Intraoperative ultrasonography in liver cancer

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Since the end of the 1970s, intraoperative ultrasonography (IOUS) has been used to guide hepatic surgery in patients with liver cirrhosis and for patients with liver metastases [1–5]. More recently, ultrasonography has enabled the development of alternatives and adjuncts to resection, such as interstitial therapy (ethanol injection, radiofrequency, and cryosurgery). These new techniques have expanded the treatment options for patients previously not considered candidates for resection. This article reviews the techniques and results of IOUS-guided liver surgery.

Technical aspects

IOUS uses flat, high-frequency echoprobes (7.5–10 MHz), which can be manipulated in deep and narrow spaces. T-shaped probes, interdigital probes, and microconvex probes are available for this purpose. Surgeons performing IOUS must have a perfect knowledge of liver anatomy as seen surgically and ultrasonographically. For surgical anatomy, the Couinaud segments are here considered [6]. After the abdominal cavity is entered, the liver must be mobilized by division of the round and falciform ligaments before liver exploration with IOUS can proceed. Gentle traction on the round ligament helps in achieving wide exposure of the liver, and by following the portal and the hepatic veins branches, the operator can study the entire liver (Fig. 1).
Indications

The indications for IOUS in liver resection include complete exploration of the liver to determine the extent of disease, guidance of liver-directed therapy procedures, and margin control in the management of tumors involving the hepatic veins.

Liver exploration

Identification and differential diagnosis of liver nodules

The hard and irregular surface of the cirrhotic liver makes the detection of small hepatocellular carcinoma (HCC) nodules by palpation difficult; IOUS allows the detection of new lesions in about 30% of cases (Fig. 2) [7]. In cases of liver metastases from colorectal carcinoma, 10% to 40% of tumors are not palpable (Fig. 3) [8,9]. In a study by Kane et al [10], 51% of the planned procedures were changed because of IOUS findings. Although progress in preoperative imaging in the past few years may have reduced the rate of changes in operative strategy from IOUS findings, these rates remain high. In a recent study, the authors found that preoperative laparoscopic ultrasonography in patients with HCC avoided useless exploratory laparotomy in 63% of patients with unresectable malignancies [11].

The risk with IOUS or laparoscopic ultrasonography in the evaluation of liver nodules is overestimating the tumor stage. In patients with HCC arising in cirrhosis, except for those nodules with mosaic ultrasonographic pattern, 84% of which are malignant, only 24% to 30% of hypoechoic nodules and 0% to 18% of hyperechoic nodules (see Fig. 2) are neoplasms.
Even intraoperative biopsy seems to be inadequate in solving this problem because of the lack of specific features to allow differentiation between early HCC, dysplastic nodules, and regenerative nodules. The only nodules that can easily be differentiated intraoperatively by IOUS from HCC or liver metastases are small hemangiomas, which are often discovered primarily at IOUS, have a typical ultrasound pattern, and change their size and appearance when compressed (Fig. 4). Further improvement in the

Fig. 2. Tiny hyperechoic nodule (arrows) visualized on laparoscopic ultrasonography. MHV, middle hepatic vein; RHV, right hepatic vein; LPV, left portal vein; P5, segment-5 portal vein branch; P8, segment-8 portal vein branch; P6-7, segment-6 and segment-7 portal vein branches.
differential diagnosis by IOUS of liver nodules may be expected with the introduction and diffusion of new ultrasonographic contrast agents.

Visualization of relationships between the tumor and blood vessels in the liver

IOUS also permits an accurate three-dimensional reconstruction of the relationships between the tumor, the hepatic veins, and the branches of the portal vein and hepatic arteries. Portal vein branches are used as landmarks in the definition of the resection line; localization of the portal vein branches is fundamental for planning the surgical strategy. Vascular and biliary invasion are signs of advanced neoplasms. IOUS remains the most accurate tool for defining vascular tumor invasion. Tumor thrombi (TT) appear on IOUS as hypoechoic masses occupying the vessel lumen. Resection of HCC in the presence of TT in the portal vein trunk confers a survival benefit in selected patients [13]. In these patients, evaluation of the extent of the TT is important to determine the operative strategy.

