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ORIGINAL ARTICLE

Is minimally invasive liver surgery a reasonable option in recurrent HCC? A snapshot from the I Go MILS registry

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Abstract

Laparoscopic liver resection (LLR) for Hepatocellular carcinoma (HCC) is a safe procedure. Repeat surgery is more often required, and the role of minimally invasive liver surgery (MILS) is not yet clearly defined. The present study analyzes data compiled by the Italian Group of Minimally Invasive Liver Surgery (IGoMILS) on LLR. To compare repeated LLR with the first LLR for HCC is the primary endpoint. The secondary endpoint was to evaluate the outcome of repeat LLR in the case of primary open versus primary MILS surgery. The data cohort is divided into two groups. Group 1: first liver resection and Group 2: Repeat LLR. To compare the two groups a 3:1 Propensity Score Matching is performed to analyze open versus MILS primary resection. Fifty-two centers were involved in the present study, and 1054 patients were enrolled. 80 patients underwent to a repeat LLR. The type of resection was different, with more major resections in the group 1 before matching the two groups. After propensity score matching 3:1, each group consisted of 222 and 74 patients. No difference between the two groups was observed. In the subgroup analysis, in 44 patients the first resection was performed by an open approach. The other 36 patients were resected with a MILS approach. We found no difference between these two subgroups of patients. The present study in repeat MILS for HCC using the IGoMILS Registry has observed the feasibility and safety of the MILS procedure.

Keywords Laparoscopic HCC · Redo surgery · Robotic · Recurrence · IGoMILS · Laparoscopic liver resection · Minimally invasive · Laparoscopic indications

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Introduction

Hepatocellular carcinoma (HCC) is the fifth cause of cancer-related deaths worldwide. In most patients, HCC occurs in case of underlying liver cirrhosis. Liver resection (LR) remains the best curative therapy. Recently, minimally invasive liver surgery (MILS) has gained broad consensus in the management of HCC [1]. The safety of MILS has also been explored in the setting of cirrhosis, suggesting its application even in the case of portal hypertension [2, 3]. Laparoscopic liver resection (LLR) is safe and feasible for all liver segments with acceptable morbidity [4], with comparable outcomes in the unfavorable segments [5]. The worldwide diffusion and results of MILS have progressively increased [6]. The recurrence of HCC after resection is a keypoint for improving long-term prognosis. In addition, surgical resection may provide a benefit in terms of long-term survival in recurrent HCC for both intra- and extra-hepatic localization [7]. MILS's role for HCC is gaining interest, showing a protective role in terms of the risk of salvage liver transplantation failure [8]. Repeat surgery can be associated with higher intra-operative bleeding and iatrogenic injury to other organs due to adhesions. Repeat laparoscopic resection has been reported as a feasible and safe procedure in different studies [9, 10].

The present study aimed to analyze the safety of repeat MILS surgery and the role of the first resection in terms of outcome in case of repeated surgery by reviewing the Italian Group of Minimally Invasive Liver Surgery (IGoMILS) registry.

Methods

The IGoMILS project is a prospective national registry of MILS. Since November 2014, all cases of LLR have been prospectively registered. We analyzed the hepatic resections for HCC reported from November 2014 to November 2018. Fifty-two centers participated in the present study; 1054 patients underwent to HCC LLR. Patients were divided into two groups based on primary or repeat resection. We defined the Group 1: first LR and Group 2: Repeat LLR. Group 1 included 974 patients with a primary LR and Group 2 included 80 patients undergoing to a redo LR. We extracted patient characteristics (including sex, age, body mass index (BMI), underlining liver disease, Child–Pugh Score, Meld Score, previous cholecystectomy, portal hypertension); surgical characteristics (including nodule diameter, nodule localization, type of resection, resection margins, duration of surgery, estimated blood loss, use of drains, conversion to open) and perioperative data (including types of complications, transfusion, length of postoperative hospital stay, CCI and mortality). HCC was related to Hepatitis C virus (HCV), Hepatitis B virus (HBV), Alcohol, Non-Alcoholic Steatohepatitis (NASH), other and on Healthy liver. The Child–Pugh score was calculated according to preoperative albumin, presence of ascites, and encephalopathy. The Model of End-stage Liver Disease (MELD) was calculated according to the Mayo Clinic definition [11]. The postoperative morbidity was classified according to the Dindo–Clavien Classification [12] and the Comprehensive Complication Index [13]. The type of resection was divided in wedge resection, segmentectomy, left lateral sectionectomy, right posterior sectionectomy, right anterior sectionectomy, bisegmentectomy, right or left hepatectomy, and others (including left or right extended hepatectomy, central hepatectomy, and ALPPS procedures). Written informed consent was obtained from all patients in accordance with the Declaration of Helsinki, and this study was approved by the institutional review board of all IGoMILS centers.

