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Research article

# Comparison of post-resection survival between hepatocellular carcinoma patients in BCLC stage A or B who experience tumor rupture and patients in BCLC stage C who do not

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ABSTRACT

*Background and aim:* Spontaneous rupture of hepatocellular carcinoma (HCC) is a life-threatening complication, and patients who experience it are formally assigned to stage T4 in the TNM system, while many clinicians informally assign them to stage C in the more widely used Barcelona Clinic Liver Cancer (BCLC) system. The present study explored whether these re-staging practices are appropriate for HCC patients who suffer tumor rupture.

*Methods:* We retrospectively reviewed the records of 1952 HCC patients who underwent hepatic resection at our hospital between January 2017 and June 2021. We compared recurrence-free and overall survival between 143 patients who had BCLC stage A or B disease at the time of spontaneous rupture and 449 patients who had BCLC stage C disease without rupture.

*Results:* Overall survival rate was significantly higher among the 143 patients (1, 3, 5-year survival rate was 80.3%, 60.4%, 51.4%) with rupture than among the 449 (1, 3, 5-year survival rate was 69.5%, 41.5%, 32.4%) with BCLC stage C disease (hazard ratio 1.65, 95% confidence interval 1.29 to 2.12). The two groups had similar recurrence-free survival (hazard ratio 1.19, 95% confidence interval 0.92 to 1.53), but most patients with rupture were able to receive interventional and potentially curative treatments after recurrence, whereas most patients in BCLC stage C received interventional or supportive care. Similar results were obtained after propensity score matching.

*Conclusion:* HCC patients who experience spontaneous rupture tumor while in BCLC stage A or B have better prognosis than patients in BCLC stage C without rupture. Our results suggest that HCC patients who suffer rupture in BCLC stage A or B should not be assigned to BCLC stage C.

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## 1. Introduction

Hepatocellular carcinoma (HCC) is the sixth most common and the third most deadly malignant tumor in the world [1]. Although HCC tumors spontaneously rupture in fewer than 3% of patients in the West, rupture occurs in 2–26% of patients in Asia [2–7]. Studies have found that even if ruptured HCC patients can be managed promptly in the event of a critical situation, their long-term prognosis is worse than that of non-ruptured HCC [8–10]. How such rupture occurs is poorly understood [11] and it is associated with extremely poor survival [12–14]. Given the complex etiology and clinical heterogeneity of HCC, accurate staging of patients using well-established systems such as the TNM system [15] and the more widely used Barcelona Clinic Liver Cancer (BCLC) system [16] is essential for guiding treatment decisions. However, whether the staging of HCC patients should change following rupture is controversial.

The most recent guidelines from Japan [17] and the USA [18] recommend assigning HCC patients who experience tumor rupture to stage T4 in the TNM system. This implies that such patients may fall within BCLC stage C, usually reserved for macrovascular invasion [16]. However, there are some studies that have been reported BCLC stage C patients appear to have substantially lower 5-year rates of overall survival after hepatic resection (<25%) [19,20] than patients who experience tumor rupture (29–49%) [10,21]. As a result, several investigators have questioned the assignment of HCC patients to stage T4 after tumor rupture [22–24]. The appropriateness of such staging may be particularly important to resolve for patients who experience tumor rupture while their disease is in BCLC stage A or B, whom some clinicians routinely assign to BCLC stage C in order to simplify treatment decision-making.

Here we assessed the appropriateness of current practices in post-rupture staging of HCC patients by comparing post-resection survival between HCC patients at our hospital who experienced rupture while in BCLC stage A or B and patients in BCLC stage C without rupture. Our findings suggest that such rupture patients should not be assigned to BCLC stage C or to TNM stage T4.

## 2. Method

### 2.1. Patients

The protocol of this retrospective study conformed to the Declaration of Helsinki (1975) and its amendments and was approved by the Ethics Review Committee of the Guangxi Medical University Cancer Hospital (LW2023005), which waived the requirement for written informed consent because patients or their legal guardians had consented, upon admission, to analysis and publication of anonymized medical data for research purposes. We extracted the medical data of HCC patients who underwent hepatic resection at our hospital between January 2017 and June 2021. Patients had been diagnosed with HCC according to the Chinese guidelines for the diagnosis and treatment of primary liver cancer [25], and they were staged according to the latest guidelines of the BCLC system [16]. In brief, patients were assigned to BCLC stage A if they had a single nodule or ≤3 nodules (each with a diameter ≤3 cm), preserved liver function, and performance status (PS) 0. They were assigned to stage B if they had multinodular tumors, preserved liver function, and PS 0. They were assigned to stage C if they had macrovascular invasion and/or extrahepatic spread, preserved liver function, and PS 1–2.

