Laparoscopic versus open liver resection for hepatocellular carcinoma: initial experience in Greece

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Abstract

Background Liver resection represents the treatment of choice for a small proportion of patients with hepatocellular carcinoma (HCC), amenable to surgery. The remarkable evolution in surgical techniques during the last decades introduced laparoscopic hepatectomy in the operative management of HCC, even in the presence of liver cirrhosis. No comparative study on laparoscopic or open liver resection for HCC has been conducted in Greece yet.

Methods Patients undergoing liver resection for HCC by one senior hepatobiliary surgeon in our Institution during the period 11/2011-02/2016 were prospectively sampled and retrospectively analyzed for the purposes of this study. Statistical analysis encompassed Student's *t*-test, Fisher's exact test, the Kaplan-Meier method/log rank test and Cox proportional hazard regression analyses.

Results Eleven patients underwent laparoscopic and 21 open liver resection, respectively. Statistical differences between the 2 groups were observed for tumor size (P=0.04), major resections (P=0.01), Pringle maneuver (P=0.008), intraoperative blood transfusion (P=0.03), and duration of operation (P=0.004). Resection margins, and tumor recurrence showed no statistical differences. Three-year postoperative survival after laparoscopic and open hepatectomy was 100%, and 67%, respectively (P=0.06). Regression analysis for patient survival revealed prognostic value for BCLC staging, γ-glutamyl transferase levels, laparoscopic hepatectomy, UICC stage, Dindo-Clavien classification, and hospital stay. Laparoscopic hepatectomy remained as independent predictor of survival by multivariate analysis (P=0.0142).

Conclusion Laparoscopic hepatectomy for HCC in chronic liver disease represents a safe and innovative treatment tool in the management of these patients under the presupposition of careful patient selection.

Keywords Laparoscopic hepatectomy, liver resection, hepatocellular carcinoma, liver cirrhosis, hospital stay

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Introduction

Hepatocellular carcinoma (HCC) represents a considerable cause of death around the world. Viral hepatitis, alcohol

overconsumption, metabolic disorders and a number of other causes may lead to hepatopathy and liver cirrhosis, a potentially precancerous condition, which may be complicated by the development of HCC [1]. A large part of the increasing documentation of HCC during the last decades has been attributed to the corresponding rising incidence of hepatitis C viral (HCV) infection [2]. Hopefully, HCV infection is going to be under control with the new anti-viral agents in the course of the forthcoming years [3,4]. However, the main problem in the therapeutic management of HCC remains the late diagnosis, since an important proportion of patients are not aware of their liver disease and the diagnosis of HCC comes to an advanced stage. Less than 40% of patients with first diagnosis of HCC are subject to potentially curative treatments such as liver transplantation, liver resection, or radiofrequency ablation (RFA) [1,2].

Liver transplantation is the best therapy for HCC in selected patients with concrete tumor characteristics, offering

dual management of both the tumor and the underlying liver cirrhosis [5,6]. As a consequence, post-transplant tumor recurrence is the lowest achieved by any treatment [7,8]. However, organ scarcity and the inappropriate tumor characteristics at diagnosis limit the widely application of liver transplantation. Expansion of the existing transplant listing criteria for HCC is considered only in some large volume transplant centers [9,13]. Thus, liver surgery represents the "gold standard" in the management of early or very early HCC [1,2,14]. Recent developments in surgical techniques, hemostatic tools and agents, anesthesia, and perioperative management made hepatic surgery feasible and safe even in patients with liver cirrhosis. However, it was only during the last 10 years, that the great evolution in laparoscopic surgery of the past 40 years was sustained in the field of liver surgery. Moreover, limited data is published on laparoscopic liver surgery for HCC in cirrhosis.

We herein report our recent institutional experience on liver resection for HCC, using laparoscopic or open technique. This series represents the first comparative study on laparoscopic versus open liver resection for HCC in Greece.

