Research Letter

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Prognostic impact of adjuvant therapy following surgical resection in primary hepatic sarcomatoid carcinoma: a retrospective cohort study

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Background: Primary hepatic sarcomatoid carcinoma (PHSC) is a rare and aggressive hepatic malignancy characterized by high recurrence rates and poor prognosis. This study aims to evaluate the efficacy of postoperative adjuvant therapy in PHSC patients after surgical resection.

Methods: The retrospective study enrolled patients with postoperatively, pathologically confirmed PHSC at a major academic medical center between December 2018 and May 2023. Patients were divided into two groups based on the receipt of postoperative adjuvant therapy. Clinical and follow-up data were retrospectively collected. The primary endpoint was disease-free survival (DFS), and the secondary endpoint was overall survival (OS). Survival curves were generated using the Kaplan–Meier method and compared via the log-rank test. Univariate and multivariate Cox regression analyses were employed to identify prognostic factors.

Results: Of 2071 patients with hepatic malignancies, 52 cases (2.5%) were pathologically confirmed as PHSC. The final analysis included 36 PHSC patients, with 19 in the treatment group and 17 in the non-treatment group. The treatment group showed significantly longer DFS compared to the non-treatment group (10.5 vs. 3.0 months, $P = 0.008$), although the difference in OS was not statistically significant (30.4 vs. 24.1 months, $P = 0.229$). Multivariable analysis identified adjuvant therapy as an independent protective factor for DFS (HR 0.24, 95% CI 0.08–0.69, $P = 0.008$).

Conclusion: Postoperative adjuvant therapy significantly prolongs DFS in patients with PHSC, although a corresponding OS benefit was not statistically demonstrated. Further multicenter prospective studies are needed to determine the optimal adjuvant therapy regimen for PHSC.

Keywords: adjuvant therapy, liver tumor, sarcomatoid carcinoma, surgical resection

Introduction

Primary hepatic sarcomatoid carcinoma (PHSC) is a rare and aggressive subtype of hepatic malignancy, characterized by a mixture of carcinomatous and sarcomatoid components[1]. Accounting for approximately 2% of resected liver specimens, PHSC typically presents carcinomatous components predominantly of hepatocellular carcinoma (HCC) type, followed by intrahepatic cholangiocarcinoma (ICC) and mixed types. Compared to conventional HCC, PHSC is associated with larger tumor burden, higher rates of vascular invasion, and poorer prognosis, with a median overall survival (OS) of approximately 10 months[2,3].

HIGHLIGHTS

- Postoperative adjuvant therapy significantly prolongs disease-free survival in primary hepatic sarcomatoid carcinoma patients (10.5 vs. 3.0 months, $P = 0.008$).
- Multivariable analysis confirms adjuvant therapy as an independent protective factor for disease-free survival (HR 0.24, 95% CI 0.08-0.69, $P = 0.008$).
- Despite longer overall survival in the adjuvant therapy group (30.4 vs. 24.1 months), the difference was not statistically significant ($P = 0.229$).

Radical surgical resection remains the primary treatment for resectable PHSC[3]. However, even after surgery, the 1-year recurrence rate approaches 80%, severely limiting long-term survival[4]. Given the challenges in preoperative diagnosis and high recurrence risk, postoperative management is crucial. Kan *et al*, in their study published in this journal involving 25 PHSC

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patients, demonstrated subsequent postoperative treatment may prolong survival[5], but the efficacy of proactive adjuvant therapy administered in the postoperative window, specifically prior to any evidence of tumor recurrence, remains unclear. Despite extensive research on adjuvant therapy for conventional liver cancer, PHSC's rarity excludes it from major trials[6], with most relevant studies limited to case reports. This represents a critical knowledge gap in the comprehensive management of this aggressive malignancy.

