Surgical strategy for liver tumors located at the hepato-caval confluence

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Liver tumors involving hepatic vein (HV) at caval confluence have been always considered an indication for major hepatectomy and/or HV reconstruction. However, careful study by means of intraoperative ultrasonography (IOUS) of tumor-vein relations and HV anatomy searching for accessory veins, together with color-Doppler IOUS analysis of portal flow, allows more conservative approaches also in these patients. Indeed, in our experience, only 12% of patients, who were operated because of liver tumors in contact or in close adjacency with one or more HVs, underwent removal of at least 3 segments: none of them required HV reconstruction, and no hospital mortality was seen. Therefore, IOUS allows sparing liver parenchyma without tumor recurrence in most patients with tumors involving HV at their caval confluence, avoiding more extended hepatectomies or HV reconstructions. This approach to complex presentations of liver tumors by the use of IOUS-guidance is a further confirmation of the importance of this tool for accomplishing a safe and effective surgical treatment.

KEY WORDS: Liver surgery, Liver tumors, Liver cirrhosis, Hepatocellular carcinoma, Liver metastases, Intraoperative ultrasonography, Contrast-enhanced intraoperative ultrasonography.

Introduction

Tumoral contact or infiltration of the main trunk of a hepatic vein (HV) close to its caval confluence has always been considered as a pattern of presentation demanding major hepatic parenchymal removal or, in cases where a conservative approach is attempted, HV reconstructions [1,2]. However, both these approaches have appreciable mortality and morbidity. Conversely, it has been shown that, in presence of infiltration of the right hepatic vein (RHV), a large inferior right hepatic vein (IRHV) allows avoidance of a right hepatectomy sparing segments 5 and 6 [3]. Experience with donor hepatectomies during living donor liver transplantation (LDLT) have shown congestion in the right paramedian sector after disconnection from the middle hepatic vein (MHV) in 78% of cases [4]. The study of the intrahepatic portal flow direction with color Doppler, once the draining hepatic vein is clamped, has optimized the need for HV reconstruction during living donor liver transplantation [4]. Resection guidance with intraoperative ultrasonography (IOUS) has reduced the need for major hepatectomies in resective liver cancer surgery. Indeed, a classification of different IOUS patterns of relationship between tumor and intrahepatic vessel predicts the risk of local recurrence and subsequent need for vascular resection [5]. All these options have in common the use of IOUS for carrying out parenchymal sparing hepatectomies in presence of tumoral contact or infiltration into the HVs, and we have recently determined their impact in surgical practice when they are systematically adopted [6]. These new perspective in the management of patients with primary and metastatic liver tumors involving the HVs at their caval confluence are discussed.

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Methods

Cirrhotic patients are selected for surgery, following a well established flow-chart [7], based essentially on the presence of ascites, and serum total bilirubin. In all the

other patients, indication for surgery is established on the basis of tumor stage, technical feasibility and volume of the remnant liver [7].
CT liver volumetry is calculated in all patients in whom a major hepatectomy could be expected. If the remnant liver volume is at least 40% of the total liver volume in case of cirrhotic liver and 35% in case of normal liver, the patient could be submitted to surgery without portal vein embolization (PVE) [4,8]. Inversely, in the event the expected remnant liver volume does not meet the required percentages of the total liver volume, PVE would be performed.

Technique

After partial mobilization of the liver by means of division of the round and falciform ligaments, IOUS is routinely performed either for staging or for resection guidance: more recently, contrast enhanced IOUS (CEIOUS) is also performed [9,10].

IOUS pattern of tumor-vessel relation
Based on IOUS findings, relationships with HV are classified as previously reported [6], and operations are carried out accordingly. A capsulated HCC at IOUS in contact with the HV itself without interruption of the vessel wall is considered to be a contact without infiltration (pattern A) (Fig. 1a, b). It is considered HV infiltration when an infiltrative type HCC or CRC liver metastases are in contact with the vessel even without vessel wall interruption (respectively patterns C and D), and in any situation where the vessel wall appears interrupted at IOUS (pattern E). Close adjacency to the HV is defined when at IOUS a CRC liver metastases appears at less than 0.5 cm from the vessel wall (pattern B).