Patients and methods

Between November 2011 and February 2016, hepatic surgery was performed in 141 patients by one senior hepatobiliary surgeon (GCS) in our institution. Data from patients with HCC were prospectively implemented in a database as follow: age, gender, date of operation, etiology of liver disease, body mass index (BMI), Child-Turcotte-Pugh (CTP) score, tumor characteristics (tumor number and size, tumor satellites, vascular invasion), regional lymph node involvement, comorbidities, Milan criteria, Barcelona clinic liver cancer (BCLC) staging classification, preoperative treatment, imaging studies, and serum tumor markers. The intraoperative data recorded included type of surgery (open versus laparoscopic), type of liver resection, additional surgical procedures (cholecystectomy, lymph node biopsy, vascular reconstruction), vascular occlusion (Pringle maneuver or total vascular occlusion), blood transfusion, and total operating time. The type of surgery was decided according to the anatomical location of the HCC; scheduled resection plan; quality and volume of the remaining liver parenchyma; and recommendations of the Louisville Statement [15]. The size of the tumor *per se* was not a criterion for choosing between open or laparoscopic approach. Major resection was defined as resection of 3 liver segments or more. Postoperative data encompassed accomplishment (or lack thereof) of direct extubation at the end of the operation, Intensive Care Unit (ICU) treatment (if any and how long), hospital stay and 30-day mortality. The postoperative morbidity was recorded and categorized according to the Dindo-Clavien classification [16]. Histopathology documentation gathered the tumor number and size, the occurrence of tumor satellites, the presence of vascular invasion or tumor thrombi, the resection margin, the tumor differentiation [17], and the classification according to the 7th edition of the Tumor/Node/Metastasis (TNM) and the Union for International Cancer Control (UICC)

systems, respectively. Follow-up data included the current patient status, recurrent disease and treatment of recurrence and cause of death.

Statistical analysis

Continuous data were expressed as median and range values and compared by Student's *t*-test. Categorical data were compared by Fisher's exact test. Patient survival was calculated using the Kaplan-Meier method and compared with the log rank test. For the identification of prognostic factors for patient survival univariate and multivariate regression analyses were performed with the Cox proportional hazard model. Differences of $P<0.05$ were considered to be statistically significant. Statistical analyses were performed using JMP (Version 8.0.2 SAS).

Results

Thirty-two patients with HCC with a median age of 65 (range 40-89) years were identified. The majority was male (n=29). Etiology of liver disease was hepatitis B viral (HBV) infection (n=17), HBV/hepatitis D viral infection (n=1), HCV infection (n=2), alcoholic liver disease (ALD, n=3), non-alcoholic steatohepatitis (NASH, n=3), or combined ALD/NASH (n=6). Only one third of patients (n=12) were aware of their liver disease and were followed by hepatologists. However, after the accomplishment of the diagnostic work-up for the liver tumor all patients received hepatology consultation and were subsequently referred to surgery. The tumor was discovered during screening in patients with known cirrhosis (HBV-induced n=8, HCV-induced n=2, ALD n=1, ALD/NASH induced n=1), during radiological investigation of abdominal pain (n=9), of weight loss (n=2), of increased levels of γ-glutamyl transferase (γ-GT) (n=4), or during follow up after liver resection for HCC (n=1). In 4 cases, the tumor was found incidentally in the context of radiological examination of rib-fracture (n=1), of follow up for neuroendocrine tumor of the lungs (n=1), and of yearly sonographic checkup (n=2).

Six patients underwent transarterial chemoembolization (TACE) and one combined TACE with RFA prior to surgery. Four additional patients were candidates for RFA, which could not be accomplished due to tumor localization and technical reasons. Eleven patients underwent laparoscopic and 21 open liver resection for HCC. All patients were followed up for recurrence every 3 months for the first postoperative year, every 4 months for the second, and every 6 months thereafter. No patient was lost to follow up.

Patient characteristics

Patient and tumor characteristics are demonstrated in Table 1. All but 2 patients had well preserved liver function prior to surgery, CTP score A. One patient with alcoholic liver

Table 1 Patients' demographics, preoperative parameters and tumor characteristics

