Laparoscopic resection of hepatocellular carcinoma. Considerations on lesions in the posterosuperior segments of the liver



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Marco Casaccia, Enzo Andorno, Stefano Di Domenico, Maximiliano Gelli, Giuliano Bottino, Umberto Valente

Advanced Laparoscopy Unit, General and Transplant Surgery Dept., "St. Martino" Hospital, University of Genoa, Italy

Laparoscopic resection of hepatocellular carcinoma. Considerations on lesions in the posterosuperior segments of the liver

AIM: The aim of this study was to evaluate retrospectively our results for laparoscopic liver resection (LLR) of hepatocellular carcinoma (HCC) including lesions in the posterosuperior segments of the liver in terms of feasibility, outcome, recurrence and survival.

MATERIAL OF STUDY: Between June 2005 and May 2009, we performed 22 LLR for HCC. The underlying cirrhosis was staged as Child A in 19 cases and Child B in 3.

RESULTS: LLR included a non anatomic resection in 15 cases and an anatomic resection in 7. A conversion to laparotomy occurred in one (4.5%) patient for hemorrhage. Mortality and morbidity rates were 0% and 18.1% (4/20). Over a mean follow-up period of 29 months (range: 19–65 months), 11 (50%) patients presented recurrence, mainly at distance from the surgical site.

DISCUSSION: A laparoscopic approach is more suitable when the lesion is located in the peripheral "laparoscopic" segments 2 to 6. Nevertheless, six resections were made in the posterosuperior segments. Although parenchymal-sparing resection is required by the presence of underlying liver disease, anatomic resection has always to be considered and pursued to reduce local recurrence. In our series the recurrence rate was similar to those reported for other laparoscopic studies and for open resection of HCC.

CONCLUSIONS: LLR for HCC in selected patients is a safe procedure with good short-term results. It can also be proposed in tumor locations with a difficult surgical access maintaining a low morbidity rate and good oncologic adequacy. This approach could have an impact on the therapeutic strategy of HCC complicating cirrhosis as a treatment with curative intent or as a bridge to liver transplantation.

KEY WORDS: Cirrhosis, Hepatocarcinoma, Laparoscopy, Liver resection.

Introduction

In recent years the progress of laparoscopic procedures and the development of new and dedicated technologies have made endoscopic hepatic surgery feasible and safe ¹⁻ ³. Almost all types of liver resection have already been performed by laparoscopy ^{4,5}. However, few major laparoscopic hepatectomies have been reported to date ^{6,7}. In fact, the use of this technique has been limited to easily accessible lesions, namely, tumors in the peripheral portion of the liver's anterolateral segments (segments 2, 3, 5 and 6, and the inferior part of 4 according to the classification of Couinaud. Accordingly, most surgeons consider that lesions located in the posterior or superior part of the liver (segments 1, 7, and 8, and the superior part of 4) are not appropriate because of the limited visualization and the difficulty of controlling bleeding ^{8,9}.

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Correspondence to: Prof. Marco Casaccia, Dipartimento Trapianti, Divisione di Chirurgia Generale e dei Trapianti d'organo, Ospedale San Martino, Università degli Studi di Genova, Monoblocco IV° piano - Largo Rosanna Benzi 10, 16132, Genova, Italia (e-mail: Marco.Casaccia@unige.it)

Because of concerns about using laparoscopy to treat malignant tumors and the fear of compromising the oncologic resection, most surgeons have concentrated on laparoscopic liver operations for benign conditions ¹⁰. Advances in laparoscopic cancer care and increasing experience of liver surgeons with laparoscopy have carved out a new role for laparoscopic surgery in the management of hepatic tumors. It is now widely accepted that laparoscopy will be increasingly used in liver surgery and the indications extended to patients with hepatocellular carcinoma (HCC) and cirrhosis ^{7,11,12}.

The aim of this study was to evaluate retrospectively our results for laparoscopic liver resection (LLR) for HCC including lesions in the posterosuperior segments of the liver in terms of feasibility, safety, outcome, recurrence and survival.

