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Laparoscopic versus robotic surgery for hepatocellular carcinoma: the first 46 consecutive cases / Magistri, P; Tarantino, G; Guidetti, C; Assirati, G; Olivieri, T; Ballarin, R; Coratti, A; Di Benedetto, F. - In: JOURNAL OF SURGICAL RESEARCH. - ISSN 0022-4804. - 217:(2017), pp. 92-99. [10.1016/j.jss.2017.05.005]

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23/04/2024 22:00

(Article begins on next page)

Accepted Manuscript

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PII: S0022-4804(17)30258-5

DOI: [10.1016/j.jss.2017.05.005](https://doi.org/10.1016/j.jss.2017.05.005)

Reference: YJSRE 14289

To appear in: *Journal of Surgical Research*

Received Date: 2 December 2016

Revised Date: 18 April 2017

Accepted Date: 1 May 2017

Please cite this article as: Magistri P, Tarantino G, Guidetti C, Assirati G, Olivieri T, Ballarin R, Coratti A, Di Benedetto F, Laparoscopic vs. Robotic Surgery for HCC: The First 46 Consecutive Cases, *Journal of Surgical Research* (2017), doi: 10.1016/j.jss.2017.05.005.

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Revised 04/18/2017

Laparoscopic vs. Robotic Surgery for HCC: The First 46 Consecutive

Cases

Robotic vs. Laparoscopic HCC resection

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This work has been presented at the 12th Annual Academic Surgical Congress, February 7-9, 2017, Las Vegas, NV.

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Disclosure statement:

None of the authors has personal interest to disclose

Author contributions:

FDB, AC and PM: study concept and design
PM: manuscript drafting
RB and CG: literature search and analysis
GA and TO: data collection and analysis
GT and AC: critical revision

Abstract:

Background: Hepatocellular carcinoma (HCC) has a growing incidence worldwide, and represents a leading cause of death in patients with cirrhosis. Nowadays, minimally invasive approaches are spreading in every field of surgery and in liver surgery as well.

Materials and Methods: We retrospectively reviewed demographics, clinical and pathological characteristics and short-term outcomes of patients who had undergone minimally invasive resections for HCC at our Institution between June 2012 and May 2016.

Results: No significant differences in demographics and comorbidities were found between patients in the laparoscopic (n=24) and robotic (n=22) group, except for the rates of cirrhotic patients (91.7% and 68.2%, respectively, $p=0.046$). Peri-operative data analysis showed that the operative time (mean, 211 min and 318 min, respectively, $p<0.001$) was the only parameter in favor of laparoscopy. Conversely, robotic assisted resections were related to less Clavien I-II post-operative complications (22 cases Vs. 13 cases; $p=0.03$). As regards resection margins, the two groups were similar with no statistically significant differences in rates of disease-free resection margins.

Conclusions: A modern hepatobiliary center should offer both open and minimally invasive approaches to liver disease in order to provide the best care for each patient, according to the individual comorbidities, risk factors, and personal quality of life expectations. Our results show that the robotic approach is a reliable tool for accurate oncologic surgery, comparable to the laparoscopic approach. Robotic surgery also allows the surgeon to safely approach liver segments that are difficult to resect in laparoscopy, namely segments I-VII-VIII.

Keywords: HCC; robotic liver surgery; MILS; Da Vinci; patient safety; surgical education

1. Introduction:

Hepatocellular carcinoma (HCC) is the most frequent primary liver neoplasm: it represents the fifth most common cancer in men (7.9% of all cancers) and the seventh in women (6.5% of all cancers)¹. It accounts for about 69,000 deaths per year and is currently the third cause of cancer-related death². Chronic liver disease is the most frequent setting of HCC development in Western countries³, mostly related to known risk factors such as chronic viral hepatitis infection, excessive alcohol consumption, non-alcoholic fatty liver disease (NAFLD), and hemochromatosis⁴. A strict surveillance of the “at-risk” population is crucial to detect and diagnose HCC early, when curative treatments are still feasible⁵.

