Original Article

Liver resection for hepatocellular carcinoma, are we going to dismiss the traditional approach?

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Background: Minimally invasive surgery has recently demonstrated results comparable to traditional surgery for recurrence-free or overall survival, even in cirrhotic patients. Laparoscopic liver resection (LLR) is gaining a central role for the treatment of hepatocellular carcinoma (HCC). The aim of our study is to analyze the evolution of traditional and minimally invasive liver resection for HCC in our Center since 2001.

Methods: We divided the cohort into two groups: group 1, patients between 2001 and 2007 and group 2, patients between 2008 and 2015. Since 2001, 429 patients were resected in our department.

Results: In group 1, we performed 42 major hepatectomies (25.3%) and 124 minor hepatectomies (74.7%). In group 2, we respectively performed 49 (18.6%) major hepatectomies and 214 (81.4%) minor hepatectomies. In group 1, 3% of patients and 44.5% in group 2 were treated by LLR. We observed an improvement of morbidity between the two groups (P<0.001), and of mortality with 3.6% in group 1 versus no mortality in group 2.

Conclusions: The number of LLR has increased since 2001. However, the complexity of HCC resection on patients with cirrhosis seems to leave a place to the traditional approach. In our experience, the traditional surgical approach has still a place for the major resection in patients with HCC.

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

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Introduction

Hepatocellular carcinoma (HCC) is the most common primary liver cancer and one of the most common malignant tumors worldwide (1). A myriad of possibilities of therapeutic options are currently available for HCC patients, which include loco-regional treatment of small and single tumor, liver resection and orthotropic liver transplantation (LT) (2). Despite less than 30% of patients with HCC are eligible for surgical resection, surgery is still the most available curative treatment (3), with a post-operative mortality rate of 5%, even in patients undergoing major hepatectomy on cirrhotic liver disease (4), and a 5-year survival of 70% (5). The extent of hepatectomy results from the balance of complete tumor removal and preservation of functional future liver remnants (FLR). In spite of this, in the majority of cases, HCC is growing from a liver with an underlying disease, reducing liver function reserve and compromising the potential regeneration (6). In this case, postoperative liver failure and post operative complication risk are higher rather than in healthy liver (7). Gruttadauria

et al. suggested that FLR should be >20–25% in patients with normal liver parenchyma, >30% in case of steatosis, hepatitis and in patients submitted to chemotherapy, and >40% in cases of chronic liver disease (8). Minimally invasive surgery has recently demonstrated results comparable to traditional surgery for recurrence-free or overall survival (9), even in cirrhotic patients (10). Furthermore recent meta-analysis concluded that laparoscopic liver resection (LLR) for HCC is superior to open approach in terms of its perioperative results and does not compromise the oncological outcomes (11). LT seems to be the ideal treatment for both tumor(s) and the underlying liver disease. However, numbers of liver graft is still low inducing to consider resection as a first option and LT in case of HCC recurrence (12,13).

The aim of our study is to analyze the evolution of traditional and minimally invasive liver resection for HCC in our Center since 2001.

Methods

Since 2001, all resected liver patients in our department were included in a prospectively maintained database. Between 2001 to December 2015, 1,463 liver resections were performed. Of them, 429 were HCC. Liver resection was performed if there was no extrahepatic metastasis observed at preoperative imaging. Evidence of tumor thrombosis was not an absolute contraindication. Liver segment resection was defined according to the Brisbane classification (14). A major resection was defined as a resection of three or more segments, and a minor resection as a resection of two or fewer segments. Surgical complications were classified as described by Dindo and colleagues (15). Major complications (Clavien-Dindo 3 and 4) and operative mortality (Clavien-Dindo 5) were considered when they occurred within 90 days after surgery or at any time during postoperative hospitalization. Liver-specific complications such ascites was defined as >10 mL/kg/day of drainage output from the abdomen after postoperative day 5 and bile leakage was defined as a bilirubin concentration in the drain fluid at least three times that of serum bilirubin on or after postoperative day 3 or as the need for radiological or operative intervention resulting from biliary collections or bile peritonitis. We divided the cohort into two groups: group 1, patients between 2001 and 2007 and group 2 patients between 2008 and 2015. All surgical procedures were performed by senior surgeon specialized in hepatobiliary surgery.

Results

Patients characteristics

Since 2001, 429 patients were resected in our department, of them 335 (78%) were male and 94 (22%) were female. Mean age was 66-year-old (range: 32–89) and the mean body mass index was 25.9. Baseline alpha-fetoprotein was 2,431.8 UI (range: 0.8–100,000), in 20 cases Child Pugh score B was observed, mean MELD score was 7.96 (6-16). A HCV related underling liver disease was observed in 308 (71.8%), a HBV in 47 (11%), alcohol in 31 (7.2%).