Guidance of resection

Hepatocellular carcinoma
Systematic segmentectomy. In patients with HCC and cirrhosis, the amount of liver to be resected must be determined carefully, with the goals of resection being complete removal of tumor while sparing the noncancerous liver parenchyma. Liver function tests and hepatic volume measurement with CT
may assist in the planning prior to resection. Tumor dissemination from the main lesion through portal vein branches cannot be detected with certainty by the pre- and intraoperative imaging modalities [14]. Therefore, the resected specimen should include at least the segmental or subsegmental portal vein in association with the tumor. It is almost impossible to correctly define the segmental boundaries without the aid of IOUS, especially in cirrhosis, because of the existing wide variations in the anatomy of portal vein branches [14].

The technique of systematic segmentectomy was devised in the early 1980s [15,16]. After liver mobilization and exploration with IOUS, the portal vein branch near the area targeted for resection is punctured under sonographic guidance using a freehand technique or by inserting the needle in a probe-adapter attached to the transducer: 3 to 5 mL of indigo carmine dye are then injected into the vessel [14]. The stained area becomes evident on the liver surface and is marked with electrocautery. If the HCC nodule is located between two adjacent liver segments, two portal vein branches afferent to the area must be punctured and injected with dye. In this case, the deepest and most dorsal vessel must be punctured first to ensure that the air bubbles in the dye do not disturb the ultrasonographic detection and puncture of the other branch.

Each portal vein branch is punctured 1 to 2 cm distal to its origin to avoid dye reflux, and the direction and velocity of the infusion are controlled at IOUS. To prolong the staining, the hepatic artery is clamped at the hilum.
before the portal vein branch is punctured. When numerous and thin vessels should be punctured, and if TT are present in the segmental portal vein branch of the segment to be removed, the dye is injected into the portal vein branches afferent to the adjacent segment; this is the so-called counterstaining technique [17].

The main advantage of IOUS-guided resection is the modification of the traditional approach to liver tissue dissection, which involves dissection in vertical planes to avoid tumor exposure on the cut surface. With IOUS, the relationship between the dissection plane and the tumor edge can be followed in real time, and the direction of the dissection plane can be modified when needed. On IOUS, the dissection plane appears as an echoic line because of air bubble and clot entrapment between the opposed cut surfaces. If the dissection plane is not clearly visible, it can be better visualized by inserting a specifically devised silicon gauze or a polyester mesh in the dissection plane. Versatile dissection planes around the tumors can avoid tumor exposure while sparing important vascular structures. This in turn results in treatments that are curative in terms of tumor excision while conservative in terms of preservation of healthy hepatic parenchyma. In patients in whom major resections are needed, IOUS also permits better design of the dissection plane, which should run along the hepatic vein to be fully anatomic.

The artifacts (air bubbles and clots) that allow visualization of the dissection plane on IOUS may mask other structures, such as the portal vein branches, which are either ligated or spared. The so-called hooking technique has been devised to permit better visualization of the point at which the portal vein branch is to be divided [18]. With the hooking technique, the portal vein branch is exposed and skeletonized, and then it is encircled with a stitch, which is visualized by IOUS as an echogenic spot with a posterior shadow. Then, under sonographic control, the stitch hooking the exposed vessel is gently pulled up, which stretches the portal vein branch slightly. The traction point is demonstrated clearly by IOUS. If the exposed portal vein branch is not clearly visible because it has collapsed, the portal triad is unclamped to enable it to fill with blood, and visualization of the portal vein branch is attempted again. If the target site is correct, the portal vein branch is ligated and divided, and segmentectomy is completed under IOUS guidance; inversely, if the exposed vessel was not the vessel targeted, it is spared, and useless sacrifice of further liver parenchyma is avoided. Some authors, inspired by an article by Hasegawa et al [19], in 1988, proposed an alternative to the hooking technique for visualizing the point at which the portal branch is to be divided, using needles inserted under sonographic guidance so that the tip was located near the deepest point to be reached during dissection [20]. The presence of needles can interfere with dissection, however.

