Intraoperative Ultrasound Guided Liver Resections: A Single Center Experience

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ABSTRACT

Background: Liver resection (LR) is the standard treatment for most focal liver lesions. Intraoperative ultrasound (IOUS) improves their diagnosis and guides the liver resection. The present paper analyses our experience in IOUS guided LR, reviewing the indications, surgical techniques, and the short-term results.

Material and Method: 198 LRs guided by IOUS in 186 patients operated in our center between January 2013 and December 2017 were included in a combined prospective and retrospective study. The median age of the patients was 60 years (mean 57, range 16-79), with a male/female ratio of 109/77, and adult/pediatric patient ratio of 185/1.

Results: Malignant lesions were the main indication for IOUS guided LR (164 LRs; 82.8%); among these, colorectal liver metastases were the main indication (66 LRs; 33.3%), followed by hepatocellular carcinoma (44 cases, 22.2%). The mean number of tumors was 3 (range 1-16), and the median diameter of the largest tumor was 40 mm (mean 51; range 3-240). IOUS found new lesions in 22.3% of cases operated for liver metastases (46 LRs), and changed the surgical strategy in 41.9% of cases (83 LRs). Major resection rate was 18.2% (36 LRs); anatomical LRs were performed in 18 cases (9.1%). The median operative time was 330 minutes (mean 334; range 90-920). The median blood loss was 700 ml (mean 900; range 250-9500), with a transfusion rate of 54.8% (108 LRs). Overall and major complication rates were 46.5% (92 LRs) and 7.6% (15 LRs), respectively, while the mortality rate was 2% (4 pts).

Conclusion: IOUS should be fully integrated in the modern liver surgery, providing improved diagnosis and optimal resection guidance, increasing resectability and surgical safety, with low perioperative morbidity and mortality.

Key words: liver resection, intraoperative ultrasound, focal liver lesions, single-center experience

Abbreviations

CT – computed tomography
FLL – focal liver lesions
FRL – future remnant liver
HCC – hepatocellular carcinoma
HV – hepatic vein
IOUS – intraoperative ultrasound
LR – liver resection
LM – liver metastases
MRI – magnetic resonance imaging

BACKGROUND

The advancement of imaging technology and intraoperative devices, along with the refinement of operative techniques and intensive care protocols played a significant role in increasing the resectability with decreased morbidity and

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mortality. Somehow surprising, even though the first applications of intraoperative ultrasound (IOUS) were recorded in the '50s, IOUS entered liver surgery more recently, mainly due to the Japanese school of surgery, represented by M. Makuuchi (1).

Despite advances in preoperative imaging techniques (MRI, CT, etc.) in the past decades, IOUS remains the most accurate diagnostic method for hepatic focal lesions, especially in case of liver metastases (LM), when the overall accuracy in detecting the lesions is about 95%, significantly superior to the preoperative imaging (about 75%) (2). However, the nodule detection may be impaired by liver steatosis or may be falsely increased by the cirrhotic liver; in these situations, the use contrast-enhanced in IOUS may surpass the difficulties (3).

However, if diagnostic IOUS is currently widely diffused worldwide, the IOUS guidance of LR is not, very few centers outside Japan having adopted it, the most successful being the one in Italy (Milan), represented by G. Torzilli, that further developed the approach (3). The present paper analyses our experience in IOUS guided LR, reviewing the indications, surgical techniques, and the short-term results.

PATIENTS

A total of 186 pts benefited from 198 LR performed in our center in the last 5 years (between January 2013 and December 2017). The median age of the patients was 60 years (mean 57, range 16-79), the male/female ratio was 109/77, and adult (over 18 years old)/pediatric patient ratio 185/1. A subgroup of 12 pts (6%) received repeated LR: 7 pts (3.5%) received one re-resection, while 5 pts (2.5%) received two re-resections; among these, 2 pts (0.1%) benefited from a two-stage approach (noncurative followed by curative LR), with (1 pt) and without (1 pt) portal vein ligation, one patient received an ALPPS procedure (Associated Liver Partition and Portal vein ligation for Staged hepatectomy). LR after portal ligation were performed in 3 pts (1.5%).

Overall, IOUS guided LR represented 15.6% of all LR performed in our center (198 out of 1267 LR). Overtime, LR progressively increased as absolute number and proportion of all operations performed in our center, from 40 LR (13.0%) in 2013 to 58 LR (23.1%) in 2017 ($p < 0.01$) (table 1).

The comorbid conditions were evaluated according to the Charlson Comorbidity Index (CCI) (4), with a median score of 7 (mean 7; range 0-13).

Table 1 - Evolvement of intraoperative ultrasound guided liver resection yearly number

Year	All operations (No of cases)	Liver resections (No of cases)	%
2013	308	40	13.0
2014	270	33	12.2
2015	216	28	13.0
2016	222	39	17.6
2017	251	58	23.1
TOTAL	1267	198	15.6

METHODS

We analyzed an HPB database with data collected prospectively (preoperative and intraoperative data) and retrospectively (postoperative data) from the medical records of patients undergoing IOUS guided LR in our center during the last 5 years. Patient demographics, indications for LR, intraoperative data (tumor location, type of LR, associated procedures, blood loss, blood transfusion, operation time), pathologist report (total number of lesions, largest tumor size and histology), and postoperative data (days of recovery, overall and major complications, and mortality within 90 days from surgery) were recorded and analyzed.

Study end-points

The primary outcome was the short-term surgical outcome, measured by postoperative complications classified according Dindo-Clavien classification (5), major (at least IIIA class according to the Dindo-Clavien classification) and overall morbidity rates, and 90-day postoperative mortality rates. The secondary end-point of the study was the evaluation of the types of the IOUS guided LR used in the present series.

Preoperative evaluation

The investigation protocol included liver function tests, specific tumor markers, and imaging, such as contrast abdominal CT scan and/or contrast magnetic resonance imaging (MRI) for the liver, thoracic CT; in selected cases, scintigraphy or positron emission tomography (PET) was considered. All patients were evaluated in our weekly multidisciplinary team meeting including surgeons, radiologists, oncologists, and gastroenterologists.