Materials and methods

Patients

Twenty-two LLR for HCC performed between June 2005 and May 2009 were retrospectively reviewed. In the same period, 51 patients underwent liver transplantation without prior resective surgery and 32 patients underwent open liver resection.

Selection criteria for laparoscopic approach in HCC patients included the following: well compensated Child's class A/B cirrhosis, esophageal varices <=grade 2, platelet count >=40 x 10^{9} /L, and solitary lesion of <=5 cm in diameter accessible to the laparoscopic approach (ie, located in the peripheral segments of the liver) and treatable by limited resection (<3 segments). Only one patient was operated on in emergency situation for an hemoperitoneum from a ruptured HCC located in segment III.

If severe impairment of the coagulation tests was assessed preoperatively (platelets <40,000 and/or international normalized ratio >1.6), patients were excluded from the procedure.

Imaging assessment of the liver included CT, MRI, or both and Doppler ultrasonography. Portal vein invasion and evidence of extrahepatic disease were considered exclusion criteria.

Most resections were intended to be anatomic (ie, resection of 1 or more anatomic segments) in order to territory of resect the portal the tumor. Segmentectomies were defined by their numbers and performed according to external segmental borders and use of intraoperative ultrasound. However, in small lesions developed in patients with portal hypertension and hepatic dysmorphy, non anatomic resections were performed. These consisted of resection of less than 1 segment including the tumor and an intended 1-cm tumor-free margin. Survival and tumor recurrence rates were studied at follow-up through liver function tests, alpha-fetoprotein, and computed tomographic or mag-

netic resonance scan at 1 month and then every 6 months.

Parameters assessed were duration of surgery, blood loss, perioperative transfusions, pathologic margins, postoperative variations of liver tests, mortality, morbidity, hospital stay, recurrence rate and survival. The results were expressed as medians (range). All comparisons between groups were performed using the Student *t*-test. P < 0.05was considered statistically significant.

SURGICAL TECHNIQUE

The patients were placed in the supine position with lower limbs apart, except for isolated resections of segment 6-7 where the left lateral decubitus position was used. The procedures were performed with CO_2 pneumoperitoneum, and abdominal pressure was electronically maintained below 11 mm Hg. In general, four trocars and a 30° optic were necessary.

The liver was examined by vision and intraoperative ultrasonography to confirm the number and size of the lesions and define their relationship with the intrahepatic vascular structures. A tourniquet for portal triad clamping was passed in few cases and the Pringle maneuver was used in one.

Hepatic transection was performed using an ultrasonic dissector (Ultracision, Ethicon, USA) in the first 4 patients and a thermofusion device (Ligasure; Covidien Italia, Segrate (Mi), Italy) in the last 18 patients.

Bipolar electrocoagulation was used for minor bleeding, and larger structures were secured with clips. Portal pedicles and major hepatic veins were divided by application of a linear stapler (Endo GIA roticulator; Covidien Italia, Segrate (Mi), Italy). The resected specimen was placed in a plastic bag and externalized, without fragmentation, through the enlarged umbilical port incision or through a suprapubic incision. This incision was immediately closed and the abdomen reinflated. The surgical field was irrigated and checked for bleeding or bile leak, and residual fluid was removed by suction. A drain was left *in situ* in all patients.

Results

Between June 2005 and May 2009, 22 liver resections for HCC were performed by laparoscopy. These 22 resections were carried out on 13 men and 9 women with a median age of 66 years (range: 47-76 years). The characteristics of the patients are summarized in Table I. Tumor location according to Couinaud hepatic segmentation is presented in Fig.1.