Propensity score matching

Propensity score (PS) matching was performed on the cohort to adjust for any difference in average outcomes for segment location selection bias. PS matching was performed by considering all significant variables between the two groups in the preliminary analysis. The matching was achieved on the basis of PS, generated by logistic regression and relied on the following eight covariates: sex (male/female); age; body mass index (BMI); previous cholecystectomy (yes/no); nodule diameter, Portal Hypertention (yes/no); Child–Pugh Score (A/B/C); and MELD Score. After estimation of PS, a regular 3:1 nearest-neighbor matching process was performed. A small caliper (0 1) was specified to improve balance.

Statistical analysis

A 3:1 PS matching was performed between the two groups to minimize selection bias in the baseline characteristics. A logistic regression model was used to estimate PS of a patient who underwent LLR for repeat resection to match with a patient who underwent LLR for a primary resection.

The effect size (Cohen *d* value) that was lower than 0.1 indicated very small differences between means, values between 0.1 and 0.3 indicated small differences, values between 0.3 and 0.5 indicated moderate differences, and values greater than 0.5 indicated large differences.

All variables were compared using the χ^2 or Fisher's exact test for categorical data, the Mann–Whitney *U* test for non-normally distributed continuous data, and

Student's *t* test for normally distributed continuous variables. Continuous variables were reported as medians and interquartile ranges (IQR). Categorical variables were reported as numbers and percentages. All data are expressed as mean ± standard deviation or median and range. A *p* value of < 0.05 was considered as statistically significant. Statistical analyses were performed using the SPSS Statistics version 22.0 (IBM SPSS).

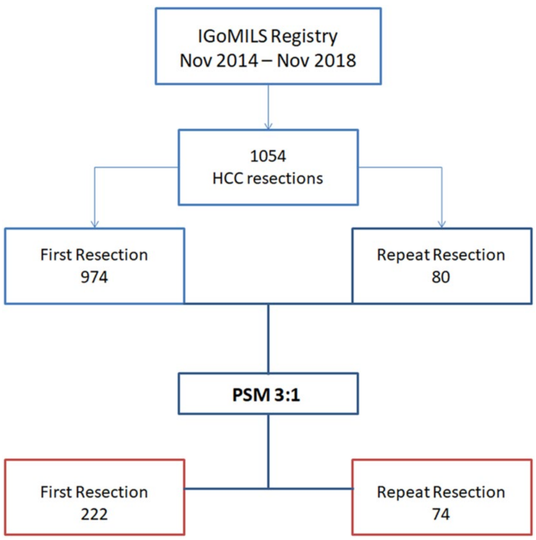


Fig. 1 Flow diagram of propensity score

Results

The IGoMILS registry includes a total of 1054 LLR for HCC. Group 1 (first LLR) consists of 974 patients and Group 2 (repeat resection) of 80 patients (Fig. 1).

No differences were observed regarding sex, BMI, Cirrhosis, Etiology (HCV, Alcohol, NASH, Healthy Liver), MELD Score, nodule localization, Pringle Maneuver, Transfusion, Surgical Time, Blood loss, Length of Stay, CCI, Morbidity, and Mortality (Tables 1, 2, 3). For HBV etiology, Child–Pugh Score, portal hypertension, previous cholecystectomies, drain, multiple resection, and conversion rate, a small difference between the two groups at the Cohen *d* value was observed. Results are further provided in Tables 1, 2, 3. Localization of the tumor is shown in Fig. 2A. The types of surgical resections in Group 2 were as follows: wedge resections (51 patients); segmentectomies (19 patients); left lateral sectionectomies (3 patients); bisegmentectomies (2 patients); left hepatectomies (4 patients); and right hepatectomy (1 patient) (Table 2).

