on SIR criteria, the bulk of events fell within Grade A or B, meaning no intervention or only minimal measures were required (~85% of treatments). Grade C complications, needing extra therapy or brief hospitalization, were observed in 5 patients (2.7%). Only 2 patients (0.9%) experienced Grade D outcomes, which prolonged hospitalization beyond 48 hours. No instances of permanent injury (Grade E) were recorded. Overall, the risk profile for AICE was favorable when delivered by experienced clinicians, with most adverse effects being limited, transient, and generally easier to manage than the typical side effects of systemic chemotherapy. Serious systemic toxicities—such as significant myelosuppression, mucosal injury, or cardiac effects—were uncommon,

presumably due to the largely localized nature of drug administration. The low rate of major complications indicates that repeated AICE is feasible with appropriate clinical support.

Table 5. Safety outcomes for 113 patients with recurrent/metastatic STS treated using AICE.

Adverse Event	Grade A (N, %)	Grade B (N, %)	Grade C (N, %)	Grade D (N, %)	Total (N, %)
Pyrexia	5 (4.4%)	2 (1.8%)	0	0	7 (6.2%)
Pain	17 (15.0%)	9 (8.0%)	0	0	26 (23.0%)
Nausea and vomiting	4 (1.9%)	0	0	0	4 (1.9%)
Abnormal liver function	0	0	1 (0.8%)	0	1 (0.8%)
Abnormal renal function	0	2 (1.8%)	0	0	2 (1.8%)
Myelosuppression	9 (8.0%)	2 (1.8%)	4 (1.9%)	2 (1.8%)	17 (15.0%)

This retrospective evaluation examined the therapeutic impact and tolerability of AICE in a substantial cohort of recurrent or metastatic STS patients. AICE showed substantial clinical activity, producing an ORR of 37.2%, a DCR of 76.1%, a median PFS of 11.0 months, and a median OS of 19.0 months in 113 patients with SIS. These findings compare favorably with historic outcomes of systemic chemotherapy alone in advanced STS. Conventional first-line doxorubicin-based regimens typically report an ORR of 18–25% and a median PFS of approximately 4–6 months in metastatic cases [25]. In contrast, AICE yielded higher tumor responses and longer disease control, implying that focused intra-arterial delivery can enhance tumor reduction and delay disease advancement. The median OS of 18.0 months in this cohort also surpassed the commonly reported 12 month median OS associated with doxorubicin in previous trials, even in studies where many patients later received second-line treatments [26]. Although comparisons across studies must be interpreted with caution, the improvement suggests a possible survival benefit. Some individuals lived beyond 2–3 years, particularly those who exhibited strong responses and were subsequently treated surgically or with other therapies. Patients receiving combined approaches (AICE along with other systemic or local modalities) tended to achieve the best outcomes, emphasizing the value of multimodal management for advanced sarcoma.

The improved treatment performance of AICE may be explained by the way the technique works. By administering chemotherapy straight into the arterial supply feeding the tumor and then immediately cutting off venous drainage, AICE creates exceptionally high drug concentrations within the tumor and prolongs exposure time [27]. This increases drug contact in the tumor microenvironment while limiting systemic distribution and toxicity [28]. As a result, tumor cell destruction is likely more effective than with standard intravenous therapy, which is restricted by dose limits and body-wide adverse effects. In addition, embolization creates ischemia, enhancing the effect of chemotherapy by promoting hypoxia and depriving tumor cells of nutrients, a combination that can induce both apoptosis and necrosis [29]. The higher ORR and DCR obtained with AICE compared to conventional chemotherapy support this collaborative effect. Comparable regional strategies, such as transarterial chemoembolization for hepatocellular carcinoma, have also achieved better local tumor control than systemic treatment alone because they combine direct cytotoxicity with ischemic injury [16]. This emphasizes the value of AICE, particularly in patients who have predominantly localized disease or tumors that show resistance to systemic drugs [30].

A further advantage of AICE is that localized drug delivery prevents patients from experiencing full-body toxicity associated with high-dose systemic chemotherapy. In our study, adverse events were mostly mild (Grade 1–2), and no fatal treatment-related events occurred. The absence of severe marrow suppression or other life-threatening effects in most patients indicates that AICE can be administered repeatedly and potentially in conjunction with other treatments without compromising patient tolerance, which is important in sarcoma management where maintaining quality of life is a key concern [31]. None of the patients in this study discontinued AICE due to toxicity, and many proceeded to receive additional therapies, reinforcing its practicality. It should be noted, however, that distinguishing the specific contribution of arterial infusion versus the intravenous component of the regimen was challenging. We did not identify definitive evidence of an abscopal effect (tumor regression outside the treatment zone) beyond what might occur with systemic chemotherapy. Thus, the improved treatment results appear attributable to the combined AICE strategy rather than a systemic immune-mediated mechanism.

