World J Surg (2019) 43:1594–1603
https://doi.org/10.1007/s00268-019-04927-x

ORIGINAL SCIENTIFIC REPORT

Short- and Long-term Outcomes after Robotic and Laparoscopic Liver Resection for Malignancies: A Propensity Score-Matched Study

Chetana Lim[1] · Chady Salloum[1] · Antonella Tudisco[2] · Claudio Ricci[3] · Michael Osseis[1] · Niccolo Napoli[2] · Eylon Lahat[4] · Ugo Boggi[2] · Daniel Azoulay[1,4]

Published online: 31 January 2019

Abstract

Objectives A laparoscopic approach improves short-term outcomes and maintains long-term outcomes compared to an open approach. In turn, the recent development of robotic surgery raises the question whether it performs as well as laparoscopic surgery. The aim of this study was to compare the short- and long-term outcomes of laparoscopic liver resection (LLR) and robotic liver resection (RLR) for malignancies.

Method From 2011 to 2017, the study population included 111 patients in the LLR group and 61 in the RLR group. Short- and long-term outcomes were compared before and after propensity score matching (PSM).

Results Operative mortality rate was nil. The intraoperative blood transfusion rate was higher during RLR (15% vs. 2%, $p = 0.0009$). Major morbidity and hospital stay were not different between the two groups. The resection margin width (LLR 7 mm vs. RLR 10 mm, $p = 0.13$) and R1 resection rates (resection margin width < 1 mm; LLR 15% vs. RLR 11%, $p = 0.49$) were similar. After PSM (55 patients in each group), the blood transfusion, major morbidity, hospital stay and R1 resection were similar between the two groups. When considering the largest subset of patients with hepatocellular carcinoma including 114 patients (66%), the 3-year overall survival rate was 80% in the LLR group and 97% in the RLR group ($p = 0.10$) and remained similar after PSM ($p = 0.27$). The 3-year recurrence-free survival rate was 50% in the LLR group and 64% in the RLR group ($p = 0.30$) and remained similar after PSM ($p = 0.26$).

Conclusions No differences were found in blood transfusion, incidence of positive resection margins and long-term outcomes between the two techniques. RLR does not compromise short-term and oncologic outcomes in patients with liver cancers.

Chetana Lim and Chady Salloum are co-first authors.

✉ Daniel Azoulay
daniel.azoulay@aphp.fr; daniel.azoulay.hmn@gmail.com

[1] Department of Hepatobiliary and Pancreatic Surgery and Liver Transplantation, Henri Mondor Hospital, 51 Avenue de Lattre de Tassigny, 94010 Créteil, France

[2] Division of General and Transplant Surgery, Cisanello Hospital, Pisa, Italy

[3] Department of Internal Medicine and Surgery (DIMEC), S. Orsola-Malpighi Hospital, Alma Mater Studiorum-University of Bologna, Bologna, Italy

[4] Department of General Surgery and Transplantation, Hepatobiliary and Pancreatic Surgery, Tel Hashomer Hospital, Tel Aviv, Israel

Introduction

The laparoscopic approach has been acknowledged as the standard approach for liver resection for malignancies in selected patients [1, 2]. While this approach maintains similar oncological outcomes to the open approach, it seems to decrease morbidity and length of hospital stay, and lead to fast rehabilitation. This is important after cancer surgery, where postoperative complications can negatively impact long-term survival and recurrence [3] and the recovery time may delay the initiation of adjuvant chemotherapy [4].

The robotic approach is increasingly performed in many specialized centers. The advantages of the robotic approach include an improved range of movements and enhanced instrument dexterity, a 3-dimensional view of the surgical field and a reduction in surgeon tremors. In addition, surgeons using the robotic approach may benefit from expertise with the laparoscopic technique, which may shorten the learning curve for applying the robotic technique [5]. Beyond the ongoing medico-economic debate about robotic technology [6], uncertainties remain regarding patient safety and oncologic concerns, such as surgical resection margin clearance.

As shown in Table 1, current comparisons of the short-term outcomes between robotic liver resection (RLR) and laparoscopic liver resection (LLR) are based on retrospective series. These reports showed low postoperative mortality (ranging from 0 to 5% for LLR and 0 to 2.8% for RLR) and similar postoperative morbidity (being high at 36% for LLR and 62% for RLR) between these two approaches (Table 1) [6–21]. While existing studies comparing the long-term oncological outcomes following these two procedures have reported no significant differences in the quality of the resection margins [6, 7, 10, 12–14, 16–21], overall survival (OS) [16, 17, 20], or recurrence-free survival (RFS) [7, 10, 17, 20], few studies have compared these 2 techniques and adjusted for confounding variables related to the choice of whether to perform LLR or RLR [6, 14, 16], and few studies have specifically focused on hepatobiliary malignancies [7, 17, 21].

The aim of this Western bicentric study was to assess whether RLR performs as well as LLR for primary and secondary liver cancers using propensity score matching (PSM) methodology.

Materials and methods

Patients

This study included all consecutive patients with primary and secondary liver cancers who underwent RLR at two Western hepatobiliary departments (Center 1: Henri Mondor Hospital, Créteil, France, and Center 2: Cisanello Hospital, Pisa, Italy) from 2011 to 2017. All these patients were compared with all patients who underwent LLR at Center 1 during the same study period.

