



OPEN Stereotactic body radiotherapy versus laparoscopic liver resection for single hepatocellular carcinoma ≤ 5 cm: a retrospective, multicenter, cohort study

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To compare the efficacy of stereotactic body radiotherapy (SBRT) and laparoscopic liver resection (LLR) for patients with single hepatocellular carcinoma (HCC) ≤ 5 cm. A retrospective analysis was conducted on a cohort of patients with HCC who underwent either LLR or SBRT at our centers. Recurrence-free survival (RFS) and overall survival (OS) were estimated using the Kaplan-Meier method and compared between groups using the log-rank test. To reduce selection bias, propensity score matching (PSM) was applied. Subgroup analyses were also performed to explore outcomes across different clinical and tumor-related characteristics. This retrospective cohort study included 383 patients from four hospitals between January 2017 and December 2019, with 268 patients in the LLR group and 115 in the SBRT group. After PSM adjustment, 98 patients were selected from each group for further analysis. The 1-, 3-, and 5-year OS rates were 94.9%, 88.8%, and 85.7% in the LLR group and 94.9%, 74.5%, and 67.3% in the SBRT group, respectively ($p = 0.005$). The 1-, 3-, and 5-year RFS rates were 86.7%, 71.4%, and 70.4% in the LLR group and 83.7%, 61.2%, and 53.1% in the SBRT group, respectively ($p = 0.011$). LLR provided better OS and RFS than SBRT. However, SBRT showed comparable OS and RFS outcomes with LLR for tumors ≤ 3 cm ($p = 0.158$; $p = 0.418$), and perivascular tumors ($p = 0.082$; $p = 0.166$). LLR is the first choice for treating single HCC ≤ 5 cm, while SBRT may be a favorable alternative for small and perivascular lesions.

Keywords Hepatocellular carcinoma, Stereotactic body radiotherapy, Laparoscopic liver resection, Treatment outcome

Hepatocellular carcinoma (HCC) ranks as the sixth most common malignant tumor and the third leading cause of cancer-related mortality¹. For patients with early-stage HCC, hepatectomy is currently the primary curative treatment². In the past decade, laparoscopic liver resection (LLR) has matured as a safe and effective alternative to traditional open liver resection (OLR)^{3–6}. As a result, LLR has increasingly become the preferred surgical approach in clinical practice. However, it is noteworthy that over 75% of HCC patients are ineligible for surgical intervention^{1,2}.

Percutaneous ablation (PA) has firmly established itself as the standard therapeutic approach for achieving curative intent in small HCC (≤ 3 cm) among patients who are not suitable for surgical intervention.

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Nevertheless, the application scope of PA is significantly limited by various factors, including the location and diameter of the tumor^{7–9}. Stereotactic body radiotherapy (SBRT) has emerged as a treatment option for HCC, yielding promising results. Usually, HCC patients are treated in line with the BCLC strategy, and per the most updated guideline, SBRT has a limited role for now for single HCC¹⁰. Numerous studies have demonstrated its effectiveness in reducing radiation-induced liver disease (RILD), enhancing local control (LC) rates, and improving survival rates^{11–14}.

Several studies have reported on the effectiveness of SBRT versus liver resection (LR) for small HCC, but results are conflicting and limited. Small sample sizes and the lack of differentiation between open and laparoscopic procedures may explain these discrepancies^{15–18}. However, after reviewing the available publications, we observed that few studies compared the long-term effects of LLR and SBRT. Given the significance of this comparison and the potential impact on clinical decision-making, this study aimed to conduct a large-scale multicenter investigation, comparing the clinical outcomes of LLR and SBRT for HCC no more than 5 cm.

Results

Patient characteristics

Between Jan 2017 and Dec 2019, a total of 383 eligible patients were identified. Of these, 268 were included in the LLR group, while 115 patients were assigned to the SBRT group. The study profile is illustrated in Fig. 1. Before PSM, the proportions of patients with hypertension, $WBC < 4 \times 10^9 / L$, PLT counts $\leq 100 \times 10^9 / L$, $TBIL > 17.1$, $PT > 13$, and $AFP > 400$ in the LLR group were lower compared to the SBRT group. After PSM, each group comprised 98 patients. No statistically significant differences were observed in patient characteristics between the two groups. The general characteristics of the patient cohort are presented in Table 1.