We also identified several factors influencing prognosis following AICE, consistent with established indicators in advanced STS. Tumor size was particularly important: patients with large masses (≥10 cm) experienced poorer

PFS and OS. Larger tumors may be less accessible to infused drugs and may contain regions with limited blood flow, restricting drug delivery even with arterial infusion. These observations are consistent with earlier research showing worse outcomes in larger tumors due to reduced drug diffusion, greater tumor burden, and more complex vascular networks [32]. Limited intratumoral drug penetration may impair AICE effectiveness. Our findings show that despite AICE, very large sarcomas remain difficult to control, and these patients may benefit from more aggressive embolization or multiple treatment cycles.

Presence of distant metastases at the time of AICE also negatively affected survival (HR ~3 for OS). Metastatic patients showed a median OS of only 12 months, compared with 36 months among those with locally recurrent disease. This reinforces that AICE, as a regional therapy, primarily benefits lesions within the treatment field and cannot independently control widespread metastases. At the same time, statistical significance ($P<0.05$) does not automatically imply clinical importance. The magnitude of the treatment effect and the width of the confidence interval are essential for interpretation. Narrow intervals suggest stronger certainty, while wide intervals indicate doubt even when the P-value meets significance [33]. In several subgroup assessments, the 95% CI for HR was wide (e.g., HR 0.55 [95% CI, 0.28–1.05]) and crossed the null value, indicating lack of significance and substantial uncertainty, preventing definitive conclusions.

Another important issue is that our study population was treated across a long time span (2011–2020), during which major developments in STS systemic therapy occurred. The introduction of new targeted agents and, in specific tumor subtypes, immunotherapy has expanded post-chemotherapy treatment options. Reviews published during this period reported improved median OS and PFS in patients receiving targeted therapies in addition to chemotherapy [34]. Patients treated in the later years of the cohort may therefore have benefited from improved systemic regimens, potentially prolonging survival independent of AICE. This temporal variability could influence survival comparisons. Future studies should include stratification by treatment year and detailed reporting of post-AICE therapies to better clarify AICE's true impact. For patients with metastatic STS, establishing disease control likely requires a combination of AICE and effective systemic agents [35]. In our cohort, some metastatic patients with extended survival were those who also received additional treatments (such as targeted drugs or second-line chemotherapy) alongside AICE, reflecting a multimodal treatment paradigm [36]. Therefore, for metastatic disease, AICE alone is unlikely to provide long-lasting tumor control. A multidisciplinary strategy incorporating AICE with systemic immunotherapy and targeted drugs is probably necessary [37]. Newer immunotherapy options, including PD-1/PD-L1 inhibitors, have shown encouraging activity in select sarcoma subtypes [38]. Combining AICE for regional control with systemic immunotherapy may improve outcomes by treating both local and distant disease progression. Pairing AICE with targeted therapies such as tyrosine kinase inhibitors (e.g., pazopanib) may also enhance control in tumors that are chemo-resistant or have inadequate vascularization. Moreover, AICE combined with immunotherapy may stimulate enhanced immune responses by promoting tumor antigen release and creating a more inflamed tumor microenvironment in metastatic SIS [39].

A substantial proportion of patients in the study (45.1%) received additional systemic treatments—including targeted agents or immunotherapy—after undergoing AICE. Those who experienced longer survival were commonly individuals who benefited from this combined treatment strategy. This indicates that the survival outcomes observed may partially reflect the influence of AICE used alongside other therapeutic approaches. We also noted that receiving three or more types of treatment was independently linked with improved OS and PFS. This supports the idea that a multidisciplinary strategy—using surgery, radiotherapy, systemic treatments, and AICE when clinically appropriate—can generate additive or synergistic advantages. The findings reinforce the significance of multimodal management in enhancing survival for STS patients. Combining AICE with radiotherapy, targeted therapy, or immunotherapy may result in enhanced therapeutic impact [40]. For instance, one patient might undergo AICE to reduce tumor burden, followed by surgery for removal, postoperative radiotherapy to strengthen local control, and systemic drugs to manage any microscopic disease. When feasible, such an intensified approach has the potential to prolong survival in sarcoma. Our results further confirm that coordinated therapy is essential for improving clinical outcomes in this complex disease. Lack of an objective tumor response (CR/PR) to AICE was associated with poorer survival, as patients whose disease remained at SD or progressed had worse prognoses. This demonstrates that tumor sensitivity to treatment remains a key factor. Individuals who responded to AICE achieved longer OS, likely because effective tumor reduction slowed progression and allowed for subsequent therapy or preservation of performance status. This observation is consistent with broader oncologic principles that deeper treatment responses often correlate with improved

survival in metastatic cancers [41], although this could also be attributed to inherent tumor biology, with less aggressive tumors responding more readily.