Because the main goal of the present study was to specifically focus on the impact of the surgical approach (i.e., RLR or LLR) on the width and incidence of positive resection margins, patients who required conversion to an open approach were excluded from the analysis. Hand-assisted or hybrid liver resections were never used in this study. The institutional review boards of both centers approved this study. Hand-assisted or hybrid liver resections were never used in this study. The institutional review boards of both centers approved this study.

All patients with a diagnosis of liver cancer were discussed at multidisciplinary meetings at each institution using the same general consensus guidelines to determine the indications for surgery and to decide whether to use the laparoscopic approach [1, 2]. A robotic or laparoscopic approach was selected according to the policies of each center, the surgeons' recommendations, the location and size of the tumors, the presence of cirrhosis, and the patient's general status.

Contraindications for LLR and RLR were patients with bulky tumors and/or close to the hilum and the inferior vena cava, those who required vascular/biliary reconstruction, and those who could not undergo pneumoperitoneum.

Surgical procedures

All procedures were performed by at least one senior surgeon (CS and CL at Henri Mondor Hospital; UB at Cisanello Hospital). The surgical techniques used for the robotic approach at these two centers have been already described in detail [6, 13, 22]. Briefly, RLR was performed using three or four arms: a 12-mm trocar was used for the 30-degree camera, and two or three 8-mm trocars were used for the robotic instruments arms. The liver parenchyma was divided using a Harmonic curved shears (Ethicon, USA). All robotic procedures were purely robotic compared to the Pittsburgh techniques [14].

All patients in the LLR group underwent pure LLR using 5 or 6 ports, as previously described [6, 13].

Table 1 Reported series comparing robotic with laparoscopic liver resection

References	LLR versus RLR (n)	Malignancy (%)	Matching	Conversion to open surgery (%)	Transfusion (%)	Mortality (%)	Morbidity (%)	Readmission (%)	Surgical margins width (mm)	R1 resection (%)	OS (%)	RFS (%)
Berber [7]	23 versus 9	100	No	LLR 0 RLR 11.1	–	0	LLR 17 RLR 11 *P* = NA	–	LLR 14 RLR 11 *P* = NS	–	–	NS
Ji [8]	20 versus 13	LLR NA RLR 61.5	No	LLR 10 RLR 0	LLR 15 RLR 0 *P* = NS	0	LLR 10 RLR 7.8 *P* = NS	–	–	–	–	–
Packiam [9]	18 versus 11	LLR 45 RLR 55	No	0	0	0	–	–	–	–	–	
Troisi [10]	223 versus 40	LLR 60.2 RLR 70	No	LLR 7.6 RLR 20	–	0	LLR 12.6 RLR12.5 *P* = 1	–	–	LLR 5.4 RLR 7.5 *P* = 0.71	–	CLM: RFS at 1 and 3 years: RLR 79 and 62 LLR 81 and 41
Wu [11]	69 versus 52	LLR 63 RLR 75	No	HCC: LLR 12.2 RLR 5	–	0	HCC: LLR 10 RLR 8 *P* = NS	–	–	–	–	–
Yu [12]	17 versus 13	LLR 29.4 RLR 76.9	No	0	0	0	LLR 11.7 RLR 0 *P* = 0.208	–	LLR 20 RLR 18.7 *P* = 0.498	–	–	–
Spampinato [13]	25 versus 25	LLR 92 RLR 68	No	LLR 4 RLR 4	LLR 16 RLR 44 *P* = 0.031	LLR 4 RLR 0 *P* = 1	LLR 36 RLR 20 *P* = 0.375	LLR 4 RLR 0 *P* = 1	–	–	–	–
Tsung [14]	114 versus 57	LLR 68 RLR 70	Yes without PSM	LLR 8.8 RLR 7	LLR 7.4 RLR 3.8 *P* = 0.372	LLR 1.8 RLR 0 *P* = 0.314	LLR 26 RLR 19.3 *P* = 0.34	–	–	–	–	–
Tranchart [15]	28 versus 28	LLR 60.7 RLR 53.6	Yes without PSM	LLR 7.1 RLR 14.3	LLR 3.6 RLR 14.2 *P* = 0.35	LLR 3.6 RLR 0 *P* = 1	LLR 17.9 RLR 17.9 *P* = 1	–	–	–	–	–
Montalti [16]	72 versus 36	LLR 70.8 RLR 75	Yes with PSM	LLR 9.7 RLR 13.9	–	LLR 0 RLR 2.8 *P* = 0.72	LLR 19.4 RLR 19.4 *P* = 1	–	–	LLR 12.5 RLR 11.1 *P* = 1	CLM: NS	CLM: NS
Lai [17]	35 versus 100	100	No	LLR 5.7 RLR 4	LLR 11.4 RLR 9 *P* = 0.74	0	LLR 20 RLR 14 *P* = 0.42	–	LLR 13.7 RLR 11.2 *P* = 0.71	LLR 8.6 RLR 4 *P* = 0.72	NS	NS

