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Short- and long-term outcomes after robotic and open liver resection for elderly patients with hepatocellular carcinoma: a propensity score-matched study

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Abstract

Background Robotic liver resection (RLR) has increasingly been accepted as it has overcome some of the limitations of open liver resection (OLR), while the outcomes following RLR in elderly patients with hepatocellular carcinoma (HCC) are still uncertain. This study aimed to evaluate the short and long-term outcomes of RLR vs. OLR in elderly HCC patients.
Methods Perioperative data of elderly patients (≥ 65 years) with HCC who underwent RLR or OLR between January 2010 and December 2020 were retrospectively analyzed. A 1:2 propensity score-matched (PSM) analysis was performed to minimize the differences between RLR and OLR groups. Univariable and multivariable Cox regression analyses were used to identify independent prognosis factors for overall survival (OS) and recurrence-free survival (RFS) of these patients.
Results Of the 427 elderly HCC patients included in this study, 113 underwent RLR and 314 underwent OLR. After the 1:2 PSM, there were 100 and 178 patients in the RLR and the OLR groups, respectively. The RLR group had a less estimated blood loss (EBL), a shorter postoperative length of stay (LOS), and a lower complications rate (all $P < 0.05$), compared with the OLR group before and after PSM. Univariable and multivariable analyses showed that advanced age and surgical approaches were not independent risk factors for long-term prognosis. The two groups of elderly patients who were performed RLR or OLR had similar OS (median OS 52.8 vs. 57.6 months) and RFS (median RFS 20.4 vs. 24.6 months) rates after PSM.
Conclusions RLR was comparable to OLR in feasibility and safety. For elderly patients with HCC, RLR resulted in similar oncologic and survival outcomes as OLR.

Keywords Robotic liver resection · Open liver resection · Hepatocellular Carcinoma · Elderly patients · Surgical outcomes

Hepatocellular carcinoma (HCC) is the fifth most common cancer and the third most common global cause of cancer-related deaths [1]. Hepatitis B virus (HBV) is closely associated with the development of HCC in the endemic Asia–Pacific regions [2]. 50 to 55% of HCC cases are attributed to chronic hepatitis B virus infection worldwide, and up to 80% in China [3]. With an increase in life expectancy in many countries, the rapid growth in the elderly population has become an important issue worldwide, especially in China. The cut-off age for elderly HCC patients varies widely in the literature from 65 to 80 years [4]. Studies have indicated that the average age at onset of HBV-related HCC is 10 years younger than that of hepatitis C virus (HCV)-related HCC [5]; the mean age at HCC diagnosis is 55–59 years old in China, while the mean age at HCC diagnosis is 63–65 years old in Europe and North America [6]. Thus, combined with previous relevant studies, 65 years is a more appropriate cut-off for elderly patients in China [4, 7, 8].

Liver resection (LR) is the first-line curative-intent therapy for HCC to date. However, elderly HCC patients with comorbidity may increase the surgical risk and cause higher morbidity and mortality [4, 9]. These age-related contraindications have prevented elderly HCC patients

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from receiving optimal surgical treatment. With the advances in surgical techniques and perioperative management in liver surgery during the last few decades, LR in elderly HCC patients has become safer [7, 10]. The rapid development of robotic surgical systems has changed the landscape of surgery over the past decade [11–13], and the potential advantages of robotic surgical system, such as articulation of instruments with almost 540° of motion, elimination of tremors, and binocular-enhanced 3D vision make the robotic approach more suitable for complicated surgeries [14, 15]. An increasing number of studies have demonstrated that the robotic liver resection (RLR) procedure allows for safety and feasibility, and major LR can be performed by a purely minimally invasive approach with the assistance of the robotic system characterized by small trauma and rapid recovery [16–18]. However, given the benefits of robotic surgery, whether RLR should be performed in elderly patients is not clear.

Our team has conducted abundant research on robotic surgery, and accumulated rich surgical experience [12, 19–21]. The present study aimed to assess the short- and long-term outcomes of RLR and open liver resection (OLR) for elderly patients with HCC, with the hope of finding out perioperative factors which can impact decision making to improve the long-term prognosis of these elderly HCC patients.

Materials and methods

Patients

A retrospective study was conducted on consecutive HCC patients who underwent RLR or OLR between January 2010 and December 2020 at Chinese People's Liberation Army (PLA) General Hospital. The inclusion criteria were patients with (1) aged 65 years or older with histopathological diagnosis of HCC; (2) good liver function with a Child–Pugh A grading/selected B (score ≤ 7); (3) R0 resection as an initial treatment after the learning curve of open or robotic hepatectomy, with no residual tumors on gross inspection and histological examination of resected specimens; and (4) no anesthesia or surgical contraindications. The exclusion criteria were patients with (1) a history of other malignant tumors and distant metastases; (2) data missing or loss to follow-up; and (3) preoperative antitumor treatment. The clinical and pathological data of these patients were retrospectively analyzed. An elderly patient was defined as a patient 65 years or older at the time of surgery based on previous reports [4, 7, 8]. This study was approved by the Ethics Committee of the Chinese PLA general hospital, and informed consent was obtained from all patients.

Preoperative assessment and hepatectomy

Routine preoperative examination included complete blood counts, liver and renal function tests, coagulation index, serum levels of alpha-fetoprotein (AFP), hepatitis B and C serology and HBV DNA load [22]. Imaging examinations included chest X-ray and contrast-enhanced CT or magnetic resonance imaging (MRI) of the abdomen. The surgical plans were consistent in both the robotic and open hepatectomy, and anatomical resection was performed for patients with good estimated residual liver function on the indocyanine green test [23]. All RLRs were performed using the da Vinci Si System (Intuitive Surgical Inc., Sunnyvale, CA, USA) [20, 24]. Both RLR and OLR were performed by seven senior surgeons from the same surgical team, all of whom have passed the learning curve of robotic and open liver resection [25–27]. Patients were informed of the advantages and disadvantages of robotic and open approaches in detail before operation, and made choices based on their own situations after they weighed the surgical risk with our team. LR of 3 or more segments was defined as major resection, while LR of less than 3 segments was defined as minor resection [4].

Postoperative surveillance and end points

Patients were regularly followed up. Investigations during the follow-up visits included AFP, liver function, and contrast-enhanced CT or MRI once every 2–3 months for the first and second year and then once every 6 months until death or loss to follow-up. The diagnosis of tumor recurrence was based on raised serum AFP levels and typical imaging findings of contrast-enhanced CT or MRI. When tumor recurrence was diagnosed, patients were subjected to appropriate treatments depending on the general condition of the patient, the liver functional reserve, and the pattern of tumor recurrence. The 90-day mortality was defined as mortality occurring within 90 days of liver resection or at any time during the hospital stay. Overall survival (OS) was measured from resection to the last follow-up or death for any reason. Recurrence-free survival (RFS) was defined as the time from LR to the date of tumor recurrence was first diagnosed or the last follow-up. Data were evaluated on June, 2021.