Therefore, we conducted this study to assess whether adjuvant therapy could improve outcomes for PHSC patients following curative-intent surgical resection, with the aim of optimizing postoperative management strategies for this challenging malignancy. To ensure the rigor and transparency of this research, we declare that no artificial intelligence (AI) or AI-assisted technologies were utilized at any stage of this study, which aligns with the TITAN 2025 guideline[7] (Supplementary Digital Content Table 1, available at: http://links.lww.com/JS9/E738).

Methods

From December 2018 to May 2023, patients with pathologically confirmed PHSC who underwent liver resection at our institution were retrospectively analyzed. Exclusion criteria included: receipt of preoperative anti-tumor treatments, diagnosis of other specific sarcoma types or concurrent malignancies, and insufficient data. Patients were divided into treatment (those receiving postoperative adjuvant therapy) and non-treatment groups. Comprehensive demographic, clinicopathological, treatment, and survival data were retrospectively collected.

Disease recurrence was defined as new intrahepatic lesions, local recurrence at the surgical margin, or distant metastases identified on routine follow-up imaging (typically contrast-enhanced computed tomography (CT), magnetic resonance imaging (MRI), or contrast-enhanced ultrasound). In instances of diagnostic ambiguity, pathological biopsy was pursued when clinically feasible and indicated. Disease-free survival (DFS), the primary endpoint, was the interval from surgical resection to first

Table 1

Baseline characteristics of PHSC patients with and without adjuvant therapy

Variables	Non–treatment (n = 17)	Treatment (n = 19)	*P* value
Demographic characteristics			
Age, median (IQR), year	55 (50, 58)	58 (53, 62)	0.153
Gender (male), n (%)	14 (82.4)	13 (68.4)	0.451
BMI, Mean ± SD, kg/m^2	23.45 ± 2.80	23.19 ± 3.04	0.790
HBsAg (positive), n (%)	15 (88.2)	17 (89.5)	1.000
ECOG stage (0), n (%)	10 (58.8)	11 (57.9)	1.000
Child–Pugh class (A), n (%)	15 (88.2)	17 (89.5)	1.000
Tumor characteristics			
AFP > 20 ng/ml, n (%)	4 (23.5)	6 (31.6)	0.717
Tumor size, median (IQR), cm	9.50 (6.1, 11.0)	6.80 (5.5, 8.8)	0.228
Multiple tumors, n (%)	5 (29.4)	4 (21.0)	0.706
Type of carcinomatous component, n (%)			0.481
HCC	8 (47.1)	11 (57.9)	
ICC	5 (29.4)	2 (10.5)	
HCC–ICC	1 (5.9)	3 (15.8)	
NA[a]	3 (17.6)	3 (15.8)	
Tumor location, n (%)			0.881
Left lobe	4 (23.5)	5 (26.3)	
Right lobe	11 (64.7)	13 (68.4)	
Both lobes	2 (11.8)	1 (5.3)	
Early stage (AJCC I + II), n (%)	7 (41.2)	13 (68.4)	0.179
Pathological features			
Satellite nodules, n (%)	2 (11.8)	3 (15.8)	1.000
Vascular invasion, n (%)	7 (41.2)	5 (26.3)	0.483
Lymph node metastasis, n (%)	2 (11.8)	4 (21.0)	0.662
Adjacent invasion, n (%)	7 (41.2)	2 (10.5)	0.055
Tumor necrosis, n (%)	9 (52.9)	11 (57.9)	0.766
Surgical data			
R0 resection, n (%)	17 (100.0)	19 (100.0)	–
Narrow margin[b], n (%)	11 (64.7)	11 (57.9)	0.742
Radical resection[c], n (%)	10 (58.8)	14 (73.7)	0.483
Major postoperative complications, n (%)	2 (11.8)	1 (5.3)	0.593

AFP, alpha–fetoprotein; AJCC, American Joint Committee on Cancer; BMI, body mass index; ECOG, eastern cooperative oncology group; HBsAg, hepatitis B surface antigen; HCC, hepatocellular carcinoma; ICC, intrahepatic cholangiocarcinoma; PHSC, primary hepatic sarcomatoid carcinoma.

[a]Tumor primarily composed of sarcomatoid component pathologically.