Table 1 continued

References	LLR versus RLR (n)	Malignancy (%)	Matching	Conversion to open surgery (%)	Transfusion (%)	Mortality (%)	Morbidity (%)	Readmission (%)	Surgical margins width (mm)	R1 resection (%)	OS (%)	RFS (%)
Croner [18]	19 versus 10	LLR 26.3 RLR 100	No	–	–	LLR 5 RLR 0 *P* = NA	LLR 16 RLR 10 *P* = NA	–	LLR 7.6 RLR 5.7 *P* = 0.882	LLR 0 RLR 0 *P* = ND	–	–
Salloum [22]	80 versus 16	LLR 60 RLR 56	Yes with PSM	LLR 3 RLR 13	LLR 0 RLR 7 *P* = 0.31	0	LLR 7 RLR 7 *P* = 1	–	–	0	–	–
Lee [19]	66 versus 70	LLR 86.4 RLR 74.3	No	LLR 12.1 RLR 5.7	LLR 1.5 RLR 4.3 *P* = 0.62	0	LLR 4.5 RLR 11.4 *P* = 0.141	–	LLR 16 RLR 15 *P* = 0.815	LLR 1.6 RLR 1.8 P > 0.99	–	–
Kim [20]	31 versus 12	LLR 77.4 RLR 58.3	No	LLR 3.2 RLR 0	–	0	LLR 25 RLR 22.6 *P* = 0.668	–	Overall: LLR 12 RLR 23 *P* = 0.840 For HCC: LLR 15 RLR 23 *P* = ND	–	NS	NS
Magistri [21]	24 versus 22	100	No	LLR 13.7 RLR 0	LLR 4.2 RLR 4.5 *P* = 0.95	0	LLR 0 RLR 62 *P* = 0.002	–	LLR 9.25 RLR 10.55 *P* = 0.59	LLR 4.2 RLR 4.5 *P* = 0.95	NS	NS
Present study (2018)	111 versus 61	100	Yes	Excluded	LLR 4 RLR 11 *P* = 0.14	0	LLR 13 RLR 22 *P* = 0.21	0	LLR 6 RLR 10 *P* = 0.054	LLR 16 RLR 11 *P* = 0.40	HCC: NS	HCC: NS

LLR laparoscopic liver resection; *RLR* robotic laparoscopic liver resection; *OS* overall survival; *RFS* recurrence-free survival; *NA* not available; *NS* not significant; *HCC* hepatocellular carcinoma; *CLM* colorectal liver metastases; *PSM* propensity score matching

Table 2 Comparison of baseline characteristics between laparoscopic and robotic hepatectomy before and after propensity score matching

	Before matching				After matching			
	Laparoscopic hepatectomy (n = 111)	Robotic hepatectomy (n = 61)	P value	SMD	Laparoscopic hepatectomy (n = 55)	Robotic hepatectomy (n = 55)	P value	SMD
Variables used for matching								
Male	83 (75)	41 (67)	0.29	0.20	41 (75)	37 (67)	0.53	0.20
Age (yrs)	63 ± 12	66 ± 10	0.19	0.26	66 ± 10	65 ± 10	0.71	0.10
Age ≥ 70 yrs	33 (30)	18 (30)	0.98	0.006	20 (36)	14 (26)	0.20	0.30
ASA score > 2	25 (23)	23 (38)	0.03	0.38	17 (31)	20 (36)	0.70	0.10
Cirrhosis	54 (49)	26 (43)	0.45	0.13	30 (55)	26 (47)	0.84	0.16
Portal vein embolization	1 (1)	1 (2)	0.67	0.33	1 (2)	0 (0)	1.00	–
Preoperative chemotherapy	33 (30)	16 (21)	0.23	0.25	15 (27)	12(22)	0.66	0.32
Major hepatectomy (≥ 3 segments)	15 (14)	9 (15)	0.82	0.006	8 (15)	4 (7)	0.36	0.42
Maximal tumor size, mm	33 ± 23	44 ± 28	0.005	0.44	40 ± 24	40 ± 24	0.96	0
Number of tumors, mean (range)	1.2 (1-3)	1.3 (1-4)	0.24	0.21	1.2 (1-3)	1.3 (1-4)	0.64	0.10
Others								
Body mass index (kg/m^2)	26 ± 6	25 ± 4	0.24	0.19	27 ± 6	25 ± 4	0.04	0.40
Repeat hepatectomy	7 (6)	1 (2)	0.16	0.77	4 (7)	1 (2)	0.36	0.91
Tumor type			0.46	0.11			0.71	0.21
Colorectal liver metastases	23 (21)	15 (25)			11 (20)	13 (24)		
Hepatocellular carcinoma	72 (65)	42 (69)			36 (66)	38 (69)		
Cholangiocarcinoma	6 (5)	2 (3)			4 (7)	2 (4)		
Other	10 (9)	2 (3)			4 (7)	2 (4)		

Results are given as mean ± standard deviation or n (%) or as stated

ASA American Society of Anesthesiologists; *SMD* standardized mean difference

The Pringle maneuver was performed before liver parenchyma division at the discretion of the surgeon [23]. Intermittent clamping was used for 15 min in patients with normal liver parenchyma, and 10 min of clamping and 5 min of unclamping were used in patients with chronic liver disease or cirrhosis. The resected liver specimen was placed in a bag and removed through a suprapubic incision. Abdominal drainage was placed at the end of the resection procedure at the discretion of the surgeon.