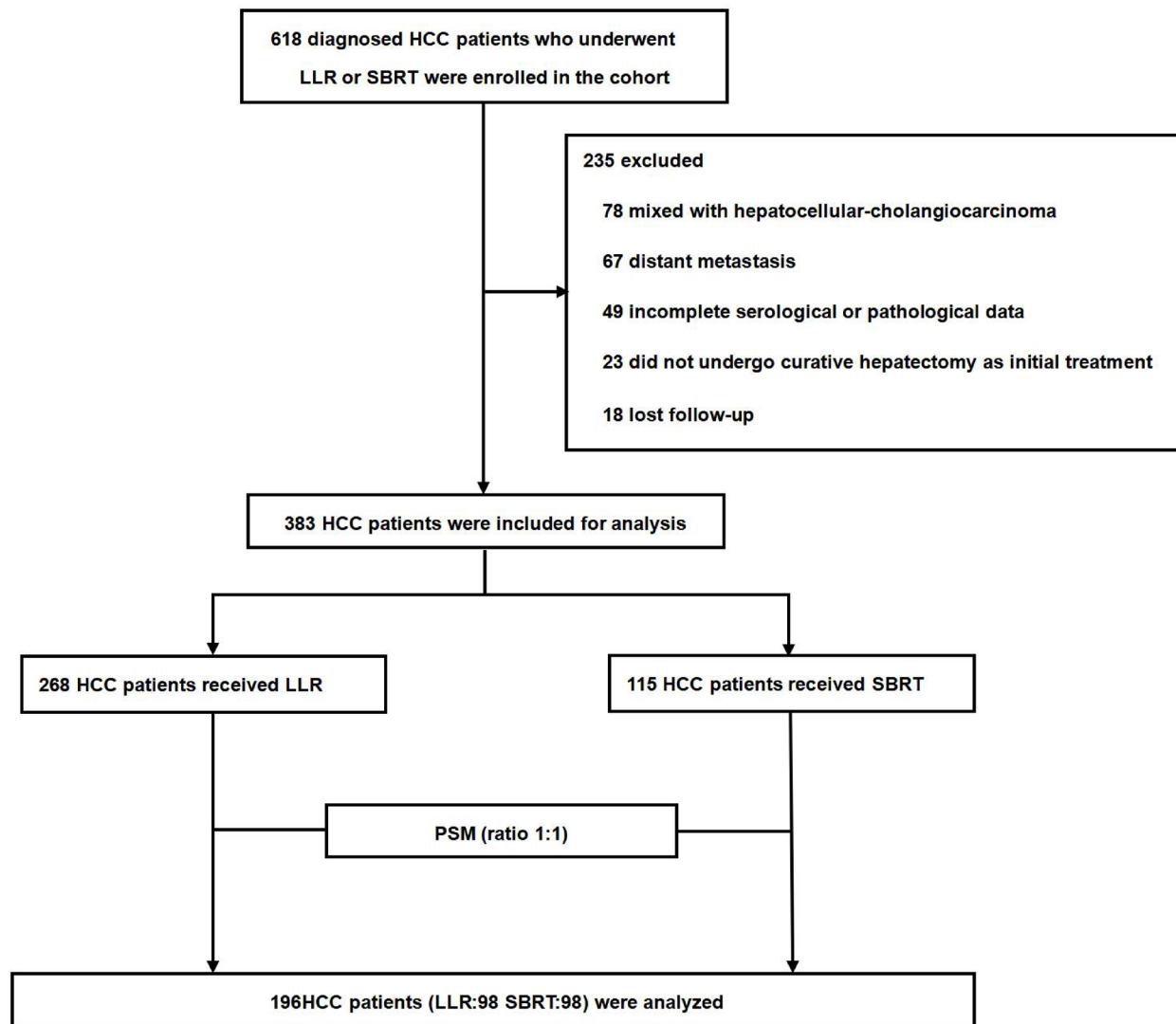


Fig. 1. The flow chart in the study. Abbreviations: HCC, hepatocellular carcinoma. LLR, laparoscopic liver resection. SBRT, stereotactic body radiotherapy. PSM, propensity score matching.

Characteristics	Before PSM			After PSM		
	LLR	SBRT	<i>p</i> value	LLR	SBRT	<i>p</i> value
	(<i>n</i> = 268)	(<i>n</i> = 115)		(<i>n</i> = 98)	(<i>n</i> = 98)	
Age > 60(%)	134(50.0%)	70(60.9%)	0.051	56(57.1%)	59(60.2%)	0.663
Sex, male(%)	221(71.3%)	89(77.4%)	0.247	75(76.5%)	76(77.6%)	0.865
Hypertension(%)	66(24.6%)	47(40.9%)	0.001	32(32.7%)	39(39.8%)	0.298
Diabetes(%)	73(27.2%)	22(19.1%)	0.092	23(23.5%)	21(21.4%)	0.732
HBV infection(%)	221(82.5%)	85(73.9%)	0.056	78(79.6%)	73(74.5%)	0.396
Child-Pugh class						
A	245(91.4%)	102(88.7%)	0.403	91(92.9%)	90(91.8%)	0.788
B	23(8.6%)	13(11.3%)		7(7.1%)	8(8.2%)	
WBC($\times 10^9/L$)						
≤ 4	33(12.3%)	49(42.6%)	< 0.001	28(28.6%)	33(33.7%)	0.440
> 4	235(87.7%)	66(57.4%)		70(71.4%)	65(66.3%)	
Platelet count($\times 10^9/L$)						
≤ 100	42(15.7%)	46(40.0%)	< 0.001	30(30.6%)	33(33.7%)	0.646
> 100	226(84.3%)	69(60.0%)		68(69.4%)	65(66.3%)	
TBIL($\mu\text{mol/L}$)						
≤ 17.1	245(91.4%)	92(80.0%)	0.002	86(87.8%)	83(84.7%)	0.534
> 17.1	23(8.6%)	23(20.0%)		12(12.2%)	15(15.3%)	
ALB (g/L)						
≤ 35	82(30.6%)	25(21.7%)	0.077	25(25.5%)	22(22.4%)	0.616
> 35	186(69.4%)	90(78.3%)		73(74.5%)	76(77.6%)	
PT (s)						
≤ 13	249(92.9%)	89(77.4%)	< 0.001	85(86.7%)	86(87.8%)	0.830
> 13	19(7.1%)	26(22.6%)		13(13.3%)	12(12.2%)	
AFP (ng/mL)						
≤ 400	242(90.3%)	93(80.9%)	0.011	88(89.8%)	86(87.8%)	0.651
> 400	26(9.7%)	22(19.1%)		10(10.2%)	12(12.2%)	
ECOG						
0	74(27.6%)	32(27.8%)	0.966	33(33.7%)	30(30.6%)	0.646
1–2	194(72.4%)	83(72.2%)		65(66.3%)	68(69.4%)	
Tumor diameter						
≤ 3	69(25.7%)	30(26.1%)	0.944	30(30.6%)	28(28.6%)	0.754
3–5	199(74.3%)	85(73.9%)		68(69.4%)	70(71.4%)	
Tumor location						
Perivascular	112(41.8%)	60(52.2%)	0.061	42(42.9%)	51(52.0%)	0.198
Other	156(58.2%)	55(47.8%)		56(57.1%)	47(48.0%)	

Table 1. Baseline characteristics between LLR and SBRT groups before PSM and after PSM. PSM, propensity score matching; LLR, laparoscopic liver resection; SBRT, stereotactic body radiation therapy; HBV, hepatitis B virus; ECOG, Eastern Cooperative Oncology Group; AFP, alpha-fetoprotein.