[b]Minimum distance from tumor edge to resection surface ≤1 cm.

[c]Radical resection was defined as R0 resection with ≤3 tumor lesions and absence of major vascular invasion or distant metastasis.

documented recurrence (as defined above) or death from any cause. Overall survival (OS), the secondary endpoint, was the interval from resection to death from any cause. Postoperative surgical complications were graded according to the Clavien–Dindo classification system, with Grade ≥III considered major[8]. For adjuvant therapy, associated adverse events (AEs) were retrospectively reviewed from available institutional records based on the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE) version 5.0[9]. In the event of death, life-threatening illness, disability, hospitalization or prolonged hospitalization, persistent or severe disability/dysfunction, or AEs will be classified as serious adverse events (SAEs).

Patients alive without an event were censored at their last follow-up or the study cut-off date. Postoperative follow-up included assessments at 1- and 3-months following resection, then typically every 3–6 months, or more frequently if clinically indicated. Standard evaluations comprised serum tumor biomarker levels, liver function tests, and imaging (contrast-enhanced CT, MRI, or contrast-enhanced ultrasound). The follow-up data for this study were censored on 1 May 2024.

Survival was analyzed using Kaplan–Meier curves and log-rank tests. To identify prognostic factors, variables with a P <0.1 in the univariate analysis were entered into a multivariate Cox regression model, where a P <0.05 was considered significant. All analyses were conducted using R software (version 4.3.0). This retrospective study received approval from our institutional ethics committee with a waiver of informed consent requirement and was conducted in accordance with the STROCSS guidelines[10].

Results

Among 2071 patients with resected liver malignancies, 52 cases (2.5%) were pathologically confirmed as PHSC. After exclusions, 36 patients were included and divided into treatment (n = 19, receiving adjuvant therapy) and non-treatment (n = 17) groups. The patient selection flowchart and adjuvant therapy details are presented in Supplementary Digital Content Figure 1 (available at: http://links.lww.com/JS9/E736) and Supplementary Digital Content Table 2 (available at: http://links.lww.com/JS9/E739), respectively. Most patients were male (75.0%) and infected with hepatitis B virus (88.9%). The median tumor size was 7.4 cm (IQR, 5.8-10.0 cm), with single tumor predominating (75.0%). Baseline characteristics were well-balanced between groups (Table 1). AJCC stage distribution showed a non-significant trend toward a higher proportion of early-stage tumors (AJCC I + II) in the treatment group (68.4% vs. 41.2%, P = 0.126). Major postoperative complications occurred in (11.8% [2/17, non-treatment] vs. 5.3% [1/19, treatment], P = 0.593, Table 1). The details of the treatment group during the adjuvant therapy phase are shown in Supplementary Digital Content Table 2 (available at: http://links.lww.com/JS9/E739), and no SAEs directly attributable to adjuvant therapy were identified in this cohort.

The median follow-up for the cohort was 25.8 months (Interquartile Range [IQR]: 14.2–36.0 months). The treatment group showed a significant improvement in DFS compared to the non-treatment group (median, 10.5 vs. 3.0 months; P = 0.008; Fig. 1A), with the 12-month DFS rate nearly doubled (42.1% vs. 23.5%). Recurrence patterns were similar between groups, with extrahepatic recurrence being predominant in both (63.6% vs. 60.0%; Supplementary Digital Content Table 3, available at: http://links.lww.com/JS9/E740). OS was longer in the treatment group but did not reach statistical significance (median, 30.4 vs. 24.1 months; P = 0.229; Fig. 1B). Multivariable Cox regression analysis (Table 2) confirmed adjuvant therapy as an independent protective factor for DFS (HR 0.24, 95% CI 0.08–0.69; P = 0.008), whereas advanced AJCC stage remained a risk factor (HR 3.88, 95% CI 1.22–12.31; P = 0.021). For OS, only adjacent invasion remained an independent risk factor (HR 3.43, 95% CI 1.13–10.42; P = 0.029). The detailed results of Cox regression analysis for DFS and OS are shown in Supplementary Digital Content Table 4 (available at: http://links.lww.com/JS9/E741) and Supplementary Digital Content Table 5 (available at: http://links.lww.com/JS9/E742), respectively.