The most used algorithm to determine the best patient treatment is that proposed by the BCLC group (Barcelona Clinic for Liver Cancer)⁶. BCLC is a multidimensional platform based on patient’s performance status, liver function calculated using the Child-Turcotte-Pugh (CTP) score, and tumor dimension. In this algorithm HCCs are divided into 5 categories. Very early (0) and Early stage (BCLC A) patients are amenable to curative treatments, such as surgical resection, liver transplantation (LT) and tumor ablation. Conversely, Intermediate stage (BCLC B) patients can only be offered a Trans-arterial chemoembolization (TACE), while Advanced stage (BCLC C) patients are treated with Sorafenib. Lastly, Terminal stage (BCLC D) patients are only offered supportive care. Despite its worldwide diffusion, this staging system is nowadays limiting because it does not take into account other important characteristics of the tumor, such as biological features, and seems too strict in its indication for intermediate and advanced patients. In fact, Villa and colleagues recently demonstrated that cancer-

specific genomic features deeply affect the prognosis⁷.

Liver resection (LR) represents one of the most valuable curative options for HCC⁸. The development of minimally invasive surgery over the past two decades has made a great impact on surgical practice and also on liver surgery. It allows accurate resections with reduced intraoperative blood loss, postoperative pain and morbidity, improved tolerance to oral feeding after surgery, shorter length of hospital stay (LOS), improved esthetics and enhanced cost-effectiveness when compared to the classical open approach. Moreover, the R0 resection rate and 5-year overall survival (OS) is similar for patients with laparoscopically treated HCC compared to those who underwent an open procedure⁹⁻¹¹. Among minimally invasive techniques, robotic surgery is spreading worldwide in every field of surgery including liver surgery.

We decided to compare our cohorts of patients who had undergone either laparoscopic liver resection (LLR) or robotic liver resection (RLR) for HCC in order to evaluate potential differences in terms of short term outcomes, safety and feasibility.

2. Materials and Methods:

Following approval by our Institutional Review Board, we retrospectively reviewed our prospectively maintained database of minimally invasive liver resections (MILR). Between January 2012 and May 2016 over 140 cases of minimally invasive liver surgery either laparoscopically and robotically were performed in our tertiary referral hospital for HPB surgery and liver transplantation (Hepato-pancreato-biliary Surgery and Liver Transplant unit, University of Modena and Reggio Emilia, Modena, Italy) with various indications. Among these, 46 patients underwent liver surgery for HCC. Within

this cohort we identified two groups, namely patients treated with either a totally laparoscopic approach (LLR) or a robotic liver resection (RLR). We introduced the daVinci Surgical System Si platform (Intuitive Surgical, Inc.) in our practice in 2014; since then, the decision between the two techniques was taken on the preference of the surgeon.

Indication to surgical resection in our center is always discussed in a multidisciplinary meeting involving surgeons, radiologists, hepatologists and oncologists. All patients affected by HCC were evaluated by preoperative examinations to determine the liver function with conventional liver function tests (including Child-Pugh classification), serum alpha-fetoprotein (AFP), hepatitis B surface antigen and anti-hepatitis C virus antibody measurements. The presence of portal hypertension was detected by platelet count, gastro-duodenal endoscopy (EGDS), and with the measurement of hepatic vein portal gradient (HVPG) when needed. Moreover, selection criteria included compensated cirrhosis or noncirrhotic liver disease, esophageal varices \leq grade 1, platelet count $\geq 50 \times 10^9$ /L, American Society of Anesthesiologists (ASA) Score ≤ 3 , and HVPG < 10 mmHg. To determine the extent of resection all patients underwent triphasic computed tomography (CT) scans using a 16-channel multidetector row helical scanner, and/or contrast enhanced magnetic resonance (MR) imaging.

An informed consent was obtained at least one day before the surgical day, including the authorization to keep audio-visual material of the surgical procedure and the authorization to keep peri-operative and follow-up data in our Institutional prospectively maintained database.

After surgery, all patients were followed at our outpatient clinic at 3 or 6 month intervals. Follow-up examinations included clinical examination, liver function tests, AFP level, and abdominal US, CT scans and MR.

ASA physical score more than three, heart failure, respiratory insufficiency and general contraindication to pneumoperitoneum were assessed as exclusion criteria from minimally invasive liver surgery (MILS).

Even if we did not establish a maximum diameter of HCC, patients presenting with extensive sub glissonian infiltration and those whose lesions infiltrated major hepatic vessels were also excluded from MILS.