AICE showed favorable tolerability in our analysis, with most treatment-related adverse events being mild to moderate. The most frequent TRAEs were mild or moderate pain (23.0%), bone marrow suppression (15.0%), and fever (6.2%). Based on SIR grading, most adverse effects were categorized as Grade A or B, meaning little to no intervention was necessary [42]. This toxicity pattern compared positively with traditional systemic chemotherapy, which is often associated with more intense hematologic or gastrointestinal side effects [43]. Catheter-associated complications were infrequent and were effectively managed when they occurred, emphasizing the value of standardized catheter insertion and attentive postoperative follow-up to further reduce risks [44]. Although only two patients (1.8%) developed renal impairment, the inability to definitively attribute these cases to cisplatin highlights the need for stronger kidney toxicity monitoring. Prior studies have identified factors such as cisplatin doses ≥100 mg/m², reduced eGFR, older age, and concomitant nephrotoxic medications as contributors to acute renal injury [45]. Future treatment pathways should include routine renal assessments before and after treatment cycles, adequate hydration strategies, and clear dose modification policies. Such measures may help maintain kidney function without compromising therapeutic gain.

Magnetic Resonance Imaging (MRI) parameters and image-derived biomarkers have shown potential in anticipating tumor characteristics and recurrence patterns in STS. Sedaghat *et al.* (2022), for example, reported that the original morphology of STS—classified as polycyclic/multilobulated or ovoid/nodular—could help predict how recurrent lesions would appear on MRI. Polycyclic/multilobulated primary tumors most frequently recurred with either ovoid/nodular or similarly complex multilobulated shapes, whereas tumors with streak-like configurations demonstrated more variable recurrence patterns [46]. These observations indicated that MRI-based structural appearance may function as a prognostic radiologic marker. Other research also linked MRI findings to tumor biology and clinical outcomes. Schmitz *et al.* (2024) showed that imaging signs, including tumor heterogeneity, adjacent edema, and contrast enhancement, were significantly associated with high-grade STS, and that radiomics-based predictive models performed strongly (AUC ~0.97) in distinguishing low- from high-grade disease [47]. In our study, although a systematic evaluation of advanced MRI biomarkers or morphologic indices was not performed for all patients, **Figure 4** clearly demonstrated treatment-related tumor shrinkage following AICE. Incorporating standardized MRI assessments—such as structural configuration, volumetric response, heterogeneity measurements, and diffusion characteristics—into future protocols may allow earlier identification of optimal candidates for AICE, more accurate response tracking, and improved selection for regional interventions.

This investigation had several limitations. First, the design was retrospective and conducted at a single institution, which could lead to selection bias, as those chosen for AICE might represent a non-random subset, potentially limiting the general applicability of the findings. Second, the absence of a dedicated control group restricted causal interpretation, meaning these results should be viewed as hypothesis-generating until confirmed in prospective, randomized, multi-institution studies. Third, the population included a mix of sarcoma subtypes and treatment histories, which may have influenced outcomes and reduced the clarity of subgroup comparisons. Fourth, these factors collectively constrained the generalizability of the results to broader patient populations. Future research should address these concerns using multicenter trial designs with defined comparison groups. Additionally, subsequent treatments beyond AICE were not uniform—some patients received systemic therapy afterward, which may have influenced survival outcomes. Nearly all participants presented with ECOG performance scores of 2–3 (96.3%), while only a small portion had scores of 0–1 (3.7%); therefore, conclusions regarding tolerability and efficacy are primarily applicable to patients with poorer performance status. The small number of ECOG 0–1 patients (n=4) prevented meaningful statistical comparison with ECOG 2–3 cases. Future studies should stratify or balance enrollment by ECOG category to determine whether individuals with better functional status derive different benefits or experience different toxicity profiles with AICE. We attempted to address these differences by evaluating multimodal therapy as a variable, which did emerge as advantageous.

Conclusion

Overall, AICE showed practical value in enhancing disease management and survival in recurrent or metastatic STS while maintaining an acceptable safety profile. Tumor dimensions, presence of metastasis, and multimodal treatment planning were identified as major prognostic factors shaping outcomes. Incorporating AICE into

comprehensive treatment frameworks and pursuing new therapeutic combinations may further improve patient prognosis. Larger, prospective, multicenter studies are needed to refine treatment strategies and validate these observations. With continuing evidence, AICE may become a key component of sarcoma treatment, complementing systemic agents and aiding in the development of personalized therapeutic pathways and treatment sequencing.

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