

# Impact of Recurrence on Survival Prognosis and Key Risk Factors in Myxofibrosarcoma: A Single-Center Retrospective Study

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**Objective:** Myxofibrosarcoma (MFS) is a rare malignant fibrogenic soft tissue tumor with high propensity for recurrence. This study retrospectively analyzed the surgical treatment outcomes of patients with myxofibrosarcoma (MFS) at a single center to evaluate the impact of recurrence on survival prognosis.

**Methods:** Clinical data from 80 patients who underwent surgical treatment for MFS between January 2015 and January 2023 were reviewed retrospectively. Postoperative follow-up was conducted to assess recurrence and overall survival. Kaplan-Meier survival analysis was used to estimate overall survival (OS) and compare survival curves. Patients were stratified into recurrence and recurrence-free groups based on recurrence status. Oncological prognosis, prognostic factors influencing survival and recurrence, and the association between recurrence and survival prognosis were examined.

**Results:** Over a median follow-up period of 40.6 months, recurrence was observed in 38 patients (47.5%), including 16 patients with multiple recurrences. A total of 17 patients (21.3%) died, and the 5-year OS rate was 70.1%. Independent prognostic factors for OS included age, tumor size, and chemotherapy. The presence of a tumor adjacent to a major vessel or nerve, as well as involvement of the upper extremity, were identified as independent risk factors for recurrence. No statistically significant differences in survival prognosis were observed between patients with and without recurrence. Additionally, survival outcomes did not differ significantly between patients with a single recurrence and those with multiple recurrences.

**Conclusion:** MFS exhibits a high recurrence rate, with multiple recurrences frequently occurring within three years postoperatively. However, both single and multiple recurrences, when managed with aggressive surgical intervention, may not have an adverse effect on overall survival. For tumors located near major vessels or nerves, achieving complete surgical resection and maintaining vigilant postoperative surveillance are essential to mitigate the risk of recurrence.

**Keywords:** neoplasms malignant, myxofibrosarcoma, survival time, disease recurrence, prognosis

## Introduction

Myxofibrosarcoma (MFS) is a rare malignant fibrogenic soft tissue tumor, accounting for approximately 5% of all soft tissue malignancies. It is characterized by aggressive behavior and a high propensity for recurrence.<sup>1-3</sup> Vanni et al summarizes as follows that the mainstay of treatment for localized disease is represented by surgical resection, with (neo)-adjuvant radio- and chemotherapy. In the metastatic setting, chemotherapy represents the backbone of treatments, however its role is still controversial, and the outcome is very poor.<sup>4</sup> Surgical resection remains the primary treatment



method; however, the myxoid-rich stromal composition of the tumor contributes to indistinct tumor margins, poor delineation between neoplastic and normal tissue, and an infiltrative growth pattern. These features complicate complete excision and increase the risk of local recurrence.<sup>5</sup> Recurrences predominantly arise near the primary site, typically manifesting within one year following surgical intervention.<sup>6</sup>

Prior studies indicated that recurrent MFS tends to exhibit greater aggressiveness and presents additional therapeutic challenges compared to primary tumors.<sup>7</sup> Although distant metastasis is uncommon, its occurrence is associated with a poor prognosis.<sup>8</sup> Furthermore, research indicates that 15% to 38% of low-grade myxofibrosarcomas may progress to high-grade malignancies with metastatic potential following recurrence.<sup>9,10</sup> However, the specific impact of recurrence on prognosis remains incompletely understood, and limited data are available on the survival outcomes of patients experiencing multiple recurrences.

We proposed the following research questions: (1) What factors influence the prognosis of survival and recurrence in myxofibrosarcoma? (2) Does recurrence affect the survival outcomes of patients with myxofibrosarcoma? (3) What are the characteristics and survival outcomes of patients with multiple recurrences of myxofibrosarcoma? This study retrospectively analyzed surgical outcomes of 80 patients with myxofibrosarcoma treated at our center, aiming to explore issues related to recurrence and survival prognosis in this disease.

