Original Article

Laparoscopic liver resection for hepatocellular carcinoma: 10 years retrospective study of laparoscopic liver resection in a single reference center

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Background: Laparoscopic liver resection (LLR) has demonstrated results comparable to traditional surgery for hepatocellular carcinoma (HCC). It has also shown good out-turns in term of postoperative outcomes and clinical results. The aim of the study is to analyze the evolution of the LLR, in term of inclusion criteria, outcomes and surgical characteristics in the decade 2009–2018 in our center.

Methods: One hundred and forty nine patients affected by HCC, who underwent LLR from January 2009 to December 2018, were retrospectively evaluated. The cohort of candidates was divided into two groups: group 1 including patients between 2009 and 2013, group 2 patients between 2014 and 2018.

Results: First of all the outcomes show an increase in the number of LLR. This value has increased both in absolute terms and considering the total amount of resection. 149 HCC patients were treated whit LLR from 2009 to 2018: most of the subjects were affected by cirrhosis (94.6%) and Child-Pugh A (88.6%). In fact, in the first period (2009–2013) patients were 52 while in the second one (2014–2018) they were 97. In both periods the types of resections performed were segmentectomies and wedge resections. The extension of the guidelines has allowed to treat a greater number of patients over 70 years old (1st 7; 2nd 30) and with a BMI greater than 30 (1st 9; 2nd 22). In the second period there was also an increase in difficult resection. In fact, 63% of the total number of resections [62] are considered difficult compared to 57% [30] in the first term. In both periods, however, most patients (1st 71.2%; 2nd 78.4) had single lesion. Moreover, a decrease in blood loss has been assessed (1st 115 mL; 2nd 108 mL), as well as a decrease in hospital stay (1st 6 days; 2nd 5 days) and an increase in the use of the Pringle maneuver to control liver vascularization (1st 23%; 2nd 31%). Finally with regard to liver transplantation, 20 transplant patients have been performed after LLR and 4 of them are still on list.

Conclusions: The number of LLR has increased since 2009. This augmentation is due to an expansion of the guidelines issued in Louisville 2008, Morioka 2014 and Southampton 2017. The study allows to state how nowadays laparoscopic surgery represents a validated technique, a safe and feasible procedure for the treatment of liver lesions caused by HCC.

Keywords: Laparoscopic liver resection (LLR); liver surgery; liver resection; hepatocellular carcinoma (HCC)

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Introduction

The role of hepatobiliary laparoscopic surgery is growing up worldwide since its introduction in the '90 when the first reports were published (1). In 1992 Gagner *et al.* has reported the first laparoscopic liver resection (LLR) for a liver tumor (2). In the last decade, the laparoscopic approach has shown encouraging results for the treatment of hepatocellular carcinoma (HCC) patients. In the beginning, LLRs were applied in the case of small wedge resections, minor hepatectomies, or for lesions located in the anterior segments (3). Moreover, the number of patients having the proper characteristics to undergo a LLR was restricted considering age, weight (BMI), and underlying liver disease. The Louisville consensus conference in 2008 (4), the first international consensus conference for the laparoscopic liver surgery, the Morioka consensus statement in 2015 (5), and the Southampton consensus guidelines in 2017 (6) laid the foundation of the modern LLR. Nowadays, this type of surgery can be performed in a higher number of HCC patients. This procedure can include patients over 70 years old, with a BMI >30 and with advanced liver disease showing excellent results in terms of surgical outcomes. Also, this technique eliminates the risk of recurrence, and it improves overall survival (7,8). The LLR could be characterized by a pure laparoscopic approach (PLLR), a hand-assisted (HALS), or hybrid one. In Europe, PLLR is the most used approach. This technique allows treating patients with both benign and malignant lesions, primitive or secondary. PLLR mainly permits to operate patients who can benefit from liver transplantation (9). According to the Brisbane classification (10), the different operations that can be carried out are left and right hepatectomy, segmentectomy, sectoriectomy, wedge, or enucleation. The classification mentioned above also gives the possibility of carrying out associated resection. An open technique is still required when the size of the tumor mass is above 5 cm, and when there are more than three nodes. LLR is the most suitable technique that can be performed to treat HCC developed in patients with cirrhosis. It is better tolerated, and it can more easily allow a second intervention or an organ transplant (11). The aim of the study is to analyze the evolution of LLR for HCC in our center in the decade that goes from 2009 to 2018. We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/dmr-20-89).