After propensity score matching, Group 1 was composed of 222 patients and Group 2 of 74 patients (Fig. 1). Nineteen centers had at least one repeat resection. The median number of repeat resection was 3 (2–6), with a median number of HCC resections of 38 (10–64). The total volume of the 19 Centers was 760 resections. The evolution of the total MILS and repeat patients is represented in

Table 1 Preoperative charateristics

	Before matching			Propensity score match		
	Group 1 (first resection)	Group 2 (redo resection)	Cohen *d*	Group 1 (first resection)	Group 2 (redo resection)	Cohen *d*
Number	974	80	–	222	74	–
Sex						
Male	726 (74.5%)	58 (72.5%)	− 0.06	165 (73.9%)	55 (74.3%)	0
Age	70 [62–76]	72.5 [66–76.75]	− 0.0001	70 [64–76]	72 [65–76]	− 0.00006
BMI	26 [24–30]	26.5 [23–30]	− 0.00007	26 [23–28]	26 [24–29]	− 0.00001
Underlying liver disease[a]						
HCV	491 (50.4%)	40 (50%)	0.02	113 (50.9%)	35 (47.3%)	0.079
HBV	204 (20.9%)	21 (26.2%)	− 0.12	36 (16.2%)	20 (27%)	− 0.29
Alcohol	141 (14.4%)	11 (13.8%)	0.028	38 (17.1%)	11 (14.8%)	0.05
NASH	119 (12.2%)	8 (10%)	0.06	24 (10.8%)	8 (10.8%)	0
Healty Liver	44 (4.5%)	4 (5%)	0	12 (5.4%)	4 (5.4%)	0
Other	106 (10.9%)	7 (8.7%)	0.06	27 (12.1%)	6 (8.1%)	0.12
Child–Pugh score						
A/B/C	886/80/3	69/11/0	− 0.16	193/27/2	66/8/0	0.081
MELD score	7 [7–9]	7 [7–9]	− 0.0001	8 [7–9]	7 [7–9]	0.00026

BMI Body Mass Index, *HCV* Hepatitis C Virus, *HBV* Hepatitis B Virus, *NASH* Non-alcoholic steatohepatitis

[a]Some patients had multiple aetiologies

Table 2 Operative findings

	Before matching			Propensity score match		
	Group 1 (first resection)	Group 2 (redo resection)	Cohen *d*	Group 1 (first resection)	Group 2 (redo resection)	Cohen *d*
Number	974	80		222	74	
Previous cholecistectomy (Yes)	91 (9.3%)	13 (16.2%)	− 0.23	33 (14.8%)	8 (10.8%)	0.11
Portal hypertension (Present)	283 (29%)	16 (20%)	0.19	52 (23.4%)	16 (21.6%)	0.026
Nodule localization (Fig. 1)			0.00012			0.0001
Nodule diameter (mm)	30 [20–45]	24 [15–30]	0.00025	27 [20–36]	25 [16–30]	0.00007
Type of resection			0.00059			0.000038
Wedge	462 (47.4%)	49 (61.2%)		119 (53.6%)	47 (63.5%)	
Segmentectomy	276 (28.3%)	21 (26.3%)		67 (30.2%)	17 (22.97%)	
Left lateral sectionectomy	81 (8.3%)	3 (3.7%)		17 (7.6%)	3 (4%)	
Right posterior sectionectomy	13 (1.3%)	–		1 (0.45%)	0 (-)	
Right anterior sectionectomy	4 (0.4%)	–		2 (0.9%)	0 (-)	
Bisegmentectomy	25 (2.5%)	2 (2.5%)		4 (1.8%)	2 (2.7%)	
Right hepatectomy	21 (2.1%)	1 (1.3%)		6 (2.7%)	1 (1.3%)	
Left hepatectomy	26 (2.6%)	4 (5%)		4 (1.8%)	4 (5.4%)	
Others**	13 (1.3%)	–		2 (0.9%)	0 (-)	
Multiple resection (Yes)	72 (7.4%)	3 (3.7%)	0.15	17 (7.6%)	3 (4%)	0.15
Surgical margin (mm)	5 [1–10]	3 [1–9.25]	0.0003	5 [1–10]	3 [1–9.5]	0.0018
Surgical time (min)	210 [150–270]	207 [150–300]	0.00002	203 [150–270]	210 [150–300]	− 0.0001
Estimated blood loss (cc)	150 [50–300]	100 [50–212]	0.00005	100 [50–200]	100 [50–225]	− 0.00002
Drain tube (yes)	802 (82.3%)	61 (76.3%)	0.21	191 (86%)	57 (77%)	0.25

**Type of resection: Others were 1 left extended hepatectomy, 1 right extended hepatectomy, 3 Central Hepatectomies, 5 first step ALPPS, 3 s step ALPPS

Fig. 3. In Group 1, 72 patients were included from Centers without patients enlisted in the repeat group.