## Materials and Methods

### General Data

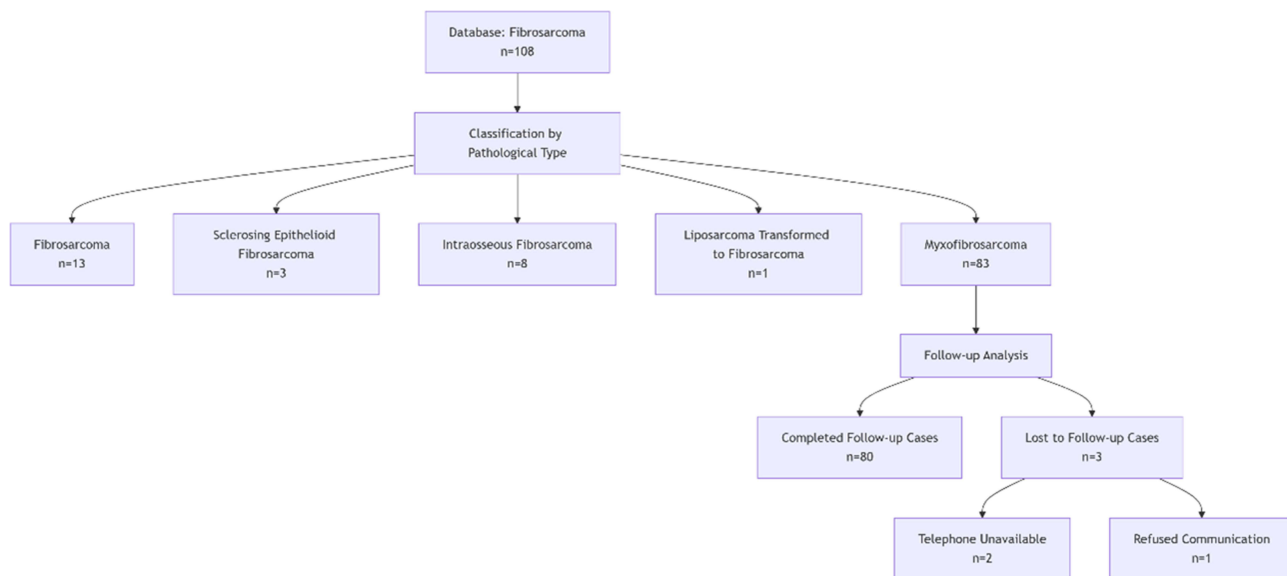
#### Inclusion and Exclusion Criteria

The inclusion criteria were defined as follows: (1) a diagnosis of myxofibrosarcoma confirmed through pathological examination, (2) surgical treatment performed at the institution, and (3) the availability of complete medical records and follow-up data.

The exclusion criteria encompassed: (1) the presence of other malignant diseases, (2) a diagnosis of primary intraosseous myxofibrosarcoma, and (3) loss to follow-up, which was defined as failure to attend outpatient appointments after discharge or non-responsiveness to follow-up calls on three separate occasions.

#### Study Participants

This retrospective study evaluated 80 patients with myxofibrosarcoma who underwent surgical intervention and had comprehensive follow-up data between January 2015 and January 2023 at a single center. The sample selection process is



**Figure 1** Patient Selection Flowchart. Flowchart demonstrates patient selection process. Myxofibrosarcoma cases were derived from database after excluding other histological subtypes. Three cases were lost to follow-up due to contact issues.

illustrated in Figure 1. The group comprised of 38 males and 42 females, with a mean age of 60 years (range: 14 to 93 years). Tumor size exceeded 5 cm in 50 cases, while 30 cases involved tumors measuring 5 cm or smaller. Tumor locations included the upper limb (15 cases), lower limb (51 cases), and trunk (14 cases).

According to the American Joint Committee on Cancer (AJCC) grading system, 31 cases were classified as grade II, 29 cases as grade IIIA, and 20 cases as grade IIIB. Unplanned surgeries had been performed in 26 patients, and tumor adjacency to a major vessel or nerve was observed in 35 patients. All surgical patients underwent intraoperative frozen section analysis of resection margins, and all achieved pathologically negative margins (R0 resection). Adjuvant chemotherapy was administered to 15 patients, while 16 patients received adjuvant radiotherapy. All patients were in good physical condition during the perioperative period, with a time from diagnosis to surgery of no more than two weeks.

In this study, tumors were considered adjacent to a vessel or nerve if no normal tissue layer was present between the tumor and the respective structure. Recurrence was defined as local tumor recurrence. Data collection was conducted with informed consent obtained from the families of all patients, and ethical approval was granted by the ethics committee of the hospital.

## Treatment

All patients underwent surgical treatment following preoperative evaluations, which included local contrast-enhanced computed tomography (CT), contrast-enhanced magnetic resonance imaging (MRI), and high-resolution CT of the chest. Extensive resection was performed, and in cases where the tumor was closely adjacent to a major vessel or nerve, resection of the vessel or nerve sheath was carried out. Adjuvant radiotherapy was administered to 16 patients, while 15 patients received adjuvant chemotherapy consisting of an anthracycline-based regimen in combination with the alkylating agent ifosfamide.

## Outcome Measures

Postoperative data were collected through outpatient reviews and telephone follow-ups. Survival time was measured from the date of diagnosis to either the last follow-up or the date of death. Follow-up assessments included verification of patient demographics (gender, age), clinical and surgical details, recurrence status, metastasis, survival status, and functional satisfaction evaluations.

Pathological grading was conducted in accordance with the AJCC standards. Functional assessment was conducted using the Musculoskeletal Tumor Society (MSTS) functional score, with patients presenting with trunk tumors excluded from this evaluation.