Survival analysis before and after PSM

Before PSM, the 1-, 3-, and 5-year OS rates were 96.6%, 89.4%, and 87.7% in the LLR group and 94.8%, 73.0%, and 66.1% in the SBRT group, respectively (Fig. 2A, $p < 0.001$). The 1-, 3-, and 5-year RFS rates were 89.9%, 76.1%, and 75.4% in the LLR group and 85.2%, 61.7%, and 54.8% in the SBRT group, respectively (Fig. 2B, $p < 0.001$).

After PSM, the 1-, 3-, and 5-year OS rates were 94.9%, 88.8%, and 85.7% in the LLR group and 94.9%, 74.5%, and 67.3% in the SBRT group, respectively (Fig. 2C, $p = 0.005$). The 1-, 3-, and 5-year RFS rates were 86.7%, 71.4%, and 70.4% in the LLR group and 83.7%, 61.2%, and 53.1% in the SBRT group, respectively (Fig. 2D, $p = 0.011$).

Subgroup analysis on the survival of HCC after PSM

In the subgroup of HCC ≤ 3 cm, there were no significant differences in OS and RFS between LLR and SBRT ($p = 0.158$; $p = 0.418$) (Fig. 3A&B). However, in the subgroup of HCC 3–5 cm, LLR provided significantly better OS and RFS than SBRT ($p = 0.012$, $p = 0.01$) (Fig. 3C&D).

In addition, in the subgroup of HCC with perivascular tumors, there were no significant differences in OS and RFS between LLR and SBRT ($p = 0.082$; $p = 0.166$) (Fig. 4A&B). But, in the subgroup of HCC with non-

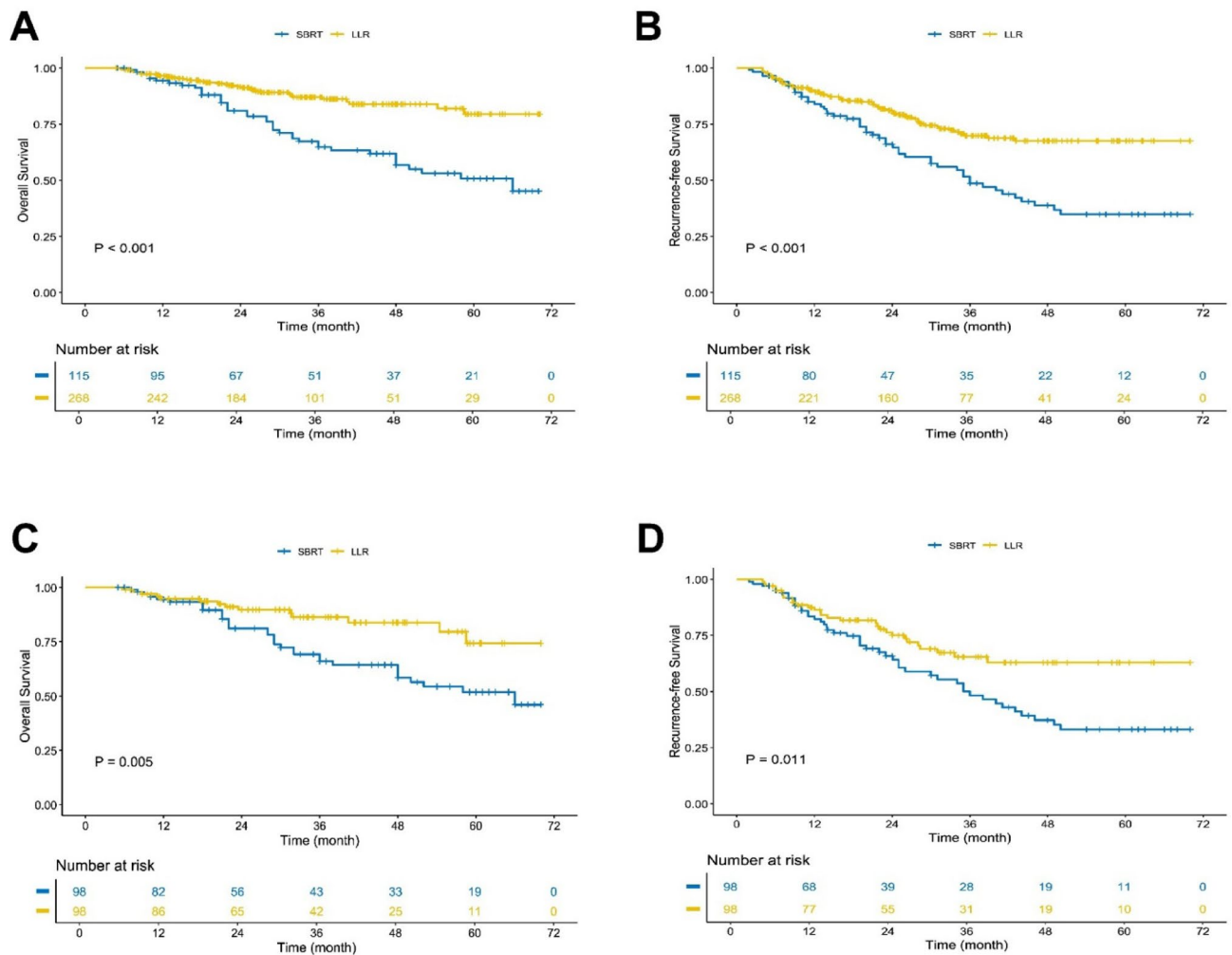


Fig. 2. Comparison of prognosis between LLR and SBRT Groups before PSM and after PSM. (A) OS before PSM; (B) RFS before PSM; (C) OS after PSM; (D) RFS after PSM. Abbreviations: OS, overall survival; RFS, recurrence-free survival; LLR, laparoscopic liver resection; SBRT, stereotactic body radiotherapy; PSM, propensity score matching.

perivascular tumors, LLR provided significantly better OS than SBRT ($p=0.041$). Although the RFS of LLR showed some advantage over SBRT, the difference was not statistically significant ($p=0.066$) (Fig. 4C&D).