The median size of the resected tumor was 3.1 cm (range: 0.9-5.0 cm). The median surgical margin was 15 mm (range: 0-40 mm) and exceeded 5 mm in 20 patients (90.9%). At hystologic examination, the severi-

TABLE I - Demographics of 22 patients with Hepatocellular Carcinoma and Liver Cirrhosis

Sex (M/F)	13/9
Age, median (range)	66 (47-76)
Ethiology of liver cirrhosis	
HCV related (%)	11 (50)
Alcoholic (%)	6 (27.3)
HBV related (%)	4 (18.2)
Mixte (%)	1 (4.5)
Liver function	
Child A (%)	19 (86.3)
Child B (%)	3 (13.7)
Laboratory tests, median (range)	
Total bilirubin (mg/dl)	1.3 (0.5-3.8)
AST (UI/L)	60 (19-207)
ALT (UI/L)	55 (19-179)
Platelet count	(109/L) 113 (40-329)
INR 1.1	(0.96-1.59)
α -feto-protein (ng/ml)	18.8 (5-809.3)

HCV: hepatitis C virus; HBV: hepatitis B virus; INR: international normalized ratio.



Fig. 1: Location of the twenty-five resected HCC nodules according to Couinaud hepatic segmentation.

ty of cirrhosis was established, showing moderate activity in 13 patients and mild activity in 9. Twenty-five HCC nodules were resected. There were 15 (68.2%) atypical and 7 (31.8%) anatomic resections. The types of liver resection and the results are detailed in Table II.

The median duration of the operation was 300 min (range: 120–560 min). The median operative blood loss was 55 ml (20-1400 ml). Bleeding resulted from parenchymal transection in all cases. Ten patients (45.4%) required blood transfusion (median 1 packed red cell unit, range: 1-4 units). Conversion to laparotomy was required in one patient (4.5%), due to important continuous bleeding during parenchymal transection (segmentectomy V). The decision to convert to laparotomy was not once taken in emergency conditions or

TABL	εII	-	Surgical	procedures	and	results.
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reputeetomy

Segmentectomy, n (%)	5 (22.8)
Left lateral lobtectomy (segments II, III), n (%)	1 (4.5)
Trisegmentectomy (segments IVb,V,VI), n (%)	1 (4.5)
Non anatomic resection, n (%)	15 (68.2)
Operative time, median (range), (min)	300 (120-560)
Blood loss, median (range), (ml)	55 (20-1400)
Conversion to laparotomy, n (%)	1 (4.5)
Surgical margin, median (range), (mm)	16 (0-40)
> 10 mm, n (%)	15 (68.2)
5-10 mm, n (%)	6 (27.3)
< 5 mm, n (%)	1 (4.5)
Morbidity, n (%)	4 (18.1)
Mortality, n (%)	0
Hospital stay, median (range), (days)	8 (5-16)

due to life-threatening bleeding or major vessel injury. One patient was operated on in emergency situation for hemoperitoneum (2500 ml) from a ruptured HCC located in segment III. An atypical resection of a 4-cm lesion was performed in this case. Eleven procedures were associated in 9 (40.9%) patients. A cholecystectomy was necessary in 5 cases to maintain a clear resection margin in HCC nodules located in segment IV or V.

Radiofrequency ablation was used to treat a second tumor located away from the resected tumor and undetected at preoperative imaging in 3 cases. Adhesiolysis was realized for previous upper quadrant surgery in 2 cases and lymphnode sampling of the hepatic pedicle was made in one case.

Specific postoperative complications occurred in four (18.1%) patients. These complications included ascites well controlled by diuretics in 2 cases, mild transient jaundice and biliary collection drained percutaneously in one case each. Median hospital stay was 8 days (range: 5-16 days). Over a mean follow-up period of 29 months (range: 19–65 months), eleven (50%) patients presented recurrence. With respect to surgery performed, all recurrences were located in another liver segment; an associated local recurrence adjacent to the stump was present in 4 patients.

No statistical differences were noted between recurrent and non recurrent patients in terms of tumor pathologic grading, presence of a capsule, presence of satellite nodules and surgical margins (18 ± 10 vs. 15.2 ± 9, respectively; P = 0.52). A statistical significance was found in tumor diameter, being larger in recurrent than in non recurrent patients (37.1 ± 11 vs. 26.7 ± 10, respectively; P = 0.048).