Of 166 patients in the group 1, 134 (80%) were male. Mean age was 66-year-old and the mean body mass index was 25.3. Baseline alpha-fetoprotein in group 1 was 2,431.7 UI, in 12 cases Child Pugh score B was observed, mean MELD score was 8 (range: 6–15).

In the second group, 201 patients (76.4%) were male. Mean age was 66-year-old and the mean body mass index was 25.8. Baseline alpha-fetoprotein in group 2 was 1,132.4 UI (range: 0.8–44,052), in 8 cases Child Pugh score B was observed, mean MELD score was 7.93 (range: 6–16).

The overall and groups patients characteristics are resumed in *Table 1*.

Operative finding

In group 1, we performed 42 major hepatectomies (25.3%) and 124 minor hepatectomies (74.7%). In group 2, we respectively performed 49 (18.6%) major hepatectomies and 214 (81.4%) minor hepatectomies. We had no difference between the two groups for major or minor surgery (P=0.09). On the other hand, an important difference was observed between the laparoscopic approaches in the two groups (P<0.00001). In group 1, 3% of patients and 44.5% in group 2 were treated by LLR. Despite this important difference, surgical time was no different, but blood transfusion has improved between the two period (P=0.02). The surgical procedure is resumed in *Table 2*.

We observed 6 deaths since the first liver resection for HCC. All of them during the first period analyzed (group 1). This results was support by an improvement of morbidity between the two groups (P<0.001). Post operative results with complication are resumed in *Table 3*.

Discussion

The number of LLR has increased since 2001. We observed an increasing of laparoscopic approach in the second group

Table 1 Patients characteristics

Characteristics	Total	2001–2007, group 1 (n=166)	2008–2015, group 2 (n=263)
Male gender, n (%)	335 (78.1)	134 (81.0)	201 (76.4)
Age (years), mean [range]	66 [32–89]	66 [32–88]	66 [38–89]
BMI	25.9 (17.7–41.5)	25.3 (17.7–36.2)	25.8 (15.3–41.5)
AFP (ng/mL), mean [range]	2,431.8 [0.8–100,000]	2,431.7 [1–100,000]	1,132.4 [0.8–44,052]
Child-Pugh class B, n (%)	20 (4.6)	12 (7.2)	8 (3.04)
Etiology, n (%)			
HBV	47 (11.0)	24 (14.6)	23 (8.8)
HCV	308 (71.8)	116 (69.8)	192 (73.0)
Alcohol	31 (7.2)	13 (7.8)	18 (6.8)
Other	43 (10.0)	13 (7.8)	30 (11.4)
MELD score, mean [range]	7.96 [6–16]	8 [6–15]	7.93 [6–16]
Tumor size (mm), mean [range]	48.7 [4–300]	52.9 [4–300]	46 [4–230]

Table 2 Surgical procedure

Surgical procedure	Total	2001–2007	2008–2015
Hepatectomies, n (%)			
Major	91 (21.2)	42 (25.3)	49 (18.6)
Minor	338 (78.8)	124 (74.7)	214 (81.4)
Laparoscopy, n (%)	122 (28.4)	5 (3.0)	117 (44.5)
Major	1	0	1
Minor	121	5	116
Operative time, min, mean [range]	197.6 [36–540]	196.8 [55–540]	198.1 [36–500]
Estimated blood loss, mL, mean [range]	188.7 [10–1,000]	198.9 [20–1,000]	182.6 [10–1,000]
Transfusion, n (%)	21 (5.1)	13 (8.4)	8 (3.0)
Pedicle clamping, n (%)	82 (19.0)	53 (33.0)	29 (11.0)
Intraoperative complications rate (%)	19 (4.4)	7 (4.3)	12 (4.6)

until reaching a stable number of LLR each year (*Figure 1*). Furthermore, we observed an improvement of morbidity between the two groups associated with no death in the second group. These results were obtained maintaining stable operative time. According with the second consensus conference held on Morioka (16), laparoscopic minor resection is often performed in our unit for HCC. Our previous study demonstrates the feasibility of a laparoscopic approach in HCC patients with chronic liver disease, even in selected Child B patients (17). On the other hand, the new loco-regional treatment, gastrointestinal therapy and anesthesiologist supports, allow to operate initial unresectable HCC. Nonetheless, surgical procedure as associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) authorize surgeon to propose curative resection in patients with previously considered unresectable HCC. The presence of macroscopic tumor thrombosis contraindicates LT and laparoscopic resection. Nevertheless, in those patients the ALPPS procedure has been described to be an effective curative treatment,