Extension of hepatectomy to the whole liver parenchyma drained by a HV involved by the tumor is considered only if tumor relations at IOUS were types C, D, or E, there are no accessory hepatic veins at IOUS (Fig. 2a, b), and color-Doppler IOUS shows hepatofugal blood flow in the feeding portal branch once the HV is clamped [4].

IOUS guidance of liver dissection
Resection guidance is carried out as has been previously described [11]. After the identification of the tumor at IOUS, the surgeon positions the flat and thin tip of the electrocautery between the probe and the liver surface: this manoeuvre results in a shadow at the IOUS image which runs deeply just below the electrocautery. In this way it is possible to define the position of the electrocautery with the tumor edge and consequently to mark with the electrocautery itself the safer edge for the incision. The adequacy of the marked edge could be furthermore checked with IOUS as the air trapped between the probe and the irregular surface of the demarcation line drawn with the electrocautery on the liver surface could be visualized at IOUS. Marking the liver surface on the opposite side of the previously accomplished marker for building the edges of the dissection plane is carried out using the finger tips: with the probe positioned on the liver surface at the site of the first superficial marker, the surgeon's finger-tip pushes the liver on the opposite side and its profile is visualized at IOUS: at this site the electrocautery is used to mark the second point through which the dissection plane should pass. Once resection is started, the dissection plane, is followed by IOUS appearing as an echoic line due to the entrapment of air bubbles and clots between the faced cut surfaces. If it is not clearly visible, it could be better visualized inserting a gauze in the dissection plane.

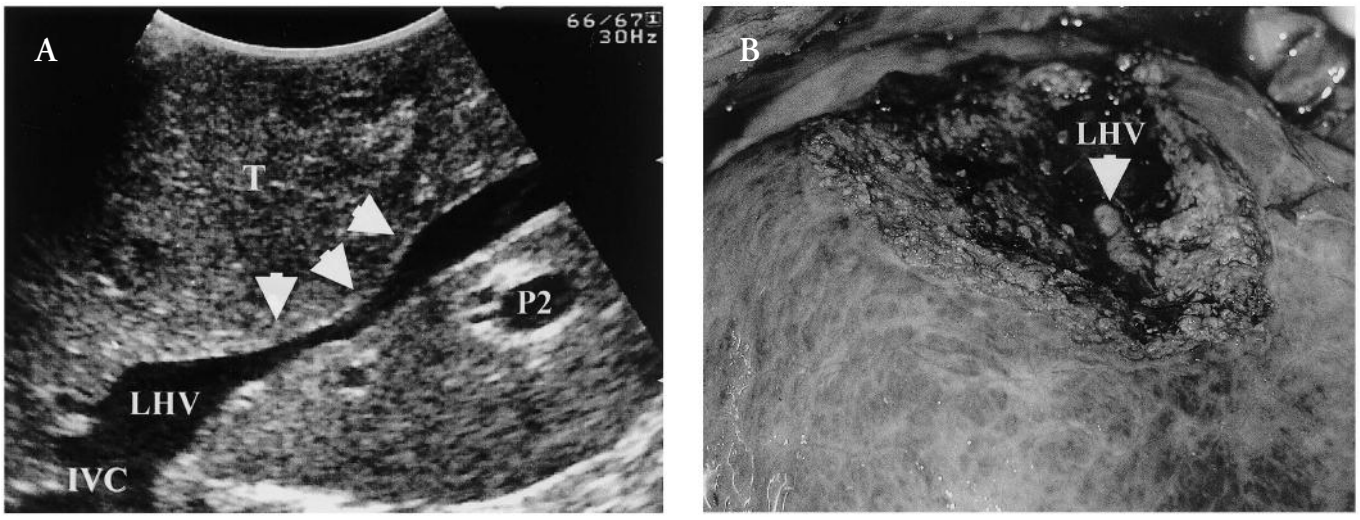

Fig. 1: a) in this, IOUS showed a small HCC compressing the left hepatic vein (LHV) close to its caval confluence: however. LHV wall is visible and does not seem invaded (arrows); b) because of IOUS findings it was possible to spare the whole left lobe limiting the operation to a limited resection exposing the LHV on the cut surface. IVC= inferior vena cava.