Factors analyzed for their potential impact on survival prognosis included gender, age, planned versus unplanned surgery, tumor size ( $\leq 5$  cm vs  $> 5$  cm), pathological grade, anatomical location (upper limb, lower limb, trunk), adjacency to a major vessel or nerve, and the administration of adjuvant radiotherapy and chemotherapy.

## Statistical Analysis

Baseline patient characteristics were summarized in tables. Continuous variables were reported as mean  $\pm$  standard deviation (mean  $\pm$  SD) for normally distributed data, or as median with interquartile range (IQR) for non-normally distributed data. Normality was assessed using the Shapiro-wilk test. Group differences were assessed using the independent samples *t*-test or the Mann-Whitney *U*-test when data did not follow a normal distribution. Categorical variables were expressed as frequencies and percentages, with group differences analyzed using the chi-square test or Fisher's exact test, as appropriate.

Overall survival (OS) was defined as the time interval from the date of surgery at the institution to either death or the last follow-up. Kaplan-Meier survival curves were constructed to estimate postoperative OS, and differences between survival curves were assessed using the Log rank test. Patients were categorized into recurrence and recurrence-free groups based on recurrence status.

Univariate and multivariate Cox proportional hazards regression models were applied to identify significant prognostic factors using stepwise regression. To ensure a comprehensive analysis, all variables with potential clinical

relevance were included in the multivariate model, regardless of their statistical significance in the univariate analysis. Results were presented as relative risks with corresponding 95% confidence intervals. All statistical analyses were performed using R software (version 4.0.5 by Posit Software, PBC, USA), with statistical significance set at  $p < 0.05$ .

## Results

### Oncologic Results

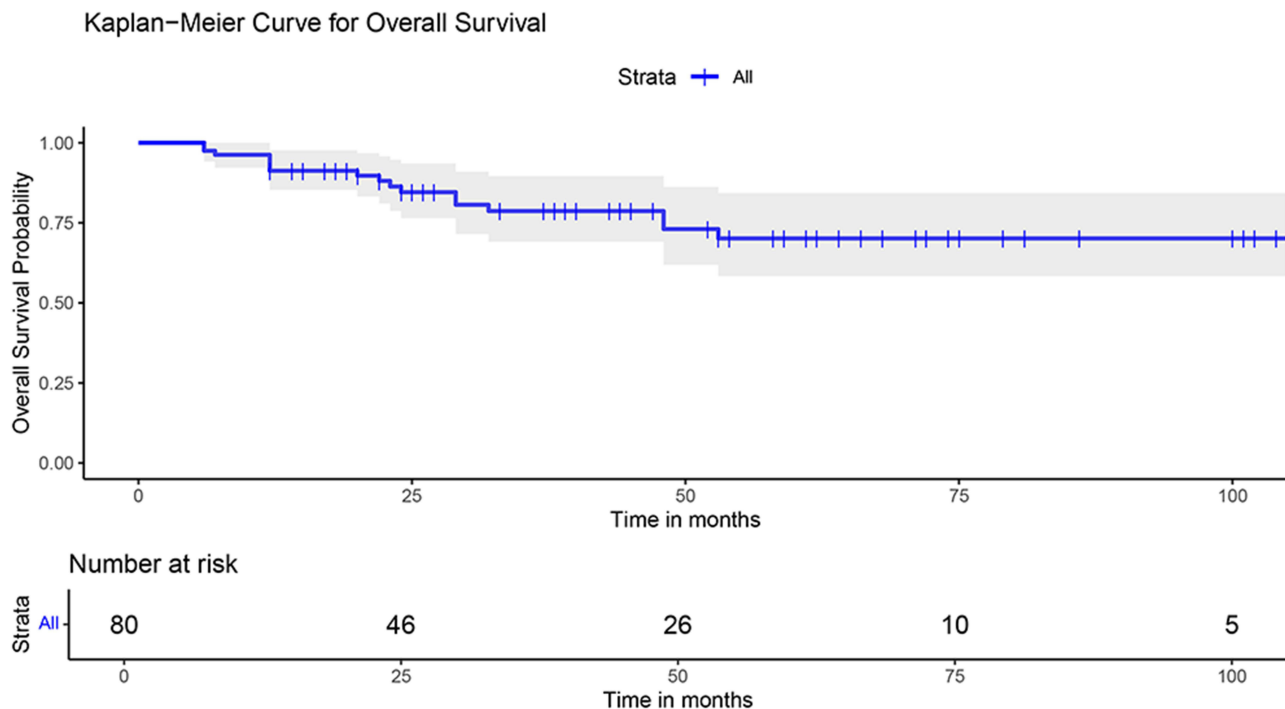
A total of 80 patients were followed up for a duration ranging from 6 to 107 months, with a mean follow-up period of 40.6 months. By the time of the last follow-up, recurrence had occurred in 38 patients, including 16 cases with multiple recurrences. A total of 17 patients had died, while 63 patients remained alive, among whom 27 had residual tumors. No patients experienced severe surgical complications.

