Editorial

Laparoscopic resection for hepatocellular carcinoma: eastern and western experiences

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Hepatocellular carcinoma (HCC) is the most common primary liver cancer (1). The incidence is rising in the last decades due to many factors, especially hepatitis C, alcoholic liver disease and non-alcoholic steatohepatitis. Moreover, the introduction of screening programs in patients with chronic liver disease has led to an increase in HCC diagnosis (1,2). In the western world, 80% to 90% of HCC cases occur in patients with liver cirrhosis (3) while this proportion is lower in some regions in Asia and sub-Saharian Africa, where hepatitis B remains as an important etiologic factor for chronic liver disease (2,4). In 1990, the annual world frequency of HCC was 437,000 cases/year (1), and in 2012 the number reached 782,200 cases/year being responsible for 746,000 deaths (5). Nowadays, HCC represents the 6th most frequent neoplastic disease in the world and the 3rd in mortality (5).

HCC treatment is complex and, for the definition of the best therapeutic strategy, many aspects have to be considered: the size and number of nodules, the presence of vascular invasion, extra hepatic spread and liver function. Currently, treatment modalities considered as curative are resection and liver transplantation (LT) (4,6).

LT have as advantage the possibility to treat simultaneously not only the tumor but the underlying liver disease, however just a limited group of patients can achieve the procedure due to long waiting lists. Dropout due to tumor progression and complications of the liver disease leading to morbidity and mortality while waiting for LT are drawbacks for the procedure. Thus, when evaluating intention to treat, LT and resection present similar results (7,8).

In the last decades, HCC resection has been more frequently performed due to technical improvements and better assessment of liver function leading to better results. The mortality rate of patients with chronic liver disease submitted to liver resection, felt from 15% in the early eighties for current 2% to 5%, with morbidity rates between 10% and 40% and transfusion rates lower than 10% in specialized centers (4,9). Moreover, liver resection presents as advantages the immediate applicability independent of the size of the tumor, lower morbidity and mortality when compared to LT and, avoidance of postoperative immunosuppression. Other advantage for resection is the possibility of histological and molecular prognostic evaluation of the specimen allowing to a better selection of patients for LT (7,10).

Liver resection is the treatment of choice for patients with HCC and non-cirrhotic livers. In these patients, even major resections can be performed without any concern about liver functional reserve provided a liver remnant larger than 25-30%. Resecability rates larger than 70% and long-term survival rates between 50% and 60% can be achieved (11). On the other hand, in patients with cirrhosis, resection is limited to those with single nodule (or oligonodular disease) and preserved liver function (4,7).

In this context, minimally invasive surgery gained space in the treatment of HCC. Many authors have shown the safety and feasibility for the procedure (12) and, when compared to conventional surgery, laparoscopic liver resection (LLR) showed advantages for patients with chronic liver disease. In comparative series, the advantages of LLR are less bleeding, lower transfusion rates, shorter hospital stay and lower rates of morbidity, especially postoperative ascites. Moreover, we should point out the absence of adhesions leading to an easier re-resection or salvage LT (13,14).

In eastern and western specialized centers, HCC present different epidemiologic and clinical characteristics leading

to different therapeutic approaches. Indeed, until recently, studies comparing eastern and western experiences with HCC are lacking. In a recent paper entitled "Laparoscopic resection for HCC: comparison between Middle Eastern and Western experience", Piardi *et al*. (15) report the results of LLR from these two different surgical schools. They included case series with more than 15 patients, comparative studies or meta-analysis. All studies were retrospective, with a total of 782 patients in western series and 541 patients in eastern series. When compared the epidemiologic data between both study populations, we can note a large number of cirrhotic patients in eastern series (between 50% and 100% of the cases), with a larger proportion of patients Child-Pugh B and C.

When comparing indications for LLR, despite some variations, the majority of groups employ the following criteria: small (<5 cm) peripheral lesions in Child-Pugh A patients, in the absence of portal hypertension or with small esophageal varices, platelet count >100,000/mL and ASA score ≤3. Most western groups consider a major vascular invasion as a contraindication for resection (11). In the Far East, the presence of portal vein tumoral thrombus does not preclude resection (16).