Perioperative management

No enhanced recovery after surgery (ERAS) protocol specifically designed for minimally invasive liver resection was registered during the study period in both centers. Both centers adopted a local protocol based on the center's experience and the literature. Briefly, whatever the surgical technique and the center, the central venous pressure was maintained < 5 mmHg during liver parenchyma transection. Intravenous fluid administration was done once the liver parenchyma transection was achieved. Oral food intake started from the day of surgery.

Postoperative computed tomography was performed at the discretion of the surgeon. Hospital discharge was decided at the discretion of the surgeon based on patient and biological results.

Following discharge, patients were followed up at the outpatient consultation 1 month after the surgery, every 3 months for the first 2 years, and every 6 months thereafter.

Definition and outcomes

Tumors located in the posterosuperior segments were those located in segments VII and VIII. Tumors located in the anterolateral segments were those located from segments II to VI. Major hepatectomy was defined as a resection involving ≥ 3 Couinaud segments. Multiple hepatectomy

Table 3 Comparison of perioperative variables between laparoscopic and robotic hepatectomy before and after propensity score matching

	Before matching			After matching		
	Laparoscopic hepatectomy (n = 111)	Robotic hepatectomy (n = 61)	P value	Laparoscopic hepatectomy (n = 55)	Robotic hepatectomy (n = 55)	P value
Intraoperative events						
Major hepatectomy	15 (14)	9 (15)	0.82	8 (15)	4 (7)	0.36
Minor hepatectomy	96 (86)	52 (85)	0.71	47 (85)	51 (93)	0.76
Segments II to VI	70	41	–	35	41	–
Segments I, VII, and VIII	18	8	–	9	7	–
Both	8	3	–	3	3	–
Anatomical minor hepatectomy	40 (36)	16 (26)	0.16	23 (42)	16 (29)	0.10
Multiple hepatectomy	8 (7)	2 (3)	0.29	3 (5)	2 (4)	0.65
Inflow clamping	33 (30)	11 (18)	0.09	18 (33)	10 (18)	0.08
Duration of inflow clamping, minutes	36 ± 21	27 ± 27	0.55	33 ± 24	31 ± 28	0.79
Operative time, minutes	263 ± 109	277 ± 156	0.48	257 ± 102	254 ± 143	0.89
Blood transfusion	2 (2)	9 (15)	0.0009	2 (4)	6 (11)	0.14
Postoperative data						
90-day mortality	0 (0)	0 (0)	–	0 (0)	0 (0)	–
90-day overall morbidity	17 (15)	15 (25)	0.13	7 (13)	12 (22)	0.21
90-day severe morbidity	2 (2)	1 (2)	0.94	0 (0)	1 (2)	0.32
Hospital stay, days	7 ± 6	9 ± 12	0.19	7 ± 5	9 ± 13	0.49
Reoperation	0 (0)	1 (2)	0.18	0 (0)	1 (2)	0.32
Readmission within 90 days	1 (1)	0 (0)	0.46	0 (0)	0 (0)	–
Specimen analysis						
Margin width (mm)	7 ± 9	10 ± 10	0.13	6 ± 7	10 ± 24	0.054
R1 resection (< 1 mm)	17 (15)	7 (11)	0.49	9 (16)	6 (11)	0.40

Results are given as mean ± standard deviation or n (%) or as stated

Severe morbidity defined as ≥ Dindo–Clavien grade 3

was defined as more than one resection. The operative time was defined as the time from incision to wound closure. The time required to dock and undock the robotic arm for RLR was included in the operative time.

Mortality was defined as mortality occurring within 90 days of liver resection or at any time during the hospital stay. All complications were assessed up to 90 days after liver resection. Readmission within 90 days after hospital discharge was recorded. Morbidity was graded according to the Clavien–Dindo classification system, and the most severe grade for each patient was retained [24]. Cirrhosis was based on noninvasive criteria or histology (METAVIR F4). R1 resection was defined as a margin width < 1 mm, and R0 resection was defined as a margin width ≥ 1 mm.

OS was measured from resection to the last follow-up visit or death for any reason. RFS was defined as the time from resection to the date of first clinical or radiological diagnosis of tumor recurrence. All data were retrieved from prospectively maintained data files at each center. Data were evaluated on May 1, 2018.

Statistical analysis

Categorical variables are shown as numbers and percentages. Continuous variables are expressed as medians and ranges. Statistical analyses were performed using the Mann–Whitney U test for nonparametric ordinal variables and the Fisher exact test for categorical variables. Survival analysis was calculated using the Kaplan–Meier method and compared using the log-rank test. A p value <0.05 was considered statistically significant. All statistical analyses were performed with SPSS software (IBM SPSS Statistics, version 23; IBM, Armonk, NY).