Intraoperative ultrasound

Ultrasound device

IOUS was always performed by the same main

surgeon, using an Esaote MyLab (Esaote Genova, Italy) with a cross-shaped high frequency (7.5-10 MHz) intraoperative probe, and, more recently, a BK 5000 (BK, Copenhagen, Denmark) with a T-shaped (5-14 MHz) and a biplane (5-12 MHz) high frequency intraoperative probes (*fig. 1*). The sterilization of the ultrasound probes was accomplished at ethylene oxide gas. The control panel of the ultrasound machine was covered with a sterile transparent plastic film in order to allow ultrasound adjustments by the surgeon. IOUS contrast agent (Sonovue®, Bracco, Milan) was used only in few cases. To reduce the use of multiple ultrasound probes, no lower frequencies probes (3.5 to 5 MHz) were used. It is worth mentioning that, in the absence of this probe which provides panoramic image of the liver (which is easier to understand and interpret), the operator needs to have adequate experience in order to be able to exclusively use the reduced field probes, such as the high-frequency ones; in this sense, a high frequency convex probe provides a wider field that a linear one with the same size. The ultrasound system was placed near the first operator, with a transparent sterile cover on the command panel, and was operated mainly by the first operator, and occasionally by the third.

IOUS protocol

The IOUS exploration was always preceded by liver mobilization consisting in dividing the round, falciform

and triangular ligaments in order to expose the entire liver surface for a complete exploration by inspection and palpation (mandatory for subcapsular nodule detection), followed by ultrasound exam, which is essential for the detection of nodules undetected at inspection & palpation.

IOUS included three main stages:

- I. Evaluation of liver anatomy
- II. Tumor staging and background liver assessment
- III. LR guidance, which includes three steps:
 - a. planning the proper LR
 - b. guiding the LR
 - c. checking the post-LR.

Liver anatomy

IOUS was of paramount importance in evaluating the intrahepatic liver vasculature (glissonian pedicles and hepatic veins) and its anatomical variants, establishing the segmental and subsegmental liver anatomy.

A first step consisted in the assessment of liver anatomy, initiated by placing the probe on the central part of the liver (segment 4) at the level of the main portal bifurcation and continued by following the two main portal pedicles and their corresponding segmental and subsegmental pedicles, and then by following the three hepatic veins (HVs) towards the hepatocaval confluence, thus delineating the liver segments.

Figure 1 - BK 5000 ultrasound machine (BK, Copenhagen, Denmark) with a T-shaped (5-14 MHz) and a biplane (5-12 MHz) high frequency intraoperative probes

Tumor staging and background liver assessment

The second stage of IOUS protocol was represented by the diagnostic stage, in which all the focal liver lesions (FLLs) signaled preoperatively were mapped and potentially new ones were detected, including the differential ultrasound diagnosis of each FLL. For a complete examination, the probe covered the entire accessible liver surface, and IOUS exploration was combined with visual exploration and palpation of the liver. Contrast enhanced IOUS was rarely included in the exploration protocol.

Surgical strategy

Patients with acceptable performance status, resectable liver disease, absence of extrahepatic disease, and sufficient future remnant liver volume (FRL) (at least 30% of total liver volume in case of normal liver parenchyma, or at least 40% in case of steatotic or cirrhotic liver) were considered suitable for LR. In cirrhotic patients, Child A cirrhosis, no significant portal hypertension, and platelets count of more than 100.000 were used as selection criteria for LR; if intra-operatively the macroscopic aspect of the liver revealed a more advanced cirrhosis than previously considered, the operation was often shifted to a tumor ablation procedure. Our pivotal surgical policy was to preserve as much liver parenchyma as possible in all cases. In

case of malignant tumors, a free margin of the resected specimen was always considered to be at least of 1 mm; in case of FLLs in contact with large vessels, tumor exposure in this particular area was accepted (6) in order to insure resectability by maximizing the FRL. For the same purpose, association of resection with different methods of tumor ablation (ethanol, radio-frequency or microwave ablation) was used in 18 (9%) small deep located malignant FLLs (12 LM and 6 HCC): 9 nodules of up to 5mm (4.5%), and other 9 of up to 2 cm (4.5%).

Guidance of liver resection

IOUS was used to guide the resection plane in all cases, in such manner to include the targeted lesions in the resected specimen while preserving the vascularization and bile drainage for the remnant liver. In case of non-anatomical LR, the resection area was delineated on the diaphragmatic surface using ultrasound guidance: the tip of the electrocautery was positioned between the ultrasound probe and the liver surface (*fig. 2*), placed in the four cardinal points in such manner to surround the targeted FLLs with safety margins in case of malignancy (accepted as few millimeters or even 0 when major intra-hepatic vascular structures in contact with a FLL was to be preserved (6)); these points were then joined to delimit the resection area on the liver surface with the electrocautery (*fig. 2*).

Figure 2 - IOUS guided delineation of the resection area for a S8 resection for HCC on micronodular cirrhosis

Figure 3 - IOUS guided delineation of the resection area for a marginal non-anatomical segment 6&7 resection for a colorectal liver metastasis

In case of marginal non-anatomical LR, the resection area was determined by placing the tip of the electrocautery between the ultrasound probe on the diaphragmatic liver surface, and the surgeon's finger on the visceral surface, in such manner to define a resection plane in between the two, including the target FLLs along with safety margins (*fig. 3*).

After the start of the resection, IOUS was used to guide the parenchymal transection plane, which was

viewed as an irregular hyperechoic line, due to the presence of air and coagulated blood between the two cut surfaces (remnant liver and specimen) (*fig. 4*). Using IOUS, the relationship between the tumor edges and the transection plane was followed in real time, and the direction of this plane was modified when needed. Thus, intricate transection plane around the tumors could be devised in order to avoid tumor exposure while sparing important vascular structures along with the corresponding

Figure 4 - IOUS guided non-anatomical segments 2, 3 and 4 for a capsulated HCC in contact with the portal pedicle for segment 3 and the horizontal portion of the left portal vein. Note the white line with a whitish shadow (indicated by arrow) that depicts the tip of a Pean clamp that guides the resection plane identifying the vessel which is in contact with (in this case, the portal pedicle for segment 3)

Figure 5 - Segmentectomy of segment 3 for a colorectal liver metastasis invading the segmental pedicle, IOUS certified that the dissected pedicle was the only one belonging to segment 3

liver parenchyma. This approach was according to the “radical but conservative” approach (7). During resection, any vessel with significant size exposed at the level of the transection plane could be identified at IOUS by the hooking technique (8): a surgical thread was placed around the target vessel which is visualized by a hyperechoic line or point with a rear shadow cone; under a gentle traction of the thread, the encircled vessel is detected at IOUS due to its angulation and occlusion. More often, we used a personal trick consisting in the placement of the tip of a clamp in contact with the vessel to be identified, which was consequently detected at IOUS using as marker the tip of the clamp (*fig. 4*). The advantages of this trick over the hooking technique is the easiness of detection of tip of a clamp at IOUS (in comparison with the thread placed around the vessels, that needs to be pulled repeatedly) and the fact that the vessel to be identified do not need to be encircled (maneuver that exposes to risk of injury, that is to be avoided in case the vessel needs to be preserved).