In this study, either ruptured HCC patient or BCLC stage C patient underwent curative surgery, including semi-elective hepatectomy, emergent hepatectomy, and sequential hepatectomy (laparotomy or TACE to achieve hemostasis, followed by hepatectomy). All patients with macrovascular invasion included in this study had portal vein tumor thrombus (PVTT) type I or II and with PS scores 0 or 1.

Tumor rupture was suspected based on sudden abdominal pain, obvious abdominal tenderness or rebound pain, and it was confirmed on the basis of imaging (ultrasonography, abdominal enhanced computed tomography, magnetic resonance imaging), increased fluid accumulation in the perihepatic area, or abdominal puncture indicating bloody ascites. Patients who experienced tumor rupture were carefully examined and their situation was discussed in multiple meetings among clinicians before hepatic resection was performed. The abdominal cavity was subjected to thorough lavage after tumor resection to reduce the risk of residual tumor cells that could cause recurrence [26,27]. None of the ruptured HCC patients in this study had macrovascular invasion.

After excluding patients in BCLC stage 0, A or B without rupture as well as patients in BCLC stage C who experienced rupture, we extracted data on the following factors likely to influence prognosis: clinicodemographic characteristics, tumor imaging, BCLC stage, platelet count (PLT), prothrombin time (PT), total bilirubin (TBil), albumin (ALB), alanine aminotransferase (ALT), alpha-fetoprotein (AFP), maximum tumor diameter, number of intrahepatic nodules, cirrhosis, portal hypertension, macrovascular invasion, and extrahepatic metastasis. We also collected data about whether HCC recurred after surgery, where it recurred and how it was treated.

### 2.2. Follow-up

As per routine procedure at our hospital, patients in this study were followed up every month within three months after discharge, then every two months until five years after discharge. Follow-up visits involved assessment of general condition, laboratory tests of liver function and tumor markers, and imaging such as ultrasonography, abdominal computed tomography or magnetic resonance imaging. If the patient died or was lost to follow-up, we attempted to contact the patient's family by telephone, text messaging, or the Internet. Follow-up data through December 31, 2022 were considered in this study.

### 2.3. Outcomes

Overall survival was defined as the interval from the first day after surgery until death or date of last follow-up. Recurrence-free survival was defined as the interval from the first day after surgery until discovery of tumor recurrence or metastasis, or until date of last follow-up in the absence of recurrence.

### 2.4. The establishment of a propensity score matching

Multivariable logistic regression was used to create cohorts for propensity score matching comparison from each of the two patient groups that were matched to each other in sex, age, PLT, PT, TBil, ALB, ALT, AFP, maximum tumor size, number of intrahepatic nodules, liver cirrhosis and portal hypertension to ensure that filter out the most suitable patients [28,29]. "Greedy nearest neighbor" matching [30,31] was performed in a 1:2 ratio of rupture patients to BCLC stage C patients, with a caliper width of 0.08.

### 2.5. Statistical analysis

Data were analyzed statistically using SPSS 26.0 (IBM, Chicago, IL, USA) and GraphPad Prism 9.0 software (GraphPad Software, San Diego, USA). Differences between the groups were considered significant if associated with $P < 0.05$.Continuous data were expressed as mean ± standard deviation, while categorical data were expressed as frequencies. Inter-group differences in continuous variables were assessed for significance using a two-sample *t*-test or corrected *t*-test or using the Wilcoxon rank sum test. Inter-group differences in categorical variables were assessed using a Pearson's chi-squared test or Fisher exact test.

The Kaplan-Meier method was used to analyze overall and recurrence-free survival after resection, and inter-group differences were assessed for significance using the log-rank test. Cox uni- and multivariable regression was performed to identify factors associated with worse survival. Subgroup analysis was used to further explore the relationship between tumor size, different BCLC stages and prognosis. Risk associations were assessed in terms of hazard ratios (HRs) and corresponding 95% confidence intervals (CIs).