PSM was performed to avoid potential confounders in patient selection [25]: age, sex (male vs. female), American Society of Anesthesiologists (ASA) score, portal vein embolization, preoperative chemotherapy, presence of

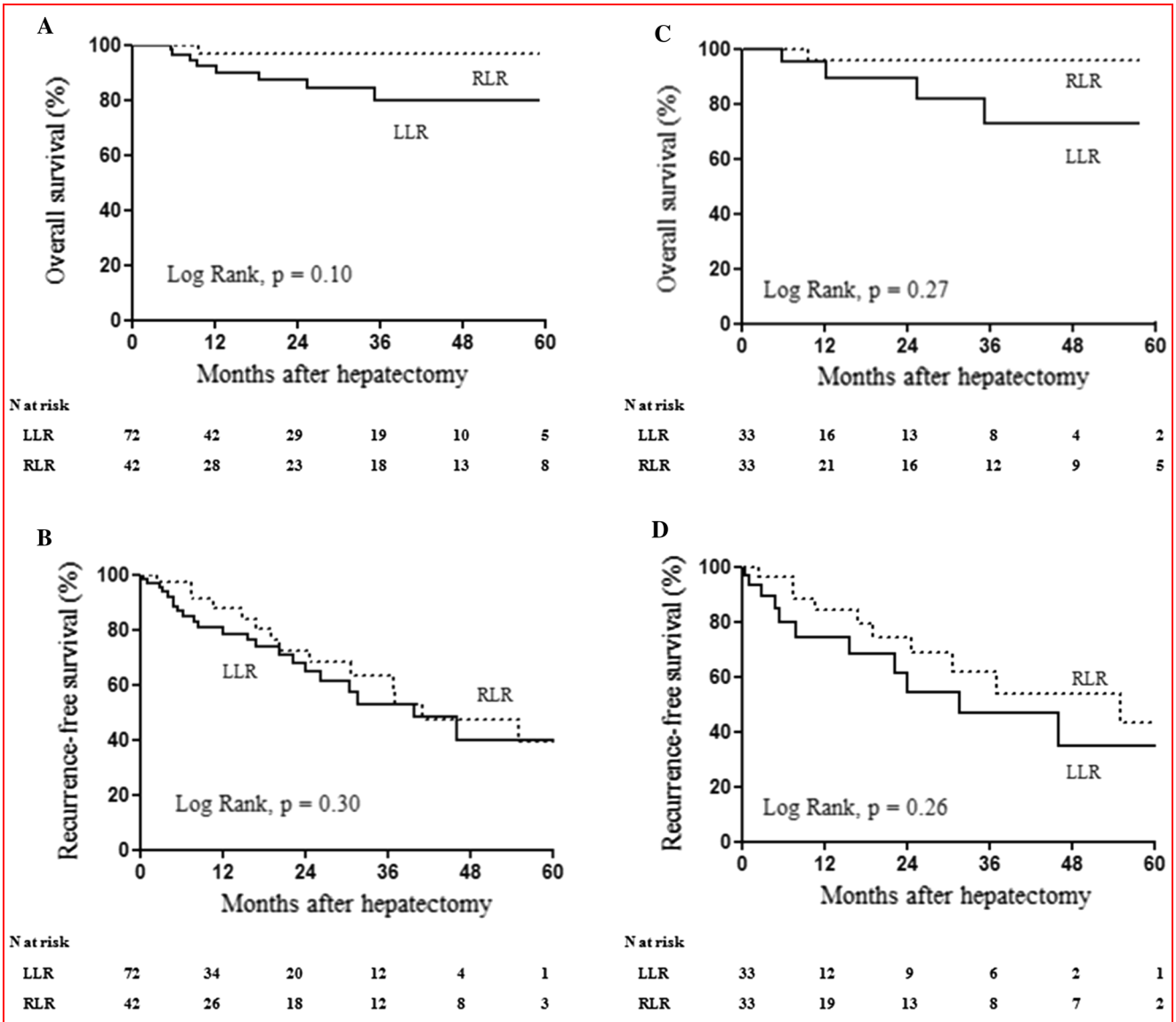

Fig. 1 Survival analysis after LLR and RLR in patients with hepatocellular carcinoma in the unmatched and matched groups of patients. **a** OS in the unmatched group of patients. **b** RFS in the unmatched group of patients. **c** OS in the matched group of patients. **d** RFS in the matched group of patients

cirrhosis, largest tumor size, largest number of tumors, and extent of liver resection (major vs. minor) were recorded. A matched group of patients was created with a 1:1 ratio. PS match method is nearest neighborhood method with the caliper width of 0.20. Standardized mean difference (SMD) was used to assess balance clinical backgrounds between the two groups. SMD < 0.1 indicated very small differences between the means; this implies that optimal balance on a variable is generally achieved; SMD between 0.1 and 0.5 indicated small/modest differences, and SMD > 0.5 indicated considerable differences.

Results

Patients

A total of 188 patients underwent LLR or RLR for hepatobiliary malignancies during the study period: 16 (9%) patients who required conversion to an open approach were excluded from the analysis including 14 in the LLR group and 2 in the RLR group. The study population included the 172 remaining patients: 111 (65%) in the LLR group and 61 (36%) in the RLR group. In the RLR group, 38 cases were from the Center 1 and 28 cases were from the Center 2.

The baseline characteristics of the LLR and RLR groups are shown in Table 2. Patients in the RLR group had higher ASA scores ($p = 0.03$) and larger tumor sizes ($p = 0.005$) than those in the LLR group, whereas the other baseline variables were not different between both groups. After PSM, 55 of 111 LLR patients could be matched (1:1) with 55 of 61 RLR patients (Table 2).