Demographics and data from past medical history were retrieved from patients' medical files, while intraoperative data were collected from the analysis of the anesthesiological chart. Estimated blood loss was calculated as the difference between volume in the suction system and irrigation volume. Operative time was considered from the induction of the pneumoperitoneum to the suture of the trocar insertion sites.

Postoperative complications were classified using the Clavien-Dindo Classification for Surgical Complications¹².

Prospectively collected data, including intraoperative variables, postoperative complications, and pathological findings were analyzed retrospectively. Continuous variables are expressed as mean \pm standard deviation (SD) or median and range and compared using Student's t-test. Categorical variables were compared using the chi-square test with Yates's correction as appropriate. Statistical significance was set for $p < 0.05$.

Statistical analysis was performed using SPSS Statistics version 19.0 (IBM, Armonk, New York, USA).

2.1 Surgical technique

LLR

For left segments and anterior right segments the patient is in 30° anti-Trendelenburg position. The surgeon performs the operation from between the divaricated legs of the patient.

We use a 10 mm umbilical port for the 30° angulated scope, a 12 mm and two 5 mm trocars.

In case of postero-lateral segments the patient is in left decubitus and the surgeon is on his left side.

Pneumoperitoneum is induced with the Verres needle technique, from the left upper abdominal quadrant. In all patients we perform intraoperative ultrasound to precisely identify the nodules and to determine the resection margin.

Pringle maneuver is not routinely performed.

The liver transection is achieved with the use of an Ultracision Harmonic Scalpel or the combination of CUSA and a bipolar-energy instrument. In our experience, we have found the application of Aquamantys useful. Vascular and biliary structures are sectioned after application of Hem-O-Lok clips (Weck, Teleflex Inc.) or titanium clips.

The sample is extracted in an Endobag through a Pfannenstiel incision or exploiting the site of a trocar incision.

The pneumoperitoneum is then re-induced and hemostasis and biliostasis is completed applying fibrin glue.

In order to prevent collection formation, we apply a Jackson-Pratt (JP) drain tube close to the resection margin.

RLR

We perform RLR using the daVinci Si Surgical System. In all cases of this series the patient is positioned supine 20° anti-Trendelenburg.

We induce pneumoperitoneum as in LLR and keep a constant endoabdominal pressure with the use of the automated insufflator AirSeal™ (Surgiquest).

The scope's trocar is generally positioned at the cross between mid-clavicular line and transverse umbilical line. We perform exploratory laparoscopy before docking the patient cart of the robot.

Three robotic 8 mm trocars are usually placed in mesogastrium (right operative arm), right flank (left operative arm) and between epigastrium and left ipocondrium (fourth arm). It is important to notice that this placement is not unique and the disposition of the trocars highly depends on patient conformation and lesion localization.

The AirSeal trocar is used by the assisting surgeon to exert retraction, apply clips or mechanical stapler and suction on the operative field.

Intraoperative ultrasound is always performed in order to precisely define the transection line as described in the literature by Guerra et al.¹³.

Liver transection is performed using robotic an Ultracision Harmonic Scalpel or combining the use of monopolar cautery and bipolar-energy forceps.

To control vessels and bleeding it is possible to use different means: titanium clips, Hem-o-Lok clips, apposition of transfixed suture. Major vessels are divided applying a vascular mechanical stapler.

After the sample is extracted, as in LLR, hemostasis and biliostasis is perfected with fibrin glue and a JP drain tube is placed.

3. Results:

Demographics:

The detailed demographics and preoperative variables analyzed in this study are reported in **Table 1**. There are no significant differences between the LLR group (N=24) and the RLR group analyzing age, sex, body mass index (BMI), ASA score, MELD and CPT score.

The only exception is a greater number of cirrhotic patients in the dLLR group (LLR Vs. RLR: 22 pts Vs. 15 pts; $p=0.046$). The etiology of chronic liver disease is homogenous among the two groups. Preoperative laboratory tests (Hemoglobin, Platelet count, INR, total bilirubin, creatinine, albumin) are comparable in both groups. We analyzed patients' comorbidity finding that they do not differ in a statistically significant way in the two groups.