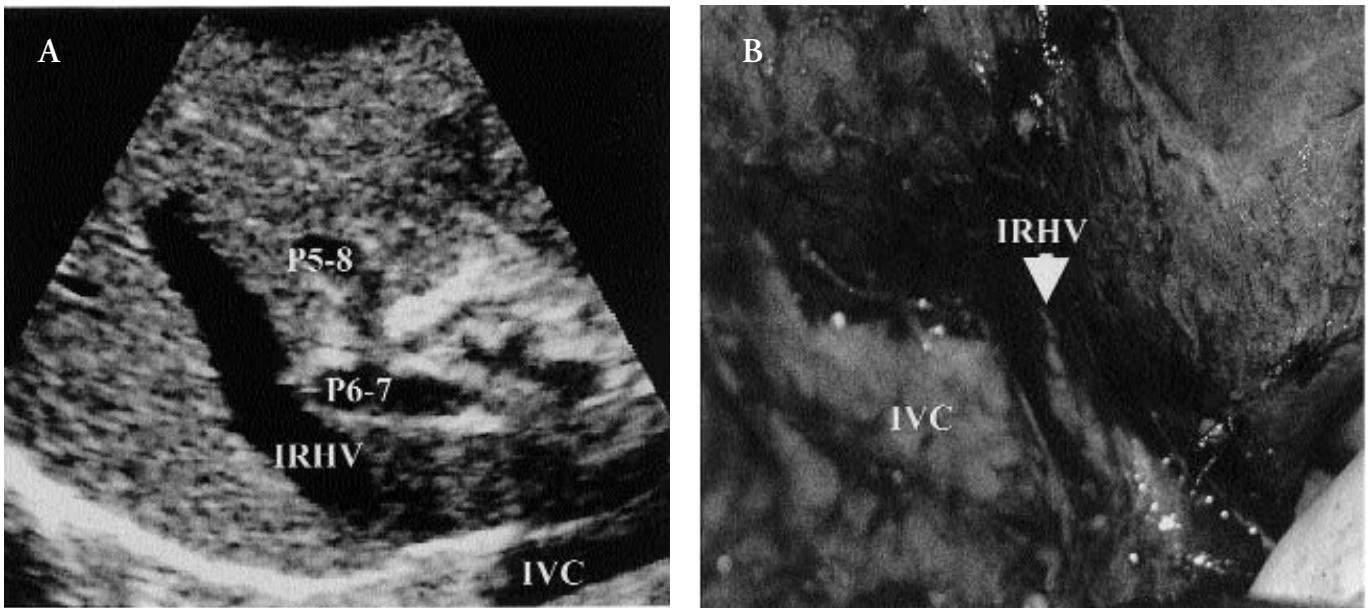

Fig. 2: a) in this patient IOUS shows an inferior right hepatic vein (IRHV) which is tipically running behind the portal branch to segments 6 and 7 (P6-7); b) after mobilization of the right liver the IRHV is confirmed. IVC= inferior vena cava.

Color-Doppler IOUS to check the portal flow direction before and after HV clamping is also repeated before finishing any operation in which it is demanded: in these patients color-Doppler ultrasonography is also carried out for further confirmation before patient's discharge.

Operative procedures

J-shaped or inverted-T laparotomies are performed routinely. For those patients with tumors involving segments 1, 4 superior, 7 and 8 close to the HV confluence into the IVC, J-shaped thoracophrenolaparotomy is considered.