The 5-year OS rate for the group was 70.1% (Figure 2), while the 5-year recurrence-free survival rate was 37.62% (Figure 3). The cumulative risk of recurrence was 35.4% at both 3 and 5 years, increasing to 40.1% at 8 years (Figure 4). The mean MSTS functional score was 25.39. Among the 63 surviving patients, 48 (76%) reported satisfaction with their quality of life, 11 (17.5%) found it acceptable, and 4 (6.5%) were dissatisfied.

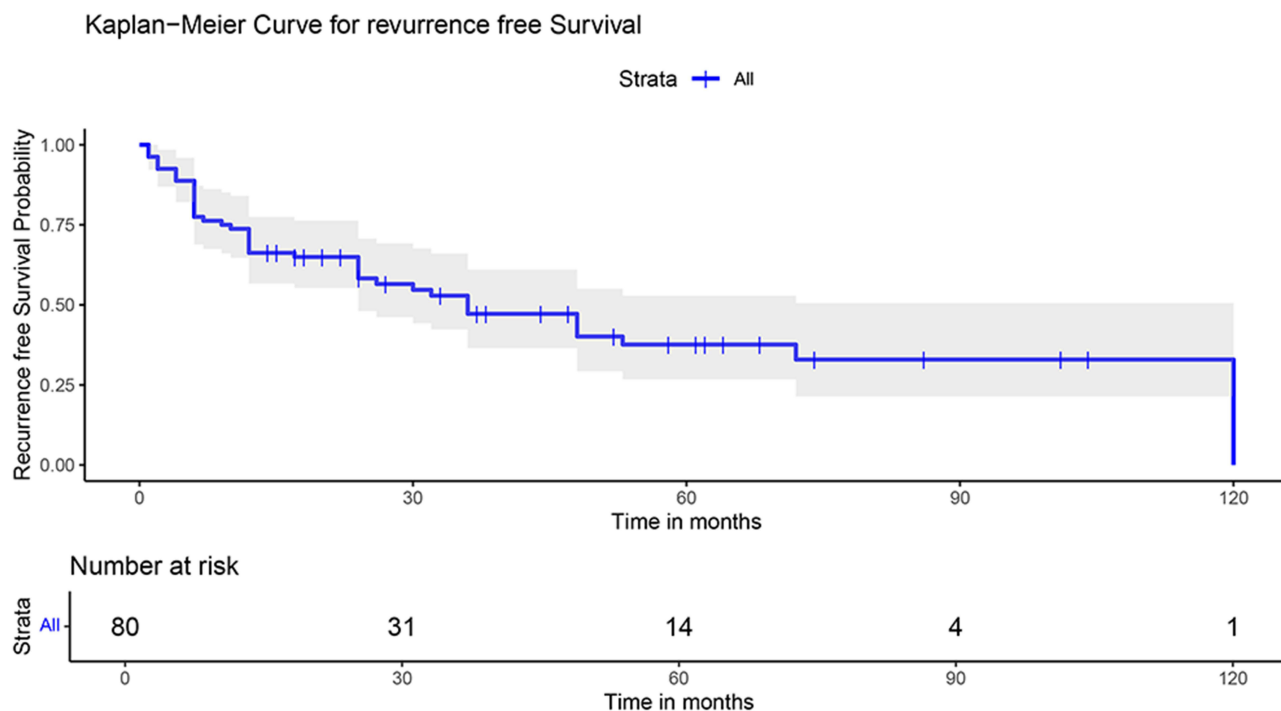
### Analysis of Prognostic Factors Affecting Survival and Recurrence

In the univariate analysis of survival prognosis, factors found to be statistically significant included age, tumor size, adjacency to a major vessel or nerve, pathological stage, and the administration of chemotherapy (Table 1). In the subsequent multivariate analysis, age, tumor size, and chemotherapy use were identified as significant prognostic factors. The risk of death increased by 6.9% for each additional year of age ( $p = 0.005$ ), and tumors larger than 5 cm were associated with a significantly higher risk of mortality ( $p = 0.032$ ). Patients who received chemotherapy were associated with a significantly high risk of death, with an HR of 3.521 ( $p = 0.037$ ).