Intraoperative outcomes:

Intraoperative data are outlined in **Table 2**. In the RLR group we performed 6 left lateral sectionectomies (LLS), 2 right hepatectomies and 14 minor resections, including 9 segmentectomies and 5 wedge resections. The LLR group had: 14 segmentectomies and 10 wedge resections, with no major hepatectomies. As reported in Table 2, the

distribution of the resection type significantly differs between the two groups. Lesions were distributed homogeneously in the different liver segments within the RLR group (31.8% in right lateral segments VI and VII; 36.4% in anterior segments IV, V, VIII; 31.8% in left lateral segments II and III). In the LLR group the majority of the lesions were localized in the right lateral segments (45.8%).

In the RLR group there was 1 case in which Pringle's maneuver was necessary with a total clamping time of 13.3 min, while in the LLR group it was never used. Operative time was significantly longer in the RLR group (LLR Vs. RLR: 211 min Vs. 318 min; $p < 0.01$), while estimated blood loss (EBL) was comparable between the two groups (LLR Vs. RLR: 320 ml Vs. 400 ml; $p = 0.12$), with a single case of necessity of blood transfusion in each group. As regards conversion to the open approach, the two groups differ in a statistically significant way. We report 4 conversion cases in the LLR group compared to no events in the RLR group (LLR Vs. RLR: 4 cases Vs. 0 cases; $p = 0.046$). Conversions were due to respiratory distress (suspected air embolism) in two cases, technical difficulties in identifying the lesion at ultrasound in one case, and major bleeding in one case.

Post-operative outcomes:

Table 3 summarizes the postoperative course. Complications were evaluated using Clavien Dindo classifications. Minor complications (Clavien Dindo class I and II) includes pleural effusion, hematomas, ascites and pneumonia. In the RLR group this type of complication was significantly less frequent than in the LLR group (LLR Vs. RLR: 22 cases Vs. 13 cases; $p = 0.03$). When analyzing specific complications, it is possible to

highlight that pleural effusion was significantly less frequent in the RLR group (LLR Vs. RLR: 10 cases Vs. 2 cases; $p=0.01$). Regarding major complications, there were no differences of incidence among the two cohorts (LLR Vs. RLR: 3 cases Vs. 2 cases; $p=0.72$).

A case of biliary leak requiring an endoscopic insertion of a biliary stent, a cardiac tamponade from a spontaneous hemopericardium and a case of hemoperitoneum were observed in the LLR group. The hemoperitoneum was treated laparoscopically performing hemostasis on the resection margin. In the RLR group there were 2 cases of pulmonary embolism treated with medical therapy.

No hepatic insufficiency nor encephalopathy were observed. Moreover, there was no perioperative mortality.

Bowel function recovery and re-alimentation after surgery were the same within the two groups. However, post-operative hospital stay (LOS) seems to be reduced in the RLR group, although without reaching statistical significance (LLR Vs. RLR: 6.2 days Vs. 5.1 days; $p=0.15$).

Histological outcomes:

Pathological data are shown in **Table 4**. Single HCCs were more frequent while multifocal tumors had a lower incidence in our cohort.

In the RLR group nodule mean size was significantly larger than in the LLR group (LLR Vs. RLR: 22.61 mm Vs. 34.06 mm; $p<0.01$). The pathological examination of the resected livers showed no significant difference regarding Edmonson-Steiner grading and prevalence of satellitosis in the two groups. However, 5 cases of microvascular

invasion were observed in the LLR group, while no cases occurred in the RLR group (LLR Vs. RLR: 5 cases Vs. 0 cases; $p=0.01$). The resection margin status does not differ between the two groups (LLR Vs. RLR: 9.25 mm Vs. 10.55 mm; $p=0.59$). In both the RLR and LLR groups one case of R1 resection (microscopic tumoral invasion) was observed (LLR Vs. RLR: 1 case Vs. 1 case; $p=0.95$).

Discussion:

Although apparently contradictory, surgical approach for HCC patients in the context of a cirrhotic liver aims to (1) obtain a radical excision and (2) preserve as much liver parenchyma as possible to prevent postoperative liver failure. Yet, both existence of an underlying liver disease and extent of LR dramatically increase postoperative complications and limit the indication for LR for patients with impaired liver function and too large tumors¹⁴.