Treatment of recurrence was possible in all patients, including chemoembolization in 8 cases, orthotopic liver transplantation in 3 cases (2 patients receiving both treatments), and percutaneous radiofrequency ablation in two.

Three (13.6%) patients died after 19, 25 and 33 months of follow-up, respectively, of severe liver function impairment and multifocal hepatic recurrence with extrahepatic metastases in one.

Discussion

LLR for HCC is limited to centers with experience in both laparoscopic surgery and the management of cirrhotic patients. Considering LLR requires an accurate assessment of the indications in terms of tumor location and underlying liver function and specific expertise and training in both hepatic and laparoscopic surgery, as well as access to adequate technology.

The most frequently required type of liver resection for small single HCC is limited anatomic resection. Such resections are particularly suitable for laparoscopy. However liver resections in cirrhotic patients are technically more difficult than in patients with a normal liver, presenting added complications, such as profuse bleeding during liver mobilization and parenchymal transection. A few reports have already suggested that laparoscopic resections may be successfully performed in patients with HCC and cirrhosis ^{13,14}.

In this study, an LLR was successfully performed in 95.5% of the patients. Only one patient required conversion to open surgery, due to important continuous bleeding during parenchymal transection (segmentectomy V). In our experience, as in other laparoscopic studies 9,14, blood loss was acceptable. This was probably due to the use of new coagulation and transection devices. Operative durations of laparoscopic liver resections are significantly longer than those of matched open counterparts ^{9,15}. This was confirmed in the present study with a 5-hour mean operative time which, however, improved with the learning curve. It is worth saying that eleven procedures were associated in 9 (40.9%) patients, further increasing the operative time. The safety of the procedure is attested by the absence of mortality and the low specific morbidity (18.1%). There were only 2 cases of transient postoperative liver failure. These findings are important since ascites and jaundice are the main complications of liver resection, even minor ones, in cirrhotic patients.

The recurrence rate was similar to those reported for other laparoscopic studies ^{2,13} and for open resection of HCC ^{16,17}. As often observed following HCC resections, most recurrences occurred away from the hepatic stump. The only local recurrences occurred in four patients after a segmentectomy V, a segmentectomy VI, and 2 atypical resections of segment VII, respectively. The parenchymal margin in our study was free of tumor cells in all patients, with a margin of less than 5 mm in only one case. However, the free parenchymal margin in the patients with recurrence near the stump was 10 mm in 2 patients and greater than 20 mm in the remaining

two. Among tumor characteristics (tumor diameter, pathologic grading, presence of a capsule, presence of satellite nodules and surgical margins), only the tumor diameter differed significantly between recurrent and non recurrent patients. A correlation between recurrence and tumor diameter has already been postulated. A retrospective study by Yeh et al. ¹⁸ analyzed the surgical outcomes of HCC concomitant with liver cirrhosis in 218 patients who underwent hepatic resection. Tumor size >2 cm was found to be a significant adverse prognostic parameter affecting recurrence and survival rates.

When considering the type of liver resection to be performed, some considerations need to be made. Segmental and non anatomic resections are more suitable for a laparoscopic approach when in the peripheral "laparoscopic" segments 2 to 6. Segments 7 and 8 are more difficult to access as the approach angle of the instruments is limited by the costal margin. The major problems then become ensuring an adequate oncologic margin and difficult-to-control bleeding from venous tributaries in the depth of the tumorectomy. In our series, 7 (31.8%) resected nodules were located in segments 7 and 8. Despite difficult location of the lesions, a non anatomic resection was completed laparoscopically in all cases. The procedures were long and technically demanding, but the use of a 30° optic joined to an extended right triangular ligament division and to a consequent lowering of the hepatic dome by use of a palpator has made it possible with respect to the surgical margins.