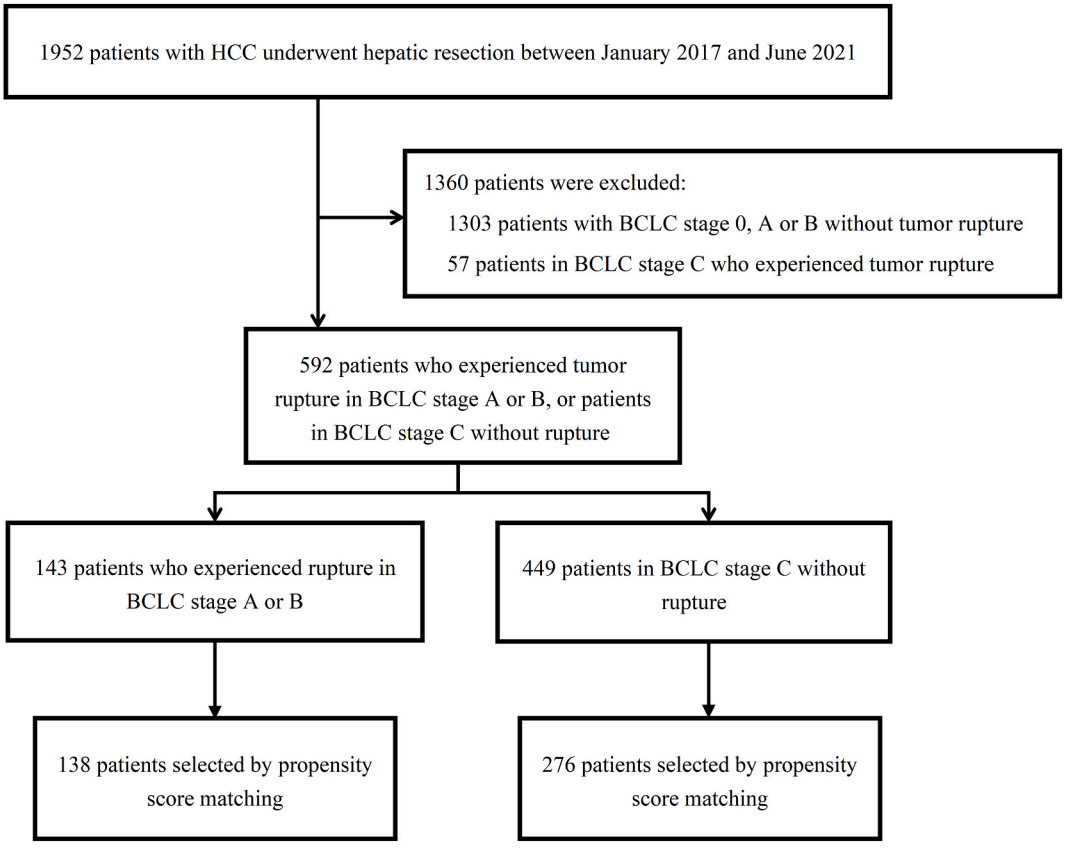


**Fig. 1.** Flow diagram of patient selection. BCLC, Barcelona Clinic Liver Cancer staging system.

## 3. Result

Of the 592 patients that we analyzed, 125 were in BCLC stage A when they experienced tumor rupture and 18 were in BCLC stage B when their tumor ruptured, while the remaining 449 were in BCLC stage C and did not experience rupture (Fig. 1). Patients in the rupture group were more likely to be female and to have total bilirubin ≥17.1 μmol/l (Table 1). Propensity score matching led to selection of 138 patients with rupture in BCLC stage A or B and 276 in BCLC stage C without rupture, and the two matched groups did not differ significantly on any of the variables examined.

When we compared the entire groups of patients, recurrence-free survival did not differ significantly between the two groups (HR 1.193, 95% CI 0.923–1.533), with rates of survival of 46.9% or 36.4% at one year, 28.1% or 21.1% at three years and 24.0% or 16.5% at five years (Fig. 2). Median survival time was 9.0 (95%CI 4.1–13.9) or 6.0 (95%CI 4.6–7.4) months. Overall survival, in contrast, was significantly better in the rupture group (HR 1.654, 95%CI 1.289–2.124). Rates of survival were 80.3% or 69.5% at one year, 60.4% or 41.5% at three years, and 51.4% or 32.4% at five years. Median survival time was 77.0 (95%CI 46.0–107.9) or 26.0 (95%CI 20.8–31.2) months. Similar results were obtained after propensity score matching (Fig. 3).