Discussion

PHSC combines carcinomatous and sarcomatoid components, with epithelial cells still identifiable morphologically, immunohistochemically, and ultrastructurally[11] (Supplementary Digital

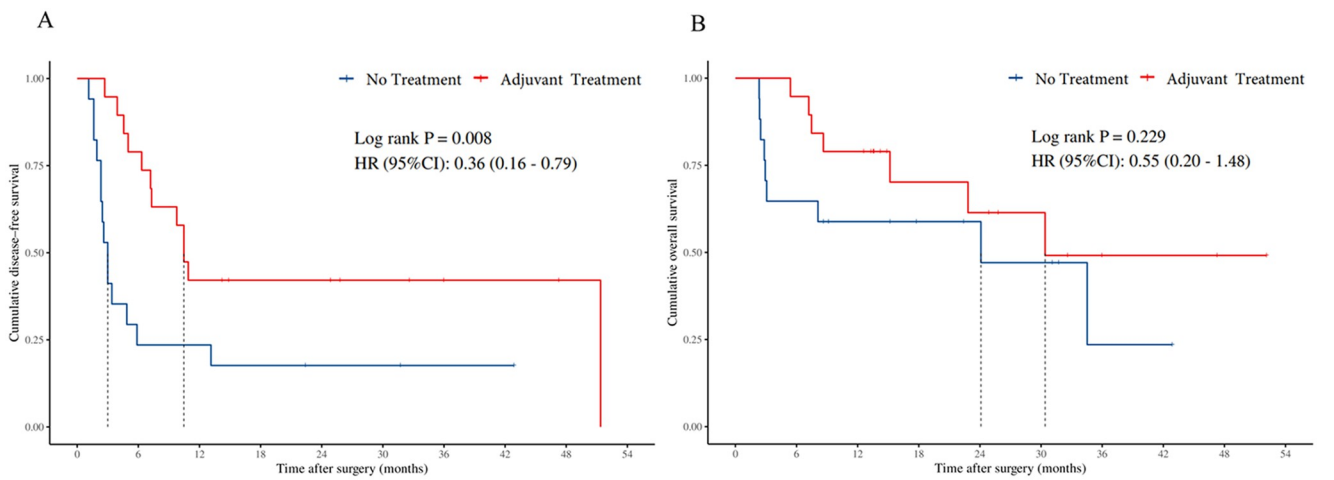

Figure 1. Kaplan–Meier curves for disease-free survival (A) and overall survival (B) according to adjuvant therapy status.

Table 2

Multivariable Cox regression analysis of factors affecting disease-free survival and overall survival

	Disease-free survival			Overall survival		
Variables	**HR**	**95%CI**	***P* value**	**HR**	**95%CI**	***P* value**
Child–Pugh class (A vs. B)	3.09	0.73–13.06	0.124			
AJCC stage (I + II vs. III + IV)	3.88	1.22–12.31	**0.021**			
Lymph node metastasis (no vs. yes)				1.11	0.24–5.19	0.896
Tumor necrosis (no vs. yes)	0.96	0.33–2.79	0.937			
Adjacent invasion (no vs. yes)	1.59	0.48–5.22	0.446	3.43	1.13–10.42	**0.029**
Adjuvant treatment (no vs. yes)	0.24	0.08–0.69	**0.008**			
Radical resection (no vs. yes)				0.44	0.13–1.53	0.197

AJCC, American Joint Committee on Cancer; CI, confidence interval; HR, hazard ratio.
Values in bold are statistically significant at the $p < 0.05$ level.