The minimally invasive approach to liver surgery had long been underestimated because it was considered too technically challenging and inadequate for a radical oncological resection. Nowadays, however, laparoscopic experience has extremely increased resulting in improved patient outcome. This change in the trend among surgeons is mainly due to both a more accurate pre-operative radiological assessment, and an improvement of intraoperative anesthesiology care and newer laparoscopic devices^{9,15,16}. Since 2003, when the first report of robotic liver surgery was published by Giulianotti et al.¹⁷, the popularity of RLRs have increased significantly. Currently, there is no formal evidence of the superiority of the robotic approach versus conventional laparoscopy, and also oncological results are similar¹⁸. MILS offers an opportunity to safely treat HCC patients even with a Child A-B cirrhotic liver, with lower rates of overall

morbidity when compared to OLR, and a lower incidence of local recurrence when compared to radiofrequency ablation (RFA)¹⁹. However, surgical resection of the liver for HCC is not merely a technical or technological issue, and the choice between different approaches should be tailored to each patient. In fact, the decision between open or minimally invasive surgery cannot be just a matter of individual ability to perform certain procedures. MLS seems more effective than OLS in patients affected by HCC with a cirrhotic liver due to several reasons. First of all, in a setting of reduced liver function and reduced functional reserve, we can benefit from less impact on the abdominal wall, gentle manipulation on the liver, respect for the venous shunts and limited surgical trauma. In addition, the intraoperative fluid loss is consistently less with MLS compared to OLS, thanks to the absence of a prolonged laparotomy with exposure of the peritoneum: consequently, fluid administration can be more conservative since generous substitutions are not needed²⁰⁻²¹. Finally, a better control of post-operative pain and early mobilization of the patient after MILS reduce respiratory complications by enhancing respiratory movements²⁰. Besides the well-known advantages of robotic surgery, such as image stability, 3-Dimensional view, flexible instruments, abolition of physiological tremor, better comfort for the surgeon and shorter learning curve¹⁸, recent data have outlined some actual clinical advantages of RLR. In particular, RLR seems to be related to shorter in-hospital stay, reduced post-operative pain and use of analgesics, while data on intraoperative blood loss are inconclusive²²⁻²⁵. Thanks to these features, RLR is ideal for delicate tissue dissection and precise intra-corporeal suturing, with a theoretical advantage in resections of lesions adjacent to major vessels, near the liver hilum, and, in general, with more complex anatomy²⁶. Therefore, we can

postulate that minimally invasive liver procedures should be considered as an independent field of surgery, with particular indication for Child A and B patients and parenchyma-sparing procedures, which should be better classified in the classical BCLC model²⁷⁻²⁹. Moreover, the robotic platform has a high value in surgical education, mainly thanks to the dual-console system, the availability of simulators and multiple plug-ins for augmented reality³⁰.

In our experience, comparing two homogeneous populations of HCC patients, we showed that the robotic approach was superior to the laparoscopic one in terms of minor post-operative complications, and thanks to its characteristics allowed us to resect slightly larger tumors without any need of conversion to laparotomy. The higher rate of pleural effusion incidence in the LLR group may be explained by the higher rate of right-posterior resections in this group, and the gentler manipulation of the diaphragm with the robotic approach. Operative time was longer than in conventional laparoscopy, both due to the docking time and the initial experience in this field of surgery. The retrospective nature of the study and the lack of randomization represent the major limitations of this work. The difference between the two groups in terms of cirrhosis rate, although statistically significant, is consistent with the extent of resection: in fact, in the LLR group wedge resections were more frequent. However, it doesn't seem to heavily affect the results: as a matter of fact, lesions localization, oncological accuracy of resection margins and major complications did not differ significantly. Moreover, the post-operative course showed that in-hospital stay was slightly shorter after RLR, although without reaching statistical significance, while 30-days mortality and major complications were comparable. However, prospective randomized trials comparing the