Subgroup analyses showed that neither subgroup's overall and recurrence-free survival differed significantly between patients who experienced tumor rupture in BCLC stage A whose largest tumor was ≤5 or >5 cm (Supplementary Fig. 1). Neither subgroup's overall and recurrence-free survival differed significantly between patients who experienced tumor rupture in BCLC stage B and patients in BCLC stage C (Supplementary Fig. 2). Patients who experienced tumor rupture in BCLC stage A, however, the overall and recurrence-free survival was significantly higher than that of BCLC stage B (Supplementary Fig. 3).

Univariate analysis associated the number of tumors and BCLC stage with recurrence-free survival of patients in BCLC stage A or B when they experienced rupture (Table 2). The same analysis associated age, serum AFP, PT, and maximum tumor diameter with recurrence-free survival in patients in BCLC stage C. Multivariate analysis showed that recurrence-free survival was associated with the number of tumors (HR 0.582, 95% CI 0.312–0.802) and BCLC stage (HR 0.574, 95% CI 0.351–0.989) in rupture patients, while it negatively correlated with serum AFP (HR 0.676, 95% CI 0.527–0.867), PT (HR 0.691, 95% CI 0.525–0.911) and tumor size (HR 0.627, 95% CI 0.449–0.876) in patients in BCLC stage C.

Univariate analysis failed to identify any factors associated with overall survival in patients with rupture, while it associated PT, portal hypertension, tumor size, and macrovascular invasion with overall survival in patients with BCLC stage C (Table 3). Multivariate analysis showed that overall survival negatively correlated with PT (HR 0.635, 95% CI 0.470–0.859) and presence of portal hypertension (HR 0.729, 95% CI 0.545–0.976) in patients in BCLC stage C.

The rate and location of tumor recurrence during follow-up did not differ significantly between the two groups of patients (Supplementary Table 1). Most cases of recurrence were either single intrahepatic or simultaneous intra- and extrahepatic metastasis and

**Table 1**
Baseline characteristics of patients in the study.

| Characteristic | Before propensity score analysis | | | After propensity score analysis | | |
|---|---|---|---|---|---|---|
| | Rupture in BCLC stage A or B (n = 143) | BCLC stage C without rupture (n = 449) | *P* | Rupture in BCLC stage A or B (n = 138) | BCLC stage C without rupture (n = 276) | *P* |
| Female | 26 (18.2) | 42 (9.4) | 0.004 | 21 (15.2) | 37 (13.3) | 0.653 |
| Age ≥60 yrs | 24 (16.8) | 84 (18.7) | 0.604 | 23 (19.4) | 57 (20.8) | 0.358 |
| Alpha fetoprotein ≥400 ng/ml | 3 (58.0) | 233 (51.9) | 0.199 | 79 (57.2) | 148 (53.8) | 0.530 |
| Platelet count ≥100 × $10^9$/l | 137 (95.8) | 418 (93.1) | 0.244 | 132 (95.7) | 253 (91.7) | 0.156 |
| Prothrombin time ≥12.1 s | 96 (67.1) | 311 (69.3) | 0.632 | 93 (70.1) | 198 (71.6) | 0.425 |
| Total bilirubin ≥17.1 μmol/l | 67 (46.9) | 153 (34.1) | 0.006 | 62 (55.1) | 121 (43.9) | 0.916 |
| Albumin ≥35 g/l | 98 (68.5) | 324 (72.2) | 0.404 | 94 (71.6) | 203 (73.5) | 0.297 |
| Alanine transaminase ≥40 U/l | 53 (37.1) | 208 (46.3) | 0.052 | 53 (38.8) | 108 (39.0) | 0.915 |
| Portal hypertension | 33 (23.1) | 104 (23.2) | 0.983 | 33 (23.9) | 62 (22.3) | 0.804 |
| Tumor size >5 cm | 119 (83.2) | 360 (80.2) | 0.421 | 114 (82.6) | 228 (82.6) | 1.000 |
| Liver cirrhosis | 107 (74.8) | 353 (78.6) | 0.342 | 103 (76.9) | 215 (78.0) | 0.537 |
| ≥3 tumors | 18 (12.6) | 59 (13.1) | 0.864 | 18 (13.4) | 38 (13.6) | 0.880 |
| Macrovascular invasion[a] | 0 (0) | 387 (86.2) | – | 0 (0) | 235 (85.2) | – |
| Extrahepatic metastasis | 0 (0) | 88 (19.6) | – | 0 (0) | 55 (20.1) | – |
| BCLC stage | | | | | | |
| A | 125 (87.4) | 0 (0) | – | 120 (87.0) | 0 (0) | – |
| B | 18 (12.6) | 0 (0) | | 18 (13.0) | 0 (0) | |
| C | 0 (0) | 449 (100) | | 0 (0) | 276 (100) | |
| Median follow-up | 44 (95% CI 35.0–53.0) | 38 (95% CI 35.3–40.7) | | 49 (95% CI 40.1–57.9) | 40 (95% CI 33.5–46.5) | |