Table 3 Post-operative complication

Complication	Total	2001–2007	2008–2015
Mortality, n (%)	6 (1.3)	6 (3.6)	0 (0)
Clavien-Dindo (%)			
0	145 (33.7)	51 (30.7)	94 (35.7)
I	182 (42.4)	61 (36.7)	121 (46.0)
II	67 (15.6)	32 (19.2)	35 (13.3)
IIIa/IIIb	11 (2.5)	8 (4.8)	3 (0.05)
IV	5 (1.1)	2 (1.2)	3 (0.05)
V	6 (1.3)	6 (3.6)	0 (0)
Overall morbidity > II, n (%)	89 (20.7)	48 (28.9)	41 (15.5)
Intensive care unit stay, days, mean [range]	0.48 [0–14]	0.57 [0–14]	0.43 [0–9]
Hospital stay, days, mean [range]	10 [0–37]	12 [0–37]	8 [2–33]

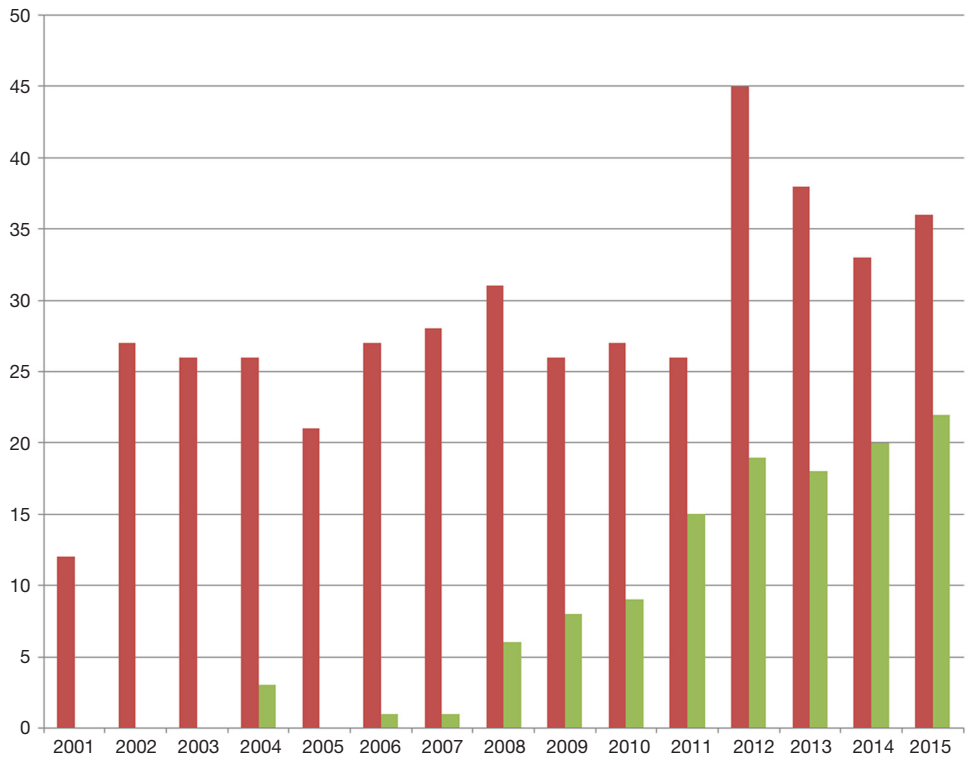

Figure 1 Evolution of laparoscopic HCC resections according with the total HCC resections since 2001. HCC, hepatocellular carcinoma.

in these cases with a traditional open surgery (18,19). Minimally invasive surgery is growing every year with impressive technical supports. Not last, the use of a robotic system can improve certain steps of minimally invasive major hepatectomy (20). Robotic ALPPS may have a place for HCC patients (21). Totally laparoscopic ALPPS is described as feasible but must be performed by experienced hands (22,23). Furthermore, performing the initial HCC resection by laparoscopy could facilitate a subsequent LT (24). On top, LLR thanks to a reduction of post-operative liver failure and ascites development in comparison to standard open (25). Moreover, LLR could be proposed in patients with clinical signs of mild portal hypertension (25). Technical difficulty for LLR seems to be overpass, in our experience we treated with laparoscopic approach HCC in each one liver segment (17). Therefore, limitation of the posterior localization of the HCC has been now overpassed (26).

However, the complexity of HCC resection on patients with cirrhosis seems to leave a place to the traditional approach.

Conclusions

Laparoscopic approach in HCC is gaining more places even in patients with cirrhosis. Major LLR in those patients is still selected cases. In our experience, the traditional surgical approach has still a place for the major resection in patients with HCC.

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Footnote

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