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Early Experience in Starting a Laparoscopic Liver Resection Program in Greece

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ABSTRACT

Background and Objectives: Laparoscopic liver resections (LLRs) have gained wider acceptance during the decade as safe and efficient procedures in the management of several benign and malignant diseases when performed by experienced surgeons. We report our initial institutional experience with LLRs performed by 1 certified hepatobiliary surgeon.

Methods: Patients undergoing LLRs by 1 senior hepatobiliary surgeon in our Institution during the period from January 2012 through January 2017 were prospectively sampled and retrospectively analyzed for the purposes of this study.

Results: Forty-two of 175 patients (24%) who had surgery for liver tumors underwent LLR. Median age was 64 years; median body mass index and Charlson comorbidity index were 27.3 kg/m^2 and 6.5, respectively. Patients underwent resections for benign (n = 22) or malignant (n = 20) lesions. Median total operating time was 115 minutes and liver resections included: 1 left hepatectomy, 11 bisegmentectomies, 7 segmentectomies, 5 wide wedge resections, 1 left lateral sectionectomy combined with segmentectomy and radiofrequency ablation, 15 liver cyst unroofing, 1 laparoscopic drainage of a pyogenic liver abscess, and 1 laparoscopic drainage of a hepatic hydatid cyst. Blood transfusion was needed in 10 patients. Six patients (14%) had postoperative complications, none of which necessitated reoperation. None of the patients was admitted to the intensive care unit after surgery, and the median hospital stay was 4 days. The tumor-free resection margin was documented in all primary or secondary oncologic cases.

Conclusions: Careful patient selection and compliance with the international recommendations are the keys for the successful introduction and evolution of an LLR program with a certified hepatobiliary surgeon with laparoscopic experience.

Key Words: Hepatocellular carcinoma, Minimally invasive liver surgery, Laparoscopic hepatectomy, Liver cirrhosis, Liver resection.

INTRODUCTION

Laparoscopic liver resections (LLRs) were initially reported in the early 90s, yet, unlike other laparoscopic procedures, their wider acceptance and performance was delayed, as initial enthusiasm was followed by great skepticism and reluctance by surgeons.[1,2] Fear of uncontrollable operative complications, such as hemorrhage and air embolism, a rather steep learning curve, absence of suitable laparoscopic instruments in combination with uncertainty of oncologic adequacy and undocumented benefits cast a shadow like a colossus over the evolution of laparoscopic hepatic surgery for nearly 2 decades. Advancement of technology on laparoscopic instruments and devices, as well as gradual acquisition of laparoscopic proficiency gradually led to a wider performance of LLRs for both benign and malignant lesions. The evolution of liver laparoscopic surgery led to the 2008 international consensus, where LLRs were eventually acknowledged as safe procedures with acceptable morbidity and mortality for both minor and major liver resections in the hands of certified hepatobiliary surgeons with experience in laparoscopic surgery.[3] During the last 20 years, indications for LLR evolved from low risk, easily accessible benign lesions to more complex and high-skill–demanding malignant tumors.[2,4,5] Despite the lack of level I evidence supporting the performance of LLRs; current evidence suggests that laparoscopic hepatic surgery is reproducible, safe, and efficient, while presenting important advantages over open liver surgery. Although LLRs are very challenging to perform and potentially time demanding, they confer significant benefits to patients, including less postoperative pain, less bleeding, reduced

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mortality, and the very important shorter hospital stay, as documented by various studies.[6–8] Notwithstanding the progress noted in LLRs in the rest of the world, in Greece the gold standard in the management of hepatic lesions remains the open approach. Similar to the international surgical community, lack of laparoscopic expertise combined with poor patient education on the benefits and adequacy of LLRs led to a slower, yet growing, adoption of minimally invasive techniques in the treatment of benign and malignant hepatic lesions.[7,9] Furthermore, the ongoing financial crisis has been an additional obstacle to the evolution of laparoscopic liver surgery in Greece. The purpose of our study was to present our initial institutional experience with LLRs performed by 1 certified hepatobiliary surgeon.