Parameter	LLR (n=11)	OLR (n=21)	P-value
Age (years)	65 (54-81)	70 (40-89)	0.47
Gender			0.26
Male	9	20	
Female	2	1	
BMI (kg/m²)	26 (21.7-40)	26.2 (23-38)	0.38
HBV infection			0.45
Yes	7	10	
No	4	11	
Co-morbidities	6 (1-7)	5 (3-9)	0.14
PLT (x10³/µL)	202 (123-372)	183 (119-699)	0.15
INR	1.09 (0.97-1.26)	1.14 (0.93-1.71)	0.49
ALT (U/L)	23 (14-54)	45 (9-273)	0.07
AST (U/L)	16 (7-56)	26 (14-378)	0.14
γ-GT (U/L)	32 (12-286)	67 (14-385)	0.13
Bilirubin (mg/dL)	0.73 (0.26-1.39)	0.63 (0.42-1.35)	0.49
Creatinine (mg/dL)	0.75 (0.6-1.1)	0.9 (0.54-1.6)	0.28
Albumin (mg/dL)	4.45 (3.4-4.8)	4 (3.3-5.2)	0.20
AFP (ng/mL)	7.7 (1.58-43.35)	25.56 (2.8-1511)	0.22
Number of tumors			1.00
Solitary	10	18	
Multifocal	1	3	
Size of largest tumor (cm)	4.7 (1.8-9.7)	6.1 (2.5-22)	0.04
BCLC staging			0.29
0	1	0	
A	7	12	
C	3	9	
Milan criteria			0.25
Within	6	6	
Out	5	15	
Tumor pre-treatment			0.68
Yes	2	6	
No	9	15	

LLR, laparoscopic liver resection; OLR, open liver resection; BMI, body mass index; HBV infection, hepatitis B viral infection; PLT, platelets; INR, international normalized ratio; ALT, alanine aminotransferase; AST, aspartate aminotransferase; γ-GT, γ-glutamyl transferase; AFP, α-fetoprotein; BCLC staging, Barcelona clinic liver cancer staging

cirrhosis had a history of variceal bleeding 10 years before; it was managed with successful endoscopic ligation, medical treatment with nonselective β-blockers and abstinence of alcohol, resulting in improvement in liver function to CTP A score. CTP B score was evident in 2 patients. Median values for platelets (PLT), international normalized ratio (INR), bilirubin, albumin, and creatinine were 196x10³/µL, 1.12, 0.69 mg/dL, 4.25 mg/dL, and 0.87 mg/dL, respectively. Median BMI and Charlson comorbidity indices were 26.05 kg/m² and 5, respectively. Twelve patients (38%) were meeting the Milan criteria. Median maximal tumor diameter was 9 cm. Most patients were BCLC stage A (n=19), whereas one patient was BCLC stage 0 and 12 patients BCLC stage C. Advanced BCLC stage was due to vascular invasion (n=6), to performance status test 1 (strenuous physical activity restricted; fully ambulatory and able to carry out light work;

n=5) or to both causes (n=1). Median α-fetoprotein (AFP) was 8.75 ng/mL. Statistical comparison of patient and tumor characteristics between patients undergoing laparoscopic or open liver resection revealed statistical difference in the size of the largest tumor (P=0.04, Table 1).

Operative procedures

Perioperative data are summarized in Table 2. Median total operating time was 180 (range 90-300) min. Liver resections included: 2 right hepatectomies, 3 left hepatectomies, one left trisectionectomy, 4 left lateral sectionectomies, one right posterior sectionectomy, 6 bisegmentectomies (segments 5/6 n=5, segments IVb/V n=1), 7 segmentectomies (5 segment VI

resections and 2 caudate lobe resections), and one left lateral sectionectomy combined with segmentectomy and RFA. Atypical resections encompassed 4 cranial mesohepatectomies (segments IVa/VIII n=1, segments IVa/VIII and partially IVb/V n=1, segments IVa/VIII and partially IVb/V and VII n=1, and segments VII/VIII n=1), one atypical right hepatectomy (segments VI/VII/VIII), and 2 wedge resections (segments VII/VIII plus segments V/VI n=1, segments II/III plus RFA segment VII). All patients received elective surgery. Lymphadenectomy and lymph node biopsy in hepatoduodenal ligament were performed in 6 and 2 patients, respectively. Almost half of patients underwent cholecystectomy (17/32). Statistical difference between patients undergoing laparoscopic or open liver resection was found for the parameters performance of major resection (P=0.01), performance of Pringle maneuver (P=0.008), duration of Pringle maneuver (P=0.0001), blood transfusion (P=0.003), and duration of operation (P=0.004) (Table 2).