In case of anatomical LR, the area was delineated by direct clamping (*fig. 5*) or by IOUS guided digital compression consisting in the compression of the portal branch (corresponding to the hepatic segments / subsegment to be resected) between the ultrasound probe and the finger of the surgeon, thus obtaining visual delineation of the area to be resected (*fig. 6*). In patients that required sectionectomies or major

hepatectomies, IOUS allowed the design of the transection plane along the middle or right portal fissure, avoiding the inadvertent injuries of the main HVs. In these patients, IOUS guided the extraglissonian approach of portal pedicles, by identifying the anatomical variants, guiding their dissection.

Control of results after LR

The IOUS control consisted in the control of

Figure 6 - Subsegmental segment 7 ischemia induced by IOUS guided finger compression of the corresponding subsegmental portal pedicle (originating from P8) that delineates the border between segment 7 and segment 8. In this case, a right posterior sectionectomy was performed for a deep located HCC in segments 6 and 7 on HBV chronic hepatitis

Figure 7 - The “bath” technique for verifying the presence in the resected specimen of the targeted lesion, a small (6 mm) non-palpable colorectal liver metastasis with a 5mm resection margin.

the remnant liver for tumor clearance and functional vascularization and bile drainage, and control of the resected specimen (immersed in sterile saline solution – the “bath” technique) for the presence of targeted small lesions and their oncological safety margins (*fig. 7*).

Surgical technique

The approach was open, routinely through a right subcostal incision that was transformed in case of large and/or multiple bilobar tumors in a Mercedes incision, and rarely through a J-shaped incision (9) (when a thoracotomy was anticipated, or in case of previous upper midline incision). In order to improve the access to the hepatocaval confluence, the xiphoid process was routinely removed. The type of resection was classified according to the anatomical nomenclature of Brisbane 2000 terminology of liver anatomy and resections (10). Major LR was defined as the removal of at least three segments. All established surgical techniques were deployed: anatomical/non-anatomical, major/minor resections; extra/intra-glissonian, extra/intra-parenchymal approach; special strategies to increase resectability, such as liver-first, two-stage, including associated liver partition and portal ligation for staged hepatectomy (ALPPS). Usually, LR was always preceded by liver mobilization. In order to facilitate the hemihepatectomies, the hanging maneuver described by Belghiti et al (11) was used whenever considered fit by the surgeon. Frequently, during right hemihepatectomies, a modified hanging maneuver was deployed, consisting in passing the tape after complete right hemiliver mobilization, sectioning the hepatocaval ligament and the right accessory HVs, and exposing the right HV at its confluence, thus avoiding the bleeding risk from the blind blunt dissection in front of the inferior vena cava.

The liver transection was exclusively performed by using the clamp crushing method (Kelly-clasia) (12), combining ligations (4.0 or 2.0 non-absorbable multifilament suture, depending on the width of the pedicle to be ligated), sutures (4.0 to 6.0 non-absorbable monofilament suture for vessels, 4.0 to 6.0 absorbable monofilament suture for bile ducts, and 3.0 or 4.0 absorbable multifilament suture for parenchyma), and use of mono-polar cautery. To limit the backflow bleeding from the HVs during liver transection, the central venous pressure was maintained whenever feasible below 5 mmHg. For vascular control, on demand intermittent portal pedicle clamping (Pringle maneuver) was routinely used deployed in periods of maximum 15 minutes of inflow occlusion with interposed intervals of liver reperfusion of minimum 5 minutes, in order to limit the ischemia-reperfusion injury; furthermore, for FLLs located in the right posterior section, the right HV was routinely controlled by tourniquet placement, and its occlusion was deployed on demand. The criteria for on demand vascular control were excessive bleeding during liver transection and/or blood loss that exceeded 500 ml. Total vascular exclusion was rarely used, in case of LR associated with inferior vena cava resection of the inferior vena cava. Bleeding and bile-leak control on the liver cut-surface was carried out using sutures, monopolar, and hemostatic adjuvants: the preferred was the fibrin sealant patch, but we also used autologous fibrin sealant (Vivostat®; Alleroed), synthetic peptides gel (Purastat®; Diamed Healthcare), or oxidized regenerated cellulose (Surgicel®, Ethicon). It is worth mentioning that we almost never used hemostatic adjuvants to stop active bleeding, but only to secure the hemostasis.

In LRs for large benign lesions during which significant

bleeding was anticipated, we successfully used the autologous blood recovery system (Cell Saver®; Haemonetics) in few cases.

Even though the routine use of abdominal drainage after LR has been challenged, and many centers do not drain in these cases anymore (13) (14), we always used drains, supporting this “old-fashioned” policy.

Technically demanding LRs (complex LRs) were defined based on the following criteria:

- Tumor feature: diameter of at least 10cm and/or more than 3 bilobar lesions;
- Background liver parenchyma: cirrhosis
- Type of LR: resection (anatomical / non-anatomical) of the middle segments (segments 4, 5, 8); right posterior sectionectomy (segments 6, 7) and non-anatomic extended (to the anterior section and/or segment 1) right posterior sectionectomy, isolated segmentectomy 1; transversal hepatectomy (segment 4, 5, 6); non-anatomic extended hemihepatectomies; trisectionectomies; two-stage hepatectomy; ALPPS
- Associated resection: portal/ arterial/ inferior vena cava resection and reconstruction, biliary resection and reconstruction, other organ resection;

Postoperative outcome

All postoperative complications occurred 90 days after surgery were recorded and classified according to Dindo-Clavien classification et al (5). Complications leading to life-threatening conditions (grade IIIA and above) were classified as major; these included postoperative bleeding, abscess, sepsis, any organ failure. Complications with no fatal potential were considered minor, such as wound infection, pleural effusion (including the ones that required percutaneous drainage), atelectasis, urinary tract infection. Liver-related complications were defined as all complications directly related with the LR, such as bile leak, cut-surface hematoma or abscess, hemoperitoneum, ascites, liver failure; self-limited bile leak was also considered a minor complication. The major complication rate was calculated based on the most severe complication for each LR. Operative mortality was defined as death during surgical procedure or within 90 post-operative days. Long-term follow-up was carried out depending on their underlying pathological condition, but was not an endpoint of this study. Survival status was established by review of the medical records and defined as the time interval between the date of LR and the date of last patient evaluation or date of death (if known).