The most frequent LLR for the treatment of patients with HCC are peripheral wedge resections, segment 6 resections, and bisegmentectomies 2-3. There is some data showing that anatomical resections can lead to better results in patients with HCC however, for single and small nodules a non-anatomical approach seems to be effective. A recent meta-analysis comparing anatomical versus non-anatomical resections in more than 1,800 patients with HCC did not show differences in survival or recurrence rates (17). Major resections for the treatment of HCC are exceptional (less than 20% of resections), but for patients with preserved liver function (Child-Pugh A) and a liver remnant larger than 40% can be done with low rates of postoperative liver failure (12,18). Selective portal vein embolization in order to increase the volume of the liver remnant and indirectly test the hypertrophy capacity of the liver is a useful tool in the therapeutic strategy (19).

In the western world most groups employ the volume of the remnant liver as a safety parameter for resection (12,15). However in the eastern world functional evaluation of the liver, mostly with indocianin green clearance, is used routinely (4,15). The meticulous evaluation of liver function employed by eastern groups may explain the liberal indication and good outcomes for liver resection even in patients Child B and C.

In the Piardi *et al*. (15) review, the laparoscopic modality employed by the majority of western series was pure laparoscopy (98.2% of the resections). On eastern series, pure laparoscopy was done in 86.3% of the cases, the hand-assisted approach in 6.5% and hybrid procedures in 7.3% of the cases. Hand-assisted and laparoscopic-assisted liver resections emerged aiming to overcome some of the limitations faced by totally laparoscopic approach and, therefore, expand the availability as well as the indications of minimally invasive liver surgery. These modalities allow surgical manipulation in a similar way of conventional surgery. Furthermore, the tactile sensation, which is partially lost on pure laparoscopic approach, is brought back. These approaches facilitate not only palpation and identification of deep lesions but also allow parenchymal compression during liver transection, making this step of the surgery safer.

The hybrid and hand-assisted approaches has been used for resection of lesions located in segments of difficult laparoscopic access (segments 1, 4a, 7, 8), multiple resections and major hepatectomies. In our series of 40 patients with HCC operated by minimally invasive approach, 14 (35%) patients were operated by these techniques, especially in cases with nodules in the posterior-superior segments or for major resections.

Laparoscopic-assisted resections are still rarely performed in western centers however, good results, along with the safety reported with this method were responsible for an increasing interest in hybrid surgery, especially in eastern centers. In a recent review, the authors observed that 88.7% of major hepatectomies were performed through hybrid technique in specialized Japanese centers (20).

Regarding operative results, transfusion rates ranged from 1.8% to 50%. Conversion rates were similar worldwide: West (5-19.4%) and East (1.8-18.6%). In a recent paper from our group with pure laparoscopic surgery, conversion rate was 13.3% (18). Morbidity is similar in eastern and western series (0-25% *vs*. 0-26.6%), as well as per-operative mortality rates (0-6.25%). All comparative studies showed lower hospital stay in the laparoscopic group.

Three-year and 5-year survival rates are also similar (west 66-93% *vs*. east 60-100%; west 55-70% *vs*. east 50-76%, respectively). Recurrence rate was also similar between groups (west 21.4-50% *vs*. east 26.9-45.5%). Comparative studies between conventional surgery and LLR did not show difference regarding overall survival and disease-free survival. In our experience, overall and disease-free 3-year survival were 76% and 58%, respectively (18).

We can conclude that the oncological results for

laparoscopic treatment of HCC presented in eastern and western series, despite retrospective, are similar to those from the conventional approach, with an apparent advantage in per operative results. Although most often used in selected cases, the expansion of LLR can be achieved with the use of hybrid and hand-assisted approaches, especially those with posterior-superior lesions requiring complex resections or major hepatectomies. Finally, LLR and its different modalities should be strongly considered in the curative treatment of HCC.

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