For the underlying liver disease, a major HBV infection was observed in Group 2 ($d = -0.29$). Portal hypertension, previous cholecystectomies, drain, multiple resection, and conversion rate confirmed a small difference between the two groups at the Cohen *d* value was observed (Table 2). A moderate difference was observed for the transfusion rate ($d = -0.31$) (Tables 2, 3). The non-anatomical resection was 119 (53.6%) and 47 (63.51%) in the first and second groups. The localization of the tumor of the two groups after PSM is represented in Fig. 2B. We performed a logistic regression to investigate the role of different variables. The lesion diameter ($p = 0.071$), the first surgery open ($p = 0.562$), and the previous wedge resection ($p = 0.358$) were not significant. We did not find any independent factor of conversion to open surgery.

No difference was observed between the two groups in terms of morbidity. In particular, in Group 1 versus Group 2, ascites rate was 6.2% and 3.7%; biliary leak 2.4% and 1.2% (Clavien-Dindo Grade ≥ III was 47.8% and 100%); abdominal collection 1.2% and 3.7% (Clavien–Dindo Grade ≥ III was 50% and 66.6%); pleural effusion 5.2% and 3.7% (Clavien–Dindo Grade ≥ III was 13.7% and 33.3%); all type of complications are described in Supplementary Table 1.

The overall conversion rate was 7.3%. The most frequent indication of conversion was the oncological radicality. Adhesion syndrome was described more often in Group 2, but no difference was observed after PSM. In 77 patients of the overall cohort, a conversion to open was required. The median operative time was 242 min, higher than the median operative time in cases of no conversion (205 min). In all conversions, the patients completed the resection as planned. Median nodule diameter was 35 mm. Forty (51.9%) of the

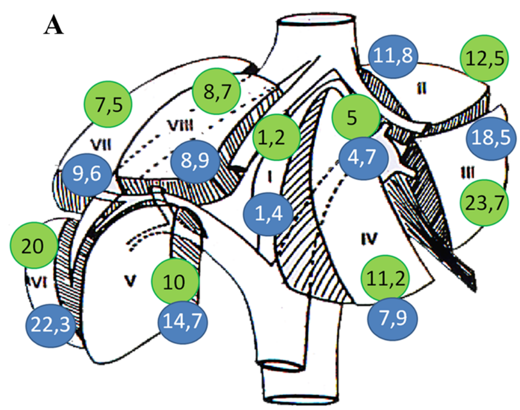
Table 3 Post-operative findings

	Before matching			Propensity score match		
	Group 1 (first resection)	Group 2 (redo resection)	Cohen *d*	Group 1 (first resection)	Group 2 (redo resection)	Cohen *d*
Number	974	80		222	74	
Conversion to open[a]	68 (6.98%)	9 (11.2%)	– 0.15	19 (8.5%)	9 (12.1%)	– 0.10
Adhesion syndrome	10 (14.7%)	3 (33.3%)	– 0.26	6 (31.6%)	3 (33.3%)	– 0.06
Bleeding	21 (30.8%)	3 (33.3%)	– 0.13	5 (26.3%)	3 (33.3%)	– 0.13
Biliary control	5 (7.3%)	0	0.12	2 (10.5%)	0 (-)	0.10
Oncological radicality	34 (51.4%)	2 (2.2%)	0.05	10 (52.6%)	2 (22.2%)	0.09
Anesthesia	2 (2.9%)	1 (1.1%)	– 0.18	0 (-)	1 (11.1%)	– 0.31
Transfusion	35 (11%)	5 (6.2%)	– 0.1	5 (2.2%)	5 (6.7%)	– 0.31
Length of Stay (days)	5 [4–6]	5 [4–6]	0.00008	5 [4–6]	5 [4–6]	0.00008
Morbidity	225 (23.1%)	17 (21.1/2%)	0.047	58 (26.1%)	17 (22.97%)	0.068
CCIndex	20.9 [8.7–26.3]	20.9 [14.8–27.9]	0.00003	20.9 [12.2–26.2]	20.9 [8.7–27.9]	0.000049
Mortality	4 (0.4%)	0	0	1 (0.45%)	0 (-)	0