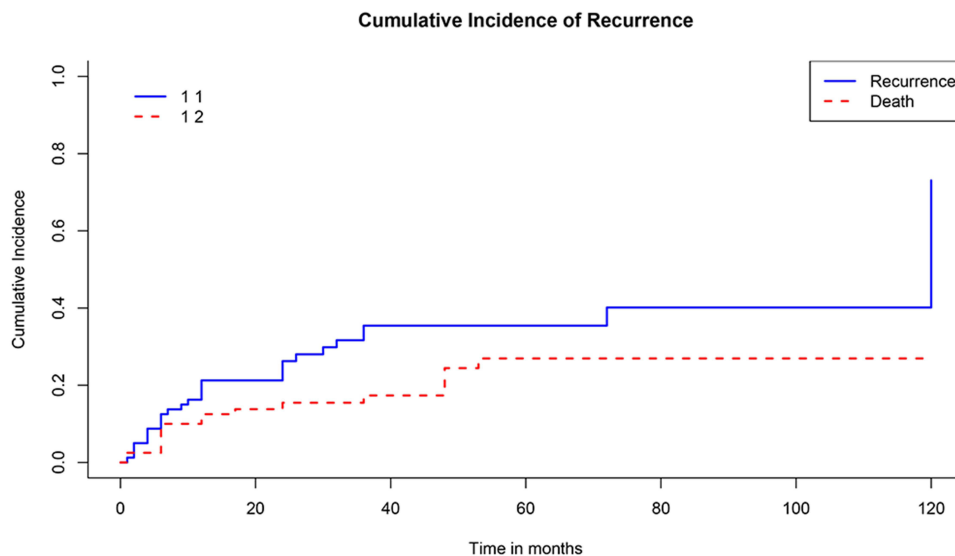
In the univariate analysis of recurrence, age, adjacency to a major vessel or nerve, and tumor location were identified as significant factors (Table 2). Multivariate analysis further indicated that tumor adjacency to a major vessel or nerve and tumor location were independent risk factors for recurrence. Patients with tumors adjacent to a major vessel or nerve



**Figure 2** Overall survival of the entire cohort. The 5-year survival rate was 70.1%.



**Figure 3** Recurrence free survival of the entire cohort. 5-year recurrence-free survival rate was 37.62%.



**Figure 4** Cumulative recurrence rate. The figure depicts how the risks of recurrence and death accumulate over time. The 3-year cumulative risk of recurrence was the same as that at 5 years, both at 35.4%, and at 8 years, it was 40.1%. The overall trend indicates that recurrence occurs more frequently than death. Recurrence remained relatively stable at the 3-year mark.

had a 156.1% increased risk of recurrence (HR: 2.561; 95% CI: 1.310–5.008;  $p = 0.006$ ) compared to those without such tumor proximity. Additionally, tumors located in the upper limbs were associated with a higher risk of recurrence (HR: 2.609; 95% CI: 1.236–5.506;  $p = 0.012$ ).

Overall, tumors adjacent to a major vessel or nerve were identified as key prognostic factors influencing both survival and recurrence in myxofibrosarcoma.

**Table 1** Univariate Analysis of Deaths in 80 Cases Myxofibrosarcoma

Characteristic	N	Event N	HRI	95% CII	p-value
<b>Gender</b>					
Female	42	11	–	–	0.378
Male	38	6	0.639	0.236, 1.729	
<b>Age</b>	80	17	1.046	1.010, 1.084	0.012
<b>Size</b>					
≤5cm	30	1	–	–	0.017
>5cm	50	16	11.60	1.537, 87.56	
<b>Vascular bundle</b>					
Not close	45	5	–	–	0.025
Close	35	12	3.294	1.160, 9.355	
<b>Location</b>					
Upper limb	15	2	–	–	
Lower limb	51	8	1.146	0.243, 5.401	0.863
Trunk	14	7	4.388	0.908, 21.21	0.066
<b>AJCC staging</b>					
II	31	1	–	–	
IIIA	29	9	11.93	1.509, 94.25	0.019
IIIB	20	7	11.73	1.443, 95.40	0.021
<b>Unplanned surgery</b>					
Primary	54	16	–	–	
Unplanned	26	1	0.138	0.018, 1.044	0.055
<b>Radiotherapy</b>					
No	64	14	–	–	
Yes	16	3	0.896	0.257, 3.118	0.863
<b>Chemotherapy</b>					
No	65	10	–	–	
Yes	15	7	3.173	1.207, 8.343	0.019

**Abbreviations:** N, Number of patients; Event N, Number of deaths; HR, Hazard Ratio; CI, Confidence Interval.

**Table 2** Univariate Analysis of Recurrence in 80 Cases Myxofibrosarcoma

Characteristic	N	Event N	HRI	95% CII	p-value
<b>Gender</b>					
Female	42	18	–	–	
Male	38	21	1.559	0.821, 2.960	0.175
<b>Age</b>	80	39	1.022	1.000, 1.043	0.050
<b>Size</b>					
≤5cm	30	17	–	–	
>5cm	50	22	0.758	0.398, 1.445	0.401
<b>Vascular_bundle</b>					
Not close	45	16	–	–	
Close	35	23	2.623	1.361, 5.055	0.004
<b>Location</b>					
Lower limb	51	19	–	–	
Upper limb	15	12	2.415	1.162, 5.019	0.018
Trunk	14	8	1.688	0.732, 3.893	0.219

(Continued)