Statistical analysis

Categorical variables were shown as numbers and percentages. Continuous variables were expressed as medians and interquartile range (IQR). Statistical analyses were performed using the Mann–Whitney *U* test for nonparametric ordinal variables and chi-square test or Fisher exact test for categorical variables. Survival analysis was calculated using the Kaplan–Meier method and compared using the log-rank test. A 1:2 propensity score matching (PSM) was performed using the nearest-neighbor matching method to minimize the differences in baseline characteristics between RLR and OLR groups. A caliper radius equal to a standard deviation of 0.1 was set to prevent poor matching. A P value < 0.05 was considered statistically significant. All statistical analyses were performed with SPSS software (IBM SPSS Statistics, version 22.0; IBM Corporation, Armonk, NY, USA).

Results

Patients characteristics

The flowchart in Fig. 1 shows how the patients were selected into this study during the period from 2010 to 2020. Finally, there were 113 elderly HCC patients in the RLR group and 314 patients in the OLR group. The presence of microvascular invasion (MVI) (P = 0.032) differed significantly between the two groups before PSM. Because some cases could not simultaneously find effective matching objects, the matching result was not an absolute 1:2. After PSM, there were 100 and 178 patients in the RLR and the OLR groups, respectively (Fig. 1), and there was no significant difference between the two groups. The detailed baseline

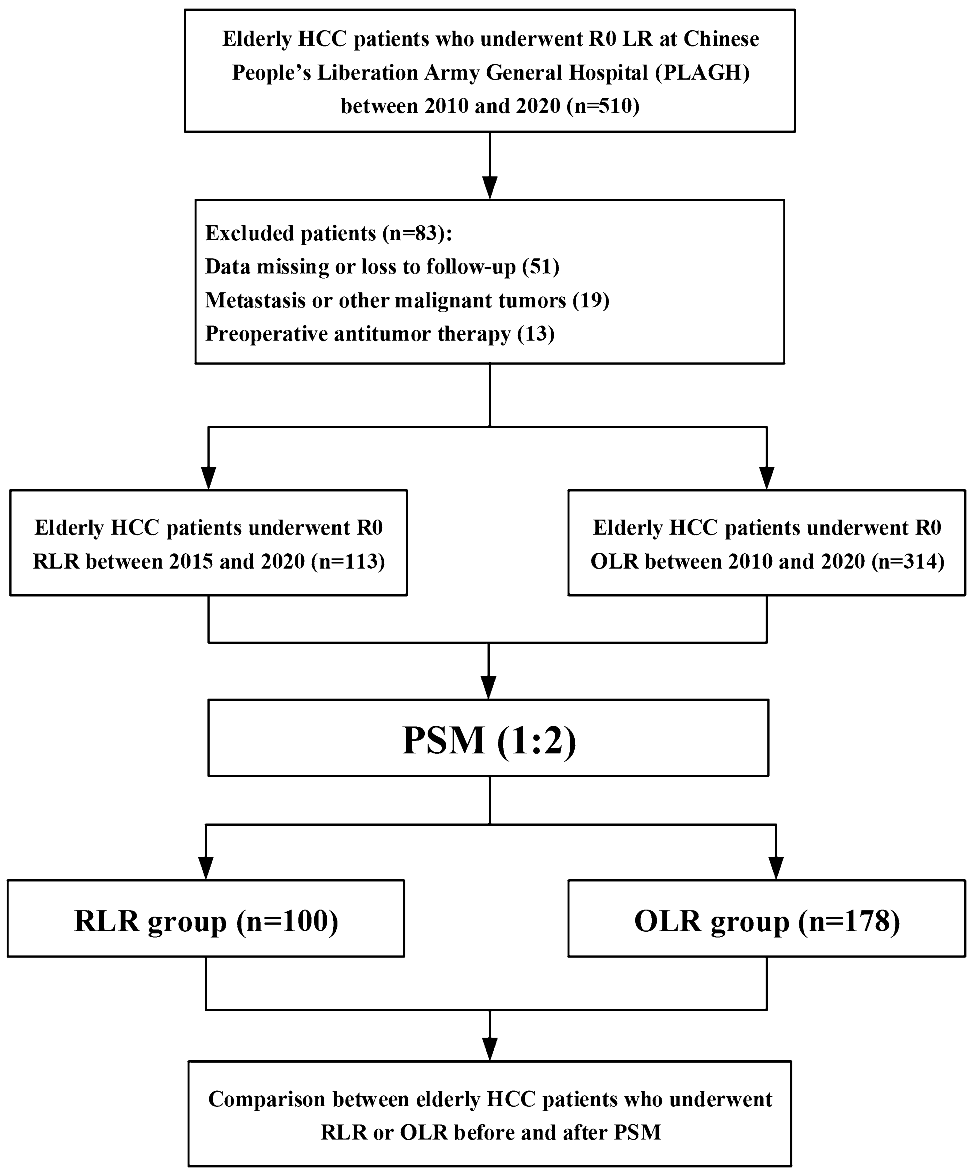

Fig. 1 Flow chart of this study showing the selection process of elderly HCC patients who underwent R0 LR. (*HCC* hepatocellular carcinoma, *LR* liver resection, *RLR* robotic liver resection, *OLR* open liver resection, *PSM* propensity score matching. Because some cases could not simultaneously find effective matching objects, the matching result was not an absolute 1:2)

characteristics of the RLR and OLR groups before and after PSM are summarized in Table 1.

Short-term outcomes after RLR and OLR for these patients before and after PSM

The perioperative outcomes of the two groups are outlined in Table 2. After PSM, there were no significant differences between the RLR group and the OLR group in operative time (205.0 min vs. 200.0 min, $P=0.493$), blood transfusion rate (9.0% vs. 12.9%, $P=0.326$), Pringle maneuver rate (57.0% vs 68.5%, $P=0.054$), total clamping time (25.0 min vs. 29.5 min, $P=0.070$), and 90-day mortality (1.0% vs. 1.1%, $P=0.999$). However, the RLR group had less estimated blood loss (150.0 ml vs. 200.0 ml, $P=0.002$), and a shorter postoperative length of stay (6.0 days vs. 9.0 days, $P<0.001$), compared with the OLR group. Interestingly, although the RLR group had a lower complications rate (7.0% vs. 17.4%, $P=0.015$), there was no significant difference in the proportion of Clavien-Dindo grade and distribution of complications between the two groups ($P=0.051$ and $P=0.977$, respectively). Other surgical outcomes of elderly HCC patients before and after PSM are shown in detail in Table 2.

Long-term outcomes after RLR and OLR for these patients before and after PSM

The two groups of elderly HCC patients who underwent RLR ($n=113$) or OLR ($n=314$) had similar OS ($P=0.390$) and RFS ($P=0.131$) rates before PSM (Fig. 2A, B and Supplementary Table 1). After PSM, patients in RLR groups also had similar median OS and 1-, 3-, and 5-year OS rates (1 year: 88.5% vs. 89.4%; 3 years: 63.5% vs. 63.2%; 5 years: 43.0% vs. 48.8%; median OS 52.8 months vs. 57.6 months, $P=0.722$), and median RFS and 1-, 3-, and 5-year RFS rates (1 year: 64.6% vs. 65.1%; 3 years: 29.8% vs. 33.2%; 5 years: 20.9% vs. 25.3%; median RFS 20.4 vs. 24.6 months, $P=0.982$). The detailed survival outcomes between the RLR and the OLR groups before and after PSM are shown in Supplementary Table 1 and Fig. 2.