[a]Conversion had two indications in four cases (bleeding + oncological in two cases; Bleeding + biliary control in one case and, oncological + Adhesion in one case). CCIndex is express only if morbidity was present

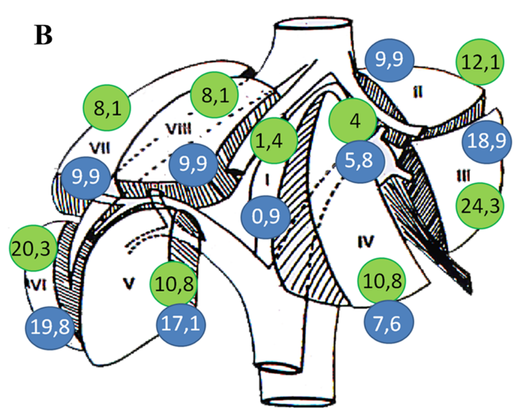
Fig. 2 **A**—Liver nodules localization in the two groups. **B**—Liver nodules localization after propensity score match

A



Segment	First resection	Redo resection
1	14 (1,4%)	1 (1,25%)
2	115 (11,8%)	10 (12.5%)
3	180 (18,5%)	19 (23,7%)
4a	46(4,7%)	4(5%)
4b	77 (7,9%)	9 (11,25%)
5	143 (14,7%)	8 (10%)
6	217 (22,3%)	16 (20%)
7	94 (9,6%)	6 (7,5%)
8	87 (8,9%)	7 (8,75%)

B



Segment	First resection	Redo resection
1	2 (0,9%)	1 (1,4%)
2	22 (9,9%)	9 (12.1%)
3	42 (18,9%)	18 (24,3%)
4a	13 (5,8%)	3(4%)
4b	17 (7,6%)	8 (10,8%)
5	38 (17,1%)	8 (10,8%)
6	44 (19,8%)	15 (20,3%)
7	22 (9,9%)	6 (8,1%)
8	22 (9,9%)	6 (8,1%)

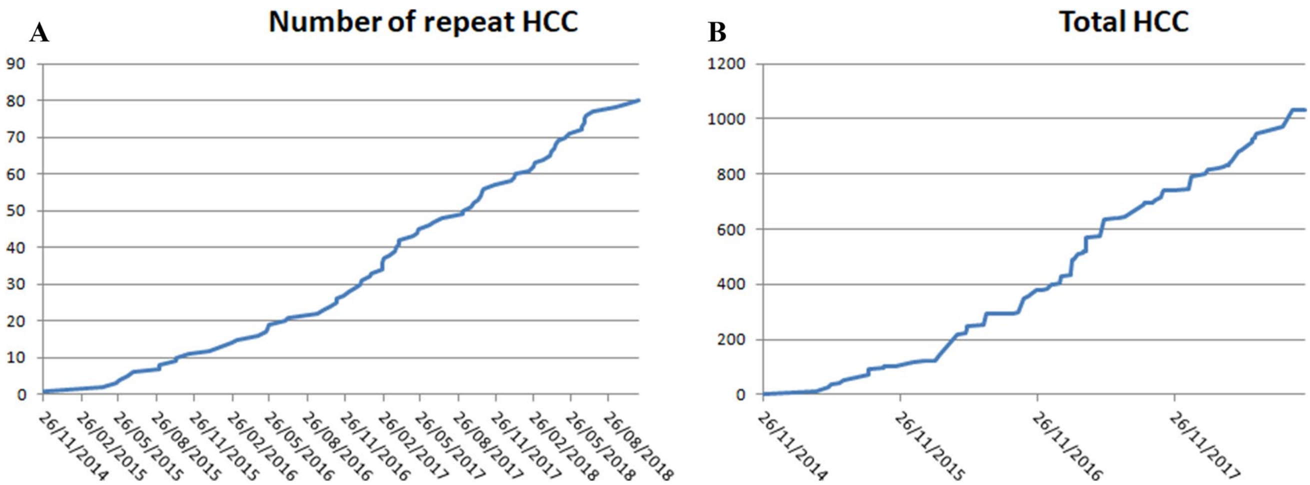


Fig. 3 Evolution of the repeat resection and the total HCC resection in the IGoMILS Registry during the study time