MATERIALS AND METHODS

Between January 1st, 2012 and January 1st, 2017 hepatic surgery was performed on 175 patients by a senior hepatobiliary surgeon (GCS) in our institution. A 12-year experience in major surgical procedures and advanced laparoscopic operations gained in German university hospitals (University Hospital, Essen, and Johannes Gutenberg University Hospital, Mainz) was applied by a senior surgeon repatriated to Greece to start an LLR program in Athens. However, the surgical and anesthesiology team progressed through the learning curve, as well as the practical and technical obstacles, as the number of cases increased. Data from patients undergoing LLR were prospectively implemented in a database as follows: age, gender, date of operation, solid or cystic tumor, diagnosis, body mass index (BMI), tumor characteristics (number and size), comorbidities, preoperative treatment, and imaging studies. The intraoperative data that were recorded included type of liver resection, additional surgical procedures (cholecystectomy and lymph node biopsy), vascular occlusion (Pringle maneuver), blood transfusion, and total operating time. Major resection was defined as the 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. Postoperative morbidity was recorded and categorized according to the Clavien-Dindo classification.[10] 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,[11] and the classification according to the 7th edition of the Tumor/Node/Metastasis (TNM) and the Union for International Cancer Control (UICC) systems. Follow-up data included current patient status, recurrent disease, treatment of recurrence, and cause of death.

No patient was lost to follow-up. All oncologic 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.

RESULTS

During the study period, 42 of 175 patients (24%) underwent LLR for solid (n = 25) or cystic tumors (n = 17). Female:male ratio was 1.2 with a median age of 64 years (range, 33–81 y). Median BMI and Charlson comorbidity index were 27.3 kg/m^2 and 6.5, respectively. Only in a minority of cases (n = 11) was the tumor discovered incidentally. Abdominal discomfort was the cardinal symptom in 15 patients. The tumor was detected during screening in patients with known cirrhosis (hepatitis B induced, n = 3; hepatitis C induced, n = 3; alcoholic, n = 1; alcoholic/nonalcoholic steatohepatitis induced, n = 1), during oncologic follow-up for rectal (n = 2) or anal (n = 1) cancer, or during radiologic investigation of jaundice (n = 2) or increased levels of γ-glutamyl transferase (n = 3).

Indications for surgery were symptomatic nonparacytic liver cyst (n = 15), hepatocellular carcinoma (HCC; n = 16), colorectal liver metastasis (CRLM; n = 2), hepatocellular adenoma (n = 3), and miscellaneous (n = 6; see **Table 1**). The timing of the LLRs of patients who received chemotherapy (n = 2) was scheduled after communication with the responsible oncologist, to minimize the potential complications caused by chemotherapy-associated steatohepatitis. In all but one case of solid tumors, single lesions were present. Four patients with cystic tumors presented with small multiple cystic lesions alongside the dominant symptomatic lesion. Median tumor size was 10 cm (range, 2–21), significantly smaller in the case of solid tumors (4 cm, range 2–10, vs 14 cm, range 7–21, in the case of cystic tumors; $P = .015$). Four patients received pretreatment of their liver tumors in the form of transarterial chemoembolization (n = 2 for HCC), or of systemic chemotherapy (n = 2 for CRLM).

Perioperative data are summarized in **Table 2**. Median total operating time was 115 minutes (range, 30–240). Liver resections included: 1 left hepatectomy, 3 left lateral sectionectomies, 8 further bisegmentectomies (segments V/VI, n = 4; segments IVb/V, n = 1; and segments VI/VII, n = 3), 7 segmentectomies (segment VI resections), 5 wide-wedge resections (segment II, n = 1; segment III,

Table 1.
Patients' and Tumor Characteristics

Parameter	Patients (N = 42)
Age (years)	64 (33–81)
Gender	
Male	20
Female	22
BMI (kg/m^2)	27.3 (21.7–40)
Tumors	
Solid	25
Cystic	17
Indications	
Benign	22
Hepatocellular adenoma	3
Nonparacytic cyst	15
Hydatid cyst	1
Hemangioma	2
Infected simple cyst	1
Malignant	20
HCC	16
Hilar cholangiocarcinoma	1
CRLM	2
Hypernephroma metastasis	1
Size of largest tumor, cm (range)	4.7 (1.8–9.7)
Tumor pretreatment	
Yes	4
No	38

Table 2.
Operative and Postoperative Data

Parameter	Patients (N = 42)
Major resection, n	
Yes	0
No	42
Type of resection, n	
Left hepatectomy	1
Wide-wedge resection	5
Left lateral sectionectomy	3
Bisegmentectomy	8
Segmentectomy	7
Liver cyst unroofing	15
Other	3
Blood transfusion, n (%)	
Yes	10 (24)
No	32 (76)
Duration of operation, min (range)	115 (30–240)
ICU treatment, n (%)	
Yes	0 (0)
No	42 (100)
Complications, n (%)	
No	36 (86)
Yes	6 (14)
Clavien-Dindo category, n (%)	
Grade I	2 (5)
Grade II	1 (3)
Grade IIIa	3 (8)
Postoperative mortality, n	0
Length of hospital stay, d (range)	4 (2–14)

n = 2; segment IV, n = 1; and segment VII, n = 1), 15 liver cyst unroofing, and, classified as other, 1 left lateral sectionectomy combined with segmentectomy and radiofrequency ablation, 1 laparoscopic drainage of a pyogenic liver abscess, and 1 laparoscopic drainage of hepatic hydatid cyst.