Intra- and postoperative outcomes

Patients in the RLR group (15%) more often required blood transfusion than those in the LLR group (2%, $p = 0.0009$; Table 3), but the difference did not reach statistical significance after PSM ($p = 0.14$; Table 3). Although not significant, hepatic pedicle clamping was more frequently used in the LLR group (30%) than in the RLR group (18%, $p = 0.09$; Table 3). This difference remained similar after PSM ($p = 0.08$; Table 3).

There was no postoperative mortality, and the two groups were similar in terms of overall and severe morbidity rates, length of hospital stay, reoperation, and readmission rates before and after PSM (Table 3).

To investigate the impact of the learning curve on RLR technique, we have divided the study period into two periods and RLR cases performed before April 2014 (March 2011–March 2014; $n = 27$) were compared with RLR cases performed after March 2014 (April 2014–December 2017; $n = 34$). Significant difference was observed in inflow clamping rate between the two groups (early period: 1/27, 4% vs. late period: 10/34, 29%; $p = 0.01$). Although statistically not significant, there was a trend toward a lower rate of blood transfusion rate after RLR performed later in this study (early period: 5/27, 19% vs. late period: 4/34, 12%; $p = 0.46$). These results show feasibility of the RLR technique with maintained safety as the RLR's experience increased.

Analysis of resection margins

The R1 resection rate was similar in both groups (15% in the LLR group vs. 11% in the RLR group, $p = 0.49$). The mean surgical margin width (7 mm in the LLR group vs. 10 mm in the RLR group, $p = 0.13$) was also similar in both groups (Table 3). These remained similar after PSM (Table 3).

Survival

During a mean follow-up period of 25 ± 22 months (median = 18; range 0.4–87.3 months), 4 (7%) patients who underwent RLR and 12 (11%) patients who underwent LLR died. The 1-, 2-, and 3-year OS rates were 93, 88, and 83%, respectively, in the LLR group and 98, 98, and 98%, respectively, in the RLR group. The 2 groups had similar OS ($p = 0.22$) and remained similar after PSM ($p = 0.12$).

The 1-, 2-, and 3-year RFS rates were 76, 61, and 44%, respectively, in the LLR group and 85, 64, and 57%, respectively, in the RLR group ($p = 0.38$) and remained similar after PSM ($p = 0.60$).

Subgroup analysis of patients with hepatocellular carcinoma (HCC)

This is the largest subset of patients including 114 patients (66% of the study population). Subanalysis was performed in these patients with HCC in the unmatched and matched cohorts of patients. Of them, 72 underwent LLR and 42 had RLR. After PSM, 33 of 72 LLR patients could be matched (1:1) with 33 of 42 RLR patients.

The R1 resection rate was similar in both groups (11% in the LLR group vs. 2% in the RLR group, $p = 0.10$). This remained similar after PSM (15% in the LLR group vs. 3% in the RLR group, $p = 0.09$).

Rates of resection margin > 10 mm (22% in the LLR group vs. 31% in the RLR group, $p = 0.30$) and anatomical resection (51% in the LLR group vs. 36% in the RLR group, $p = 0.11$) were similar in both groups. This remained similar after PSM for margin width > 10 mm (18% in the LLR group vs. 30% in the RLR group, $p = 0.25$). For anatomical resection, this difference reached statistical significance after PSM (61% in the LLR group vs. 36% in the RLR group, $p = 0.049$).

The 3-year OS rate was 80% in the LLR group and 97% in the RLR group ($p = 0.10$; Fig. 1a) in the unmatched groups of patients and remained comparable in the matched groups of patients ($p = 0.27$; Fig. 1c). In the unmatched groups of patients, the 3-year RFS rate was 50% in the LLR group and 64% in the RLR group ($p = 0.30$; Fig. 1b); this rate remained comparable in the matched groups of patients ($p = 0.26$; Fig. 1d).

Analysis of the entire cohort including converted patients

Although this was not the main goal of this study, we performed an analysis of the entire cohort ($n = 188$) including the 16 (9%) patients who required conversion to open surgery to investigate the fact that excluding converted patients might have artificially increased blood transfusion in RLR group (because of a lower rate of conversion in these patients).

In this analysis, 125 patients (66%) in the LLR group were compared with 63 patients (34%) in the RLR group. Among these 16 converted patients, 10 had HCC, 5 had colorectal liver metastases, and 1 had cholangiocarcinoma. Although not significant, the conversion rate was higher in

the LLR group (14/125, 11%) than in the RLR group (2/63, 3%; $p = 0.06$). When compared to non-converted patients, transfusion rate (8/16, 50% vs. 11/172, 6%; $p < 0.0001$) was significantly higher in converted patients. When including converted patients in such analysis, blood transfusion rate was similar between RLR (3/63, 5%) and LLR (9/125, 7%) groups ($p = 0.95$).

Discussion

This bi-institutional propensity score-matched study found that blood transfusion rate, postoperative morbidity, surgical margins, and long-term outcomes were similar between the LLR and RLR for hepatobiliary malignancies.