77 cases had a nodule in the unfavorable segments. In the 19 centers registered repeat resection, 51 conversions were observed. In 36 patients, conversion was performed to reach the oncological radicality, including difficulty to detect the nodule, margin doubt, difficulty to complete the resection by MILS technique. The other events, for which a laparotomic conversion was requested, were bleeding, biliary stasis, and anesthesia necessity. Due to the small sample size and the small number of events the differences between the two groups were difficult to analyze.

Patients with a first resection by open approach versus MILS approach were analyzed in Group 2. In 44 patients, the first resection was performed by an open approach, 36 patients were resected with a MILS approach (5 of those with the robotic approach). First resection in Group 2 was as follows: wedge resection (43 patients); segmentectomy (26 patients); left lateral sectionectomy (3 patients); right posterior sectionectomy (3 patients), and a major resection (5 patients) (Table 4). No differences between these two subgroups of patients were found. Operative time, blood loss, conversion rate, and length of stay were similar. Overall morbidity was similar; however, when a complication was present, the CCI seemed to be higher when the first resection was performed by a MILS approach ($p = 0.049$).

Discussion

The present study reports a prospective national multicentric study of repeat LLR for patients with HCC before and after PS matching. Repeat LR with a MILS approach has been successfully achieved in 80 patients. Operative and postoperative outcomes were similar between the two groups. A propensity score match was carried out to eliminate potential selection bias.

In the present series, the non-anatomical resection rates were 47.4% and 61.2% in Groups 1 and 2, respectively. The role of anatomical resection for HCC is still debating, and lots of studies have compared the two types of resections [14–17]. According to a comparative Asian study including 385 cases (Taiwanese 105, Japanese 280), after PSM, the disease-free survival (DFS) and overall survival (OS) data were not significantly different between the two groups at 5-year follow-up [14]. The surgical eradication of HCC with anatomical resection is based on adequate clearance of the tumor together with the surrounding microenvironment niche. The margin safety should be correlated to tumor biology [15].

A recent analysis comparing laparoscopic anatomical versus non-anatomical resections for HCC in a single center includes 231 patients. The authors reported the long-term outcomes of the non-anatomical group not inferior to those of the anatomical group [16]. Moreover, the size of the tumor nodule is important. In the case of small HCC < 3 cm non-anatomical resection outcomes are comparable to anatomical resection [17]. In the present study, tumor nodule diameters were 30 mm for the first resection group and 24 mm for the repeat group (Table 2).

The role of repeat MILS compared to the primary resection has been investigated in high experienced European centers' early experience [18]. The authors observed an increased operative time and blood loss. However, this initial experience was performed with different indications and only 10% of HCC.

MILS's benefit for recurrent HCC has been demonstrated with a significant increase in term of disease-free survival compared to open repeat surgery in a single-surgeon study [19]. The above-mentioned salient results may be overstated due to the small cohort and need to be confirmed with multicentric studies. The first review of 103 cases of MILS for

Table 4 Sub-analysis inside the repeat group

	Group redo-open	Group redo-MILS	*p* value
	44	36	
Sex			
Male/Female	31/13	27/9	
Age	72 [65.5–76.5]	73.5 [66–76.5]	0.555
BMI	25 [23–28]	27 [22–29]	0.297
Underlying liver deasese			
HCV	23	17	0.658
HBV	12	9	0.821
Alcohol	4	7	0.185
NASH	3	5	0.300
Healty liver	4	0	0.065
Other	3	4	0.505
Child–Pugh score			
A/B/C	37/7/0	32/4/0	
MELD Score	7 [7–8.5]	7.5 [6–9]	0.804
Previous Cholecis-tectomy	7	6	0.928
Portal Hypertension	7	9	
nodule diameter (mm)	25 [15–35.5]	22 [15–30]	0.812
First liver resection			
Wedge	28	23	0.373
Segmentectomy	11	8	
Left lateral sec-tionectomy	1	2	
Bisegmentectomy	–	2	
Major hepatectomy	3 left 1 OLT	1 right	
Surgical margin (mm)	3 [1–5]	5 [0–10]	0.602
Surgical time (min)	197 [120–315]	210 [150–240]	0.954
Estimated blood loss (cc)	100 [50–250]	100 [40–200]	0.716
Drain tube (yes)	35	26	0.455
Conversion to open	4	5	0.514
Transfusion	2	3	0.505
Length of stay (days)	5 [4–6]	4.5 [4–6.5]	0.863
Morbidity	6	11	0.076
CCIndex	14.8 [8.7–22.6]	20.9 [20.9–29.6]	0.49
Mortality	–	–	–