two techniques may clarify the role of the two minimally invasive approaches, in particular focusing on the role of the learning curve. As reported in literature, confidence with minimally-invasive liver procedures improves with experience resulting in a significant decrease in operative time³¹. However, the difference in the learning curve of minimally-invasive approaches between a fully trained HPB surgeon and a “minimally-invasive native surgeon” should be taken into account. In other words, the new generation of residents and young surgeons will be more involved in novel technological applications in the field of surgery, such as virtual reality, augmented reality and simulation, reflecting the evolution of our society³². Therefore, a comparison between classical-open trained and minimally-invasive oriented trained surgeons may be of great interest. Our data confirm that the major advantage of the robotic platform when compared to conventional laparoscopy is the technology itself, that adds value when precise vessel dissection or major suturing are needed. The name daVinci is particularly indicated for this valuable MILS tool. Not only because of the genius of Leonardo da Vinci in engineering, but also because it recalls the importance of the multidisciplinary approach. When the young Leonardo da Vinci attended the workshop of Andrea del Verrocchio, his mentor, in Florence, the approach to fine arts was in fact “multidisciplinary”: sculptors and painters worked along side each other every day generating influences between them that led to da Vinci’s famous volumetric and sculptural effect in painting. Today we have understood that a multidisciplinary approach is the only way to improve the medical and surgical art. Surgeons, together with radiologists, developed advanced imaging techniques for the pre-operative study of the patient and, in the same way as Renaissance artists, nowadays we step from the

real plane into a virtual plane, getting the best performance possible. However, we are trying to close the path going back from the virtual plane to a “realistic” plane, through the application of 3D reconstruction and 3D printing techniques, which give the surgeon more accurate information on patient-specific anatomy, enhancing patient safety.

Conclusions:

A multidisciplinary approach to the patient affected by HCC is essential in order to provide the best treatment according to patient-specific background, anatomy and expectations. The robotic platform allows for more comfortable and precise vessel dissection and major suturing, with comparable results in terms of oncological radicality but safer post-operative course and reduced in-hospital stay when compared to both conventional laparoscopy and open surgery.

Acknowledgements:

We would like to thank the nursing staff of the “Hepatopancreatobiliary Surgery and Liver Transplantation Unit” of the “Policlinico” University Hospital of Modena, for their efforts for the pre-, intra- and post-operative wellness of patients and enthusiasm towards new technologies.

The study was conducted according to the principles of the Declaration of Helsinki

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Table 1. General demographic features and preoperative data of the two cohorts

	LLR (n=24)	RLR (n=22)	Overall <i>P</i>
Sex ratio (M/F)	15/9	18/4	0.15
Age (Mean \pm SD)	66.56 \pm 11.82	60.88 \pm 9.85	0.09
Liver disease			
<i>Cirrhosis (n°)</i>	22 (91.7%)	15 (68.2%)	
<i>Pre-cirrhotic liver disease (n°)</i>	2 (8.3%)	7 (31.8%)	0.046
Liver disease's etiology			
<i>HBV (n°)</i>	8 (33.3%)	4 (18.2%)	0.25
<i>HCV (n°)</i>	12 (50%)	13 (59.1%)	0.55
<i>NAFLD/NASH (n°)</i>	2 (8.3%)	3 (13.6%)	0.57
<i>Alcohol</i>	2 (8.3%)	3 (13.6%)	0.57
αFP (ng/dl) median (range)	15.25 (2-622)	4.6 (3-5065)	0.41
Preoperative Laboratory tests (mean \pm SD)			
<i>Hemoglobin (g/dl)</i>	13.45 \pm 1.50	13.57 \pm 1.88	0.83
<i>Platelet count (x10³/mm³)</i>	130 \pm 54.9	137 \pm 69.4	0.73
<i>INR</i>	1.17 \pm 0.29	1.19 \pm 0.14	0.80
<i>Total serum bilirubin (mg/dl)</i>	1.01 \pm 0.52	1.14 \pm 0.94	0.56
<i>Creatinine (mg/dl)</i>	0.75 \pm 0.15	0.88 \pm 0.37	0.19
<i>Albumin (g/l)</i>	3.91 \pm 0.51	3.92 \pm 0.51	0.98
ASA score			
1	0	0	n.a.
2	16 (66.7%)	14 (63.6%)	0.8
3	8 (33.3%)	8 (36.3%)	0.8
4	0	0	n.a.
BMI, Mean \pm SD	26.5 \pm 3.81	26.8 \pm 3.73	0.83
Comorbidities			
<i>Heart failure</i>	3 (12.5%)	2 (9.1%)	0.72
<i>Respiratory insufficiency</i>	1 (4.2%)	1 (4.5%)	0.95
<i>Chronic kidney disease</i>	2 (8.3%)	2 (9.1%)	0.93
<i>Diabetes</i>	4 (16.7%)	3 (13.6%)	0.78
<i>Hypertension</i>	15 (62.5%)	15 (68.2%)	0.69
<i>Esophageal varices</i>	12 (50%)	6 (27.3%)	0.12
Child-Pugh-Turcotte score			
<i>CPT A</i>	21 (87.5%)	20 (90.9%)	0.92
<i>CPT B</i>	3 (12.5%)	2 (9.1%)	0.72
MELD, Median (range)	9 (7-14)	9 (6-13)	0.82