Pathology

Pathology data are summarized in Table 3. Vascular invasion and tumor thrombi were documented in 15 (47%) and 10 (32%) patients, respectively. Lymph nodes were negative in all cases where lymphadenectomy or lymph node biopsies were performed (n=8 in total). Tumors were classified to UICC stages I, II, IIIA, and IIIB, in 13, 8, 5, and 6 instances, respectively. Tumor differentiation according to the Edmonson and Steiner grading system was stage I, II, III, and IV, in 5, 10, 14, and 3 patients, respectively. Tumor-free resection margin (R0-resection) was identified in 29 of 32 patients (91%). Liver cirrhosis was histologically documented in 20 patients (63%). No statistical differences in pathology characteristics were assessed between patients undergoing laparoscopic or open liver resection (Table 3).

Morbidity and mortality

Direct extubation at the end of the operation was accomplished in all patients. Six patients were transferred to the ICU for postoperative monitoring. Ten patients experienced minor complications. Bile leakage and bleeding occurred in 2 and 1 patients, respectively, and were treated conservatively. One patient experienced aspiration pneumonia the 8th postoperative day after right hepatectomy; he was re-intubated, transferred to the ICU but died the 25th postoperative day of sepsis. Median hospital stay was 7 days. No statistical significance in postoperative outcomes between patients undergoing laparoscopic or open liver resection was identified (Table 4).

Follow-up data

Nine patients developed tumor recurrence during the postoperative follow up. In all but one patient the sites of

Table 2 Perioperative data concerning surgical details and blood transfusion

Parameter	LLR (n=11)	OLR (n=21)	P-value
Major resection			0.01
Yes	0	9	
No	11	12	
Type of resection			
Right hepatectomy	0	2	
Left hepatectomy	0	3	
Left trisectionectomy	0	1	
Right posterior sectionectomy	0	1	
Left lateral sectionectomy	3	2	
Bisegmentectomy	4	2	
Segmentectomy	4	3	
Others	0	7	
Pringle maneuver			0.008
Yes	2	15	
No	9	6	
Pringle maneuver duration (min)	0 (0-15)	20 (0-60)	0.0001
Blood transfusion			0.003
Yes	4	19	
No	7	2	
Duration of operation (min)	120 (90-180)	200 (90-300)	0.004

LLR, laparoscopic liver resection; OLR, open liver resection; ICU, intensive care unit

Table 3 Pathology results

Parameter	LLR (n=11)	OLR (n=21)	P-value
Vascular invasion			0.25
Yes	3	12	
No	8	9	
Tumor thrombi			0.11
Yes	1	9	
No	10	12	
UICC Stage			0.153
I	6	7	
II	4	4	
IIIA	1	4	
IIIB	0	6	
Histological grade			0.455
Well differentiated	1	4	
Moderately differentiated	4	6	
Poorly differentiated	6	8	
Undifferentiated	0	3	
Resection margin			0.53
Positive	0	3	
Negative	11	18	

LLR, laparoscopic liver resection; OLR, open liver resection; UICC, union for international cancer control

recurrence was the liver; the patient who developed intra- and extrahepatic tumor recurrence has undergone a repeated liver resection for a multifocal stage IIIB HCC 8 months after an atypical right hepatectomy for a stage II HCC; he was

treated with TACE and sorafenib but died 5 months after the second liver resection. TACE was the treatment of recurrence in 4 additional patients, whereas one patient underwent conventional chemotherapy. Currently 26 patients are alive after a median follow up of 18 (range 6-48) months. One-year and 3-year postoperative survival after laparoscopic and open hepatectomy was 100% and 100%, and 79% and 67%, respectively (P=0.06, marginal significance, Fig. 1).
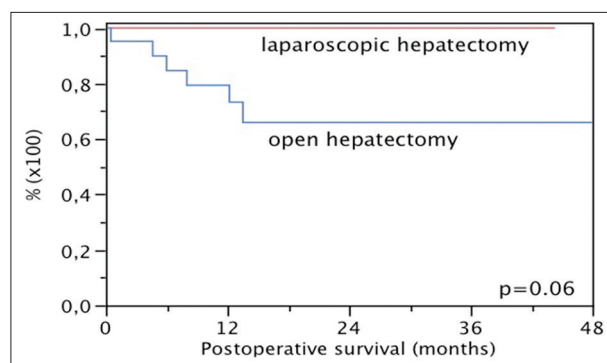
Prognostic factors for patient survival