Liver mobilization Is accomplished according to the side of tumor location and the hepatic vein involved is isolated at its caval confluence by an extra-parenchymal approach, and encircled with a tourniquet for future clamping. Similarly, accessory veins are also taped if any. Liver dissection is accomplished, under intermittent clamping by the Pringle maneuver [12], using Pean-forceps crush-clamping and bipolar electrocautery for vessel coagulation: each vessel thicker than 2 mm was ligated with thin (2/3-0) sutures.

Clamping of one or more HV is considered during liver dissection in case of contact or infiltration with the tumor, and for the time needed to dissect the area of tumor-vessel relation: anyway, it is not routinely recommended. Inversely, placement of surgeon's left hand behind the mobilized liver, is performed during hepatic dissection to pull up the liver with the aim of reducing the backflow bleeding by compression. First operator stays routinely on the right side of the patients; he stays on the left side of the patient, in case of tumor-vessel relation with the LHV only or both with LHV and MHV and the aim is to spare both these vessels.

Total vascular exclusion is considered in case of tumor contact with the IVC larger than 2/3 of vessel circumference and/or in presence of tumoral invasion of the IVC lumen.

The level of anesthesia is maintained by general and epidural anesthesia thereby reducing the quantity of inhalation agents and intravenous drugs. Fluid restriction (of 4-5 ml/kg/h) and reduction of the respiratory tidal volume to around 60% just before starting liver dissection are the techniques adopted to decrease the thoracic and right atrial pressures, keeping the central venous pressure (CVP) between 0 and 4 cm H_2O and, consequently, limiting the backflow-bleeding from the hepatic veins and/or their tributaries. Hydrocortisone (100 mg) is injected intravenously (iv) before starting vascular occlusion to protect the liver during warm ischemia.

The cut surface of the liver is secured by 2/3-0 sutures, electrocautery, fibrillar oxidated regenerated cellulose (Fibrillar Tabotamp, Ethicon, USA) and fibrin glue (Tissucol, Baxter, USA): a careful examination is made to rule out bile leakage, and cholangiography is not performed for this purpose [13].

Closed suction drains are always left in the peritoneal cavity with the tip facing the cut surface of the liver.

Discussion

Major hepatectomies still represent around half of the liver resections carried out in most series [14-18]. However, they are still associated with appreciable rates of mortality and major morbidity including liver insufficiency [19], which occurs in 33% of patients who do not undergo PVE and in 10% of those who had PVE [20]. Therefore, the need for reducing the rate of major liver parenchy-

ma sacrifice is a priority in hepatic surgery [21], especially considering that most of the patients who need hepatectomy have a cirrhotic or steatotic liver. In presence of infiltrated HVs at their caval confluence removal of major portions of liver parenchyma is generally expected because of fear of hepatic congestion in the undrained hepatic segments [22-25]. An accepted alternative to this approach is to follow a parenchymal sparing strategy by means of reconstruction of the resected HV with grafts [1,2]. This strategy, although accomplished for safety reasons, is associated with mortality, major morbidity and blood transfusion rates similar to those of major hepatectomies [1,19].

On the other hand, more than half of livers examined in autopsy series seemed to have venous anastomosis, which put the HVs and their drained areas into communication among themselves [26-28]. Based on these findings Sano et al. showed how color-Doppler IOUS could predict liver congestion [4]. Color-Doppler IOUS and the search for the presence of accessory veins such as the IRHV are tricks which should lead to spare liver parenchyma in liver resection once a HV has to be ligated at its caval confluence. Muratore et al. reported that IRHV detection allowed avoidance of a right hepatectomy in 6 of 11 cases with CRC liver metastases invading the RHV in a series of 332 patients operated on for that disease [29].