Univariable and multivariable cox regression analyses on survival outcomes in all elderly HCC patients after hepatectomy

The univariable analyses for OS and RFS of elderly HCC patients after hepatectomy are shown in **Table 3**. In the multivariate cox regression analyses, BCLC stage B-C (Hazard ratio [HR] 1.525; 95% confidence interval [CI] 1.054–2.206; $P=0.025$), AFP > 400 ng/mL (HR 1.625; 95% CI 1.186–2.227; $P=0.003$), cirrhosis (HR 1.413; 95% CI 1.011–1.975; $P=0.043$), and the presence of MVI (HR 2.762; 95% CI 2.010–3.795; $P<0.001$) were independent risk factors for OS in all elderly HCC patients. In addition, AFP > 400 ng/mL (HR 1.384; 95% CI 1.077–1.779; $P=0.011$), the presence of MVI (HR 2.033; 95% CI 1.609–2.569; $P<0.001$), and histological differentiation (moderate vs. well, HR 1.653; 95% CI 1.174–2.326, $P=0.004$; poor vs. well, HR 1.630; 95% CI 1.185–2.243, $P=0.003$) were independent risk factors for RFS in all elderly HCC patients. Surgical approaches did not significantly affect the long-term survival of these patients (Table 3 and Fig. 3).

Discussion

The present investigation on short- and long-term outcomes of a large cohort of elderly HCC patients (≥ 65 years) undergoing RLR or OLR at a tertiary cancer center demonstrated that the robotic approach was advantageous over open approach in terms of short-term outcomes, such as intraoperative blood loss, postoperative complications, and postoperative length of hospital stay. In addition, this PSM study also indicated that the long-term survival outcomes for elderly HCC patients were similar between the RLR and OLR groups.

The probability of developing a malignant tumor in the elderly is much higher than that in the young population, which makes an increase in demand for surgery for elderly patients with malignant tumors [28]. Several studies have reported that elderly patients have higher incidences of cardiopulmonary diseases, and worse tolerance to surgical stress than young patients [8, 9], and increasing age is also associated with worse outcomes in elderly patients with severe liver injury [9]. With the aging of the population, the number of elderly HCC patients undergoing hepatectomy is increasing. Nevertheless, hepatectomy is one of the most complex operations with high morbidity and mortality. The decision to perform hepatectomy in elderly patients can be difficult [4, 8, 10].

Advances in surgical techniques and improvements in postoperative management have expanded the indications for liver resection, making it safe for elderly patients [4, 10]. As minimally invasive techniques and instruments continue to improve, minimally invasive LR (laparoscopic or robotic) produced better perioperative and comparable oncologic outcomes than OLR for HCC [10, 19, 29]. A recent study aimed to compare the outcomes between laparoscopic liver resection (LLR) and OLR in elderly patients (≥ 65 years) demonstrated that the short- and long-term benefits of LLR are evident in geriatric oncological liver surgery patients. Although the operation time in the LLR group was longer than that in the OLR group after matching, the median hospitalization in the LLR group was

Table 1 The baseline characteristics of elderly HCC patients undergoing RLR or OLR before and after PSM

Variables	Before PSM			After PSM¶		
	RLR group (*n* = 113)	OLR group (*n* = 314)	*P* value	RLR group (*n* = 100)	OLR group (*n* = 178)	*P* value
Age, years						
< 75	90 (79.6)	251 (79.9)	0.947	81 (81.0)	143 (80.3)	0.893
≥ 75	23 (20.4)	63 (20.1)		19 (19.0)	35 (19.7)	
Sex						
Female	22 (19.5)	76 (24.2)	0.305	22 (22.0)	34 (19.1)	0.563
Male	91 (80.5)	238 (75.8)		78 (78.0)	144 (80.9)	
ASA grade						
≤ II	87 (77.0)	242 (77.1)	0.986	76 (76.0)	138 (77.5)	0.771
III	26 (23.0)	72 (22.9)		24 (24.0)	40 (22.5)	
HCC etiology						
HBV	92 (81.4)	258 (82.2)	0.537	82 (82.0)	149 (83.7)	0.887
HCV	6 (5.3)	26 (8.3)		4 (4.0)	9 (5.1)	
HBV and HCV	2 (1.8)	5 (1.6)		2 (2.0)	3 (1.7)	
Others	13 (11.5)	25 (8.0)		12 (12.0)	17 (9.6)	
BCLC stage						
0-A	98 (86.7)	273 (86.9)	0.953	87 (87.0)	160 (89.9)	0.463
B-C	15 (13.3)	41 (13.1)		13 (13.0)	18 (10.1)	
Diabetes						
No	83 (73.5)	257 (81.8)	0.057	76 (76.0)	144 (80.9)	0.335
Yes	30 (26.5)	57 (18.2)		24 (24.0)	34 (19.1)	
AFP, ng/mL						
≤ 400	86 (76.1)	231 (73.6)	0.597	74 (74.0)	130 (73.0)	0.861
> 400	27 (23.9)	83 (26.4)		26 (26.0)	48 (27.0)	
ALB, g/L						
< 35	12 (10.6)	28 (8.9)	0.594	9 (9.0)	15 (8.4)	0.870
≥ 35	101 (89.4)	286 (91.1)		91 (91.0)	163 (91.6)	
ALT, U/L						
≤ 44	76 (67.3)	231 (73.6)	0.201	74 (74.0)	134 (75.3)	0.813
> 44	37 (32.7)	83 (26.4)		26 (26.0)	44 (24.7)	
TBIL, μmol/L						
≤ 17	87 (77.0)	220 (70.1)	0.160	74 (74.0)	132 (74.2)	0.977
> 17	26 (23.0)	94 (29.9)		26 (26.0)	46 (25.8)	
PT, seconds						
≤ 13	70 (61.9)	185 (58.9)	0.573	60 (60.0)	112 (62.9)	0.630
> 13	43 (38.1)	129 (41.1)		40 (40.0)	66 (37.1)	
PLT, 10^9/L						
< 100	33 (29.2)	65 (20.7)	0.065	27 (27.0)	42 (23.6)	0.528
≥ 100	80 (70.8)	249 (79.3)		73 (73.0)	136 (76.4)	
Child–Pugh grade						
A	95 (84.1)	278 (88.5)	0.221	85 (85.0)	155 (87.1)	0.628
B7	18 (15.9)	36 (11.5)		15 (15.0)	23 (12.9)	
Cirrhosis						
No	35 (31.0)	90 (28.7)	0.643	30 (30.0)	54 (30.3)	0.953
Yes	78 (69.0)	224 (71.3)		70 (70.0)	124 (69.7)	
No. of tumors						
Solitary	94 (83.2)	264 (84.1)	0.825	83 (83.0)	155 (87.1)	0.352
Multiple	19 (16.8)	50 (15.9)		17 (17.0)	23 (12.9)	