The hooking technique is particularly useful in ventral or dorsal subsegmentectomy of segment 8. The portal trunk to this segment may show bifurcation of its dorsal branch and ventral trunk close to the origin of
segment-5 portal vein branch. In this instance, there is a risk of ligating and dividing the segment-5 portal vein branch instead of the planned segment-8 portal vein branch, which could lead to ischemia of segment 5. The hooking technique under IOUS control enables identification of the encircled branch and allows the surgeon to decide with certainty whether it should be ligated. Another example in which the hooking technique is useful is with inferior segment-4 resection [21]. The segment-4 portal vein branches are generally divided into two subsegments for the superior and the inferior portion, but the most common branching pattern can be recognized in just half of cases [22]. These branches, rather than being punctured under IOUS guidance, can be approached by dissecting along the umbilical fissure. Once the portal vein branch is exposed, the vessel can be encircled with a suture and pulled under IOUS control to verify whether it is the branch leading to the inferior portion of segment 4 (Fig. 5). The appropriate portal vein branch can be ligated and divided, with the ischemic subsegment corresponding to the inferior subsegment of segment 4. The discolored area is then marked with electrocautery in preparation for liver dissection.

Postresectional control. There are two potential applications of IOUS in postresectional control after resection. One is the “water bath” technique, which consists of real-time verification that the targeted nodule is completely included in the resected specimen; this technique consists in the examination of the specimen that has been previously immersed in a container filled with saline [23]. The second application consists in the

Fig. 5. (A) The portal branch (arrows) to inferior segment 4 (P4 inf) is identified by intraoperative ultrasonography (IOUS). (B) P4 inf is exposed, encircled, and pulled with a stitch, and the traction modifies its profile on IOUS (arrows).
verification of the liver cut surface of the specimen refilled with saline to ensure the absence of residual tumor or satellite nodules.

Comments. The aforementioned methods for resection of HCC guarantee that resections are both anatomic and limited, and thus safe but oncologically acceptable. Two studies showed that prognosis of patients with HCC who underwent segmentectomy proved to be significantly better than that of patients who underwent limited resection [14,24]. In addition, a recent study in which 107 consecutive patients with HCC underwent liver resections reported no perioperative mortality [25]. Procedures that are not guided by IOUS can lead to dangerous and nontherapeutic major resection or incomplete operations. Of patients who undergo liver resection without IOUS guidance, 16% to 18% have positive resection margins [26,27]; inversely, none of the patients who underwent liver resection under the guidance of IOUS had positive resection margins [27].

Liver metastases

Today, complete tumor clearance resulting in a survival benefit can be achieved in many patients undergoing liver resection for metastatic disease, even in those with bilobar disease or vascular invasion [28]. Advances in surgical technique and preoperative portal vein embolization have further contributed to this improvement in outcomes [29,30]. An important factor in the emergence of liver resections that are curative and safe is the use of IOUS. In patients with hepatic colorectal metastases, there is probably no need for anatomic resection [31], but complete tumor clearance is mandatory. To achieve this goal, IOUS is essential.

Definition of the area to be resected. After identification of the tumor, the surgeon, under IOUS guidance, can use the electrocautery to mark the border of the lesion on the surface of the liver just above the nodule. To carry out this maneuver, the flat and thin tip of the electrocautery is positioned between the transducer and the liver surface: this results in an echogenic shadow that runs deeply just below the electrocautery (Fig. 6). With this technique, it is possible to define the position of the electrocautery in relationship to the edge of the tumor. The electrocautery is then used to mark the boundaries of the nodule to be resected on the liver surface and to select the safest resection margin. Furthermore, the adequacy of the marked edge can be checked with IOUS because the air trapped between the probe and the irregular surface of the demarcation line drawn with the electrocautery on the liver surface can be visualized.