**Table 2** (Continued).

Characteristic	N	Event N	HRI	95% CII	p-value
<b>AJCC staging</b>					
II	31	17	–		
IIIA	29	15	0.942	0.466, 1.907	0.869
IIIB	20	7	0.596	0.245, 1.453	0.255
<b>Unplanned_surgery</b>					
Primary	54	28	–	–	
Unplanned	26	11	1.035	0.513, 2.092	0.923
<b>Radiotherapy</b>					
No	64	31	–	–	
Yes	16	8	1.106	0.505, 2.421	0.801
<b>Chemotherapy</b>					
No	65	29	–	–	
Yes	15	10	1.744	0.843, 3.605	0.134

**Abbreviations:** N, Number of patients; Event N, Number of recurrences; HR, Hazard Ratio; CI, Confidence Interval.

## The Impact of Recurrence on Survival Prognosis

Statistical analysis comparing patients with and without recurrence demonstrated significant differences in age, tumor adjacency to a major vessel or nerve, and tumor location (Table 3), findings that were consistent with the univariate analysis of recurrence. However, no statistically significant difference in mortality was observed between the two groups ( $p = 0.079$ ), indicating that recurrence did not have a significant impact on overall survival prognosis in this group.

Additionally, a comparative statistical analysis was performed between patients with a single recurrence and those with multiple recurrences (Table 4). No statistically significant differences were identified between the two groups in the analyzed parameters, and mortality rates did not differ significantly ( $p = 0.076$ ). These findings indicate that multiple

**Table 3** Comparison of Factors Between Patients with or Without Recurrence

Characteristic	Total Patient (N = 80)	Patients Without Recurrence (n= 41)	Patients with Recurrence (n = 39)	p-value
<b>Gender</b>				0.376
Female	42(52.5%)	24 (58.5%)	18 (46.2%)	
Male	38	17 (41.5%)	21 (53.8%)	
<b>Age</b>	59.0 [53.0;69.0]	57.0 [52.0;65.0]	67.0 [55.5;71.0]	0.020
<b>Size</b>				0.386
≤5cm	30(37.5%)	13 (31.7%)	17 (43.6%)	
>5cm	50 (62.5%)	28 (68.3%)	22 (56.4%)	
<b>Vascular_bundle</b>				0.014
Not close	45(56.2%)	29 (70.7%)	16 (41.0%)	
Close	35 (43.8%)	12 (29.3%)	23 (59.0%)	
<b>Location</b>				0.011
Upper limb	15 (18.8%)	3 (7.32%)	12 (30.8%)	
Lower limb	51 (63.7%)	32 (78.0%)	19 (48.7%)	
Trunk	14 (17.5%)	6 (14.6%)	8 (20.5%)	
<b>AJCC staging</b>				0.354
II	31 (38.8%)	14 (34.1%)	17 (43.6%)	
IIIA	29 (36.2%)	14 (34.1%)	15 (38.5%)	
IIIB	20 (25.0%)	13 (31.7%)	7 (17.9%)	

(Continued)

**Table 3** (Continued).

Characteristic	Total Patient (N = 80)	Patients Without Recurrence (n= 41)	Patients with Recurrence (n = 39)	p-value
<b>Unplanned_surgery</b>				0.575
Primary	54 (67.5%)	26 (63.4%)	28 (71.8%)	
Unplanned	26(32.5%)	15 (36.6%)	11 (28.2%)	
<b>Radiotherapy</b>				1.000
No	64 (80.0%)	33 (80.5%)	31 (79.5%)	
Yes	16 (20.0%)	8 (19.5%)	8 (20.5%)	
<b>Chemotherapy</b>				0.210
No	65 (81.2%)	36 (87.8%)	29 (74.4%)	
Yes	15 (18.8%)	5 (12.2%)	10 (25.6%)	
<b>Death</b>				0.079
No	63 (78.8%)	36 (87.8%)	27 (69.2%)	
Yes	17 (21.2%)	5 (12.2%)	12 (30.8%)	