The parameters age, gender, BMI, etiology of liver disease, Charlson's comorbidity index, BCLC staging, AFP, creatinine, γ-GT, laparoscopic hepatectomy, blood transfusion, operative time, UICC stage, tumor grade, R0 resection, Dindo-Clavien classification of postoperative complications, and hospital stay were evaluated by univariate analysis. Parameters that are

taken into account in the BCLC staging, such as tumor number, tumor size, vascular invasion, Milan criteria, PLT count, INR, bilirubin, and albumin, were not separately assessed. BCLC staging (P=0.0177), γ-GT (P=0086), laparoscopic hepatectomy (P=0.0209), UICC stage (P=0.008), Dindo-Clavien classification (P=0.0158), and hospital stay (P=0.0271), were found to be significant predictors of patient survival by univariate Cox proportional hazard regression analysis (Table 5). Since UICC stage, Dindo-Clavien classification and hospital stay are not predictable preoperatively, only BCLC staging, γ-GT, and laparoscopic hepatectomy were included in the multivariate analysis. Performance of laparoscopic hepatectomy remained as the unique independent predictor of survival by multivariate Cox proportional hazard regression analysis (P=0.0142).

Discussion

Although the first reports on laparoscopic liver resections were published in the early 1990s [18,19], and the first laparoscopic hepatectomy for HCC in 1995 [20], for many years most hepatobiliary surgeons were very restrained regarding the performance of laparoscopic liver resections. An increasing controversy between enthusiasm and skepticism on the new technique led to the organization of the 1st World Consensus Meeting on laparoscopic hepatectomy in 2009 [15], where indications and contra-indications for the new technique were thoroughly discussed and the pillar for the modern hepatic surgery was set. It was then, that laparoscopic hepatectomy was acknowledged as a "safe and effective approach to the management of surgical liver disease in the hands of trained surgeons with experience in hepatobiliary and laparoscopic surgery". Afterwards, a significant evolution in this field was noted, and the spectrum of laparoscopic liver resections was opened from liver biopsies and liver cysts deroofing up to typical and atypical hepatectomies for benign and malignant diseases and to live donor hemihepatectomy for transplantation [21,22]. Last achievement is the performance of laparoscopic multiple metastasectomies for colorectal liver metastases and of laparoscopic hepatectomy in the cirrhotic liver [23-25].

Some comparative studies and systematic reviews have already been published on the surgical outcomes of laparoscopic versus open liver procedures [26-28]. Among the documented benefits that a laparoscopic liver resection in comparison to the open approach might offer are the decreased blood loss and requirement for blood transfusion, the reduced operative time, the lower overall postoperative morbidity, the less postoperative pain and the shorter hospital stay [26-28]. Concerns for uncontrolled bleeding, compromised tumor margin or the port-site metastases have not been confirmed [26-28]. In addition, according to the current knowledge, patient survival and recurrence-free survival seem not to be influenced by the kind of procedure [28].

As demonstrated in recent comparative studies in Table 6, tumor size, operative time, blood loss, and hospital stay were reported between 2 and 8.5 cm, 185 and 365 min, 80 and 1085 mL, and 6 and 17 days in median values, respectively.

Table 4 Postoperative outcomes regarding postoperative management, morbidity and mortality and oncological outcomes

Parameter	LLR (n=11)	OLR (n=21)	P-value
ICU treatment			0.07
Yes	0	6	
No	11	15	
Complications			0.25
No	9	12	
Yes	2	9	
Dindo-Clavien category			
Grade I	1	0	
Grade II	1	8	
Grade V	0	1	
Postoperative mortality	0	1	0.11
Length of hospital stay (days)	5 (4-14)	8 (5-25)	0.09
Tumor recurrence			0.11
Yes	1	8	
No	10	13	

LLR, laparoscopic liver resection; OLR, open liver resection; ICU, intensive care unit

Figure 1 Kaplan-Meier patient survival analysis according to the type of hepatectomy

Table 5 Univariate and multivariate Cox proportional hazards regression analysis for patient survival