Statistical analysis

Continuous parameters were expressed as median, mean and ranges. Categorical variables were expressed in absolute number and percentage. The Mann-Whitney test was applied to compare nonparametric data and the chi-squared test or Fisher's exact test were applied for analysis of categorical variables. The level of statistical significance was set at <0.05.

RESULTS

Indications for LR

The indications for IOUS guided LR are depicted in table 2.

IOUS found new lesions in 22.3% of cases operated for LM (46 cases) (fig. 8). The median number of resected lesions was 1 (mean 2.6; range 1-16); 42 LRs (21.2%) were performed for more than 3 FLLs. The median diameter of the main lesion was 40 mm (mean 51; range 3-240); 23 LRs (11.6%) were performed for lesions larger than 100 mm. Lesions were most frequently located in the right hemiliver (92 LRs; 46.5%) (table 3). The background liver is described in table 4.

LR technique

The surgical approach was always open using a right

Table 2 - Type of resected lesions as diagnosed at pathology

Tumor type	No of cases	%
Malignant tumors	158	79.8
Colorectal liver metastases	66	33.3
Hepatocellular carcinoma	44	22.2
Other malignant tumors	12	6.1
Non-colorectal liver metastases	19	9.6
Peripheral cholangiocarcinoma	7	3.5
Klatskin tumor	7	3.5
Gallbladder cancer	2	1.0
Hepatoblastoma	1	0.5
Benign tumors	26	13.1
Haemangioma	13	6.6
Adenoma	5	2.5
Focal nodular hyperplasia	4	2.0
Other benign tumors	4	2.0
Other benign lesions	13	6.6
Liver hydatid cyst	6	3.0
Liver abscess	6	3.0
Caroli disease	1	0.5
Liver trauma	1	0.5
TOTAL	198	100

Table 3 - Topography of the focal liver lesions

Lesion topography	No of LRs	%
Right hemiliver	92	46.5
Left hemiliver	23	11.6
Bilobar	81	40.9
Segment 1 (alone)	2	1.0
TOTAL	198	100.0

Table 4 - Background liver

Background liver	No of LRs	%
Normal liver	127	64.1
Liver cirrhosis	23	11.6
Chronic hepatitis	29	14.6
Steatosis	34	17.2
Impaired liver after chemotherapy	76	38.4

Figure 8 - New small non-palpable liver metastasis found at intraoperative ultrasound

subcostal approach that was transformed in a Mercedes incision in case of multiple bilobar FLLs and/or large FLLs. The J-shaped incision was used only when a previous upper midline incision was present (22 cases; 11.1%), and a thoraco-laparotomy was used in 2 cases (1%). IOUS changed the planned LR in 83 cases (41.9%). Major resection rate was 18.2% (36 LRs). Anatomical resections were performed in 16 cases (8.1%) (*table 4*); out of these, 8 (4%) had associated limited non-anatomical LRs. According to the established

criteria, 112 (56.6%) were technically complex (*table 5*). Twenty-three LRs (11.6%) were performed on cirrhotic liver. Associated ethanol injection and thermal tumor ablation were associated to LR in 9 cases (4.5%) each. Extrahepatic simultaneously organ resections were performed 10.6% of cases (21 LRs), among which colorectal resections were performed in 7.6% of cases (15 LRs). The median operative time was 180 minutes (mean 204; range 45-920). The median operative time was 330 minutes (mean 334; range 90-920). The median blood loss was 700ml (mean 900; range 250-9500), with a transfusion rate of 54.8% (108 LRs).

Table 5 - Type of liver resection (LR)

Type of liver resection	No of pts	%
Major resections	36	18.2
Minor resections	162	81.8
Anatomical resections	16	8.1
Trisectionectomy	2	1.0
Right hemihepatectomy	7	3.5
Left hemihepatectomy	1	0.5
Central LR (anatomic)	2	1.0
Bisegmentectomy	6	3.0
Posterior right sectionectomy	14	7.1
Anterior right sectionectomy	2	1.0
Non-anatomical resections	182	91.9
Extended right hemihepatectomy	12	6.1
Extended left hemihepatectomy	12	6.1
Extended bisegmentectomy	6	3.0
Extended right posterior sectionectomy	7	3.5
Central LR (non-anatomic)	14	7.1
Other limited non-anatomical resection	131	66.2

Surgical outcome

Overall and major (at least IIIA according to Dindo-Clavien classification) complication rates were 46.5% (92 LRs) and 7.6% (15 LRs), respectively. We underline that pleural effusion that needed percutaneous drainage (4 cases; 2%) was not considered a major complication, as pleural effusion is a common complication after LR, the indication for drainage is not standardized, and it does not have a vital risk; moreover, in case of thoraco-laparotomy, pleural effusion needing percutaneous drainage is exceptional, so considering this a major complication would bias the comparison with published data by centers that favor this type of approach.

Among all liver-related complications, cut surface collection were the most frequent (23 LRs; 11.6%),

Table 6.