Then, we categorized tumors into two anatomical subgroups: anteroinfero-lateral portion of the liver (segments 2, 3, 4b, 5, and 6) and postero-superior portion of the liver (segments 1, 7, 8, and 4a). For tumors located in the postero-superior portion, there was no statistically significant difference in OS or RFS between the LLR and SBRT groups ($p=0.185$ and $p=0.428$, respectively). For tumors located in the anteroinfero-lateral portion, the LLR group demonstrated a significantly better OS and RFS compared to SBRT ($p=0.015$ and $p=0.013$, respectively) (Fig. 5).

Within the HBV (hepatitis B virus) subgroup, LLR was associated with significantly better OS compared to SBRT ($p=0.020$), and showed a trend toward improved RFS, although the difference did not reach statistical significance ($p=0.084$). In contrast, RFS and OS appeared generally comparable between LLR and SBRT within the HCV (hepatitis C virus), ALD (alcohol-related liver disease), and NASH (non-alcoholic steatohepatitis) subgroups (Figure S1).

Univariate and multivariable analyses of predictors of OS and RFS

After PSM, AFP < 400 and LLR were independent prognostic factors in improving OS, while non-perivascular tumor location, LLR, and PLT > 100 were independent prognostic factors in improving RFS in the Cox proportional hazard model (Table 2). We found that tumor diameter was not the influencing factor of OS and RFS.

Toxicity and complications

Among the 268 patients undergoing LLR, complications occurred in 22 patients, resulting in a complication rate of 8.2% (22/268). The specific complications were as follow: 7 patients experienced Grade 1 complications

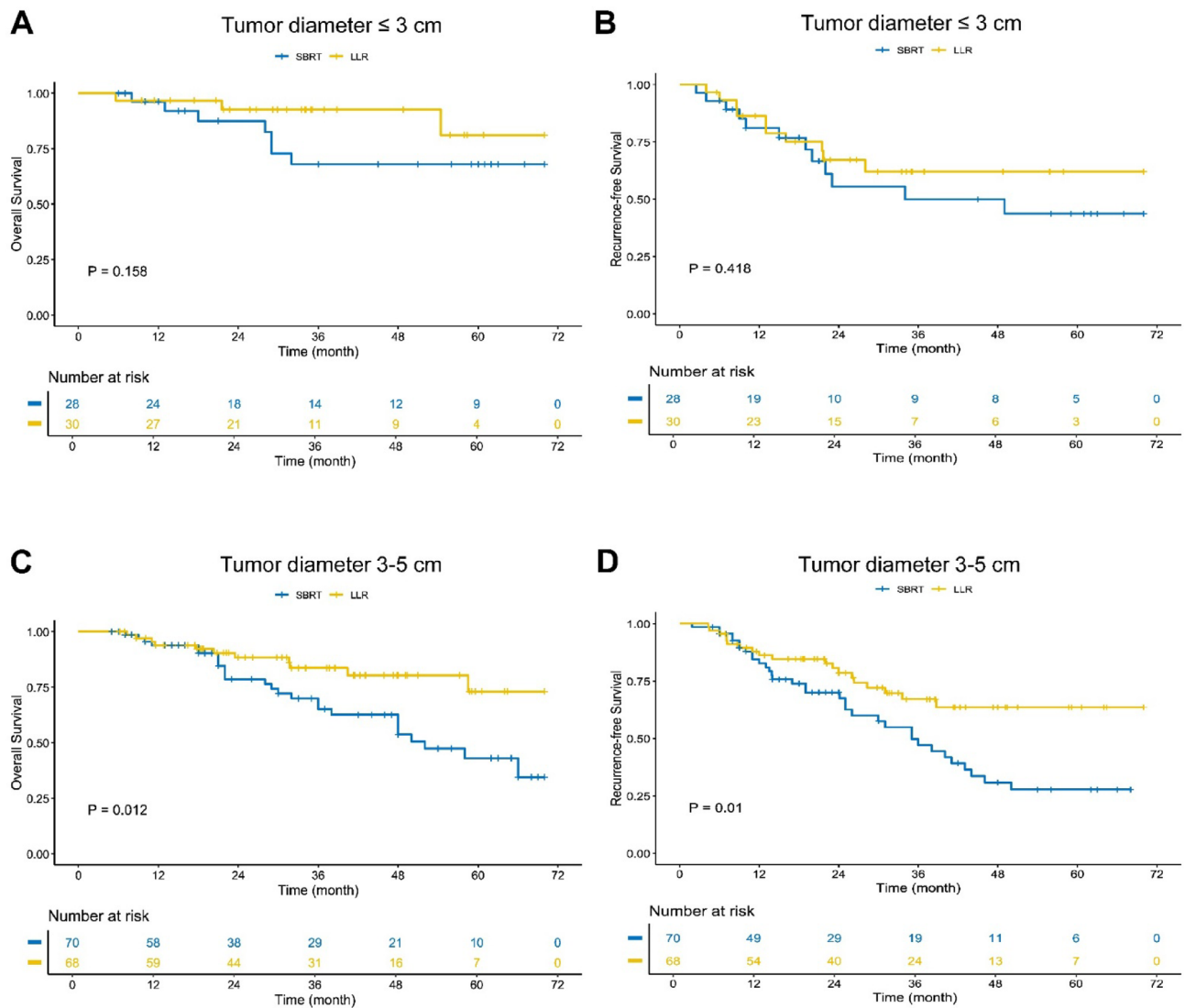


Fig. 3. Comparison of prognosis between LLR and SBRT Groups in tumor diameter subgroups after PSM. (A) OS in the ≤ 3 cm tumor diameter subgroup; (B) RFS in the ≤ 3 cm tumor diameter subgroup; (C) OS in the 3–5 cm tumor diameter subgroup; (D) RFS in the 3–5 cm tumor diameter subgroup. Abbreviations: OS, overall survival; RFS, recurrence-free survival; LLR, laparoscopic liver resection. SBRT, stereotactic body radiotherapy. PSM, propensity score matching.