Values are n (%), unless otherwise noted.
[a] All patients had portal vein tumor thrombus type I or II and the PS scores were all 0 or 1.BCLC, Barcelona Clinic Liver Cancer staging system.

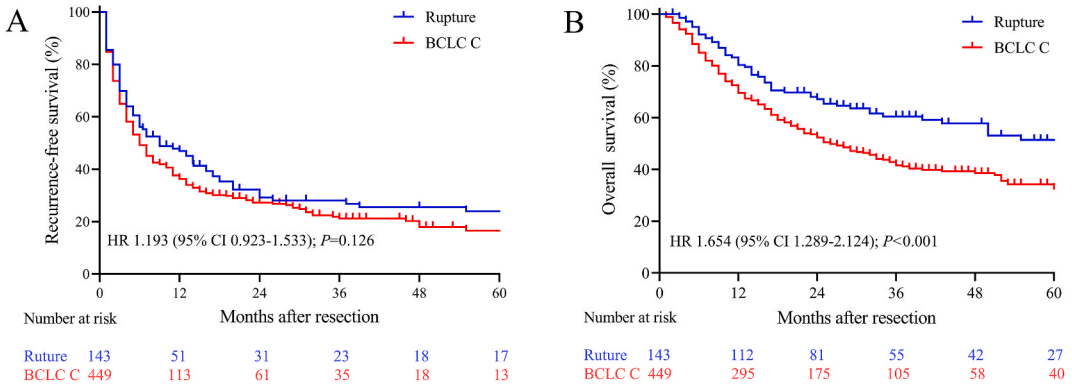


**Fig. 2.** Comparison of cumulative (A) recurrence-free survival or (B) overall survival between all patients who experienced tumor rupture in BCLC stage A or B, and all patients in BCLC stage C without rupture. BCLC, Barcelona Clinic Liver Cancer staging system; HR, hazard ratio.

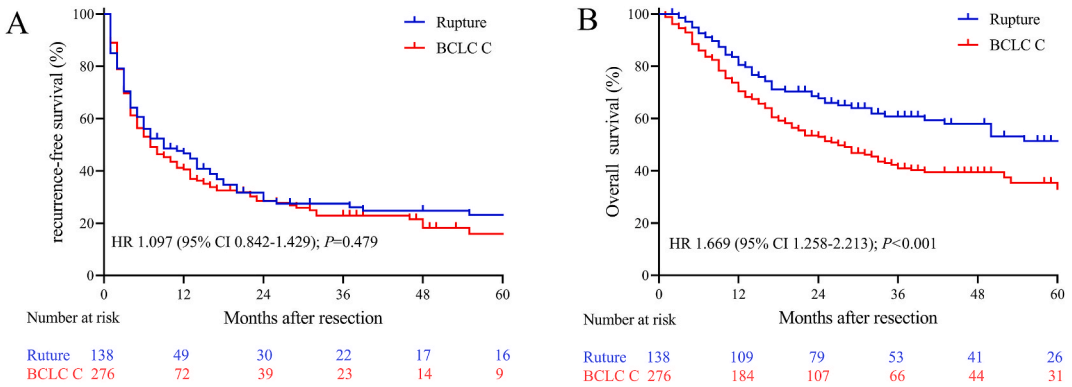


**Fig. 3.** Comparison of cumulative (A) recurrence-free survival or (B) overall survival between propensity score-matched subgroups of patients who experienced tumor rupture in BCLC stage A or B, or patients in BCLC stage C without rupture. BCLC, Barcelona Clinic Liver Cancer staging system; HR, hazard ratio.

approximately 1% patients in only peritoneal metastasis. In contrast, the two groups differed in which treatments they received after recurrence. Most treatments for patients with rupture were interventional or potentially curative, including transarterial chemoembolization, hepatic resection, local ablation and percutaneous ethanol injection; whereas most treatments for patients in BCLC stage C were interventional or supportive care (Supplementary Tables 2–3). In addition, to estimate the impact of tumor rupture and stage, multivariate Cox regression analysis of the entire cohort with the group variable (rupture in BCLC stage A or B vs BCLC stage C without rupture) as a parameter revealed that tumor rupture was associated with tumor recurrence and mortality (Supplementary Table 4).