**Table 4** Comparison of Clinical Characteristics Between Patients with One Recurrence vs Multiple Recurrences

Characteristic	Patients with Recurrence (N= 39)	Patients with One Recurrence (n= 23)	Patients with Multiple Recurrences (n= 16)	p-value
<b>Gender</b>				1.000
Female	18 (46.2%)	11 (47.8%)	7 (43.8%)	
Male	21 (53.8%)	12 (52.2%)	9 (56.2%)	
<b>Age</b>	64.1+12.8	66.8+13.9	60.2+10.0	0.092
<b>Size</b>				0.097
≤5cm	17 (43.6%)	7 (30.4%)	10 (62.5%)	
>5cm	22 (56.4%)	16 (69.6%)	6 (37.5%)	
<b>Vascular_bundle</b>				1.000
Not close	16 (41.0%)	9 (39.1%)	7 (43.8%)	
Close	23 (59.0%)	14 (60.9%)	9 (56.2%)	
<b>Location</b>				0.576
Upper limb	12 (30.8%)	6 (26.1%)	6 (37.5%)	
Lower limb	19 (48.7%)	11 (47.8%)	8 (50.0%)	
Trunk	8 (20.5%)	6 (26.1%)	2 (12.5%)	
<b>AJCC staging</b>				0.168
II	17 (43.6%)	7 (30.4%)	10 (62.5%)	
IIIA	15 (38.5%)	11 (47.8%)	4 (25.0%)	
IIIB	7 (17.9%)	5 (21.7%)	2 (12.5%)	
<b>Unplanned_surgery</b>				0.734
Primary	28 (71.8%)	17 (73.9%)	11 (68.8%)	
Unplanned	11 (28.2%)	6 (26.1%)	5 (31.2%)	
<b>Radiotherapy</b>				1.000
No	31 (79.5%)	18 (78.3%)	13 (81.2%)	
Yes	8 (20.5%)	5 (21.7%)	3 (18.8%)	
<b>Chemotherapy</b>				0.711
No	29 (74.4%)	18 (78.3%)	11 (68.8%)	
Yes	10 (25.6%)	5 (21.7%)	5 (31.2%)	
<b>Death</b>				0.076
No	12 (30.8%)	10 (43.5%)	2 (12.5%)	
Yes	27 (69.2%)	13 (56.5%)	14 (87.5%)	

**Table 5** Clinical Characteristics and Management Strategies for Recurrent Myxofibrosarcoma

Category	Details
Disease Characteristics	- High recurrence rate of myxofibrosarcoma - Multiple recurrences are common, especially within 3 years after surgery
Treatment Strategies	- Aggressive surgical intervention for both single and multiple recurrences - Aggressive surgical intervention does not have a significant negative impact on overall survival prognosis
Management of Special Cases	- Complete surgical resection should be prioritized for tumors located adjacent to major vessels or nerves - Close postoperative surveillance is essential to monitor for potential recurrence
Postoperative Management	- Regular follow-up examinations are required, especially within 3 years after surgery - Monitor for signs of recurrence

recurrences do not adversely affect overall survival prognosis in this group. We have compiled a table of clinical recommendations (Table 5), which may provide practical guidance for surgical strategy and follow-up monitoring.

## Discussion

Five-year survival rates for myxofibrosarcoma have been reported in the literature to range from 61% to 84%.<sup>11–13</sup> In a review of 158 cases, Sanfilippo identified tumor size, pathological grade, and resection margin as significant prognostic factors influencing survival.<sup>14</sup> Similarly, Chiel conducted an analysis of prognostic factors in the largest group of myxofibrosarcoma cases to date (908 patients), reporting a median OS of 155 months. Advanced age, tumor size, and pathological grade were identified as significant prognostic factors.<sup>12</sup>

The impact of unplanned surgery on prognosis remains a subject of debate. The retrospective analysis by Kazutaka of 100 cases found that unplanned resection was significantly associated with five-year disease-free survival.<sup>6</sup> However, Isaac reported no significant difference in five-year OS between patients undergoing planned and unplanned surgeries.<sup>15</sup> Findings from the present study also indicated that unplanned surgery did not influence OS, which aligns with the majority of recent studies suggesting that unplanned surgery does not have a significant impact on prognosis.

In this study, age, tumor size, and chemotherapy administration were identified as prognostic factors. Myxofibrosarcoma is generally considered to exhibit limited sensitivity to chemotherapy.<sup>16–18</sup> In this study, postoperative chemotherapy was administered to patients meeting one or more of the following criteria: tumor size greater than 10 cm, high-grade sarcoma, tumor location adjacent to major blood vessels or nerves, recurrent tumors, or age under 70 years. These patients demonstrated a higher risk of mortality, which may be attributed to the limited efficacy of chemotherapy in treating myxofibrosarcoma. Additionally, patients selected for chemotherapy typically presented with more advanced or high-risk disease.

Recurrence is a prominent characteristic of myxofibrosarcoma and has been reported to be associated with histologically invasive tumor growth.<sup>16,19,20</sup> The five-year recurrence rate documented in the literature ranges from 19.1% to 33.9%.<sup>17,21,22</sup> In this study, cumulative incidence plots for death and recurrence demonstrated that recurrence occurred more frequently than mortality, a finding consistent with the known clinical behavior of myxofibrosarcoma.

Tumor diameter greater than 5 cm and positive surgical margins have been identified in previous studies as factors contributing to recurrence.<sup>23</sup> Findings from this study further indicated that tumor adjacency to a major vessel or nerve, as well as tumor location in the upper limb, were associated with an increased risk of recurrence. Given the technical challenges associated with achieving complete resection of tumors in these locations, inadequate surgical margins may contribute to the higher recurrence rates observed.