Given the current absence of available randomized controlled studies or ongoing prospective studies (as assessed on August 11, 2018, at ClinicalTrial.gov) comparing RLR with LLR for the management of liver cancer, we used PSM to minimize the risk of patient selection bias that can occur in a retrospective comparative series. Matching analyses and PSM comparing LLR and RLR have been performed in only 4 [6, 14–16] and 2 studies [6, 16], respectively. The main caveats of these studies are as follows: they included patients with benign diseases [10–12, 15] (ranging from 29 to 40% in the LLR group and 25–46% in the RLR group), or they specifically focused on patients who underwent robotic and laparoscopic left lateral sectionectomy [6] or those who had tumors located in the posterosuperior segments of the liver [16].

With equally matched groups, the present study did not demonstrate any differences in blood transfusion, inflow clamping, operative time, length of hospital stay, overall or severe morbidity, and mortality between the 2 groups. However, there is one point which should be addressed. Before matching, the rate of intraoperative blood transfusion was found significantly higher in the RLR group than in the LLR group. Although this was not the main goal of the study, the analysis of the entire cohort including converted patients allowed to support the fact that excluding converted patients might have artificially increased blood transfusion in RLR group (because of a lower rate of conversion in these patients).

Yet, blood loss and transfusion may lead to impaired perioperative [26, 27] and oncologic outcomes (intrahepatic cholangiocarcinoma [26], colorectal liver metastases [28], and hepatocellular carcinoma [29]). As patients requiring conversion to open surgery may have higher rate of blood loss and transfusion, excluding converted patients may also introduce a bias in the analysis of survival. Although an analysis including converted patients would represent real-life situation, the limited number of converted patients (9%) and the presence of various types of malignant disease do not allow for robust survival analysis.

The similar readmission rate between both groups in the current study is an important finding, as this endpoint has been previously reported in only one study [13]. Here again, further larger studies are needed to draw any conclusions on this assertion.

Margin status did not appear to be altered by RLR when compared to LLR in the current study. This finding has been confirmed in other recent studies (Table 1) [7, 12, 17, 18, 21]; however, patient selection bias likely influenced these results. Indeed, as already mentioned, previous studies included patients with benign diseases (Table 1) [12, 18] and patients in whom conversion to an open approach was required (ranging from 4% to 11% in the RLR group and 6% to 14% in the LLR group; Table 1) [7, 17, 21].

The high OS rate (> 80% at 3 years) observed after minimally invasive liver resection in the current study may be explained by the selection of patients with low tumor burden and noncirrhotic underlying liver parenchyma (53%). The heterogeneity of malignancies does not allow for general extrapolation of the 3-year OS and RFS rates of 98 and 57%, respectively, after RLR. These survival rates are particularly higher than the 3-year OS and RFS of 56% and 38%, respectively, observed in a recent international multicenter study that included 61 patients who underwent RLR [30]. In addition to the issue of patient selection, this finding may be partly explained by our mean follow-up period, which was limited to 25 months. However, when we limited long-term outcome comparisons to the largest subset of patients with hepatocellular carcinoma (66% of the study population), the 5-year OS and RFS rates for patients with hepatocellular carcinoma were similar between the two groups.

This study has some limitations. First, its retrospective nature may have led to patient selection bias. Second, although the sample size is one of the largest series to date [30], it still may lack sufficient power to obviate type 2 error. Third, the high OS rate (> 80% at 3 years) in this study compared with that reported in the recent study published by Khan et al. [30] (56%) was likely related to patient selection and inclusion of patients without cirrhosis (> 50% in each group) who frequently had tumors located in the more anterolateral segments of the liver (> 60% in each group), which are more suitable for minimally invasive liver resection.

This study has several strengths, including the large number of patients who underwent surgery within a short and recent period. To our knowledge, this is the first and largest European matched study on RLR versus LLR to date. In contrast to the technique used in a recent

international multicenter study [14, 30], all RLR procedures were considered purely robotic because our technique included robotic docking for all patients prior to mobilization and adhesiolysis.

In conclusion, this study did not demonstrate any differences in short- and long-term outcomes or in the quality of surgical margin clearance among patients who underwent robotic or laparoscopic approaches for hepatobiliary cancer.