Methods

From 1st January 2009 to 31st December 2018, 149 HCC patients underwent LLRs at the department of general surgery and organ transplant of the San Camillo-Forlanini Hospital in Rome. Since 2001, a prospective database was maintained, which includes all patients treated in the department. The group of 149 patients was then divided into two groups: group 1, including patients treated from 1st January 2009 to 31st December 2013, and group 2 made up of patients operated from 1st January 2014 to 31st December 2018. In both groups, the inclusion criteria for this type of surgery, as well as the surgical characteristics and the possibility of a redo surgery OR a liver transplant, were evaluated. A preoperative assessment was made for each patient, including age, gender, BMI, Child-Pugh score, and MELD score, completed by studying the patient's general condition using the ECOG scale (12). The diagnoses of HCC were based on the appropriate imaging approaches, including triple-phase computed tomography (CT), magnetic resonance imaging (MRI), and ultrasound scan (US). The perioperative data collected were surgical times, Pringle maneuver, blood loss, operative time, morbidity, and hospital length of stay. As regards the histopathological data evaluated in this study, the total number, size, and relative position of the nodules inside the hepatic parenchyma, TNM, and histological characteristics were assessed on Edmondson and Steiner grade. Evaluations provided by the development of the consensus conferences made on the subject were used to classify the resections into "easy" and "difficult" (5-7). All surgical procedures were performed by a surgeon specialized in hepatobiliary surgery. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki (as revised in 2013). All patients have signed informed consent for scientific research. In the present study, review by the ethics committee wasn't required as it's a retrospective study.

Results

One hundred forty-nine patients were resected during the study time, 52 were in the first group, and 97 in the second group. The majority of the operated patients were male 113 (75.8%), and the rest of them [36] were female (24.2%).

Table 1 Patients characteristics

Patients characteristics	2009–2013 (n=52)			2014–2018 (n=97)		
	Average	%	Total	Average	%	Total
Age	63			65		
Male		78.8	41		74.2	72
Female		21.2	11		25.8	25
BMI	26.84			26		
Cirrhosis		94.2	49		94.8	92
Child-Pugh A		82.5	33		91.3	84
Child-Pugh B		17.5	7		8.7	8
Nr Child			40			92
MELD <10		70.6	24		73.9	68
MELD >10		29.4	10		26.1	24
HCV		53.8	28		50.5	49
Alcohol		5.8	3		6.2	6
HBV		7.7	4		12.4	12
HCV, HBV and alcohol		0.0	0		1.0	1
HBV and alcohol		1.9	1		3.1	3
HCV and HBV		1.9	1		4.1	4
HCV and alcohol		7.7	4		7.2	7
Other		21.2	11		15.5	15
ECOG 0–I		85.7	36		74.0	71
ECOG II–III		14.3	6		26.0	25

BMI, body mass index; MELD, Model of End Staged liver Disease; HCV, hepatitis C virus; HBV, hepatitis B virus; ECOG, Eastern Cooperative Oncology Group performance status.

The median age was 65 years old (range, 36–87), and the median of body mass index (BMI) was 26.20 (range, 17–48). As regards the causes of underlying liver disease was in 77 cases, a hepatitis C virus, in 16 cases, a hepatitis B virus and in 9 patients, a previous alcohol abuse. Moreover, in 5 patients, there was a liver disease due to a simultaneous HBV and HCV infection. Only in one patient, a simultaneous presence of HCV, HBV, and alcoholic liver disease was observed. Cirrhosis was present in 141 (94%) patients, 117 (88.6%) patients had a Child-Pugh Score A, the remaining 20 cases (11.4%) were Child-Pugh Score B (both B7 and B8). In 4 patients, it was not possible to calculate the Child due to a lack of data. The MELD score was classified as higher or lower than 10: 73.6% had a MELD score <10 while 26.4% MELD >10; 77.5% of the patient had ECOG 0–I while 22,5 ECOG II–III. Patients' characteristics are summarized in *Table 1*.