Table 1 (continued)

Variables	Before PSM			After PSM¶		
	RLR group ($n=113$)	OLR group ($n=314$)	*P* value	RLR group ($n=100$)	OLR group ($n=178$)	*P* value
Tumor size, cm						
≤5	67 (59.3)	190 (60.5)	0.821	61 (61.0)	109 (61.2)	0.969
>5	46 (40.7)	124 (39.5)		39 (39.0)	69 (38.8)	
Microvascular invasion						
Absent	60 (53.1)	130 (41.4)	**0.032**	50 (50.0)	85 (47.8)	0.719
Present	53 (46.9)	184 (58.6)		50 (50.0)	93 (52.2)	
Tumor encapsulation						
Complete	69 (61.1)	208 (66.2)	0.323	65 (65.0)	117 (65.7)	0.902
Incomplete or absent	44 (38.9)	106 (33.8)		35 (35.0)	61 (34.3)	
Histological differentiation						
Well	15 (13.3)	60 (19.1)	0.352	15 (15.0)	35 (19.7)	0.623
Moderate	34 (30.1)	83 (26.4)		30 (30.0)	51 (28.7)	
Poor	64 (56.6)	171 (54.5)		55 (55.0)	92 (51.7)	
Type of hepatectomy						
Minor	71 (62.8)	186 (59.2)	0.503	62 (62.0)	113 (63.5)	0.806
Major	42 (37.2)	128 (40.8)		38 (38.0)	65 (36.5)	

Data are presented as *n* (%). Bold text hinted that these variables were statistically significant. ¶, because some cases could not simultaneously find effective matching objects, the matching result was not an absolute 1:2

HCC hepatocellular carcinoma, *PSM* propensity score matching, *RLR* robotic liver resection, *OLR* open liver resection, *ASA* American Society of Anesthesiologists, *HBV* hepatitis B virus, *HCV* hepatitis C virus, *BCLC* Barcelona Clinic Liver Cancer stage, *AFP* α-fetoprotein, *ALB* albumin, *ALT* alanine aminotransferase, *TBIL* total bilirubin, *PT* prothrombin time, *PLT* platelet

significantly shorter than that in the OLR group [8]. Nomi et al. [10] also indicated that LLR for HCC is associated with good short-term outcomes in patients compared with OLR, and LLR is safe and feasible in selected octogenarians with HCC.

Since Giulianotti et al. first reported the application of robot-assisted laparoscopic system in segmental hepatic resection in 2003 [14, 30], the robotic surgical system has gradually been accepted by surgeons for its advantages in overcoming the inherent limitations of laparoscopic surgery by increased flexible manipulation and improved three-dimensional visualization, which makes surgical operations easier [19, 23, 31], whereas robotic surgical systems also lack tactile feedback, tissue resistance and haptics, which can be confusing for beginners [26]. According to previous reports, 25–45 cases were needed to overcome the learning curve for robotic major hepatectomy, and result in superior outcomes [25–27]. Previous studies also demonstrated that RLR could be applied for challenging major resection in patients with cirrhotic liver disease after learning curve with less postoperative pain and shorter hospital stays without compromising oncological outcomes [17, 23]. Our team has been committed to the research of RLR for a long time and has reported on a series of studies to prove that RLR is safe and feasible [12, 19–21]. Nevertheless, there are still no reports on RLR for elderly patients and whether elderly patients could also benefit from RLR is still unknown [4, 7, 10].

In the present study, the perioperative and oncological outcomes of RLR in elderly HCC patients were compared with OLR. The results showed that the perioperative outcomes were similar between groups after PSM, but the RLR group had less intraoperative blood loss, and a shorter postoperative LOS, compared with the OLR group. In addition, previous studies reported that the overall rate of postoperative complications was 10.4–21.4% for LLR and 16.9–33.5% for OLR in elderly HCC patients. We also proved that the RLR group had a lower complications rate compared with those in the OLR group (7.0% vs. 17.4% after PSM, $P=0.015$), which indicated that the robotic approach has many unique advantages in elderly patients because of less surgical trauma and rapid postoperative recovery [19]. Some previous studies reported that the postoperative 90-day mortality of elderly HCC patients after LR ranged from 0.4 to 3.9% [4, 8, 32, 33]. In this study, the postoperative 90-day mortality was 1.0% in the RLR group after PSM, which is consistent with previous research.

The long-term survival benefits of LR are evident in geriatric oncological liver surgery patients as previous reports [7, 8, 32] with 5-year OS rate ranged from 35.0 to 49.4%. In this study, there were no significant differences in the long-term survival outcomes of elderly HCC patients between

Table 2 The surgical outcomes of elderly HCC patients undergoing RLR or OLR before and after PSM

Variables	Before PSM			After PSM		
	RLR group (*n* = 113)	OLR group (*n* = 314)	*P* value	RLR group (*n* = 100)	OLR group (*n* = 178)	*P* value
Operative time, min	205.0 (155.0, 235.0)	200.0 (145.0, 245.0)	0.255	205.0 (161.3, 235.0)	200.0 (145.0, 245.0)	0.493
Estimated blood loss, ml	150.0 (100.0, 250.0)	200.0 (100.0, 300.0)	**0.035**	150.0 (62.5, 250.0)	200.0 (100.0, 300.0)	**0.002**
Conversion to laparotomy	3 (2.7)	–		3 (3.0)	–	
Blood transfusion						
Yes	9 (8.0)	42 (13.4)	0.128	9 (9.0)	23 (12.9)	0.326
No	104 (92.0)	272 (86.6)		91 (91.0)	155 (87.1)	
Pringle maneuver						
Yes	65 (57.5)	224 (71.3)	**0.007**	57 (57.0)	122 (68.5)	0.054
No	48 (42.5)	90 (28.7)		43 (43.0)	56 (31.5)	
Total clamping time, min	25.0 (15.0, 35.0)	30.0 (18.3, 44.8)	**0.022**	25.0 (16.0, 35.5)	29.5 (18.0, 45.5)	0.070
Complications						
Yes	10 (8.8)	54 (17.2)	**0.03**3	7 (7.0)	31 (17.4)	**0.015**
No	103 (91.2)	260 (82.8)		93 (93.0)	147 (82.6)	
Clavien-Dindo grade						
I-II	8 (7.1)	38 (12.1)	0.090	5 (5.0)	24 (13.5)	0.051
> II	2 (1.8)	16 (5.1)		2 (2.0)	7 (3.9)	
Type of complications[a]						
Ascites	4 (3.5)	14 (4.5)	0.979	2 (2.0)	8 (4.5)	0.977
Liver failure	0 (0.0)	2 (0.6)		0 (0.0)	1 (0.6)	
Hepatic insufficiency	1 (0.9)	6 (1.9)		0 (0.0)	4 (2.2)	
Pulmonary complications	2 (1.8)	16 (5.1)		1 (1.0)	7 (3.9)	
Infectious complications	3 (2.7)	14 (4.5)		3 (3.0)	9 (5.1)	
Bile Leakage	1 (0.9)	4 (1.3)		1 (1.0)	4 (2.2)	
Bleeding	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	
Others	3 (2.7)	12 (3.8)		2 (2.0)	7 (3.9)	
Postoperative LOS, day	6.0 (4.0, 7.0)	9.0 (5.0, 10.0)	< **0.001**	6.0 (4.0, 7.0)	9.0 (4.0, 10.0)	< **0.001**
90-day mortality	2 (1.8)	6 (1.9)	0.999	1 (1.0)	2 (1.1)	0.999

Data are presented as *n* (%) or median (IQR), Bold text hinted that these variables were statistically significant.