Patient/tumor parameters		P-value	
		Patient survival	
		Univariate analysis	Multivariate analysis
Age (years)	65 (40-89)	0.7748	
Gender		0.2001	
Male	29		
Female	3		
BMI (kg/m²)	26 (21-40)	0.8927	
Etiology of liver disease		0.5833	
HBV	17		
Other	15		
Co-morbidities	5 (1-9)	0.2763	
BCLC staging		**0.0177**	0.2559
0	1		
A	19		
C	12		
AFP (ng/mL)	8.75 (1.58-1511)	0.0652	
Creatinine (mg/dL)	0.87 (0.54-1.6)	0.4345	
γ-GT (U/L)	60 (12-385)	**0.0086**	0.3722
Laparoscopic hepatectomy		**0.0209**	**0.0142**
Yes	11		
No	21		
Blood transfusion		0.5182	
Yes	23		
No	9		
Operative time (min)	180 (90-300)	0.1924	
UICC stage		**0.008**	
I	13		
II	8		
IIIA	5		
IIIB	6		
Tumor grade		0.4617	
Well	5		
Moderate	10		
Poor	14		
Undifferentiated	3		
R0 resection		0.0843	
Yes	29		
No	3		
Dindo-Clavien category		**0.0158**	
0	21		
1	1		
2	9		
5	1		
Hospital-stay (days)	7 (4-25)	**0.0271**	

Data are expressed as median and range values. Statistical significant P-values are highlighted with bold characters

BMI, body mass index; HBV, hepatitis B virus; BCLC staging, Barcelona clinic liver cancer staging; AFP, α-fetoprotein; γ-GT, γ-glutamyl transferase; UICC, union for international cancer control

Three-year patient survival was 60.7-100% and 41.8-100% for laparoscopic and open resections, respectively. In most studies, disease-free survival showed no statistical differences [29-35].

In the present series, patients with HCC undergoing laparoscopic live surgery (Fig. 2) had statistically smaller tumors (P=0.04) compared with patients undergoing open

Table 6 Literature data on recent comparative studies on laparoscopic and open liver resections for hepatocellular carcinoma

Author	Procedure	N	Tumor size	Operative time	Blood loss	Hospital stay	3-year survival	DFS
Leong, *et al* [28]*								
	lap	42		250	495	7		52%
	open	110		349	1085	11		38%
	P-value			<0.001	<0.001	<0.001		0.035
Komatsu, *et al* [29]								
	lap	38	4.7	365	100	7	73%	50%
	open	38	8.5	300	80	10	69%	29%
	P-value		0.006	<0.001	0.094	0.079	0.951	0.219
Meguro, *et al* [30]								
	lap	60	2.3	277	110		83%	43%
	open	200	3.5	312	420		63%	28%
	P-value		<0.001	0.001	<0.001		0.004	0.048
Xiao, *et al* [31]								
	lap	41		242	272	9	78%	70%
	open	86		235	450	14	82%	68%
	P-value			0.589	0.001	<0.001	0.448	0.808
Martin RC 2nd, *et al* [32]*								
	lap	100	6.7		336	6.2	60%	20%
	open	254	8.5		755	9.3	41%	26%
	P-value		0.07		<0.001	0.001	0.499	0.826
Kim, *et al* [33]								
	lap	70	2.5	215		12	65%	51%
	open	70	2.4	282		17	65%	54%
	P-value		0.55	0.001		0.44	0.610	0.773
Kim, *et al* [34]								
	lap	29	3.5	210	485	7	100%	54%
	open	29	4.2	203	261	13	92%	40%
	P-value		0.278	0.681	0.065	<0.001	>0.05	>0.05
Kobayashi, *et al* [35]								
	lap	24	2	198	110	11	100%	50%
	open	27	2.2	185	450	17	100%	62%
	P-value		0.3371	0.7598	0.0019	<0.0001		