(including 6 cases of fever and 1 case of wound infection); 15 patients experienced Grade 2 complications (including 9 cases of ascites and 6 cases of minor bile leakage); 2 patients experienced Grade 3 complications (bile leakage requiring percutaneous drainage).

All 115 patients in the SBRT group completed the radiation therapy plan. Complications occurred in 7 patients, resulting in a complication rate of 6.1% (7/115). Grade 1 complications, including 5 cases of vomiting and 2 cases of anorexia. Grade 2 complications include 1 case of abdominal pain and 2 cases of ALT/AST elevation. No toxicities of Grade ≥ 3 were observed. All 7 patients recovered after drug treatment.

Therefore, no patients died from the toxicities or complications of LLR or SBRT (Table 3).

Discussion

To the best of our knowledge, this is the first study analyzing the long-term efficacy of SBRT compared to LLR for single HCC ≤ 5 cm. The present research indicates that LLR significantly outperformed SBRT in terms of OS and RFS, both before and after PSM. However, for small or perivascular tumors, LLR may lose its superiority, and the outcomes of both treatments were comparable. In terms of treatment-related side effects, LLR was associated with more adverse reactions compared to SBRT, which has been shown to be safe and well-tolerated in treating patients with HCC.

Previous studies have identified tumor diameter as an independent prognostic factor for HCC^{19–21}. However, in our study focusing on HCC with a diameter ≤ 5 cm, we found that tumor diameter did not influence RFS and OS outcomes between LLR and SBRT. In the HCC ≤ 3 cm subgroup, we found that LLR and SBRT showed

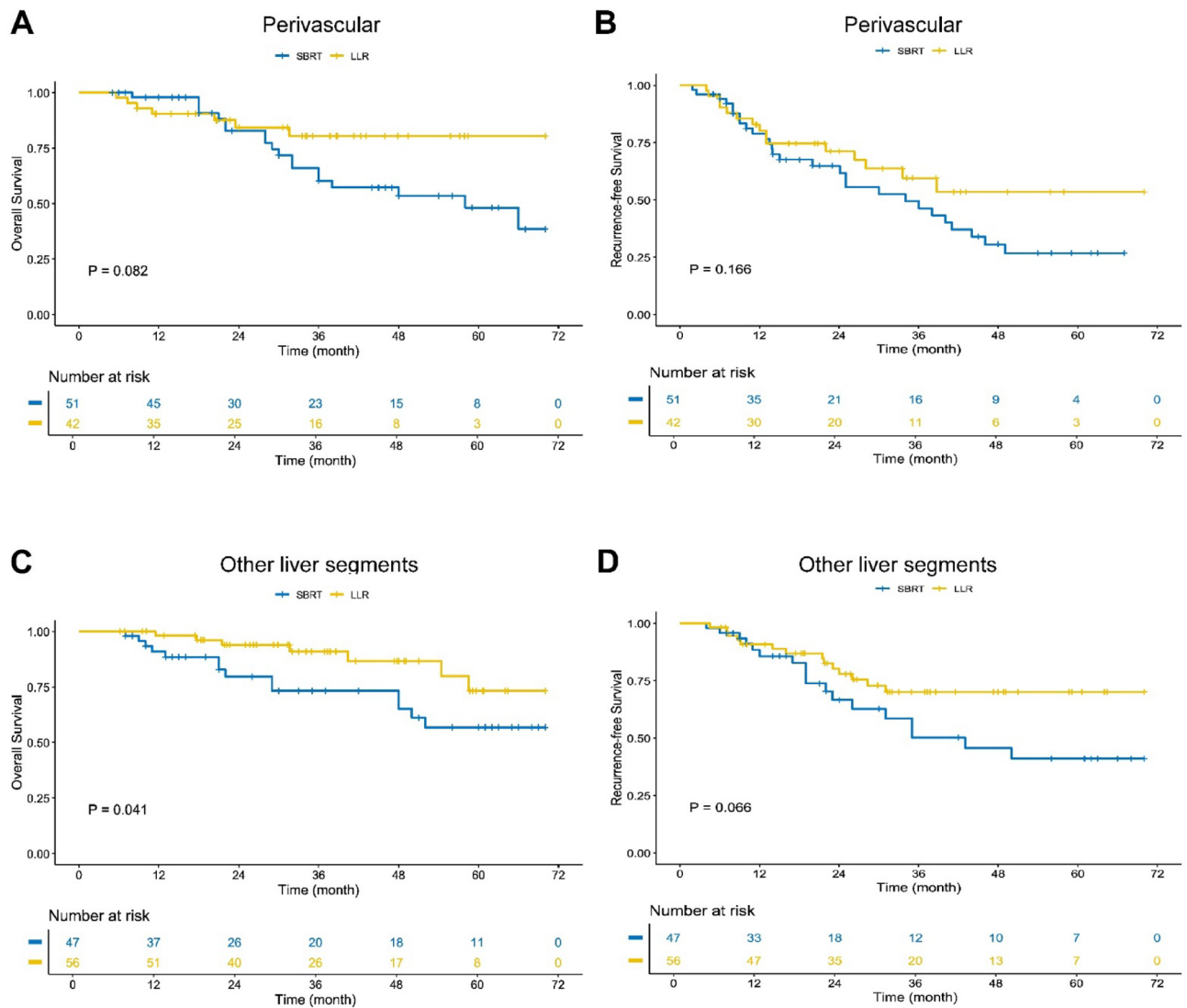


Fig. 4. Comparison of prognosis between LLR and SBRT Groups in tumor location subgroups based on proximity to vascular structures after PSM. **(A)** OS in the perivascular tumor subgroup; **(B)** RFS in the perivascular tumor subgroup; **(C)** OS in the subgroup with tumor located in other liver segments; **(D)** RFS in the subgroup with tumor located in other liver segments. Abbreviations: OS, overall survival; RFS, recurrence-free survival; LLR, laparoscopic liver resection. SBRT, stereotactic body radiotherapy. PSM, propensity score matching.