In the first group, 41 patients (78.8%) were male. The median age was 63 years old, and the median of BMI was 26.8; 7 cases Child-Pugh B were observed and 9 cases with MELD >10; only 6 patients had an ECOG II-III before surgery. In the second group, 72 patients (74.2%) were male. The median age was 65 years old, and the median of BMI was 25.88; 13 cases Child-Pugh B were observed and 24 cases with MELD >10; 25 patients had an ECOG II–III before surgery.

Operative findings

In group 1, 51 minor hepatectomies and only one major hepatectomy were performed with laparoscopic technique. Most of the resections performed were wedges, 26 (46.2%). Eighteen segmentectomies and six left lobectomies were also carried out. Only six interventions required an associated resection, three of which were wedges and three segmentectomies. In this period, according to Morioka and Southampton criteria, 30 (50.7%) "difficult" resections were performed. The Pringle maneuver has been set up 13 times, hepatic pedicle clamping was required in 3 cases. The medium of the blood loss was 115 mL, and no blood transfusion was required. The average intervention time is 2 hours and 50 minutes. However, it has been noted that "difficult" hepatectomies have an average of 2 hours and 49 minutes while the "easy" ones have an average of 2 hours and 34 minutes. The medium of the length of stay was 6 days. In group 2, 93 minor and 4 major hepatectomies (one of which was a right hepatectomy) were performed (9). The most practiced resections were segmentectomies, 48, followed by wedges 22. Associated resections were performed in 10 patients with multifocal lesions, the majority of which were segmentectomies. In this group, 62 (63.9%) "difficult" resections were performed. The Pringle maneuver was prepared in 30 interventions, while clamping was then carried out in 17 of these (average clamping duration 24 minutes, intermittent technique). The medium of blood loss was 108 ml; in one case, a blood transfusion was required. The medium of surgical procedure time was 2 hours and 48 minutes: 3 hours and 2 minutes for the "difficult" hepatectomies while 2 hours and 29 minutes for the "easy" one. The medium of hospitalization was five days. The surgical procedures are shown in *Table 2*. Histological findings in group 1 of 52 HCC patients undergoing LLR 22 (44%) had T1, 26 T2 (52%), and 2 T3 (4%). Thirty-seven patients had one nodule, ten patients had two nodules; two patients had three nodules, three patients had more than 3 nodules. Among 37 people with only one nodule, 29 patients had it located in segments SII to SVI, considered easily attackable by the IWATE criteria. In contrast, 8 of them had this lesion in the posterosuperior segments I-VII-VIII. In 4 patients, the lesions had a diameter greater than 5 cm. In group 2 of HCC patients 28 (30.8%) had a T1, 62 (69.1%) T2 and 2 (1.1%) T3. The majority of patients, 76 (78.4%), had only one nodule, which was located in easily attackable segments (SII-SVI) in 74.7% of cases, while in the 25.3% of cases, it was located in difficult segments (SI-SVII-SVIII). Fourteen patients had 2 nodules, nine of which easy and five difficult. In 9 (9.8%) patients, the lesion had a diameter greater than 5 cm. All the histological findings are shown in *Table 3*.