*Multicenter data

DFS, disease-free survival
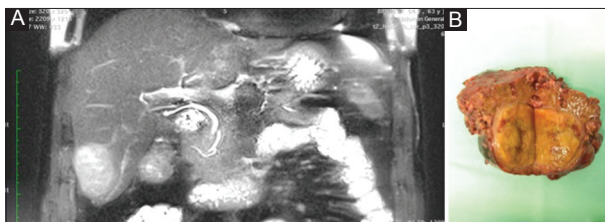
Figure 2 (A) Magnetic resonance imaging and (B) specimen, of a patient with hepatocellular carcinoma in segment VI in cirrhosis undergoing laparoscopic hepatectomy

liver surgery (Fig. 3), resulting in statistically less major resections (P=0.01), less requirement for Pringle maneuver (P=0.008) and intraoperative blood transfusion (P=0.03), and shorter duration of operation (P=0.004). Noteworthy, in all other patient and tumor characteristics, pathology results and postoperative outcomes, no statistical difference between the 2 groups was detected. Hospital stay, though shorter in the laparoscopic group (5 versus 8 days in the open group), gained only marginal significance in the present series (P=0.09). Three-year postoperative survival after laparoscopic and open hepatectomy was 100%, and 67%, respectively (P=0.06).

A point of discussion and criticism in our series might be the fact that 12/32 patients were BCLC stage C due to vascular invasion (n=6), to performance status test 1 (n=5) or to both causes (n=1). BCLC algorithm proposes the first-line treatment options for patients with HCC. However, this algorithm is not binding. The heterogeneity of HCC, the modern individualized patient approach, the local institutional facilities, the fact that vascular invasion represents a contra-indication to liver transplantation but not to liver resection and the contemporary perioperative support to patients with performance status 1 are some factors that allowed us to carefully select patients with BCLC stage C to liver resection. Moreover, as the initiators of the BCLC system very recently underline, "*several factors affect treatment of advanced stage, so that each patient with HCC*

should be carefully evaluated and treatment should be selected based on individual features" [36].

One limitation of this study was the small volume of the groups. However, data was sampled within a relative short period of time (4 years and 3 months), patients were evaluated and operated by the same senior hepatobiliary surgeon (reducing in this way the biases of patient selection for surgery, selection of operative procedure and operative technique), and this series is the first comparative study on laparoscopic versus open liver resection, regardless of indication, in Greece.
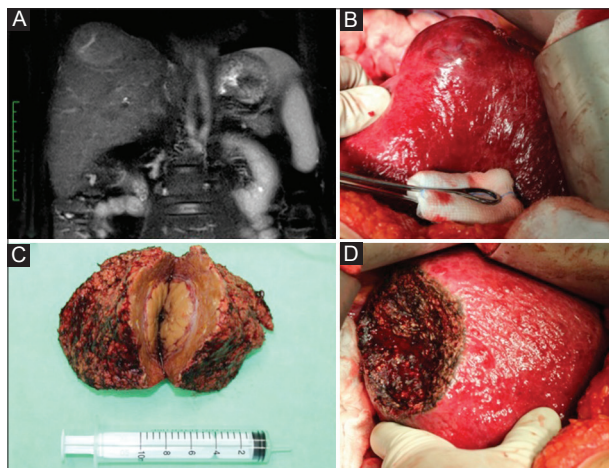
Figure 3 Magnetic resonance imaging (A), operative field before (B) and after hepatectomy (D) as well as operative specimen (C) of a patient with hepatocellular carcinoma in segment VII in cirrhosis undergoing open hepatectomy

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Summary Box

What is already known:

- Liver resection is the standard of care for selected patients with hepatocellular carcinoma (HCC)
- Laparoscopic hepatectomy represents the new trend in the operative management of HCC and finds increasing application during the last decade
- Limited comparative data on open versus laparoscopic hepatectomy for HCC have been published in Europe

What the new findings are:

- First comparative study on laparoscopic versus open liver resection for HCC in Greece
- Laparoscopic hepatectomy favored intraoperative outcomes without compromising pathology and postoperative outcomes
- Laparoscopic hepatectomy was an independent predictor of patient survival by multivariate analysis

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Despite the small study volume, Cox proportional hazard regression analysis for patient survival revealed 6 prognostic factors, BCLC staging, γ-GT levels, laparoscopic hepatectomy, UICC stage, Dindo-Clavien classification, and hospital stay. Laparoscopic hepatectomy remained as independent predictor of survival by multivariate Cox proportional hazard regression analysis (P=0.0142).

In conclusion, laparoscopic hepatectomy claims a notable proportion in the management of patients with HCC in chronic liver disease. Careful patient selection is of cardinal importance for the success of this innovative and promising method.

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