Complex LR	No of pts	%
Criteria		
Maximum tumor diameter more than 100 mm	15	7.7
More than 3 bilobar lesions	42	21.2
Liver cirrhosis	23	11.6
Trisectionectomy, right/left extended (non-anatomical) hepatectomy, central LR (anatomical/ non-anatomical), two-stage hepatectomy, ALPPS	42	21.2
Main bile duct resection	9	4.5
Portal resection	3	1.5
Inferior vena cava resection	2	1.0
Other organ resection	21	10.6
Number of simultaneous criteria		
1	82	41.4
2	27	13.6
3	2	1.0
4	1	0.5
TOTAL	112	56.6

followed by ascites (19 LR; 9.6%) (table 7). Among major complications, cut-surface collection were the most frequent most severe complication after LR (2 LR;

Table 7 - All liver-related complications recorded after LR

Liver-related complications	No of LR	%
Cut surface collection	23	11.6
Bile leakage	14	7.1
Ascites	19	9.6
Liver failure	5	2.5
Hemoperitoneum	1	0.5
Liver haematoma	1	0.5
Angiocholitis	1	0.5
Localized liver necrosis	0	0.0
Vascular thrombosis	0	0.0

1%) (table 8). Mortality rate was 2% (4 pts). Median postoperative hospital stay was 8 days (mean 12; range 4-45).

DISCUSSION

LR is the mainstay treatment for large benign tumors, and primary and metastatic liver tumors, especially in case of colorectal LM (15). Ultrasound is one of the most used imaging techniques in current medical practice, due to its noninvasiveness, rapidity

Table 8 - Dindo-Clavien classification of main complication in each case that benefitted from IOUS guided liver resection

	I	II	IIIA	IIIB	IVA	IVB	V	TOTAL	%
Liver									
Bile leakage	1	10	1	0	0	0	0	12	6.1
Cut surface collection	0	12	2	0	0	0	0	14	7.1
Liver failure	0	1	0	0	0	0	1	2	1.0
Angiocholitis	0	1	0	0	0	0	0	1	0.5
Hemoperitoneum	0	0	0	1	0	0	0	1	0.5
Ascites	7	4	0	0	0	0	0	11	5.6
Respiratory system									
Bronchial pneumonia	0	1	0	0	0	0	0	1	0.5
Pleural effusion	0	12	0	0	0	0	0	12	6.1
Respiratory failure	0	0	0	0	2	0	1	3	1.5
Digestive system									
Pancreatic fistula	0	1	0	0	0	0	0	1	0.5
Duodenal fistula	0	0	1	0	0	0	0	1	0.5
Intestinal Clostridium infection	0	1	0	0	0	0	0	1	0.5
Renal system									
Kidney failure	0	3	0	0	2	0	0	5	2.5
Cardiovascular system									
Deep vein thrombosis	0	1	0	0	0	0	0	1	0.5
Neurologic system									
Neurological disorders	0	1	0	0	0	0	0	1	0.5
Systemic complications									
MODS	0	0	0	0	0	0	2	2	1.0
Fever	0	11	0	0	0	0	0	11	5.6
Other abdominal complications									
Wound infection	0	7	0	0	0	0	0	7	3.5
Intraabdominal abscess	0	1	0	1	0	0	0	2	1.0
Wound evisceration	0	2	1	1	0	0	0	3	1.5
TOTAL	8	69	4	3	4	0	4	92	46.5

and repeatability, and has real potential for improvement of performance. Following the experience of IOUS pioneers in liver surgery - Makuuchi M (Japan) (16), Lane RJ (Great Britain) (17), Sigel B (United States) (18), and Bismuth H (France) (19), IOUS became a standard diagnostic tool in liver surgery in the mid-1980s (20), and due to Makuuchi M (Japan), IOUS became a guiding tool in LR (21).

Intraoperative ultrasound

IOUS of the liver, by removing the "ultrasonic barriers" (such as the abdominal wall or intestinal gas) and the use of high frequency probes (5-10 MHz), has a significant increase in image and diagnostic accuracy due to its unmatched spatial resolution, and therefore remains an essential tool for hepatobiliary surgeons.

IOUS assists the surgeon in assessing intraoperatively with precision and in real time the disease, providing important information for optimal treatment strategy and surgical procedure, including tumor ablation techniques. Furthermore, IOUS optimizes LR by insuring the preservation of proper vascularization and bile drainage of the remnant liver, decreasing significantly the immediate postoperative complications related to ischemic parenchyma, such as liver insufficiency, bile leak, and cut surface abscess. In this way, IOUS guidance also improves the long-term oncological results, as remnant liver ischemia may be associated with early tumor recurrence (22).

Therefore, IOUS brings four major benefits in liver surgery, that have a remarkable impact on surgical management (23), allowing the surgical procedures to be properly changed or adapted, thus avoiding intraoperative incidents or incomplete treatment:

1. Complementary investigation to preoperative imaging methods in depicting the vascular anatomy, liver segmentation and tumor mapping (24);
2. Acquisition of information needed to establish intraoperative tactics and techniques, including tumor vascular invasion or thrombosis (25);
3. Guiding the liver resection (LR) and/or interventional tumor ablation procedures (TA);
4. Verifying the outcome of these procedures, in terms of tumor clearance and proper vascularization and biliary drainage of the remnant liver.

Although there are still skeptical opinions about the usefulness of IOUS in liver surgery (26), many studies have clearly demonstrated its value, stating that modern LR should be ultrasonically guided (21). To the best of our knowledge, our center is the second European center that successfully implemented the

IOUS guided LR in a large series of patients, after the one in Milan (Italy).

Training and learning curve

IOUS requires a thorough knowledge of general ultrasound, liver anatomy and segmentation, of normal and abnormal findings in the liver (27,28), and of the artifacts that may be encountered in the setting of liver surgery, so a thorough specialized training should be integrated into the surgeon's education program. In this sense, diagnostic IOUS was progressively learned by the main author starting with 2001, during resident ship, while the training in IOUS guidance of LRs was carried out in a high-volume specialized center lead by G. Torzilli (Humanitas Clinical Institute, Milan, Italy) (2006-2012), during which skills for both LR and IOUS guidance were acquired. The learning curve for IOUS guided LR was covered since 2013 (29), in a high-volume specialized center, under the supervision of an experienced HPB surgeon, I. Popescu.

We emphasize that IOUS, both diagnostic and for LR guidance, was performed by the same surgeon that performed the surgery. In this way we consider that best results, including in terms of decision making and surgical planning, are obtained when diagnostic IOUS is performed by the surgeon and not by the radiologist, while the IOUS guidance during LR can only be performed by the surgeon who performs the LR.