First liver resection open vs mils

BMI Body Mass Index, *HCV* Hepatitis C Virus, *HBV* Hepatitis B Virus, *NASH* Non-alcoholic steatohepatitis, CCIndex is express only if morbidity was present

repeat HCC reported ten studies demonstrating the increasing experience with redo surgeries [20]. Previous surgeries in the reported review were open and MILS, major resection, multiple tumors, and nodules in the unfavorable segments [20].

Repeat hepatectomy, open or laparoscopic, continues to be a challenging surgical procedure. As previously described, the initial differences, like higher operative time and blood loss [18], have been overcome with the increasing surgeon experience [21, 22]. Two recent meta-analyses have studied the outcome of repeat MILS [23, 24]. These two studies have observed no differences in term of operative time, but a reduction in terms of blood loss, postoperative complication, major complication, and length of stay. A noteworthy finding is the higher R0 resection rate reported in the MILS group. The laparoscopic magnification imaging and the improvements of surgical instruments and surgeons' experience can explain the R0 divergence.

A European multicentric study comparing open VS laparoscopic repeat resection for colorectal liver metastases reported a shorter operative time, less use of the Pringle maneuver and, a shorter length of stay in the laparoscopic group [25]. Moreover, as reported in other series, the R0 rate was higher in the laparoscopic group. A review of the literature is resumed in Table 5. The present study is the largest national prospective study.

One potential indication for the conversion is the presence of abdominal adhesions. However, in our study, the adhesion syndrome was not the first indication and was not significant between the groups. Laparoscopic surgeon well knows that the pneumoperitoneum tensing up adhesions allows easier adhesiolysis than an open approach. Interestingly, the conversion rate was similar in the sub-analysis between patients with a first open surgery versus laparoscopic. This result should encourage choosing a MILS approach in patients with a previous open LR. Considering that the annual number of repeat LR for HCC is a relatively rare event, and that repeat resection is in selected patients an alternative to salvage liver transplantation, there is still no standardized indication to perform repeat resection by a MILS approach. In the present study, looking at the previous LR for Group 2, a major resection was performed in five patients (Table 4). Moreover, one of them was a liver transplanted patient for HCC. A laparoscopic approach resected the recurrence nodule [26].

A world collaborative study compared open versus laparoscopic repeat resection and confirmed a significative minor operative time and intraoperative blood loss [27]. However, this study did not observe a shorter length of stay. Nevertheless, the overall survival and disease-free survival was similar between the open and the MILS group. In the case of recurrence in the contralateral liver segment of the previous resection, a laparoscopic approach seems to improve the patient's outcome [28].

The present study may have some limitations. First, this is a minimally invasive surgery registry and the open surgery is not included. Second, as a National Registry, all centers are allowed to enroll patients, which includes also

Table 5 Review of repeat laparoscopic liver resection for Hepatocellular Carcinoma