## 4. Discussion

The lack of consensus about how to stage HCC in patients who experience tumor rupture can complicate and delay treatment decisions, which may lead to worse prognosis. Here we compared the survival between patients who experience rupture at earlier BCLC stages A and B and patients in the final BCLC stage C who did not experience rupture. We found better overall survival among the former group, although not necessarily better recurrence-free survival. Nevertheless, in the event of recurrence, more of the former group of patients were able to benefit from interventional and potentially curative therapies. Our results suggest that HCC patients who experience spontaneous rupture tumor while in BCLC stage A or B should not be assigned to BCLC stage C.

Our finding of similar recurrence-free survival between the two groups of patients may reflect that HCC involving rupture appears to involve faster growth, greater tumor vascularization and generally greater malignancy than HCC without rupture [9,32,33]. This may raise the risk of recurrence to a level similar to that in patients in BCLC stage C, who often have macrovascular invasion or extrahepatic metastasis [34–36]. On the other hand, some studies have suggested that tumor rupture does not significantly affect prognosis of HCC patients after hepatic resection [14,37,38]. Further work should explore whether tumor load before rupture and intervention after rupture strongly influence recurrence-free survival.

Relatively few patients in our study experienced peritoneal metastasis. This may reflect the role thorough lavage of the abdominal cavity after hepatic resection, a standard practice at our hospital that is believed to stop spread of cancer cells that could give rise to recurrence. Similar findings were confirmed by other clinical studies and experimental study [26,27].

**Table 2**
Uni- and multivariate analyses to identify factors associated with tumor recurrence.

| Factor | Rupture in BCLC stage A or B | | | | BCLC stage C without rupture | | | |
|---|---|---|---|---|---|---|---|---|
| | Univariate analysis | | Multivariate analysis | | Univariate analysis | | Multivariate analysis | |
| | HR (95% CI) | *P* | Hazard ratio (95% CI) | *P* | HR (95% CI) | *P* | HR (95% CI) | *P* |
| Sex (male *vs* female) | 1.807 (0.960–3.402) | 0.067 | | | 1.158 (0.741–1.810) | 0.520 | | |
| Age, yr (≥60 *vs* < 60) | 1.153 (0.612–2.173) | 0.659 | | | 1.442 (1.027–2.026) | 0.035 | 1.378 (0.74–1.950) | 0.070 |
| AFP, ng/ml (<400 *vs* ≥ 400) | 0.681 (0.440–1.054) | 0.084 | | | 0.625 (0.490–0.798) | <0.001 | 0.676 (0.527–0.867) | 0.002 |
| PLT, × $10^9$/l (<100 *vs* ≥ 100) | 0.851 (0.269–2.696) | 0.785 | | | 0.774 (0.452–1.326) | 0.351 | | |
| PT, sec (<12.1 *vs* ≥ 12.1) | 0.949 (0.608–1.482) | 0.818 | | | 0.653 (0.498–0.858) | 0.002 | 0.691 (0.525–0.911) | 0.009 |
| TBil, μmol/l (<17.1 *vs* ≥ 17.1) | 0.938 (0.615–1.429) | 0.764 | | | 0.940 (0.880–1.477) | 0.321 | | |
| ALB, g/l (<35 *vs* ≥ 35) | 1.018 (0.573–1.469) | 0.720 | | | 1.175 (0.739–1.286) | 0.858 | | |
| ALT, U/l (<40 *vs* ≥ 40) | 0.963 (0.624–1.485) | 0.864 | | | 0.809 (0.636–1.028) | 0.083 | | |
| Portal hypertension (absence *vs* presence) | 0.854 (0.520–1.403) | 0.534 | | | 0.888 (0.665–1.186) | 0.422 | | |
| Tumor size, cm (≤5 *vs* > 5) | 0.971 (0.622–1.845) | 0.804 | | | 0.592 (0.427–0.822) | 0.002 | 0.627 (0.449–0.876) | 0.006 |
| Liver cirrhosis (absence vs presence) | 0.778 (0.486–1.246) | 0.296 | | | 0.959 (0.720–1.276) | 0.772 | | |
| Tumor number (<3 *vs* ≥ 3) | 0.531 (0.285–0.758) | 0.016 | 0.582 (0.312–0.802) | 0.046 | 0.840 (0.732–1.478) | 0.828 | | |
| BCLC stage (A *vs* B) | 0.574 (0.303–0.939) | 0.025 | 0.574 (0.351–0.989) | 0.049 | ND | | | |
| Macrovascular invasion (absence *vs* presence) | ND | | | | 0.925 (0.651–1.316) | 0.666 | | |
| Extrahepatic metastasis (absence *vs* presence) | ND | | | | 0.912 (0.675–1.233) | 0.550 | | |