With tumors located in segments 2, 3, 4a, 5, and 6, another way to precisely draw the tumor edge on the liver surface with the aid of IOUS is to use the fingertips. With the transducer positioned on the liver surface, the surgeon uses his or her fingertip to push on the opposite surface and the profile of the tumor is visualized by IOUS (Fig. 7). This technique defines
the relationship between the fingertip and the tumor edge, and the resection area can be marked precisely on the liver surface.

*Dissection of metastases and postresectional control.* The concepts that apply for IOUS guidance of the dissection plane and postresectional control in patients undergoing resection of HCC also apply to patients undergoing resection of liver metastases.

*Comments.* Complete surgical clearance of all tumor tissue, even in cases of multiple colorectal liver metastases, is justified if one assumes that every
single nodule is secondary to the primary tumor rather than the result of intrahepatic metastatic spread [29]. Yamamoto et al [31] showed that the occurrence of satellite nodules around the main metastatic lesion is rare and that wedge (nonanatomic) resection, even with tumor-free margins less than 5 to 10 mm, is justified as long as there is no exposure of tumor on the cut surface. Therefore, a major surgical goal is tumor-free margins, which are considered to be a major factor of outcome [32,33]. The other goal in patients with liver metastases is avoidance of unnecessary parenchymal resection. IOUS with the techniques described previously, which include a safe rounded dissection plane, allows curative but limited resection. With this approach, it has been possible to carry out resections with a relatively low rate of major hepatectomy (21%) [28]. These results further confirm that liver resection should be an imaging-guided procedure, and only in this case, could still be considered the treatment of choice for liver tumors. These principles of resection result in a high success rate and should be compared with the results of radiofrequency ablation, which are associated with a recurrence rate as high as 39% in the first year of follow-up [5].

**Management of tumors involving hepatic veins**

Tumor invasion of the hepatic veins normally mandates sacrifice of the area of the liver parenchyma drained by these vessels, which limits the use of curative surgical treatment, especially in cirrhotic patients, because of the large volume of liver parenchyma to be removed. Although portal vein embolization [29,30] has lessened the consequences of such resections, parenchymal sparing remains an important goal.

A thick inferior right hepatic vein is present in 20% to 24% of patients [34–36] and is not always detectable with preoperative imaging techniques. Recognition and preservation of a thickened inferior right hepatic vein allows sparing of segment 6 in case of infiltration of the right hepatic vein and allows for alternate anatomic resections otherwise not feasible [37]. IOUS enables the detection of the inferior right hepatic vein, which runs behind the portal branch to segments 6 and 7 (Fig. 8). Furthermore, if there is single hepatic vein involvement by tumor, the detection with color Doppler IOUS of collateral vessels connecting the territory of the involved hepatic vein with the adjacent ones allows the sparing of the liver parenchyma drained by the involved hepatic vein. The sacrifice of the liver tissue drained by the hepatic vein infiltrated by the tumor can be avoided also if, based on color Doppler, the portal vein branch to this area of the liver does not show reversed blood flow once the infiltrated hepatic vein is clamped. The absence of blood flow reversal indicates the still-sufficient blood drainage for this portion of the liver. If none of the conditions mentioned previously is noted (reversal of flow or absence of collaterals), hepatic vein reconstruction is mandatory [38]. In this case, color Doppler also enables verification of the graft patency after the reconstruction and
can be used to guide the removal of clots with a balloon catheter in the case of obstruction.

Summary

IOUS has become increasingly important for surgical resection in patients with cirrhosis and healthy liver. IOUS is important in the diagnosis and staging of liver cancer and as an element of the surgical technique, and IOUS can now be considered a fundamental tool for hepatobiliary and other surgical procedures [3]. The American College of Surgeons has recently recognized the need for surgeons to have specific training in ultrasonography. Meanwhile, dedicated monographs on IOUS have been published in the United States, Chile, and Europe [39–42].

References