References	Country	Study period	Group	Number	Age	Gender (M/F)	Child–Pugh	Previous MILS/Open	Nodule diameter	Operative time	Blood loss	Major resection	Morbidity	Conversion	Lenght of stay (days)
Kanazawa [32]	Japan	2006–2011	ReLLR	20	70	15/5	19/1	5/15	1.7[0.7–3.5]	239	78	–	1 (5%)	2 (10%)	9
			ROR	20	65	19/1	17/3	–	2.2 [1.3–4.1]	211	612	–	16 (80%)	–	19
Chan [33]	China	2004–2013	ReLLR	11	61	8/3	11/0	5/6	2 [1–4.5]	200	100	0	2 (18%)	0	6
			ROR	22	62	16/6	-	–	2 [1–5]	188	340	0	1 (4.5%)	-	5
Zhang [34]	China	2014	ReLLR	31	54	26/5	–	0/31	2.5 ± 1.0	116.7	117.5	0	–	0	4.5
			ROR	33	59	27/6	–	0/33	3.8 ± 1.1	148.2	265.9	0	–	–	6.0
Liu [35]	China	2008–2015	ReLLR	30	56	23/7	30/0	9/21	2.1[1–5]	200.5	100	1 (3.3%)	2 (6.7%)	4 (13.3%)	9.5
			ROR	30	48	28/2	27/2	-	2.45[1–4.3]	207.5	400	3 (10%)	10 (30%)		13.5
Ogawa [22]	Japan	2014–2018	ReLLR	28	73	21/7	28/0			233	50		3 (10.7%)	0	7
			LLR	76	71	58/18	68/8			258	50		6 (7.9%)	2 (2.5%)	7
Goh [19]	Singapore	2005–2017	ReLLR	20	68.5	18/2	–	13/7	2 [1.15–2.7]	315	200	2 (10%)	2 (10%)	3 (15%)	4
			LLR	185	63	138/47	–	–	2.8[2–4.2]	225	300	20 (10.8%)	5 (25%)	27 (14.6%)	4
Belli [9]	Italy	2004–2008	ReLLR	12	69	–	–	8/4	40 [30–48]	72.5	–	0	4(27%)	–-	7.4
Onoe [21]	Japan	2007–2018	ReLLR	30	70.9	23/7	30/0	9/21	12.5 [.8–35]	276	100	-	2 (6.75%)	2 (6.75%)	10
			ROR	42	72	30/12	34/8	6/36	17.5 [5–60]	292	435	-	6 (14.3%)		14.5
Gon [28]	Japan	2008–2019	ReLLR	23	72	18/5	23/0	2/21	1.9 [1.2–2.5]	286	10	–	2 (8.7%)	1	9
			ROR	23	72	18/5	23/0	0/23	2 [1.3–2.6]	348	420	–	3 (13%)		15
Morise [27]	International	2007–2017	ReLLR	238	67.1	181/57		57/181	27.5 ± 28.8	272	268		36 (15%)		10.4
			ROR	238	66.4	184/54		51/187	27.7 ± 26.4	232	497		31 (13%)		9.6
Present serie	Italy	2014–2018	ReLLR	74	72	55/19	66/8	36/44	25 [16–30]	210	100	5 (6.7%)	17 (23%)	9 (12.1%)	5
			LLR	222	70	165/57	193/27		27 [20–36]	203	100	10 (4.5%)	58 (26.1%)	19 (8.5%)	5

ReLLR Redo Laparoscopic Liver Resection, *ROR* Redo Open Resection, *LLR* Laparoscopic Liver Resection non-hepatobiliary referral centers with smaller volumes of LLR per year. Third, a selection bias towards offering repeat resection only to those patients with a lower expected surgical difficulty. According to the literature, the incidence of intrahepatic recurrence after LR is about 50% at 5 years for patients with solitary HCC [29–31] and, in half of the cases, it is an early recurrence [30]. The number of recurring patients on the IGoMILS registry may be higher. Moreover, patients who underwent repeat hepatectomy for recurrences had a better prognosis than those who underwent other treatments [31]. Also, the IGoMILS Registry does not include open approach cases, which precludes the direct comparison of open versus LLR surgery. Nevertheless, we also want to acknowledge the participation of the 52 centers in this study, with 18 reporting at least one LLR in Group 2. The present study is the first study based on a National prospective database, which is an essential difference with previous publications. The large number of centers included in the study, involving at least 51 surgeons from various centers, reinforces the value of our results; repeat MILS for HCC seems achievable and safe. The prevalence of LLR for HCC in Italian centers is growing, with an increasing trend in offering MILS approach also for recurrent HCC.

Conclusion

The IGoMILS experience in repeat MILS for HCC has observed the feasibility and safety of the procedure in both previous surgeries, either open or MILS. The repeat LR MILS experience and the number of centers approaching recurrent HCC with MILS are growing every year in Italy.

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