Content Figure 2, available at: http://links.lww.com/JS9/E736). To our knowledge, this is the first cohort study evaluating the efficacy of pre-recurrence adjuvant therapy after surgical resection, offering novel clinical evidence for improving the prognosis. Our study provides evidence that postoperative adjuvant therapy significantly improves DFS in PHSC patients and is an independent protective factor for DFS. The significant improvement in median DFS (10.5 vs. 3.0 months) represents a clinically meaningful outcome that may enhance quality of life by delaying disease progression and permitting additional therapeutic interventions upon recurrence. In terms of safety, the incidence of major postoperative complications was comparable between the two groups, and no SAEs attributable to adjuvant therapy were found in our existing records.

While prior studies report median OS for PHSC patients of approximately 10 months[1,2], our cohort exhibited a markedly longer median OS exceeding 24 months in both adjuvant therapy and non-adjuvant therapy groups. This improvement likely reflects a lower proportion of terminal stage (AJCC IV) patients in our cohort (8.3%), the achievement of R0 resection in all patients, and the implementation of intensive postoperative management strategies. The prolonged OS aligns with findings from Wang *et al* and Hwang *et al*, who reported improved survival in selected patients with sarcomatoid HCC[3,4].

In the current study, the lack of a statistically significant OS benefit despite improved DFS ($P = 0.229$) parallels observations in conventional HCC adjuvant therapy studies[6] . This observation is not uncommon in adjuvant settings for highly aggressive cancers and may be attributed to several factors: both groups (82% in treatment group, 60% in non-treatment group) received intensive salvage therapies upon recurrence, potentially mitigating survival differences; second, the heterogeneity of adjuvant treatment approaches likely resulted in variable therapeutic responses among patients (Supplementary Digital Content Table 3, available at: http://links.lww.com/JS9/E740), potentially diluting the efficacy in the treatment group; third, despite a trend toward a 6.3-month OS benefit in the treatment group, limited by sample size, a more comprehensive assessment of survival advantage may require extending observation time or conducting multicenter studies to improve statistical power.

Currently, there are no established guidelines for adjuvant therapy in PHSC, and treatment decisions primarily rely on multidisciplinary team consensus, resulting in highly individualized approaches[12]. In our study, therapeutic strategies were tailored based on the predominant carcinoma component: patients with HCC-dominant histology received either TACE or systemic targeted therapy, while those with ICC-dominant features underwent gemcitabine-based chemotherapy. Moreover, the potential efficacy of adjuvant therapy in PHSC may be underpinned by its distinct molecular characteristics. Morisue *et al* reported higher PD-L1 expression in sarcomatoid components compared to carcinomatous elements, suggesting that immunotherapy-based regimens could be beneficial[13]. Supporting this notion, case reports have documented promising immunotherapeutic responses in PHSC patients[14]. Consistently, one patient in our study who received PD-1 antibody plus tyrosine kinase inhibitor achieved a recurrence-free survival of 32.60 months by the end of observation, further supporting the potential of combination immunotherapy as an adjuvant strategy for PHSC.

Conclusion

This study provides evidence that postoperative adjuvant therapy significantly improves DFS in PHSC patients following surgical resection. These findings support the consideration of adjuvant therapy in postoperative management, especially in patients with advanced stages. Future studies should focus on optimizing regimens and identifying patients most likely to benefit.

Ethical approval

This research was approved by the Ethics Committee of West China Hospital, Sichuan University (Approval Number: 2024-180).

Consent

As it is a retrospective study, according to national legislation and institutional requirements, written informed consent is not required for this study.

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Author contributions

All authors contributed significantly to the conceptualization and design of this study. J.J., D.H., J.W., and G.Q. were primarily responsible for data collection and conducting the preliminary analyses. J.J. and H.W. performed the advanced statistical analyses. J.J. and J.H. collaborated closely to interpret the data, providing critical insights and explanations. The drafting and comprehensive revision of the manuscript were carried out by J. J., H.W., and J.H. All authors have thoroughly reviewed and approved the final manuscript.

Conflicts of interest disclosure

The authors have no relevant financial or non-financial interests to disclose.

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Provenance and peer review

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Data availability statement

Anonymized data are available upon reasonable request.

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