Discussion

The number of LLR has increased since 2009. In the last ten years, there has been a greater development of the laparoscopic technique for the treatment of liver lesions. This augmentation is due both to the discovery of new technologies and to the extension of the guidelines that have taken place over the years. In the first period evaluated, the inclusion criteria adopted were the Louisville ones [2008], which led to a total of 52 LLR. In the second group, where Morioka 2014 was adopted and then expanded from Southampton 2017, 97 patients were treated. More patients were eligible to LLR with the extension of the guidelines. Taking BMI into consideration, in the first group, there were nine patients with a BMI >30, while in the second group, patients were 22. In the first group, there were seven patients with more than 70-years-old. In the second one, there were 30. The increase in the inclusion criteria associated with improved surgical outcomes has led surgeons to approach by laparoscopy HCC patients assuming an important role compared to traditional open surgery. This increase can be seen in *Figure 1*, where it is proved that with the growth of HCC patients treated surgically, the number of resections performed laparoscopically has increased. In particular, *Figure 1* highlights the fact that LLR stabilized around 40% of the total amount of interventions in HCC.

The extensions obtained in Morioka and Southampton also led to an increase in difficult resections carried out during the second period. The main clinical advantage of LLR is the significantly lower rate of postoperative complications. This is ensured by the fact that the abdominal wall is preserved, and kinetics of the diaphragm is conserved (13) in association with the hemostatic effect of the pneumoperitoneum that allows reducing blood losses (14). Although in the two periods examined, most of the patients treated had only one lesion. We observed that in the second-period, resections increased in patients with more than one lesion. This result, according to a recent meta-analysis (15), confirmed this technique's validity of LLR for HCC. Finally, thanks to all the benefits of LLR, performing the initial HCC resection by laparoscopy could facilitate a subsequent LT (9). In the last decade the percentage of LLR is increased for three main reasons: the high volume of liver resection per year, the high number

Table 2 Surgical characteristics

Surgical characteristics	2009–2013			2014–2018		
	Average	%	Total	Average	%	Total
Main resections						
Major hepatectomy		1.9	1		4.1	4
Minor hepatectomy		98.1	51		95.9	93
Segmentectomy		34.6	18		50.0	48
Left lateral sectionectomy		11.5	6		15.6	15
LobectDx		0.0	0		0.0	0
Wedge		46.2	24		22.9	22
Wedges		3.8	2		7.3	7
Left hepatectomy		1.9	1		2.1	2
Right hepatectomy		0.0	0		1.0	1
Central hepatectomy		0.0	0		0.0	0
Posterior sectionectomy		1.9	1		1.0	1
Anterior sectionectomy		0.0	0		0.0	0
Associated resections		12	6		10	10
Wedge		6	3		2	2
Segmentectomy		6	3		7	7
Segmentectomy + wedge		0	0		1	1
Pringle maneuver		25	13		31	30
Pedicle clamping		5.8	3		17.5	17
Blood loss (mL)	115			108		
Blood transfusion			0			1
Operative time (min)	170			168		
Hospital stay (day)	6.04			5.80		

of advanced abdominal laparoscopic procedures and the enlarged knowledge of liver transplant units. LLRs have led to several advantages such as a decrease in post-operative pain, blood loss, morbidity and average length of the stay. This technique has also accelerated the time of recovery (3-7). We have also to consider that using LLR in the first approach allows a secondary resection or a transplant in a more easy way compared to an open approach. In fact, LLR reduces the formation of adhesions (7-9). Concerning the oncological outcomes, such as resection margins' negativity and non-progression of the disease, LLRs can be compared to an open technique (16,17). From the point of view of the surgical technique we can see how a laparoscopic approach improves the exposure of the organ and allows cleaner access. These characteristics are essential in order to preserve nearby structures and hepatic parenchyma remaining (3-9). Despite the advances in LRR there are some drawbacks related to this technique. First of all, LRRs are characterized by the absence of three-dimensional images and tactile sensitivity. These features led to a different perspective of neighbouring organs. Consequently, this procedure can be performed only in specialized centers. Moreover, LRRs can be carried out only by surgeons who have experience both with laparoscopic approach and open surgery. LRRs can be therefore executed only in those centers where hepatic surgeries are frequently