HCC hepatocellular carcinoma, *PSM* propensity score matching, *RLR* robotic liver resection, *OLR* open liver resection, *IQR* interquartile range, *LOS* length of stay

[a]Duplications present

the RLR and OLR groups. Therefore, with similar oncology benefits and safety, RLR for selected elderly patients with HCC is worthy of consideration.

Recent studies indicated that age itself is not a contraindication to surgery, and selected elderly patients have similar oncologic outcomes following hepatectomy for HCC compared with younger patients [4, 32]. In the present study, multivariable analyses also demonstrated that advanced age was not an independent risk factor for long-term survival outcomes, while BCLC stage, AFP level, MVI, and cirrhosis were independent prognostic factors for OS; and AFP level, MVI and tumor differentiation were independent prognostic factors for RFS of these patients. The long-term survival outcomes of advanced HCC patients are severely damaged, and the presence of MVI, high AFP level, and poorly histological differentiation often indicate that the prognosis is dismal [34, 35]. Besides, the impairment of liver function as a result of cirrhosis restricts the treatment options, and cirrhosis is also known to predispose to multicentric hepatocarcinogenesis and increase the risk of recurrence after resection of HCC [36]. Hence, for elderly HCC patients with the above risk factors, closer postoperative follow-up and aggressive postoperative treatment may prolong their survival outcomes [35, 37].

This study also had several limitations. First, this is a retrospective study with its potential inherent biases, even though PSM was used to reduce selection biases. Second, patients in the present study were also treated exclusively in China. However, the majority of patients with HCC had a background of HBV-related cirrhosis in

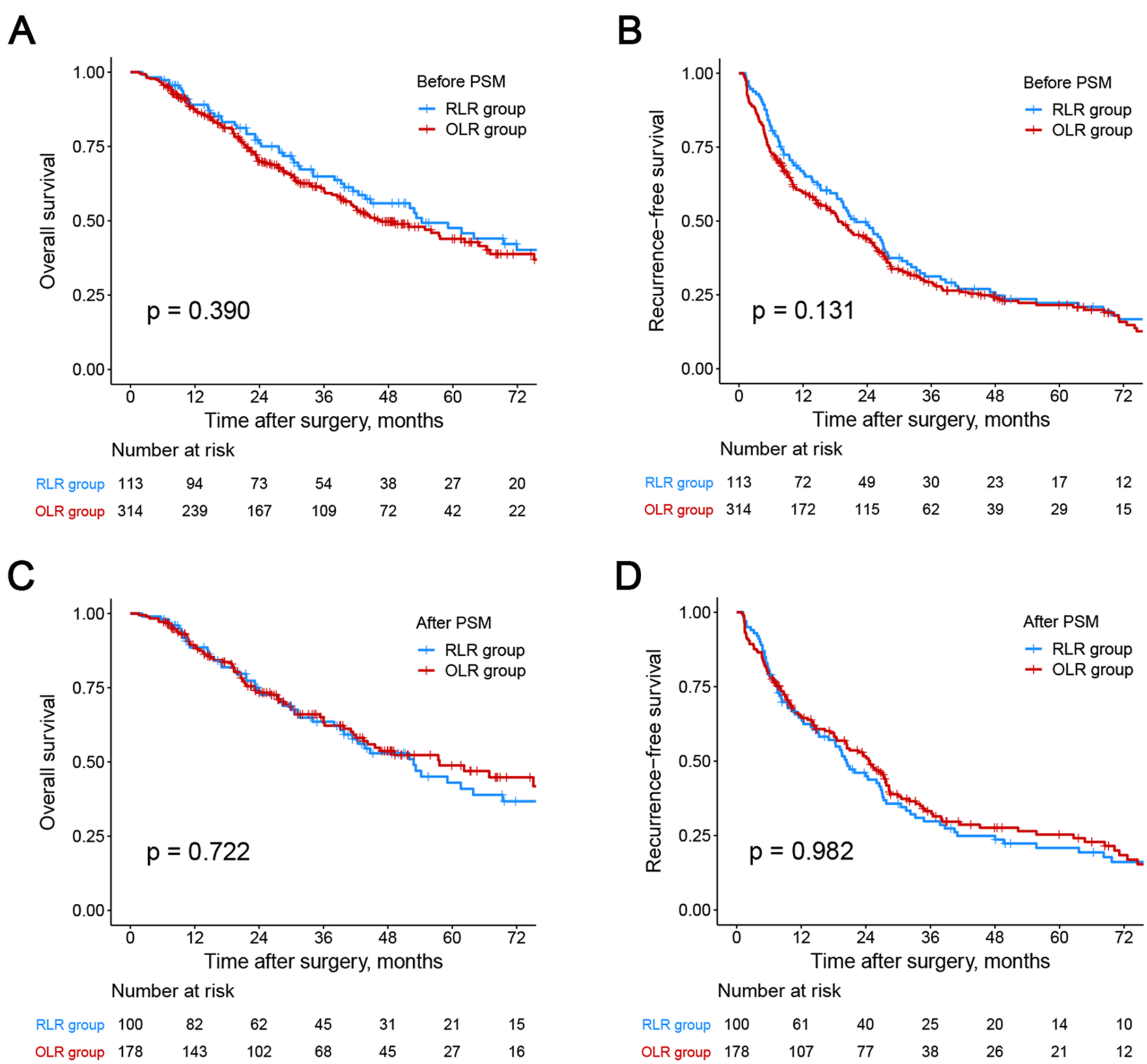

Fig. 2 Kaplan–Meier curves estimating OS and RFS of elderly HCC patients before and after PSM. **A**, **B** OS and RFS of elderly HCC patients who underwent RLR or OLR before PSM; **C**, **D** OS and RFS of elderly HCC patients who underwent RLR or OLR after PSM. (*HCC* hepatocellular carcinoma, *PSM* propensity score matching, *RLR* robotic liver resection, *OLR* open liver resection, *OS* overall survival, *RFS* recurrence-free survival)

China. Thus, data from the present study need to be externally validated in Western patients to ensure whether the results are universal to other populations of patients such as alcohol or nonalcoholic-related HCC. Finally, this was a single-center report with a large sample size which can limit the application of the results to other low-volume robotic surgery centers. We will initiate better designed multicenter and prospective studies to compare RLR with OLR for elderly patients in the future.