no significant differences in OS and RFS, which was consistent with previous research¹⁷. However, in the 3–5 cm subgroup, LLR demonstrated significantly higher OS and RFS compared to SBRT. A meta-analysis found that the OS of SBRT was superior to HCC lesions ≤ 3 cm compared to > 3 cm ($p = 0.015$)¹⁴. However, this study included patients with HCC lesions larger than 5 cm, which may have confounded the results and contributed to the observed difference in outcomes. Previous studies comparing LR and SBRT for single (≤ 5 cm) HCC have not analyzed tumor location in detail^{16–18}. Perivascular HCC refers to neoplastic tissue that is either closely adhered to or located within 1 cm of major intrahepatic vessels and ducts²². This anatomical peculiarity complicates the achievement of adequate surgical margins, which are imperative for curative resection and must be maintained at a distance of ≥ 1 cm from the tumor edge. A prospective study has demonstrated that preoperative radiotherapy markedly enhances OS in perivascular HCC²². In the present study, no significant differences in OS and RFS were observed between LLR and SBRT in treating perivascular HCC. Conversely, for tumors located in non-perivascular regions, LLR demonstrated improved OS and comparable RFS when compared to SBRT. Previous findings suggest that the therapeutic efficacy of SBRT appears to be independent of tumor proximity to major vessels¹⁴. In contrast, for LLR, tumors situated away from vascular structures (non-perivascular) are more likely to allow for wider surgical margins, potentially contributing to better oncologic outcomes. This discrepancy in resection margin adequacy may partly explain the observed differences in treatment efficacy between LLR and SBRT. In perivascular regions, where achieving sufficient margins is technically challenging due to the proximity to vital vascular structures, LLR may be less advantageous. Meanwhile, SBRT, which relies on precise radiation

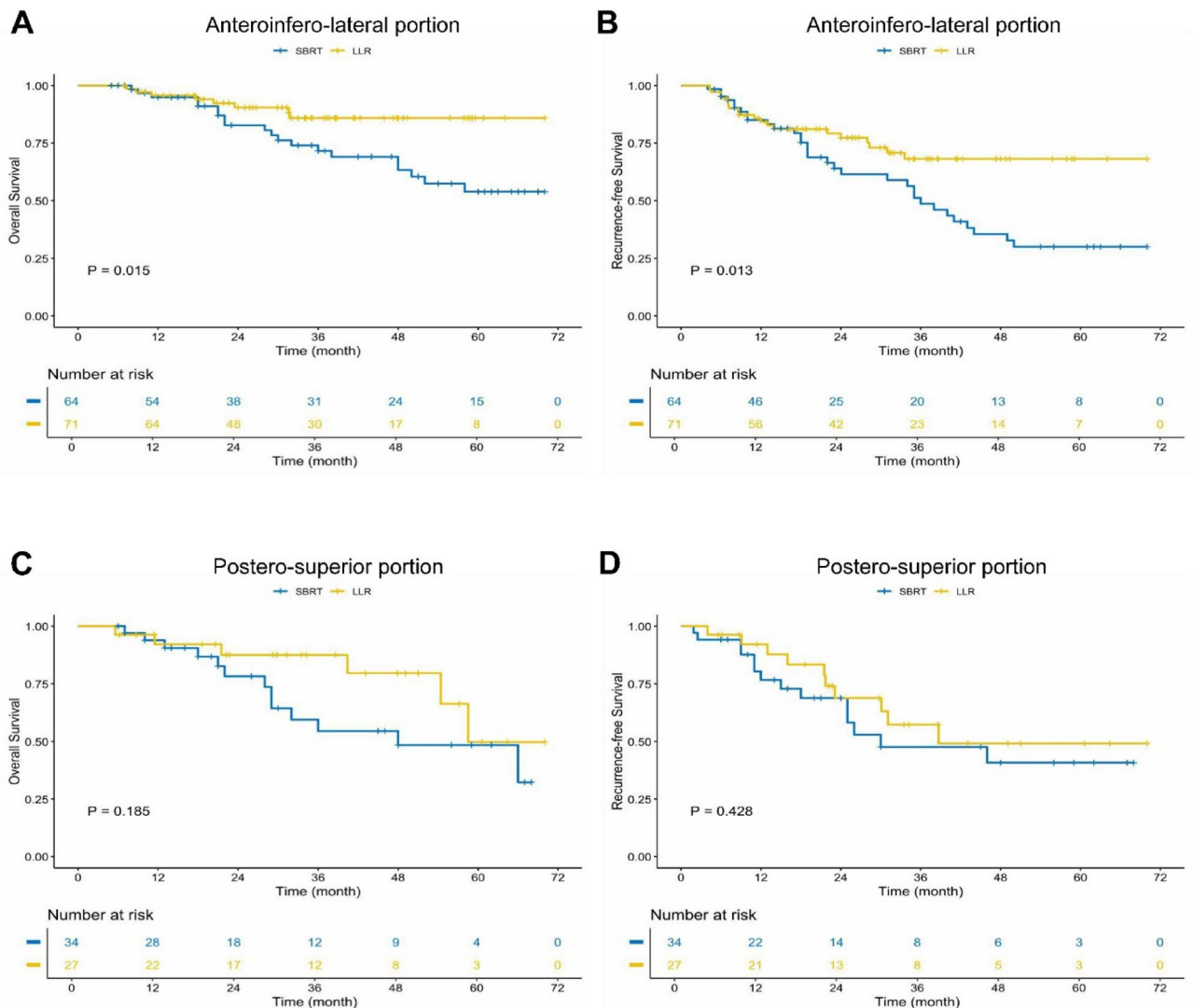


Fig. 5. Comparison of prognosis between LLR or SBRT Groups in tumor location subgroups after PSM, according to technical difficulty of LLR. **(A)** OS in the anteroinfero-lateral portion tumor subgroup; **(B)** RFS in the anteroinfero-lateral portion tumor subgroup; **(C)** OS in the postero-superior portion tumor subgroup; **(D)** RFS in the postero-superior portion tumor subgroup. Abbreviations: OS, overall survival; RFS, recurrence-free survival; LLR, laparoscopic liver resection. SBRT, stereotactic body radiotherapy. PSM, propensity score matching.