Although parenchymal-sparing resection is required by the presence of underlying liver disease and impaired liver regeneration, anatomic resection has always to be considered and pursued. In fact, it has been shown to reduce local recurrence and improve survival in HCC patients when compared with non anatomic wedge resections ^{19,20}

This is attributed to the mode of dissemination of HCC through microvascular portal invasion, which justifies anatomic resection of a portal territory around the tumor. According to previous studies ^{10,21}, we can state that a laparoscopic approach to a limited resection for a single lesion in segment 7 or 8 would only be suitable where the lesion is particularly small and superficial. A single larger lesion must, therefore, be considered for either an open limited resection or a laparoscopic right hemihepatectomy. Besides the advantages of minimally invasive surgery, another important issue includes preservation of abdominal collateral venous circulation, which may contribute to the absence of postoperative ascites, and avoidance of peritoneal adhesions, valuable in these patients who may require repeat operations for tumor recurrence. This advantage is particularly appreciated in patients undergoing liver transplantation, as it occurred in 3 patients of our series. Absent or limited postoperative adhesions were noted at this time.

In conclusion, our study shows that LLR for small peripheral HCC in patients with chronic liver disease

and preserved liver function is a safe procedure with good short-term results. It also can be proposed in tumor locations with a difficult surgical access maintaining a low morbidity rate and good oncologic adequacy. It suggests that LLR represents an acceptable alternative to open resection in this setting and could have an impact on the therapeutic strategy of HCC complicating cirrhosis, as a treatment with curative intent or as a bridge to liver transplantation.

Riassunto

Il trattamento chirurgico dell'epatocarcinoma in pazienti affetti da cirrosi epatica è sempre stato controverso per i limiti dovuti agli alti tassi di morbilità legati alla procedura e per l'alto tasso di recidiva di malattia.

Nel corso degli anni, con l'affinamento delle tecniche chirurgiche unitamente all'impiego di una strumentazione sempre più appropriata, l'impiego della laparoscopia nella chirurgia dei tumori epatici è andata sempre più diffondendosi con risultati incoraggianti.

Scopo di questo studio è stato quello di analizzare retrospettivamente una serie di pazienti operati di resezione laparoscopica per epatocarcinoma, valutandone i risultati sia dal punto di vista chirurgico che dal punto di vista dell'"outcome"oncologico.

Nel periodo compreso tra Giugno 2005 e Febbraio 2009 sono state effettuate 22 resezioni laparoscopiche per epatocarcinoma. L'età dei pazienti presentava una mediana di 66 anni. Sotto il profilo della funzione epatica lo stadio della cirrosi è stato valutato di grado Child A in 19 casi e Child B in 3.

Il tipo di resezione laparoscopica è stato anatomico in 7 casi e non anatomico in 15. Sono state associate 11 procedure in 9 pazienti (40.9%). La mediana delle dimensioni tumorali è stata di 3.1 cm mentre la mediana dei margini della resezione è stata di 15 mm.

A causa di un grave sanguinamento un paziente ha necessitato la conversione dell'intervento in laparotomia (4.5%). I tassi di mortalità e morbilità operatori sono stati dello 0% e del 18.1% (4/20), rispettivamente.

La degenza mediana è stata di 8 giorni (range 5-16 giorni). Durante un follow-up medio di 29 mesi (range: 19-65 mesi), 11 (50%) pazienti hanno presentato recidiva di malattia a livello epatico, più frequentemente a distanza dalla sede chirurgica.

Un trattamento della recidiva è stato possibile in tutti i pazienti, incluso il trapianto ortotopico di fegato in 3 pazienti.

In conclusione si può asserire che in pazienti selezionati la resezione epatica laparoscopica può rappresentare un valido trattamento dell'epatocarcinoma poiché la procedura chirurgica appare sicura in mani esperte e con buoni risultati a breve-medio termine. Può essere proposta anche in caso di lesioni poste in sedi di difficile accesso chirurgico quali i segmenti epatici postero-superiori pur mantenendo un tasso accettabile di complicanze ed una buona adeguatezza oncologica.

Questo tipo di approccio laparoscopico deve essere tenuto presente nella strategia terapeutica della cirrosi epatica complicata da epatocarcinoma quale valida opzione terapeutica con intento curativo o come trattamento "ponte" verso il trapianto epatico.

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