The role of tumor adjacency to a major vessel or nerve as a prognostic factor for recurrence in soft tissue sarcomas remains unclear in the literature. In a retrospective analysis of preoperative MRI scans from 46 patients with soft tissue sarcomas, Panicek found no significant differences in local recurrence, distant metastasis, or disease-specific survival between cases with and without major vessel or nerve encasement.<sup>17</sup> However, based on the findings of the present study, it is proposed that due to the distinct characteristics of myxofibrosarcoma, tumor adjacency to a major vessel or nerve

may contribute to an increased risk of postoperative recurrence. In contrast, when analyzed collectively across various soft tissue sarcoma subtypes, this factor may not demonstrate statistical significance due to heterogeneity among tumor types.

For myxofibrosarcomas located adjacent to a major vessel or nerve, surgical intervention should prioritize achieving complete resection, including routine dissection of the membrane surrounding vascular and nerve bundles. Additionally, postoperative surveillance should be conducted rigorously to monitor for potential recurrence. In cases where vascular or nerve invasion is present, both resection and reconstruction are necessary to optimize treatment outcomes.

Analysis of this study revealed no significant difference in mortality between patients with and without recurrence ( $p = 0.079$ ), suggesting that recurrence may not have a definitive impact on OS prognosis. Additionally, the cumulative recurrence risk was 35.4% at both three and five years, increasing to 40.1% at eight years, indicating that recurrence predominantly occurred within the first three years following surgery. Therefore, intensive postoperative surveillance, particularly through MRI, is essential within the first three years to facilitate early detection and intervention for recurrent disease.

Patients diagnosed with myxofibrosarcoma may experience multiple recurrences over the course of their lifetime. Willems indicated that recurrence in myxofibrosarcoma may be associated with increased tumor aggressiveness, a higher risk of metastasis, and reduced survival.<sup>24</sup> However, this association was not observed in the present study. Among the 80 patients included in this group, 39 (48.8%) experienced recurrence, with multiple recurrences occurring in 16 of these cases (41%). No statistically significant differences were identified between patients with single versus multiple recurrences in terms of clinical parameters, and mortality rates did not differ significantly between the two groups ( $p = 0.076$ ). While mortality appeared higher in multiple recurrence group, this difference did not reach statistical significance. However, due to the limited sample size, post hoc power analyses for this comparison indicated limited statistical power, suggesting that the sample size may have been insufficient to detect a true effect. Nevertheless, we believe that the use of wide or aggressive surgical excision, particularly in tertiary care settings where many patients with recurrent disease were referred, may have mitigated the potential negative impact of recurrence on overall survival and contributed to the lack of statistically significant difference observed.

It is worth noting that although surgery remains the mainstay of treatment for myxofibrosarcoma, some progress has been made in adjunctive multimodal therapies in recent years. Regarding the MFS chemoresponse to anthracyclines where great intra-histotype heterogeneity has been observed. Indeed, this could lead to a biomarker-driven treatment stratification, complementing clinical findings on recurrence, survival, and chemotherapy use. In this regards, recent preclinical work has demonstrated considerable variability in chemosensitivity among MFS tumors, underscoring the importance of biomarker-guided patient selection for systemic therapy.<sup>25,26</sup> Additionally, the use of blood-based biomarkers may offer a promising approach for future research on survival prognosis.<sup>27</sup>

This study has several limitations. First, as a retrospective analysis, the potential for selection and recall bias cannot be excluded. Second, the relatively small sample size may limit the generalizability of the findings as well as the statistical power of the results. However, this limitation is inherent to the study of myxofibrosarcoma, a rare tumor subtype that accounts for only a small fraction of soft tissue sarcomas. Despite this, our cohort contains a large single-institution datasets examining recurrence-related prognosis in this disease. Third, the follow-up period was limited, and long-term survival data were not available. Future research should aim to include a larger patient cohort and extend follow-up durations to improve the understanding of prognostic factors in myxofibrosarcoma and to inform clinical management strategies.

## Conclusion

Myxofibrosarcoma demonstrates a high recurrence rate, with multiple recurrences occurring frequently, primarily within the first three years following surgery. Both single and multiple recurrences, when managed with aggressive surgical intervention, may not appear to negatively impact overall survival prognosis. For myxofibrosarcomas located adjacent to a major vessel or nerve, complete surgical resection should be prioritized, and close postoperative surveillance is essential to monitor for potential recurrence.

## Abbreviations

AJCC, American Joint Committee On Cancer; MRI, Magnetic Resonance Imaging; MSTs, Musculoskeletal Tumor Society; MFS, Myxofibrosarcoma; RR, Relative Risk.

## Data Sharing Statement

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

## Ethics Approval and Consent to Participate

This study was conducted with approval from the Ethics Committee of the Second Affiliated Hospital of Zhejiang University. Approval number is 2024-0999. This study was conducted in accordance with the declaration of Helsinki. Written informed consent was obtained from all participants.

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## Disclosure

The authors declare that they have no competing interests for this work.

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