Table 3 Histological findings

Histological findings	2009–2013		2014–2018	
	%	Total	%	Total
Grading (I & II = yes)	28.8	15	41.7	40
Grading (III & IV = no)	71.2	37	58.3	56
TNM T1	42.0	21	30.8	28
TNM T2	54.0	27	68.1	62
TNM T3	4.0	2	1.1	1
Single nodule	71.2	37	78.4	76
Nodule location SII-SVI	77.8	28	74.7	56
Nodule location SI/SVII/SVIII	22.2	8	25.3	19
Two nodules	19.2	10	14.4	14
Nodule location SII-SVI	80.0	8	64.3	9
Nodule location SI/SVII/SVIII	20.0	2	35.7	5
Three nodules	3.8	2	6.2	6
Nodule location SII-SVI	50.0	1	33.3	2
Nodule location SI/SVII/SVIII	50.0	1	66.7	4
Four nodules	3.8	2	0.0	0
Five nodules	1.9	1	1.0	1
Diameter nodule >50 mm	7.7	4	9.8	9
Diameter nodule >30 mm	23.1	12	38.1	37

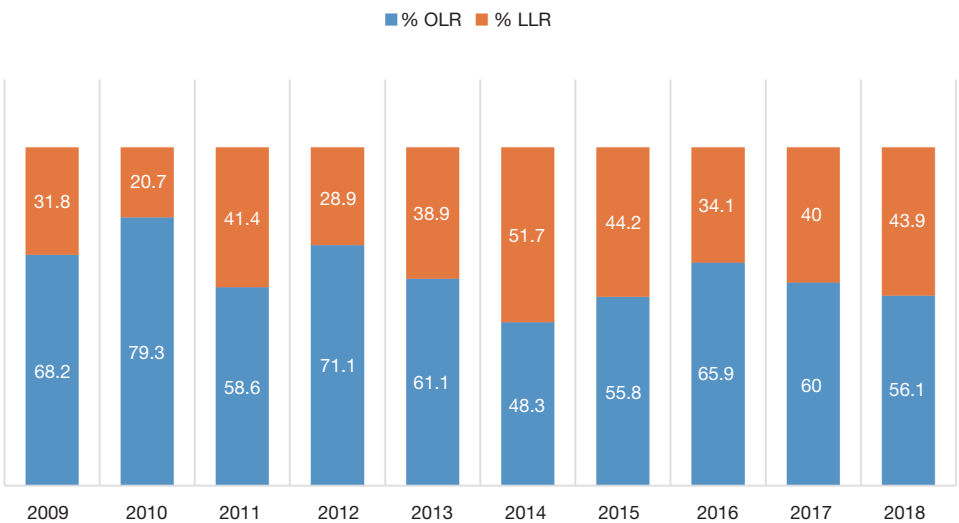

Figure 1 Evolution of LLR HCC resection, comparison between LLR and OLR since 2009. LLR, laparoscopic liver resection; HCC, hepatocellular carcinoma; OLR, open liver resection.

carried out (7). Lastly, not all tumors can be removed using a laparoscopic approach. This can be related to an excessive size of the tumor mass and its possible multifocality, in particular if there are more than 3 lesions (18). The new advantage difficult locations and complex right-sided resections remain in majority of cases performed by open surgery. To this we can add a better visualization and manipulation of these segments and a greater bleeding control. Moreover, the minimally invasive approach has a protective factor in case of a salvage liver transplantation for recurrence (11). The LLR can be achieved even in patient with previous liver transplant (19).

With the evolution of LLR for HCC, the role of open approach surgery seems to lose the throne (20). The main limitation of our study is the monocentric analysis and the retrospective period.

In conclusion, we compared two period time of surgical practice in our center for HCC patients. The laparoscopic approach improved the possibility to treat more patients, more sick, and more older. The postoperative outcomes were improved too. The minimally invasive approach will became the gold standard of care for HCC patients in the next future.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at http://dx.doi.org/10.21037/dmr-20-89

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki (as revised in 2013). All patients have signed informed consent for scientific research. In the present study, review by the ethics committee wasn't required as it's a retrospective study.

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