References

1. Buell JF, Cherqui D, Geller DA et al (2009) The international position on laparoscopic liver surgery: the Louisville Statement, 2008. Ann Surg 250(5):825–830
2. Wakabayashi G, Cherqui D, Geller DA et al (2015) Recommendations for laparoscopic liver resection: a report from the second international consensus conference held in Morioka. Ann Surg 261(4):619–629
3. Doussot A, Lim C, Lahat E et al (2017) Complications after hepatectomy for hepatocellular carcinoma independently shorten survival: a western, single-center audit. Ann Surg Oncol 24(6):1569–1578
4. Kawai T, Goumard C, Jeune F et al (2018) Laparoscopic liver resection for colorectal liver metastasis patients allows patients to start adjuvant chemotherapy without delay: a propensity score analysis. Surg Endosc 32(7):3273–3281
5. Efanov M, Alikhanov R, Tsvirkun V et al (2017) Comparative analysis of learning curve in complex robot-assisted and laparoscopic liver resection. HPB (Oxford) 19(9):818–824
6. Salloum C, Lim C, Lahat E et al (2016) Robotic-assisted versus laparoscopic left lateral sectionectomy: analysis of surgical outcomes and costs by a propensity score matched cohort study. World J Surg 41(2):516–524. https://doi.org/10.1007/s00268-016-3736-2
7. Berber E, Akyildiz HY, Aucejo F et al (2010) Robotic versus laparoscopic resection of liver tumours. HPB (Oxford) 12(8):583–586
8. Ji WB, Wang HG, Zhao ZM et al (2010) Robotic-assisted laparoscopic anatomic hepatectomy in China: initial experience. Ann Surg 253(2):342–348
9. Packiam V, Bartlett DL, Tohme S et al (2012) Minimally invasive liver resection: robotic versus laparoscopic left lateral sectionectomy. J Gastrointest Surg 16(12):2233–2238
10. Troisi RI, Patriti A, Montalti R, Casciola L (2013) Robot assistance in liver surgery: a real advantage over a fully laparoscopic approach? Results of a comparative bi-institutional analysis. Int J Med Robot 9(2):160–166
11. Wu YM, Hu RH, Lai HS, Lee PH (2014) Robotic-assisted minimally invasive liver resection. Asian J Surg 37(2):53–57
12. Yu YD, Kim KH, Jung DH et al (2014) Robotic versus laparoscopic liver resection: a comparative study from a single center. Langenbecks Arch Surg 399(8):1039–1045
13. Spampinato MG, Coratti A, Bianco L et al (2014) Perioperative outcomes of laparoscopic and robot-assisted major hepatectomies: an Italian multi-institutional comparative study. Surg Endosc 28(10):2973–2979
14. Tsung A, Geller DA, Sukato DC et al (2014) Robotic versus laparoscopic hepatectomy: a matched comparison. Ann Surg 259(3):549–555
15. Tranchart H, Ceribelli C, Ferretti S et al (2014) Traditional versus robot-assisted full laparoscopic liver resection: a matched-pair comparative study. World J Surg 38(11):2904–2909. https://doi.org/10.1007/s00268-014-2679-8
16. Montalti R, Scuderi V, Patriti A et al (2015) Robotic versus laparoscopic resections of posterosuperior segments of the liver: a propensity score-matched comparison. Surg Endosc 30(3):1004–1013
17. Lai EC, Tang CN (2016) Long-term survival analysis of robotic versus conventional laparoscopic hepatectomy for hepatocellular carcinoma: a comparative study. Surg Laparosc Endosc Percutan Tech 26(2):162–166
18. Croner RS, Perrakis A, Hohenberger W, Brunner M (2016) Robotic liver surgery for minor hepatic resections: a comparison with laparoscopic and open standard procedures. Langenbecks Arch Surg 401(5):707–714
19. Lee KF, Cheung YS, Chong CC et al (2016) Laparoscopic and robotic hepatectomy: experience from a single centre. ANZ J Surg 86(3):122–126
20. Kim JK, Park JS, Han DH et al (2016) Robotic versus laparoscopic left lateral sectionectomy of liver. Surg Endosc 30(11):4756–4764
21. Magistri P, Tarantino G, Guidetti C et al (2017) Laparoscopic versus robotic surgery for hepatocellular carcinoma: the first 46 consecutive cases. J Surg Res 217:92–99
22. Salloum C, Subar D, Memeo R et al (2014) Laparoscopic robotic liver surgery: the Henri Mondor initial experience of 20 cases. J Robot Surg 8(2):119–124
23. Lim C, Osseis M, Lahat E et al (2018) Extracorporeal pringle maneuver during laparoscopic and robotic hepatectomy: detailed technique and first comparison with intracorporeal maneuver. J Am Coll Surg 226(5):e19–e25
24. Clavien PA, Barkun J, de Oliveira ML et al (2009) The Clavien–Dindo classification of surgical complications: five-year experience. Ann Surg 250(2):187–196
25. Lonjon G, Porcher R, Ergina P et al (2016) Potential pitfalls of reporting and bias in observational studies with propensity score analysis assessing a surgical procedure: a methodological systematic review. Ann Surg 265(5):901–909
26. Gomez-Gavara C, Doussot A, Lim C et al (2017) Impact of intraoperative blood transfusion on short and long term outcomes after curative hepatectomy for intrahepatic cholangiocarcinoma: a propensity score matching analysis by the AFC-IHCC study group. HPB (Oxford) 19(5):411–420
27. Lyu X, Qiao W, Li D, Leng Y (2017) Impact of perioperative blood transfusion on clinical outcomes in patients with colorectal liver metastasis after hepatectomy: a meta-analysis. Oncotarget 8(25):41740–41748
28. Postlewait LM, Squires MH 3rd, Kooby DA et al (2016) The relationship of blood transfusion with peri-operative and long-term outcomes after major hepatectomy for metastatic colorectal cancer: a multi-institutional study of 456 patients. HPB (Oxford) 18(2):192–199
29. Kuroda S, Tashiro H, Kobayashi T et al (2012) No impact of perioperative blood transfusion on recurrence of hepatocellular carcinoma after hepatectomy. World J Surg 36(3):651–658. https://doi.org/10.1007/s00268-012-1425-3
30. Khan S, Beard RE, Kingham PT et al (2018) Long-term oncologic outcomes following robotic liver resections for primary hepatobiliary malignancies: a multicenter study. Ann Surg Oncol 25(9):2652–2660. https://doi.org/10.1245/s10434-018-6629-9