Tumor staging and background liver assessment

As diagnostic purposes, IOUS can locate preoperatively known liver lesions and detect further FLLs during surgery, thus assisting in planning the type of LR (30). IOUS detects non-palpable FLLs with maximum accuracy and may reveal FLLs undetected at preoperative imaging during intraoperative palpation in 10%-35% of cases (31) (32). Indeed, in our experience, IOUS detected new LM in 22.3% of cases. On the contrary, IOUS depicts with difficulty superficial (subcapsular) small FLLs, but these are readily detected at intraoperative inspection and palpation. Thus, in order to perform a complete and correct liver assessment, IOUS has to be accompanied by intraoperative inspection and palpation (33). Another scenario in which IOUS has difficulty in depicting small FLLs (under 1cm) are the isoechoic ones (with similar echogenicity as the parenchyma); this situation is usually encountered when exploring a steatotic liver, and may be overcome by the intraoperative use of contrast-enhanced ultrasound agents (3) (34), that we did not routinely performed. Therefore, IOUS should be systematically performed in order not to overlook occult FLLs. When a FLL is identified, its relationship with

adjacent vascular structures can be accurately assessed by IIOUS (35).

IIOUS is a key diagnostic tool in LM, reaching a sensitivity unmatched by no other imaging technique, ranging from 93-100% (36), while MRI or CT has only 84%, and percutaneous ultrasound only 71% (23,37). IIOUS has proven accuracy for the LM detection, with 94% sensitivity and specificity, 92% positive predictive value, and 96% negative predictive value (38,39). In hepatocellular carcinoma (HCC) on cirrhosis, the information provided by IIOUS is not always useful for the differential diagnosis with regenerative nodules, so that only 20-30% of small FLLs detected at IIOUS in this scenario are neoplastic (40). Thus, while 84% of mixt (hyper- and hypoechoic) FLLs are malignant, hypoechoic FLLs are malignant only in 24-30% of cases, and hyperechoic only in 0-18% of cases; moreover, the biopsy does not seem to be useful in these situations (40,41). Thus, if mixt FLLs clearly need treatment (42), in case of hypo- or hyperechoic FLLs, only the intra-operative use of contrast-enhanced ultrasound agents may provide a diagnosis (43,44).

IIOUS optimizes LR by detecting all lesions and ensuring appropriate oncological safety margin (45,46), thus improving the long-term survival of patients. Consequently, IIOUS has become a standard adjuvant method in liver resection (LR) for both primary and secondary tumors (21,47,48,49), having a decisive role in choosing the parenchymal dissection plane in liver resections (43). Information provided by IIOUS modified the surgical technique in 19.5-83% of cases for malignant FLLs (38,50, 51, 52,53,54). More recent studies report a percentage of 4-7% (55,56), which may be explained by the advances in preoperative imaging techniques, but especially by the surgical strategy adopted in those studies, with preference for major LR, so that tumors detected de novo at IIOUS localized in the resected hemiliver did not influence the surgical technique, at the cost of sacrificing a significant volume of functional liver parenchyma. In case of conservative LR, the impact of IIOUS on surgical strategy remains particularly important, thus allowing the sacrifice of a minimum volume of functional hepatic parenchyma (7).

It is well known that conventional LR in cirrhotic patients has a high rate of postoperative complications, mainly due to liver failure (up to 64% of cases) (57). Ability to perform anatomical LR, especially in patients with HCC on cirrhosis, without mortality or major complications (58) is mainly due to the use IIOUS (59), which is the best imaging method for staging tumors in the liver and step-by-step guidance of the parenchymal transection. Some authors proved that segmentectomy

or subsegmentectomy in HCC is superior in terms of local recurrence compared to non-anatomical limited resection (21). However, in our experience we favored limited non-anatomical LR instead of the anatomical ones.

The presence of portal tumor thrombosis in HCC is no longer an absolute contraindication for LR because it has been demonstrated that long-term survival benefits can be obtained (60). This extension of the surgical guidelines is partly due to the use of IIOUS, because in these cases the correct tumor staging and the knowledge of the type of vascular infiltration are fundamental. IIOUS guided ligation of the portal pedicle upstream of intravascular tumor thrombosis, reduces the risk of thrombus detachment and migration into the portal system of the remnant liver in 4 cases (2%).

Tumor mapping and staging was performed by IIOUS in all cases of our series. During 46 LRs for colorectal LM (22.3%), IIOUS found 53 new lesions undetected at preoperative imaging. In 67 cases with malignancy (33.8%), IIOUS found that the preoperatively known FLLs were more locally advanced than previously believed. In 83 of these cases (41.9%), IIOUS modified the surgical strategy and technique. Moreover, IIOUS evaluated the quality of liver parenchyma, detecting with ease advanced liver steatosis or fibrosis.

In our series, the majority of resected lesions were malignant (79.8%). The most common indication for LR was colorectal LM (33.3%), followed by HCC (22.2%), in accordance to published data (61). In case of colorectal LM, resection is considered the gold standard treatment and offers the best chance of long-term survival (62,63). In our experience, benign tumors represented only 13.1% of all LRs, hemangioma being the most frequent indication for LR among benign lesions (6.6%). In what the background liver parenchyma is concerned, LR were performed on liver cirrhosis in 11.6% of cases.

Surgical strategy

Despite significant advances in preoperative imaging techniques (MRI, CT, etc.) in the last decade, IIOUS remains the most accurate diagnostic method for hepatic focal lesions, that often changes surgical planning and patient management (2,37,23). In our series, IIOUS changed the surgical planning in 41.9% of cases, mainly due to new FLLs detected at IIOUS and/or more advanced FLLs that was preoperatively considered (increased size, contact/invasion of major vessels, tumor thrombosis). Moreover, IIOUS allowed conservative LRs in case of FLL invading one of the main HVs, by documenting compensatory collateral venous circulation

towards the other(s) HVs and/or centrifugal flow in the corresponding portal pedicles once the involved HV is temporarily occluded by clamping or IOUS guided digital compression (64,65). The acceptance of minimum oncological resection margin and even tumor exposure when in contact with major vessels significantly increased the resectability. Using these policies, FLLs considered otherwise unresectable, or resectable using more extensive procedures with higher risk of morbidity and mortality, were resected with low morbidity and mortality.