Abbreviations: AFP, alpha fetoprotein; ALB, albumin; ALT, alanine aminotransferase; BCLC, Barcelona Clinic Liver Cancer staging system; CI, confidence interval; HR, hazard ratio; ND, not done; PLT, platelet count; PT, prothrombin time; TBil, total bilirubin.

Our subgroup analysis showed similar overall and recurrence-free survival between patients who experienced tumor rupture in BCLC stage B and patients in BCLC stage C without rupture. However, patients who experienced tumor rupture in BCLC stage A had significantly improved the overall and recurrence-free survival compared with patients who experienced tumor rupture in BCLC stage B. This leads us to suggest that it may be appropriate to increase the staging of HCC patients by one step in the BCLC system following rupture, such that those who experience rupture in stage A are assigned to stage B and those who experience rupture in stage B are assigned to stage C. This idea should be explored in future work.

At the same time, future work should address several shortcomings in the present study, including its retrospective design and small sample. The small sample may help explain, for example, why we observed similar survival between patients who experienced rupture in BCLC stage A and whose largest tumor measured ≤5 or >5 cm, despite the known association between larger tumor and worse survival among HCC patients who experience tumor rupture [39,40]. In addition, most of our patients were chronically infected with hepatitis B virus, similar to HCC patient populations elsewhere in Asia but unlike patient populations in the West [41,42]. Our results should be validated and extended in other populations. Concurrently, by reporting only outcomes in patients with rupture and subsequent hepatic resection, this study does not provide the full spectrum of features of this phenomenon, which may have implications for survival beyond what might be expected when examining outcomes in patients who did not " selected " to undergo resection. This limitation should be equally acknowledged, as surgery is only one treatment option for HCC. Finally, resection is not first choice of BCLC C patients and may thus weaken the underlying rationale of using BCLC C patients who underwent resection as comparison.

## 5. Conclusion

This retrospective study showed that overall survival of HCC patients with BCLC stage A or B rupture was better than that of patients with BCLC stage C, although the two groups showed similar recurrence-free survival. Our results suggest that HCC patients who suffer rupture in BCLC stage A or B should not be assigned to BCLC stage C.

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**Table 3**
Uni- and multivariate analyses to identify factors associated with mortality.

| Factor | Rupture in BCLC stage A or B | | | | BCLC stage C without rupture | | | |
|---|---|---|---|---|---|---|---|---|
| | Univariate analysis | | Multivariate analysis | | Univariate analysis | | Multivariate analysis | |
| | HR (95% CI) | *P* | HR (95% CI) | *P* | HR (95% CI) | *P* | HR (95% CI) | *P* |
| Sex (male *vs* female) | 1.294 (0.636–2.634) | 0.477 | | | 1.155 (0.561–1.304) | 0.467 | | |
| Age, yr (≥60 *vs* < 60) | 1.017 (0.484–1.737) | 0.791 | | | 1.030 (0.747–1.420) | 0.859 | | |
| AFP, ng/ml (<400 *vs* ≥ 400) | 0.659 (0.384–1.130) | 0.130 | | | 0.915 (0.711–1.178) | 0.491 | | |
| PLT, × $10^9$/l (<100 *vs* ≥ 100) | 1.817 (0.656–5.034) | 0.250 | | | 1.054 (0.634–1.751) | 0.839 | | |
| PT, sec (<12.1 *vs* ≥ 12.1) | 0.794 (0.441–1.430) | 0.442 | | | 0.595 (0.442–0.801) | 0.001 | 0.635 (0.470–0.859) | 0.003 |
| TBil, μmol/l (<17.1 *vs* ≥ 17.1) | 0.818 (0.491–1.363) | 0.441 | | | 0.950 (0.726–1.242) | 0.705 | | |
| ALB, g/l (<35 *vs* ≥ 35) | 1.047 (0.600–1.826) | 0.872 | | | 1.248 (0.944–1.651) | 0.120 | | |
| ALT, U/l (<40 *vs* ≥ 40) | 0.936 (0.551–1.588) | 0.805 | | | 0.823 (0.646–1.071) | 0.153 | | |
| Portal hypertension (absence *vs* presence) | 0.700 (0.370–1.325) | 0.273 | | | 0.674 (0.507–0.897) | 0.007 | 0.729 (0.545–0.976) | 0.034 |
| Tumor size, cm (≤5 *vs* > 5) | 0.420 (0.168–1.053) | 0.064 | | | 0.699 (0.499–0.978) | 0.037 | 0.726 (0.517–1.021) | 0.066 |
| Liver cirrhosis (absence *vs* presence) | 0.769 (0.442–1.340) | 0.355 | | | 0.829 (0.613–1.121) | 0.224 | | |
| Tumor number (<3 *vs* ≥ 3) | 0.529 (0.259–1.081) | 0.079 | | | 0.943 (0.643–1.383) | 0.764 | | |
| BCLC stage (A *vs* B) | 0.614 (0.331–1.123) | 0.081 | | | ND | | | |
| Macrovascular invasion (absence *vs* presence) | ND | | | | 0.648 (0.421–0.996) | 0.048 | 1.375 (0.888–2.127) | 0.153 |
| Extrahepatic metastasis (absence *vs* presence) | ND | | | | 0.531 (0.404–1.589) | 0.480 | | |