All but 1 patient underwent elective surgery. An 81-year-old patient with a pyogenic liver abscess associated with a 21-cm infected hepatic cyst in liver segment VII/VIII was operated on urgently because of deterioration of his clinical condition and unsuccessful radiologic puncture. Thirteen patients underwent cholecystectomy (35%). Pringle maneuver was performed in 4 patients. Blood transfusion was necessary in 10 patients (24%), 9 from the solid and 1 from the cystic tumor group. Direct extubation at the end of the operation was accomplished in all patients. No patient was transferred to the ICU. Six patients experienced complications, 3 minor and 3 major. There were 2 grade I complications (wound infections opened at the bedside), one grade II complication (bleeding treated conservatively), and 3 grade IIIa complications. The latter complications encompassed 2 bile leakages treated with endoscopic retrograde cholangiography and stent placement and percutaneous drainage of a biloma, as well as one wound dehiscence repaired under local anesthesia.

In 2 instances the initial diagnosis was not confirmed in the pathology report. A young woman was operated on for a presumed hepatocellular adenoma but the final diagnosis was atypical focal nodular hyperplasia. In the

second case, a male patient was operated on for hepatocellular carcinoma in cirrhosis but histology revealed an intrahepatic cholangiocarcinoma in cirrhosis. A tumor-free resection margin (R0) was documented in all primary or secondary oncologic cases (n = 20). Among the primary malignant liver tumors were 10 pT1, 5 pT2, and 1 pT3a tumors. Microvascular invasion was documented in 4 patients with HCC. Malignancy was histologically ruled out in all cases of cystic tumors. The median hospital stay was 4 days. During the follow-up 2 patients died due to progression of their metastatic disease from hypernephroma or hilar cholangiocarcinoma. At this writing, 40 patients are alive and in good physical condition after a median follow-up of 27 months (range, 2–61 months).

DISCUSSION

Laparoscopic liver surgery has undergone a major evolution during the past decade. Although initially confronted with restrain and reluctance by the surgical community, LLR is currently considered a safe and adequate approach in the management of liver lesions in the hands of experienced surgeons. Despite the fact that the first reports date back to the early 90s,[1,2] the first well-defined series of LLRs were not reported until almost 10 y later.[4,12] Descottes et al[12] and Cherqui et al[4] each described their initial experience with LLR with 15 and 30 patients, respectively, undergoing surgery for benign and malignant diseases including HCC with underlying liver cirrhosis. Their results were promising and set the foundations for wider performance of LLRs. Several equally small initial-experience series followed, reporting results for benign and malignant lesions using pure or hand-assisted laparoscopic approaches.[13–15] In 2007, a series of 300 minimally invasive hepatectomies was reported by Koffron et al.[16] The increasingly encouraging outcomes in multiple series led to the 2008 international consensus (Louisville. Kentucky, USA), where, following thorough evaluation, LLRs were recognized as safe and efficient procedures when performed by proficient hepatobiliary surgeons.[3] The following year, a world review of LLRs including 2804 patients was published.[17] The study confirmed that LLR is a safe approach with adequate morbidity and mortality rates for both minor and major hepatic resections; in addition 3- and 5-year survival rates for HCC and colorectal cancer liver metastases were reported to be comparable to open liver resection (OLR) in selected patients. The road was then wide open for experienced surgeons to perform more LLRs, and in the following years, several institutions and surgeons reported their initial experiences with minor and major LLR in progressively larger study groups with equally positive short- and long-term results.[5,6,18–20]

Our initial experience with LLRs coincided with an escalating financial crisis in Greece, which greatly affected the national healthcare system.[21] The rising rates of unemployment along with a general climate of uncertainty led an important proportion of population away from seeking medical assistance promptly.[22] Such a phenomenon is decisive, given the fact that certain malignant lesions need to be treated surgically within a certain time frame for adequate oncological results. If not, treatment options including laparoscopic resection, in our case, can be limited. Recession, along with strictly imposed austerity measures, led to crippling cutbacks in healthcare funds and consequently in purchase of medical equipment. Access to suitable laparoscopic equipment, which is essential for the performance of these procedures, was limited. More important, the continued economic crisis led to a direct reduction of available ICU bed capacity, creating yet another hurdle, as postoperative ICU close monitoring may be essential. In addition, poor education of the public concerning the benefits of laparoscopic hepatic surgery was an obstacle that we encountered. Patient skepticism toward LLR was partially triggered by a proportion of hepatologists in Greece who remained anchored to traditional open liver resection (OLR) for the management of HCC. A lack of anesthesiology experience with major abdominal laparoscopic procedures constituted another significant restriction.