Guidance of liver resection

IOUS also assisted the LR procedure, by delimitating the resection area, guiding the plane of transection, marking target vascular structures to be sectioned or, on the contrary, preserved (43). IOUS was also used to assess the immediate results after LR, checking the remnant liver for proper vascular flow and tumor-clearance. IOUS allowed treatment of small unpalpable lesions in 43 cases (21.7%). Moreover, IOUS allowed resection of nodules in contact with large vessels insuring tumor exposure only in the area in contact with the respective vessel, scenario that do not expose to significant risk for cut surface tumor recurrence (6). Accidental tumor exposure (tumor exposure when in contact with parenchyma), being encountered in 9 malignant tumors, excluding the capsulated HCC where tumor exposure was accepted. Additional confirmation of the value in IOUS guided LR is proven that the margins of the resected specimens after conventional LR were more frequently infiltrated by tumor (16-18% of cases) than the ones after IOUS guided LR (46,66). Indeed, in our experience insuring oncological security margins was feasible by IOUS guidance.

Control of results after LR

At control of the remnant liver, IOUS detected remnant nodules in 6 cases (5 cases with multiple bilobar colorectal LM, 1 case with multifocal HCC), and remnant tumor tissue on the cut surface in 3 cases (R2 resection) (1 case with colorectal LM, 1 case with cholangiocarcinoma, and 1 case with infiltrative HCC) and assisted in the re-resection of the involved area in all cases insuring a complete tumor removal, except one (multifocal HCC), in which tumor ablation by ethanol injection was performed for a small (1 cm) residual nodule.

In all but 2 cases, IOUS confirmed the integrity of main biliary and vascular structures of the remnant liver; in these 2 cases, further limited LR was performed in order to excise the impaired parenchyma.

Surgical technique

Method for parenchymal transection

A recent randomized controlled trial comparing four different transection methods in liver resection showed that the clamp crushing method remained the most efficient device in terms of resection time, blood loss, and blood transfusion frequency, when compared with CUSA, hydrojet and the dissecting sealer, and was also the least expensive (67). Clamp crushing was the standard method for parenchymal transection in our series of IOUS guided LR not only for its simplicity and efficacy but also for the ability to provide a very versatile method of changing the orientation of the transection plane while insuring a smooth cut surface that is very easy to be depicted at IOUS. Moreover, this method allows a minimum destruction of parenchyma due to the thin clamp, allowing the surgeon to transect in very tight spaces, such a tumor located close to / in contact with a large vessel. Another feature of this method that we consider useful during IOUS guided LR is the "tactile" feedback of the clamp during the crushing movements, allowing differentiating between parenchyma and large vessels, or between parenchyma and tumor tissue during intentional or unintentional tumor exposure.

Intraoperative bleeding

Despite advances in surgical and anesthetic techniques, blood transfusion is still required in 10–33% of patients undergoing elective liver resection (68,69). Major bleeding and the subsequent blood transfusion have been shown to increase post-operative morbidity and mortality (70). However, it is debatable whether it is due to a cause-effect relationship or just due to more complex LRs. Perioperative blood transfusions were associated with a higher rate of recurrence and lower survival after LR for early HCC (71), but there we found no clear evidence in case of colorectal LM, peripheral cholangiocarcinoma, and advanced HCC (71,72). Our policy was to reduce blood loss as much as possible by meticulous technique and vascular control by intermittent on demand Pringle maneuver, avoiding massive bleeding in a short period of time. Total vascular exclusion was used in 1 case, in which inferior vena cava thrombectomy was also performed. However, the blood loss was influenced by liver status (cirrhosis and advanced steatosis) ($p=0.03$) and complexity of LR ($p<0.01$). The overall transfusion rate in our experience was 54.8%, higher in comparison

to published data, fact that could be explained by the higher percentage of complex LR (56.6%).

Lowering the central venous pressure below 5 cm H₂O in order to decrease the backflow bleeding during LR (73) was used whenever feasible by decreasing the infusions to 1 ml/kg/hour, the tidal volume to 7 ml/kg, respiratory rate to 12-18/min, the airway pressure below 5 mmHg, by patient positioning in anti-Trendelenburg (head up), use of diuretics, analgesics and venodilators agents.

Major vs minor hepatectomy

Major LR represent up to 50% of LR performed in the majority of the centers and its decrease in favor of liver parenchyma sparing resection is one of the priorities of liver surgery. This strategy is sometime laborious and time consuming, but increases resectability rate, reduces the morbidity and mortality rates, and often allows future re-resections (74). Consequently, the parenchyma sparing approach in LR has become the standard treatment in colorectal LM (75,76), especially in case of small ones located in the right hemiliver. IIOUS guidance significantly facilitates this conservative approach in LR, making feasible LR that are impossible to perform using the conventional approach. In this sense, we avoided major hepatectomies by replacing them with multiple non-anatomical LR, sectionectomies, extended sectionectomies (such as posterior right sectionectomy extended to the anterior section), or limited central hepatectomy. In our experience, the major resection rate was relatively low (18.2%) considering the advanced disease presentation of most cases. These findings are consistent with our policy to limit major resections in order to preserve the functional parenchyma as much as possible, avoiding postoperative liver insufficiency and favoring potential re-resections.

Anatomical vs non-anatomical resection

Anatomical LR is recommended in patients with HCC, according with the theory of cell tumor dissemination through the portal branches of the involved liver segment (77,78,79,80). However, this policy is not generally accepted. The best option for an anatomical yet conservative LR in HCC is the subsegmentectomy. IIOUS guided subsegmentectomy may be accomplished by tattoo technique or by digital compression, both being proven safe, feasible and effective, the first being however considered as standard procedure (81). We did not systematically perform anatomical LR in HCC, but we performed IIOUS guided segmentectomy or subsegmentectomy using direct exposure or digital compression of the corresponding portal pedicle in

case of HCC/LM invading the subsegmental portal pedicle in 9 cases.

In colorectal LM, multiple comparative studies of anatomical versus non-anatomical LR showed similar results regarding the status of resection margins, recurrence and survival (82,83). Our policy clearly favored non-anatomical LR (91.9%), even in HCC. Non-anatomical LR was preferred for maximizing the FRL volume (thus avoiding the risk of liver failure) and minimizing the risk of major biliary and/or vascular injuries. Major anatomical LR was usually performed only in selected cases with focal lesions/traumatic extensive laceration involving most of the hemiliver, with malignant tumors invading one the main portal pedicles, and for Klatskin tumors.