In conclusion, for the first time this study demonstrated that RLR was safe and feasible in elderly patients, with similar short or long-term outcomes compared with OLR. Carefully selected elderly patients should be considered for RLR.

Table 3 Univariable analysis for OS and RFS of elderly HCC patients ($n=427$)

Variables	OS			RFS		
	B	HR (95% CI)	*P* value	B	HR (95% CI)	*P* value
Age, years, ≥ 75 vs. < 75	−0.095	0.910 (0.643–1.286)	0.592	−0.068	0.934 (0.715–1.221)	0.619
Sex, male vs. female	−0.103	0.902 (0.648–1.254)	0.539	−0.076	0.927 (0.716–1.200)	0.565
ASA grade, III vs. ≤ II	−0.081	0.922 (0.654–1.299)	0.643	0.001	1.001 (0.774–1.294)	0.996
HCC etiology						
HCV vs. HBV	0.425	1.530 (0.948–2.469)	0.082	0.033	1.033 (0.678–1.574)	0.880
HBV & HCV vs. HBV	0.428	1.535 (0.678–3.476)	0.304	0.035	1.035 (0.488–2.195)	0.928
BCLC stage, B-C vs. 0-A	0.548	1.730 (1.198–2.497)	**0.003**	0.312	1.367 (1.000–1.867)	**0.049**
Diabetes, yes vs. no	0.034	1.035 (0.739–1.450)	0.841	-0.040	0.961 (0.738–1.252)	0.769
ALB, g/L, ≥ 35 vs. < 35	−0.273	0.761 (0.487–1.189)	0.231	−0.339	0.713 (0.498–1.019)	0.064
ALT, U/L, > 44 vs. ≤ 44	−0.177	0.838 (0.609–1.153)	0.277	−0.121	0.886 (0.694–1.131)	0.330
AFP, ng/mL, > 400 vs. ≤ 400	0.610	1.840 (1.344–2.518)	< **0.001**	0.507	1.660 (1.298–2.122)	< **0.001**
TBIL, μmol/L, > 17 vs. ≤ 17	0.055	1.056 (0.774–1.441)	0.730	0.011	1.011 (0.795–1.285)	0.932
PT, seconds, > 13 vs. ≤ 13	−0.221	0.802 (0.596–1.079)	0.145	−0.162	0.851 (0.680–1.063)	0.155
PLT, 10^9/L, ≥ 100 vs. < 100	0.065	1.067 (0.771–1.476)	0.697	0.236	1.266 (0.974–1.645)	0.078
Child–Pugh grade, B7 vs. A	0.227	1.254 (0.844–1.864)	0.262	0.302	1.352 (0.95–1.838)	0.054
Cirrhosis, yes vs. no	0.376	1.456 (1.045–2.030)	**0.027**	0.222	1.248 (0.979–1.592)	0.074
No. of tumors, multiple vs. solitary	0.451	1.570 (1.108–2.227)	**0.011**	0.231	1.260 (0.943–1.684)	0.118
Tumor diameter, cm, > 5 vs. ≤ 5	0.312	1.367 (1.025–1.821)	**0.033**	0.397	1.487 (1.193–1.855)	< **0.001**
MVI, present vs. absent	1.080	2.945 (2.149–4.035)	< **0.001**	0.798	2.221 (1.765–2.795)	< **0.001**
Complete tumor capsule, no vs. yes	0.216	1.242 (0.931–1.655)	0.140	0.099	1.104 (0.883–1.382)	0.386
Histological differentiation						
Moderate vs. Well	0.343	1.409 (0.893–2.224)	0.141	0.559	1.749 (1.246–2.456)	**0.001**
Poor vs. Well	0.671	1.955 (1.302–2.936)	**0.001**	0.685	1.984 (1.453–2.708)	< **0.001**
Surgical approach, OLR vs. RLR	0.139	1.149 (0.837–1.576)	0.391	−0.189	0.828 (0.647–1.059)	0.133
Type of hepatectomy, major vs. minor	−0.027	0.974 (0.728–1.302)	0.857	−0.200	0.818 (0.655–1.023)	0.078
Operative time, min, > 180 vs. ≤ 180	0.143	1.154 (0.861–1.546)	0.338	0.135	1.144 (0.917–1.428)	0.232
Blood loss, ml, > 200 vs. ≤ 200	0.112	1.119 (0.840–1.491)	0.443	0.100	1.105 (0.886–1.378)	0.374
Complications						
Clavien-Dindo grade ≤ II vs. no	−0.213	0.808 (0.502–1.302)	0.382	−0.040	0.960 (0.677–1.361)	0.820
Clavien-Dindo grade > II vs. no	0.197	1.217 (0.677–2.191)	0.512	0.008	1.008 (0.589–1.725)	0.977

Bold text hinted that these variables were statistically significant

HCC hepatocellular carcinoma, *OS* overall survival, *RFS* recurrence-free survival, *HR* Hazard Ratio. *B* coefficient, *CI* confidence interval, *RLR* robotic liver resection, *OLR* open liver resection, *ASA* American Society of Anesthesiologists, *HBV* hepatitis B virus, *HCV* hepatitis C virus, *BCLC* Barcelona Clinic Liver Cancer stage*, AFP* α-fetoprotein, *ALB* albumin, ALT, alanine aminotransferase, *TBIL* total bilirubin, *PT* prothrombin time, *PLT* platelet. *MVI* Microvascular invasion