Despite the ominous financial situation in our hospitals and country, the introduction of LLR gained significant ground as a more cost-efficient procedure based on the following facts: (1) high operative costs of the OLRs at the time were admissible; at the beginning of our program, costs of 1-use medical equipment or expendable material used during open laparoscopic resections by other hepatobiliary surgeons in our hospital were as high as up to 10,000€ per operation; (2) ICU stay was a prerequisite for almost all patients undergoing liver resections because of the long duration of the OLR performed by previous surgeons; and (3) median hospital stay after OLR was longer than 2 weeks. Notwithstanding the limiting financial data combined with the previous institutions' experience with OLR, our program succeeded and became established, as (1) we used multipurpose laparoscopic medical instruments for repeated use in LLR, which were purchased at our personal cost; (2) LLRs required no ICU bed coverage, as a result of good patient selection and careful preoperative patient optimization[23]; and (3) we reduced median hospital stay to 4 d. Such critical modifi-

cations allowed us to reduce costs and develop the program despite the yearly reductions in the budget. The "paradox" of starting an LLR program during an ongoing financial crisis makes our small-volume series unique.

Major LLRs are routinely performed only in specialized high-volume centers, and thus remain highly challenging, even to experienced surgeons.[5] Wider performance of LLR has been increasingly adopted in smaller centers, yet arbitrary practice may hide a wolf in sheep's clothing, as patients with extensive malignant or asymptomatic benign lesions may undergo unnecessary or even major LLR. The indications for our resections were in strict accordance with the international consensus standards, avoiding redundant liver resections while respecting the parenchyma sparing as standard of care.[3] Moreover, our initial experience included uncomplicated lesions as defined by the difficulty score for LLR proposed in the second international consensus meeting.[24] The mean tumor size was 4 cm for solid lesions (range, 1.8–9.7 cm) and the majority (n = 21) were located in peripheric segments (II–VI), whereas LLR for significantly larger tumors situated in more difficult-to-access segments was avoided and the open approach was preferred. Resections for all benign diseases including focal nodular hyperplasia (FNH) and liver adenomas were performed solely for symptomatic cases, whereas nonessential or major resections were avoided in these patients. Of note, the percentage of our performed LLRs compared to all our hepatic resections was 24%, consistent with that of some international high-volume hepatic surgery centers.[6] Complication rates of LLRs reported in literature vary significantly whereas our series included only 3 (8%) major complications that did not require general anesthesia to resolve (Clavien-Dindo IIIA). Finally, as far as the oncologic adequacy of LLR in our patients is concerned, our current mean follow-up period (27 months) does not allow us to draw solid conclusions, but our results, based on follow-up imaging and laboratory data, to date could be deemed excellent.

It is noteworthy that 11 patients with resected HCC had chronic liver disease: 6 had HBV infection, 3 had HCV infection, and 2 had alcoholic and nonalcoholic steatohepatitis. Eight of the patients had known cirrhosis and some degree of portal hypertension (PHT). The Barcelona Clinic Liver Criteria (BCLC) classification, which is recommended for HCC treatment strategies, advocates that surgery may not be beneficial in the presence of cirrhosis with solitary >5 cm or multiple tumors with known PHT.[25] Nevertheless, it is reported that selected patients with larger tumors and PHT may profit from the performance of hepatic resection although it is not suggested by the BCLC.[26] Moreover, several studies highlight the advantages of LLR in this high-risk patient group, including shorter hospital stay, less blood loss, decreased morbidity rates, and fewer complications such as intractable ascites.[27–29] Careful preoperative evaluation, selection, and optimization of patients with cirrhosis who have tumors that are easily accessible laparoscopically are of principal importance.

CONCLUSION

In conclusion, our initial experience with 42 cases of LLR in a Greek center, on the one hand, highlights the difficulties and obstacles when introducing a novel surgical method in a health care system, but on the other hand, demonstrates the safety, feasibility, and positive results of LLR, provided that both careful patient selection and compliance with the international recommendations are ensured.

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