targeting rather than physical excision, is less affected by tumor location relative to vascular anatomy. These differences highlight the importance of individualized treatment planning based on tumor characteristics and anatomical considerations.

Based on the IWATE criteria²³, tumors located in the anteroinfero-lateral segments of the liver (segments 2, 3, 4b, 5, and 6) are generally considered more suitable for LLR, while those in the postero-superior segments (segments 1, 7, 8, and 4a) pose greater challenges^{2,4}. This difficulty is mainly attributed to the limited accessibility of these regions through standard trocar placements and the restricted flexibility of laparoscopic instruments, which may compromise the ability to achieve adequate resection margins. In the present study, LLR was associated with significantly better OS and RFS than SBRT for tumors located in the anteroinfero-lateral segments. However, no significant differences were observed in tumors located in the postero-superior segments. Based on these findings, we suggest that while LLR may offer superior outcomes for HCCs ≤ 5 cm located in accessible regions of the liver, SBRT remains an effective alternative treatment option for tumors located in anatomically challenging areas such as the postero-superior segments or those in perivascular regions.

In terms of perioperative outcomes, the mean hospital stay was significantly shorter in the SBRT group (5.6 days) compared to the LLR group (10.5 days). The complication rate in the LLR group was 8.2%, while that of the SBRT group was 6.1%. These findings suggest that SBRT offers favorable short-term safety profiles and less invasiveness compared to LLR.

Characteristic	HR Comparison	OS						RFS					
		Univariate analysis			Multivariate analysis			Univariate analysis			Multivariate analysis		
		HR	95% CI	p value	HR	95% CI	p value	HR	95% CI	p value	HR	95% CI	p value
Age	>60 vs. ≤60,year	1.60	0.87–2.96	0.133				1.79	1.09–2.93	0.021	1.63	1.00–2.67	0.052
Sex	Female vs. male	1.60	0.75–3.43	0.228				1.55	0.86–2.77	0.144			
Hypertension(%)	Yes vs. no	1.06	0.59–1.90	0.859				0.84	0.52–1.36	0.484			
Diabetes(%)	Yes vs. no	1.46	0.76–2.82	0.262				1.19	0.70–2.02	0.525			
HBV infection	Yes vs. no	0.64	0.34–1.20	0.167				0.91	0.54–1.55	0.74			
Child–Pugh class	A or B	1.22	0.44–3.41	0.705				1.34	0.62–2.98	0.461			
WBC	>4 vs. ≤4,×10 ⁹ /L	0.63	0.34–1.14	0.127				0.83	0.51–1.35	0.456			
Platelet count	>100 vs. ≤100,×10 ⁹ /L	0.49	0.27–0.89	0.018	0.64	0.35–1.16	0.142	0.46	0.29–0.73	<0.001	0.52	0.33–0.83	0.006
TBIL	>17.1 vs. ≤17.1,μmol/L	1.81	0.88–3.76	0.110				1.17	0.59–2.14	0.715			
ALB	>35 vs. ≤35,g/L	1.35	0.71–2.57	0.355				1.01	0.59–1.73	0.983			
PT	>13 vs. ≤13,s	0.91	0.39–2.16	0.836				0.90	0.45–1.81	0.765			
AFP	>400 vs. ≤400,ng/ml	0.33	0.14–0.65	0.001	0.39	0.20–0.79	0.009	0.48	0.27–0.88	0.017	0.55	0.29–1.03	0.066
ECOG	0 vs. 1–2	1.75	0.89–3.44	0.107				1.05	0.54–1.72	0.843			
Tumor diameter	≤3 vs. 3–5,cm	1.77	0.88–3.57	0.109				0.99	0.60–1.92	0.953			
Tumor location	Perivascular vs. other	1.48	0.83–2.63	0.184				1.66	1.05–2.62	0.030	1.65	1.02–2.65	0.040
Treatment methods	LLR vs. SBRT	2.38	1.27–4.46	0.007	2.21	1.18–4.16	0.014	1.82	1.14–2.56	0.012	1.62	1.01–2.59	0.045

Table 2. Univariate and multivariate Cox regression analysis of factors associated with OS and RFS after PSM. HCC, hepatocellular carcinoma; OS, overall survival; RFS, recurrence-free survival; PSM, propensity score matching; LLR, laparoscopic liver resection; SBRT, stereotactic body radiation therapy; HBV, hepatitis B virus; ECOG, Eastern Cooperative Oncology Group; AFP, alpha-fetoprotein.

Characteristics	LLR (n = 268)	SBRT (n = 115)
Total n (%)	22 (8.2%)	7 (6.1%)
Grade 1	fever, n = 6 wound infection, n = 1	vomiting, n = 5 anorexia, n = 2
Grade 2	ascites, n = 9 minor bile leakage, n = 6	abdominal pain, n = 1 ALT/AST elevation, n = 2
Grade 3	bile leakage, n = 2	0

Table 3. Treatment-related toxicity and complications in LLR and SBRT groups. LLR, laparoscopic liver resection; SBRT, stereotactic body radiation therapy.