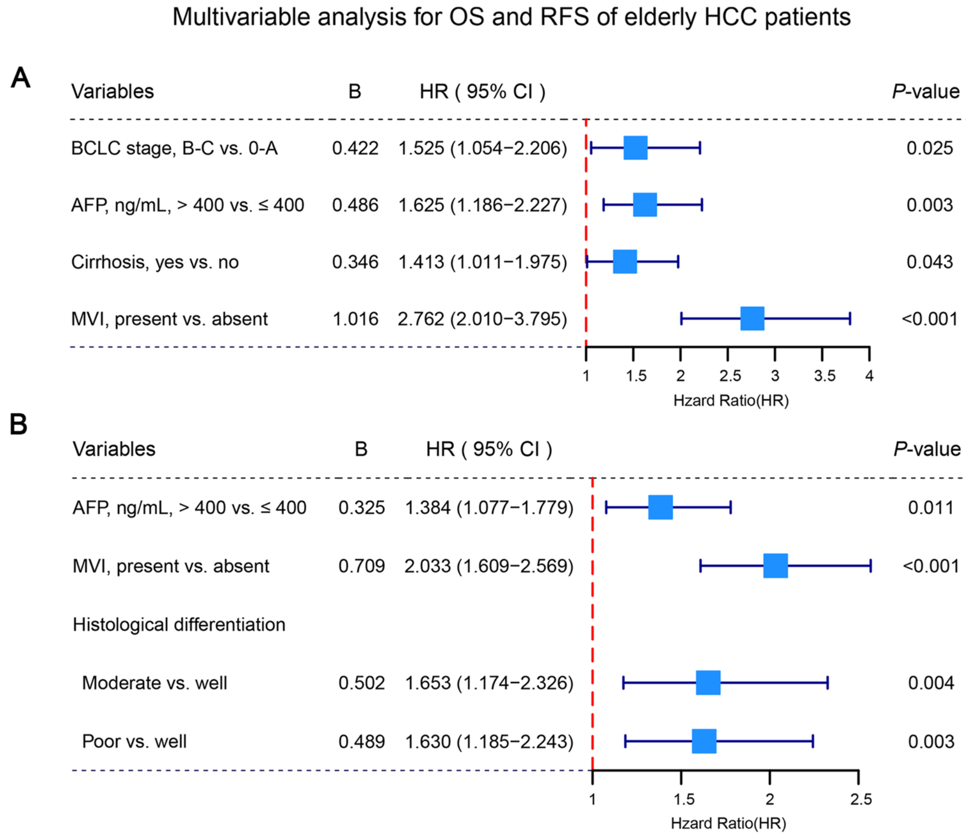

Fig. 3 Forest-plot of multivariable analysis for OS and RFS in elderly patients with HCC after LR. **A** forest-plot of multivariable analysis for OS; **B** forest-plot of multivariable analysis for RFS. (*HCC* hepatocellular carcinoma, *LR* liver resection, *OS* overall survival, *RFS* recurrence- free survival)

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Data availability The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Disclosures Dr. Xiu-Ping Zhang, Shuai Xu, Ming-Gen Hu, Zhi-Ming Zhao, Zhao-Hai Wang, Guo-Dong Zhao, Cheng-Gang Li, Xiang-Long Tan, and Rong Liu have no conflicts of interest or financial ties to disclose.

Ethical approval
This study was approved by the Ethics Committee of the PLA general hospital, and written informed consent was obtained from all patients.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F (2021) Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 Countries. CA: A Cancer J Clin 71(3):209–249
2. Forner A, Reig M, Bruix J (2018) Hepatocellular carcinoma. Lancet 391:1301–1314
3. Omata M, Cheng A-L, Kokudo N, Kudo M, Lee JM, Jia J, Tateishi R, Han K-H, Chawla YK, Shiina S, Jafri W, Payawal DA, Ohki T, Ogasawara S, Chen P-J, Lesmana CRA, Lesmana LA, Gani RA, Obi S, Dokmeci AK, Sarin SK (2017) Asia-Pacific clinical practice guidelines on the management of hepatocellular carcinoma: a 2017 update. Hepatol Int 11:317–370
4. Wang H-Q, Yang J, Yan L-N, Zhang X-W, Yang J-Y (2014) Liver resection in hepatitis B related-hepatocellular carcinoma: clinical outcomes and safety in elderly patients. World J Gastroentero 20:6620–6625
5. Nishikawa H, Kimura T, Kita R, Osaki Y (2013) Treatment for hepatocellular carcinoma in elderly patients: a literature review. J Cancer 4:635–643
6. El-Serag HB (2012) Epidemiology of viral hepatitis and hepatocellular carcinoma. Gastroenterology 142(6):1264–1273
7. Chen Z-L, Zhang C-W, Liang L, Wu H, Zhang W-G, Zeng Y-Y, Gu W-M, Chen T-H, Li J, Zhang Y-M, Wang H, Zhou Y-H, Li C, Diao Y-K, Lau WY, Wu M-C, Shen F, Yang T, Liang Y-J (2020) Major hepatectomy in elderly patients with large hepatocellular carcinoma: a multicenter retrospective observational study. Cancer Manag Res 12:5607–5618