Table 2. Intraoperative outcomes

	LLR (n=24)	RLR (n=22)	Overall P
Lesion's localization			
<i>Right posterolateral segments (VI, VII)</i>	11 (45.8%)	7 (31.8%)	0.34
<i>Anterior segments (IV, V, VIII)</i>	5 (20.8%)	8 (36.4%)	0.25
<i>Left lateral segments (II, III)</i>	8 (33.3%)	7 (31.8%)	0.91
Resection type			
<i>Wedge / segmentectomy</i>	24 (100%)	14 (63.6%)	<0.01
<i>Left lateral sectionectomy</i>	0 (0%)	6 (27.3%)	<0.01
<i>Right hepatectomy</i>	0 (0%)	2 (9.1%)	0.14
Operative time, mean ± SD	211 ± 78.13	318 ± 113.5	<0.01
Devices used for parenchymal transection	Ultracision, CUSA, Bipolar forceps	Ultracision, monopolar cautery, bipolar forceps.	
Pringle's maneuver	0 (0%)	1 (4.5%)	0.30
Mean clamping time (minutes)	/	13.3	
EBL, median (range)	328 (100 – 1100)	400 (50 – 1500)	0.12
Need for blood transfusion	1 (4.2%)	1 (4.5%)	0.95
Open conversion rate	4 (16.7%)	0 (0%)	0.046

Table 3: Post-operative outcomes

	LLR (n=24)	RLR (n=22)	Overall <i>P</i>
Clavien Dindo classification of surgical complications			
<i>No complications</i>	0 (0%)	7 (31.8%)	0.002
<i>I-II</i>	21 (87.5%)	13 (59.1%)	0.03
<i>III-IV</i>	3 (12.5%)	2 (9.1%)	0.72
Specific complications			
<i>Pleural effusion</i>	10 (41.7%)	2 (9.1%)	0.01
<i>Ascites</i>	4 (16.7%)	5 (22.7%)	0.61
<i>Pulmonary embolism</i>	0 (0%)	2 (9.1%)	0.14
<i>Pneumonia</i>	4 (16.7%)	6 (27.3%)	0.39
<i>Biliary leak</i>	1 (4.2%)	0 (0%)	0.34
<i>Hemoperitoneum</i>	1 (4.2%)	0 (0%)	0.34
<i>Abdominal wall hematoma</i>	0 (0%)	2 (9.1%)	0.14
<i>Other</i>	4 (16.7%)	2 (9.1%)	0.46
Re-intervention (n°)	1 (4.2%)	0 (0%)	0.34
Bowel function recovery (days), median (range)	2 (1-3)	2 (1-3)	0.86
Re-alimentation (days), median (range)	2 (1-5)	2 (1-5)	0.93
Length of hospital stay (days), mean ± SD	6.2 ± 2.57	5.1 ± 2.4	0.15
30-days mortality	0 (0%)	0 (0%)	n.a.

Table 4: results of the pathological examination

	LLR (n=24)	RLR (n=22)	Overall <i>P</i>
N° of nodules			
<i>Single HCC</i>	21 (87.5%)	19 (86.4%)	0.91
<i>Multifocal HCC</i>	3 (12.5%)	3 (13.6%)	0.91
Mean dimension (mm), mean ± SD	22.61 ± 11.33	34.06 ± 13.50	<0.01
Edmonson-Steiner grading system			
<i>G1</i>	4 (16.7%)	5 (22.7%)	0.61
<i>G2</i>	14 (58.3%)	8 (36.3%)	0.14
<i>G3</i>	6 (25%)	9 (40.9%)	0.17
Satellitosis	2 (8.3%)	5 (22.7%)	0.18
Microvascular invasion	0 (0%)	5 (22.7%)	0.01
R0	23 (95.8%)	21 (95.5%)	
R1	1 (4.2%)	1 (4.5%)	0.95
Resection margin (mm), mean (range)	9.25 (1-20)	10.55 (1-40)	0.59