The present study has several limitations that warrant consideration. Firstly, the study design was retrospective, which introduces the potential for selection bias. Although PSM was utilized to mitigate the effects of baseline characteristic imbalances, the results should be further validated through well-designed prospective studies. Secondly, all study participants were from China, with approximately 80% of patients having concurrent HBV infection. We observed that LLR provides superior OS and comparable RFS to SBRT in the HBV-related subgroup. However, no significant differences were found between LLR and SBRT in patients with HCV-, ALD-, or NASH-related HCC. Given the small sample sizes in these subgroups, we believe these findings may be due to limited statistical power. Therefore, future multi-center studies including patients from diverse geographic and etiological backgrounds are planned to improve the external validity of our results. Lastly, our study exclusively included patients with early-stage solitary HCC and a diameter ≤ 5 cm. Therefore, the efficacy of LLR and SBRT for treating early-stage multifocal or larger diameter (≥ 5 cm) HCC remains unknown. Future research should aim to address these limitations to provide a more comprehensive understanding of the treatment outcomes across different patient populations and disease stages.

In conclusion, our study indicates that LLR provides better RFS and OS than SBRT in HCC patients with a single nodule ≤ 5 cm. However, for patients with solitary HCC ≤ 3 cm or located near major blood vessels, SBRT may be considered an effective and viable alternative treatment option.

Methods

Ethical considerations

The study was approved by our institution's institutional ethics committee (No.:KXKS2025011). All methods were performed in accordance with the relevant guidelines and regulations, including the Declaration of Helsinki. Due to the study's retrospective nature, the institutional ethics committee waived the need for written informed consent.

Patients

Eligibility criteria for inclusion in the study were as follows: (1) Diagnosis of HCC confirmed by a surgeon and/or radiologist via imaging studies, laboratory tests, or pathological examination; (2) presence of a single tumor with a maximum lesion diameter of 5 cm or less; (3) an Eastern Cooperative Oncology Group performance status (ECOG PS) score ranging from 0 to 2; (4) no history of prior therapy; (5) absence of portal vein tumor thrombosis and distant metastases; and (6) classification in Child–Pugh Class A or B (CP-A or CP-B).

The treatment plan was established by a multidisciplinary team (MDT), and patient preferences were also considered in determining the appropriate treatment modality. For patients with well-preserved liver function, laparoscopic liver resection was considered the primary option. If there were surgical contraindications such as thrombocytopenia, ascites, or inadequate coagulation, ablation was considered an alternative. When ablation posed significant risks (e.g., to the hepatic vasculature, main bile duct, or intestinal loop) or achieving an adequate resection or ablation margin was challenging, SBRT was contemplated.

The treatment procedure of SBRT group

Before performing SBRT with the G4 CyberKnife system (Accuracy, USA), each patient had four to six fiducial markers implanted. Following the determination of the treatment site through CT simulation, an oncologist delineated the gross tumor volume (GTV) and identified organs at risk (OARs), which included the stomach, liver (excluding tumorous areas), esophagus, duodenum, kidneys, spinal cord, and bowel. A planning target volume (PTV) was then created by expanding the GTV by 3–5 mm, ensuring that the OARs were avoided. Prescribed doses ranged from 48 to 54 Gy across 5–8 fractions, with the isodose curve covering 100% of the GTV. Treatment planning utilized the CyberKnife Multiplan system (version 4.0.2). The tolerance doses for the OARs were guided by the AAPM TG-101 report²⁴.

The treatment procedure of LLR group

LLR was performed following established techniques as described in the literature²⁵, with all procedures involving anatomical liver resection.

Toxicity reaction evaluation

Treatment-related toxicities were evaluated and graded based on the Common Terminology Criteria for Adverse Events (CTCAE) version 4.03 for SBRT. Additionally, post-surgical complications were assessed and classified according to the Clavien–Dindo classification system.

Follow-up study

Each patient was consistently monitored every 2–3 months during the initial years, and subsequently every 3 months until the end of this study or death, depending on which occurred first. The follow-up assessments comprised biochemical evaluations, such as liver function tests and serum alpha-fetoprotein levels, as well as imaging studies, including abdominal contrast-enhanced CT or MRI scans.

Definitions and evaluation of data

The primary endpoint was recurrence-free survival (RFS). The second endpoint was overall survival (OS). RFS was calculated beginning at the onset of LLR/SBRT until tumor recurrence. OS was assessed starting from the initiation of LLR/SBRT until the final follow-up appointment or mortality. Perivascular HCC refers to liver malignancies situated in distinct segments, including S1, S4, S5, and S8, where the neoplastic tissue is either intimately adhered to or situated within a proximity of 1 centimeter to major intrahepatic vessels and ducts²².

Statistical analysis

The utilization of propensity score matching (PSM) analysis aimed to decrease the impact of selection biases and potential confounding variables. The covariates included in the propensity score calculation were: age, white blood cell (WBC) count, platelet count (PLT), total bilirubin (TBIL), prothrombin time (PT), alpha-fetoprotein (AFP) level, tumor diameter, tumor location, and performance status. Following the PSM evaluation, instances were paired through 1:1 nearest neighbor matching with a caliper distance of 0.02 standard deviations of the logit of the PS. Cases that did not match were eliminated. OS and RFS were computed utilizing the Kaplan–Meier technique. The comparison between LLR and SBRT was conducted via the log-rank test. Univariate and multivariable hazard ratios were assessed employing the Cox proportional hazard model. The baseline variables of the two groups were compared using the χ^2 test or Fisher's exact test. A $p < 0.05$ was considered statistically significant. All statistical computations were carried out using R version 4.0.2 (Stanford University, CA, USA) and SPSS version 27.0 (IBM Corp., Armonk, NY, USA).

Data availability

Research data are stored in an institutional repository and will be shared upon request to the corresponding author.

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Declarations

Competing interests

The authors declare no competing interests.

Additional information

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