Abbreviations: AFP, alpha fetoprotein; ALB, albumin; ALT, alanine aminotransferase; BCLC, Barcelona Clinic Liver Cancer staging system; CI, confidence interval; HR, hazard ratio; ND, not done; PLT, platelet count; PT, prothrombin time; TBil, total bilirubin.

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The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the manuscript. The corresponding authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

## Research background

Many clinicians assign hepatocellular carcinoma (HCC) rupture patients to stage T4 in the TNM system, while some assign them to stage C in the more widely used Barcelona Clinic Liver Cancer (BCLC) system. The appropriateness of such restaging after rupture is unclear, especially for patients who experience rupture in BCLC stage A or B. The present study evaluated the appropriateness of restaging HCC patients to BCLC stage C after they experience tumor rupture in stage A or B.

## Research methods

This retrospectively study performed compared recurrence-free and overall survival between 143 patients who had BCLC stage A or B disease at the time of spontaneous rupture and 449 patients who had BCLC stage C disease without rupture. Analyses were performed on the entire two groups, as well as on subsets from the two groups that were matched to each other 1:2 based on propensity scoring.

## Research results

Overall survival rate was significantly higher among patients with rupture than among those without rupture, while the two groups had similar recurrence-free survival. Most patients with rupture were able to receive interventional and potentially curative treatments after recurrence, whereas most patients in BCLC stage C received interventional or supportive care. Similar results were obtained after propensity score matching.

## Research conclusions

HCC patients who experience spontaneous rupture tumor while in BCLC stage A or B have better prognosis than patients in BCLC stage C. Our results suggest that HCC patients who suffer rupture in BCLC stage A or B should not be assigned to BCLC stage C.

## Research perspectives

abrLarge, multi-center studies are needed to optimize the staging of HCC patients who experience rupture within the BCLC staging system.

## Data availability statement

All available data have been included in the article. More original data can be obtained from the corresponding authors in accordance with privacy/ethical restrictions.

## Ethical declarations

The protocol of this retrospective study conformed to the Declaration of Helsinki (1975) and its amendments and was approved by the Ethics Review Committee of the Guangxi Medical University Cancer Hospital (LW2023005), which waived the requirement for written informed consent because patients or their legal guardians had consented, upon admission, to analysis and publication of anonymized medical data for research purposes.

## CRediT authorship contribution statement

**Su Jia-Yong:** Writing – review & editing, Writing – original draft, Formal analysis. **Wang Hong-Liang:** Formal analysis, Data curation. **Luo Ding-Wen:** Formal analysis. **Chen Qing-Qing:** Data curation. **Cai Yu-Tong:** Data curation. **Tan Jun-Shao:** Formal analysis. **Chen Mei:** Data curation. **Tian Wei:** Data curation. **Xie Rong-Wei:** Visualization. **Ma Liang:** Conceptualization. **Guo Ping-Ping:** Writing – review & editing. **Zhong Jian-Hong:** Conceptualization, Writing – review & editing.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e27355.

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