A strategy which takes into account all IOUS findings, including IOUS pattern of tumor-vein relations [5], color-Doppler IOUS of portal branches once draining HV is clamped [4], and detection of the IRHV [3,29] or any other accessory vein, has been applied and reported [6]: this policy led us to limit the number of major hepatectomies without the need for HV reconstruction in presence of neoplastic involvement of one or more HVs. Indeed, we did major hepatectomies only in 12% of patients (3 out of 25), who had involved one or more HVs. This allowed complex surgery without mortality and with minimal major morbidity (4%), which consisted in one case of pleural effusion requiring percutaneous drainage. Furthermore, no patients had local recurrence at a mean follow-up of 21 months (range 6-60). Minimizing the rate of major hepatectomies has several positive consequences for patients' outcome. Indeed, only four had normal liver among the 25 considered, while more than two thirds of them were cirrhotic or had liver steatosis. In these patients the reported risk of postoperative liver failure ranges from 5 to 7%, with mortality rates ranging from 1 to 7% [19,30]. Inversely, we did not experience postoperative mortality, re-operations, major morbidity and liver failure. Furthermore, the low rate of patients transfused with blood in our experience with liver tumors at the caval confluence (12%), which is largely below that reported in most series submitted to major hepatectomies (28-91%) [14-19,30], although in part due to a chosen policy of restricting blood administration [31], is certainly also related to the low percentage of major hepatectomies. Furthermore, more conservative resections maximize the possibility of repeated resections should the patients present new lesions, either metastases from CRC or HCC, which are more likely to occur in other areas of the liver than the site of the previous tumor: repeated resections have a positive impact on patients' survival [32-35].

The other option which consist of HV reconstruction is associated with not negligible rates of mortality (12%), liver failure (25%) and blood transfusion with a mean of 4 packs of blood per patient [1]. This is probably related to the complex procedures demanded for this approach which required in some cases an ex-vivo resection. These results, when compared with those we have reported [6], indicate that HV reconstruction is less safe than our approach.

The absence of tumor recurrences we observed at the site of resection, when HVs were spared in spite of their ultrasonographic contact with HCC or less than 0.5 cm close adjacency with CRC liver metastases, should induce to reconsider the need for a 1 cm tumor-free margin [5,6]. On the other hand, some authors have recently reported that 1 cm tumor-free surgical margin is not a significant prognostic factor after limited resection for CRC liver metastases [36-38]. Conversely, in the case of HCC there is no evidence that a 1 cm safety margin is needed if tumor clearance is obtained [39-41].

Furthermore, our experience may suggests that PVE itself may not be justified in these patients due to the low probability of undergoing a major hepatectomy: indeed, in the rare event after HV resection the drained liver is congested but the volume of the remnant liver is not enough to allow a major hepatectomy, vein reconstruction could be a reasonable option [1,2].

In conclusion, when IOUS is systematically and properly used, tumor contact with one or more HV exceptionally leads to more aggressive major hepatectomies or liver resections with associated HV reconstruction.

Riassunto

I tumori del fegato che coinvolgono le vene sovraepatiche in prossimità della loro confluenza nella vena cava inferiore vengono comunemente ritenuti un'indicazione alla resezione epatica maggiore o, in casi selezionati, alla ricostruzione vascolare. Tuttavia, uno studio accurato con l'ecografia intraoperatoria (EIO) per definire i rapporti tra tumore e vene sovraepatiche e per ricercare eventuali vene accessorie, associato ad un'analisi dei flussi portali con il color-Doppler, permettono di assumere un atteggiamento più conservativo anche in questi pazienti. Infatti, nella nostra esperienza solo il 12% dei pazienti ha ricevuto un'epatectomia maggiore pur in presenza di lesioni epatiche alla confluenza sovraepatico-cavale ed in contatto con una o più vene sovraepatiche: di questi pazienti nessuno è stato sottoposto a ricostruzioni vascolari, e la mortalità peroperatoria è stata nulla. In defini-

tiva, l'EIO permette di effettuare resezioni conservative e senza recidive locali anche in presenza di tumori primitivi o secondari situati alla confluenza sovraepatico-cavale, evitando così il ricorso ad epatectomie maggiori o ricostruzioni vascolari. Questa modalità di approccio a tumori di difficile aggressione chirurgica è l'ulteriore conferma della necessità di una guida ecografica in chirurgia epatica perché si possano effettuare interventi sicuri ed efficaci.

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