8. Kim JM, Kim S, Rhu J, Choi G-S, Kwon CHD, Joh J-W (2020) Elderly hepatocellular carcinoma patients: open or laparoscopic approach? Cancers 12(8):2281
9. Gorman E, Bukur M, Frangos S, DiMaggio C, Kozar R, Klein M, Pachter HL, Berry C (2020) Increasing age is associated with worse outcomes in elderly patients with severe liver injury. Am J Surg 220:1308–1311
10. Nomi T, Hirokawa F, Kaibori M, Ueno M, Tanaka S, Hokuto D, Noda T, Nakai T, Ikoma H, Iida H, Komeda K, Ishizaki M, Hayami S, Eguchi H, Matsumoto M, Morimura R, Maehira H, Sho M, Kubo S (2020) Laparoscopic versus open liver resection for hepatocellular carcinoma in elderly patients: a multi-centre propensity score-based analysis. Surg Endosc 34:658–666
11. Gotohda N, Cherqui D, Geller DA, Abu Hilal M, Berardi G, Ciria R, Abe Y, Aoki T, Asbun HJ, Chan ACY, Chanwat R, Chen K-H, Chen Y, Cheung TT, Fuks D, Han H-S, Hasegawa K, Hatano E, Honda G, Itano O, Iwashita Y, Kaneko H, Kato Y, Kim JH, Liu R, López-Ben S, Morimoto M, Monden K, Rotellar F, Sakamoto Y, Sugioka A, Yoshiizumi T, Akahoshi K, Alconchel F, Ariizumi S, Benedetti Cacciaguerra A, Durán M, Garcia Vazquez A, Golse N, Miyasaka Y, Mori Y, Ogiso S, Shirata C, Tomassini F, Urade T, Wakabayashi T, Nishino H, Hibi T, Kokudo N, Ohtsuka M, Ban D, Nagakawa Y, Ohtsuka T, Tanabe M, Nakamura M, Yamamoto M, Tsuchida A, Wakabayashi G (2022) Expert consensus guidelines: how to safely perform minimally invasive anatomic liver resection. J Hepato-Bil-Pan Sci 29:16–32
12. Liu Q, Zhao Z, Zhang X, Wang W, Han B, Chen X, Tan X, Xu S, Zhao G, Gao Y, Gan Q, Yuan J, Ma Y, Dong Y, Liu Z, Wang H, Fan F, Liu J, Lau WY, Liu R (2021) Perioperative and oncological outcomes of robotic versus open pancreaticoduodenectomy in low-risk surgical candidates: a multicenter propensity score-matched study. Ann surg. https://doi.org/10.1097/SLA.0000000000005160
13. Cheung T, Wang X, Efanov M, Liu R, Fuks D, Choi G, Syn N, Chong C, Sucandy I, Chiow A, Marino M, Gastaca M, Lee J, Kingham T, D'Hondt M, Choi S, Sutcliffe R, Han H, Tang C, Pratschke J, Troisi R, Goh B (2021) Minimally invasive liver resection for huge (≥10 cm) tumors: an international multicenter matched cohort study with regression discontinuity analyses. Hepatobil Surg Nutr 10:587–597
14. Liu R, Wakabayashi G, Kim H-J, Choi G-H, Yiengpruksawan A, Fong Y, He J, Boggi U, Troisi RI, Efanov M, Azoulay D, Panaro F, Pessaux P, Wang X-Y, Zhu J-Y, Zhang S-G, Sun C-D, Wu Z, Tao K-S, Yang K-H, Fan J, Chen X-P (2019) International consensus statement on robotic hepatectomy surgery in 2018. World J Gastroentero 25:1432–1444
15. Liu R, Zhang T, Zhao Z-M, Tan X-L, Zhao G-D, Zhang X, Xu Y (2017) The surgical outcomes of robot-assisted laparoscopic pancreaticoduodenectomy versus laparoscopic pancreaticoduodenectomy for periampullary neoplasms: a comparative study of a single center. Surg Endosc 31:2380–2386
16. Wang Z-Z, Tang W-B, Hu M-G, Zhao Z-M, Zhao G-D, Li C-G, Tan X-L, Zhang X, Lau WY, Liu R (2019) Robotic vs laparoscopic hemihepatectomy: a comparative study from a single center. J Surg Oncol 120:646–653
17. Lim C, Salloum C, Tudisco A, Ricci C, Osseis M, Napoli N, Lahat E, Boggi U, Azoulay D (2019) Short- and long-term outcomes after robotic and laparoscopic liver resection for malignancies: a propensity score-matched study. World J Surg 43:1594–1603
18. Chiow AKH, Fuks D, Choi G-H, Syn N, Sucandy I, Marino MV, Prieto M, Chong CC, Lee JH, Efanov M, Kingham TP, Choi SH, Sutcliffe RP, Troisi RI, Pratschke J, Cheung T-T, Wang X, Liu R, D'Hondt M, Chan C-Y, Tang CN, Han H-S, Goh BKP (2021) International multicentre propensity score-matched analysis comparing robotic versus laparoscopic right posterior sectionectomy. Br J Surg 108:1513–1520
19. Hu M, Chen K, Zhang X, Li C, Song D, Liu R (2020) Robotic, laparoscopic or open hemihepatectomy for giant liver haemangiomas over 10 cm in diameter. Bmc Surg 20:93
20. Hu M, Liu Y, Li C, Wang G, Yin Z, Lau WY, Liu R (2019) Robotic versus laparoscopic liver resection in complex cases of left lateral sectionectomy. Int J Surg 67:54–60
21. Hu M-G, Wang J, Yin Z-Z, Liu R (2021) First two-stage robotic ALPPS in HCC patients with hepatic vein invasion: a step-by-step procedure from a clinical case. World J Surg Oncol 19:58
22. Marrero JA, Kulik LM, Sirlin CB, Zhu AX, Finn RS, Abecassis MM, Roberts LR, Heimbach JK (2018) Diagnosis, staging, and management of hepatocellular carcinoma: 2018 practice guidance by the American association for the study of liver diseases. Hepatology 68:723–750
23. Chen P-D, Wu C-Y, Hu R-H, Chou W-H, Lai H-S, Liang J-T, Lee P-H, Wu Y-M (2017) Robotic versus open hepatectomy for hepatocellular carcinoma: a matched comparison. Ann Surg Oncol 24:1021–1028
24. Wang Z-Z, Zhao G-D, Zhao Z-M, Gao Y-X, Xu Y, Yin Z-Z, Liu Q, Lau WY, Liu R (2019) An end-to-end pancreatic anastomosis in robotic central pancreatectomy. World J Surg Oncol 17:67
25. Efanov M, Alikhanov R, Tsvirkun V, Kazakov I, Melekhina O, Kim P, Vankovich A, Grendal K, Berelavichus S, Khatkov I (2017) Comparative analysis of learning curve in complex robot-assisted and laparoscopic liver resection. HPB (Oxford) 19:818–824
26. Liu Q, Zhang T, Hu M, Zhao Z, Zhao G, Li C, Zhang X, Lau WY, Liu R (2020) Comparison of the learning curves for robotic left and right hemihepatectomy: a prospective cohort study. Int J Surg 81:19–25
27. O'Connor VV, Vuong B, Yang S-T, DiFronzo A (2017) Robotic minor hepatectomy offers a favorable learning curve and may result in superior perioperative outcomes compared with laparoscopic approach. Am Surg 83:1085–1088
28. Liu Q, Zhao Z, Zhang X, Zhao G, Tan X, Gao Y, Lau WY, Liu R (2020) Robotic pancreaticoduodenectomy in elderly and younger patients: a retrospective cohort study. Int J Surg 81:61–65
29. Han DH, Choi SH, Park EJ, Kang DR, Choi GH, Choi JS (2016) Surgical outcomes after laparoscopic or robotic liver resection in hepatocellular carcinoma: a propensity-score matched analysis with conventional open liver resection. Int J Med Robot Comput Assist Surg 12:735–742
30. Giulianotti PC, Coratti A, Angelini M, Sbrana F, Cecconi S, Balestracci T, Caravaglios G (2003) Robotics in general surgery: personal experience in a large community hospital. Arch Surg 138:777–784
31. Diana M, Marescaux J (2015) Robotic surgery. Br J Surg 102:e15–e28
32. Xing H, Liang L, Wang H, Zhou Y-H, Pei Y-L, Li C, Zeng Y-Y, Gu W-M, Chen T-H, Li J, Zhang Y-M, Wang M-D, Zhang W-G, Pawlik TM, Lau WY, Shen F, Wu M-C, Yang T (2020) Multicenter analysis of long-term oncologic outcomes of hepatectomy for elderly patients with hepatocellular carcinoma. HPB (Oxford) 22:1314–1323
33. Yamada S, Shimada M, Morine Y, Imura S, Ikemoto T, Arakawa Y, Saito Y, Yoshikawa M, Miyazaki K (2021) Significance of frailty in prognosis after hepatectomy for elderly patients with hepatocellular carcinoma. Ann Surg Oncol 28:439–446
34. Han J, Li Z-L, Xing H, Wu H, Zhu P, Lau WY, Zhou Y-H, Gu W-M, Wang H, Chen T-H, Zeng Y-Y, Wu M-C, Shen F, Yang T (2019) The impact of resection margin and microvascular invasion on long-term prognosis after curative resection of hepatocellular carcinoma: a multi-institutional study. HPB (Oxford) 21:962–971
35. Han K, Kim JH (2015) Transarterial chemoembolization in hepatocellular carcinoma treatment: barcelona clinic liver cancer staging system. World J Gastroentero 21:10327–10335

36. Poon RTP (2009) Differentiating early and late recurrences after resection of HCC in cirrhotic patients: implications on surveillance, prevention, and treatment strategies. Ann Surg Oncol 16:792–794
37. Zhang X-P, Wang K, Wei X-B, Li L-Q, Sun H-C, Wen T-F, Chai Z-T, Chen Z-H, Shi J, Guo W-X, Xie D, Cong W-M, Wu M-C, Lau WY, Cheng S-Q (2019) An Eastern hepatobiliary surgery hospital microvascular invasion scoring system in predicting prognosis of patients with hepatocellular carcinoma and microvascular invasion after r0 liver resection: a large-scale, multicenter study. Oncologist 24:e1476–e1488