In our series, for major hepatectomies, the preferred approach was extra-glissonian (assisted by IIOUS) whenever feasible, which we considered more straightforward when compared to the intra-glissonian approach. For the right sectionectomies, we perform the anatomical resection by primarily dissecting the corresponding pedicle whenever favored by portal anatomy (superficially located anterior or posterior pedicle determined at IIOUS), otherwise the preferred approach was trans-parenchymal in the plane of the corresponding portal fissure determined by IIOUS. Even though this type of LR is not generally accepted as anatomical, it is logical to admit that, for example, a LR conducted in a IIOUS guided plane placed laterally to the right HV, exposing the later, and intersecting the right posterior pedicle at origin, leaving no ischemic tissue on the cut surface, is indeed an anatomical LR. In few cases of right posterior sectionectomy, we used the induced portal ischemia of subsegments of segment 6 and segment 7 adjacent to segment 5 and segment 8, or counter-portal ischemia of the subsegment 8 dorsal and segment 5 to delineate the resection area, by IIOUS guided finger compression of the corresponding pedicles.

Oncological resection margin

The oncological security margin was initially considered to be of at least 1 cm (84,85,86). Because of this principle, many patients were considered not resectable, and therefore did not benefit from this treatment. In the new era of chemotherapy, the efficacy of LR for LM with reduced oncological security margin was sustained by numerous studies, proving that the thickness of the surgical margin is at least of 1 mm (87,88); the concept seems to be also valid in case of HCC (89). More recently, even no surgical margin at all (tumor exposure) was proven not correlated with reduced overall survival in both HCC

(90,91) and LM, where similar overall survival rates following negative margin status (R0) and microscopically positive margin status (R1) may be obtained using an aggressive approach consisting in combined chemotherapy and repeat surgery (92). Moreover, in case of colorectal LM, pathological studies have proved that micro metastases, satellitosis and Glisson sheath extension are extremely rare (93,94).

It is worth mentioning that the margin status assessment is difficult, being dependent of the transection techniques used that vaporize, aspirate, ablate or fracture the parenchyma adjacent to the tumor, leading to an underestimation of the width of the resection margin; in other words, the more parenchyma is destructed during parenchymal transection, the less width of resection margin may be obtained. Moreover, the pathologist often cannot differentiate between tumor exposure on the resected specimen (R1 margin status) and residual tumor on the liver cut surface (R2 margin status). In this scenario, IOUS guidance offers precision, assisting in avoiding to leave residual tumor on the liver cut surface; moreover, in case that happens, IOUS can detect it during the control of the remnant liver and assists in the re-resection of the involved area, insuring a complete tumor removal. However, tumor biology rather than width of surgical margin seems to correlate with liver recurrence and overall survival.

In our series, in LM the standard approach was to obtain R0 margin status. However, we did not exclude patients from resection if tumor exposure (no security margin) was contemplated in order to preserve major vessels in contact with tumor, and therefore insure resectability. We underline that tumor exposure in contact with parenchyma was avoided and considered an error, according to a policy that was recently validate (6). Moreover, in these particular cases we avoid to leave macroscopic tumor tissue on the remnant liver (macroscopically positive R2 margin status) by using the IOUS guidance; however, in 3 cases IOUS discovered residual tumor on the cut surface and assisted in completing the resection. On the contrary, when tumor invasion was seen at IOUS, an upfront LR including the territory of the invaded vessels was performed whenever feasible. The IOUS criteria for tumor invasion, similar to ones described by Torzilli et al (7), were: intravascular thrombosis, abnormal vessel wall appearance, more than 180 degrees contact between tumor and vessel, and upstream bile duct dilation (in case of portal pedicles). When the main trunk of a major HV was invaded, its territory was not included in the LR when IOUS depicted collateral communicating veins with the adjacent venous territory, such as with

middle HV territory when main right HV resection was contemplated, right HV and/or left HV territories when main middle HV resection was contemplated, or with middle HV territory when main left HV resection was contemplated), or significant accessory right HV were present when main right HV resection was contemplated.

Complex liver resection

In this study, technically complex LRs were identified based on the above-mentioned criteria with the purpose to analyze the disease severity, as well as the surgical expertise. Therefore, almost half of all LRs were complex (47.2%), meaning that, unfortunately, patients often were referred to surgery in advanced stages necessitating substantial surgical expertise. Complex LR was the main factor influencing the postoperative outcome, with major complication and mortality rate of 11.9% and 6.5%, respectively, compared to 2.9% and nil in the rest of the series, respectively ($p < 0.01$ and $p < 0.01$, respectively). In our opinion, the complexity of LR should always be considered when analyzing the results of a certain series, reflecting both the morbidity rate and the expertise. Moreover, patients with complex presentations of liver tumors should always be evaluated by a multidisciplinary team in a highly-specialized center, otherwise a significant part of them would be submitted to useless explorative laparotomies, incomplete or risky procedures, or they would not be referred to LR at all.

Vanishing lesions

The increased use of more effective chemotherapy regimens for downstaging or as neoadjuvant therapy commonly induces the “disappearance” of LM at preoperative imaging. IOUS has a key-role in this situation, as it is able to detect them, even when not detectable at intraoperative exploration and palpation, and more important, to guide their resection, even in case of deep-localized FLLs. It is worth mentioning that steatosis may impair the IOUS capacity to detect small LM. Other approaches in case of vanishing lesions may be: decreased time and/or aggressiveness of chemotherapy, treatment using local ablation techniques combined with fusion imaging, anatomical resection of the involved territory, or “wait and see” treatment strategy. However, IOUS guided LR may be an option, as in all cases of vanished preoperative lesions but one, we successfully detected and treated the lesion; in that particular case, where one of 4 lesions preoperatively known was not detected by IOUS, a re-resection was performed after 6 months during which the lesion along with another new one were resected.

Increase of resectability

We applied all strategies to improve resectability in patients unresectable with upfront conventional LR due to large tumor volume that would require the resection of an excessive amount of functional parenchyma, with high risk of liver failure (95,96). However, we favor upfront LR policies (97):

- Two-stage hepatectomy (98,99), recommended in multiple bilobar LMs, The drawbacks are the necessity of two operations (each associated with specific morbidity and mortality) and the failure to perform the second stage due to tumor progression in 19-24% patients (98,100).
- ALPPS (Associating Liver Partition and PVL for Staged hepatectomy) procedure is a novel surgical technique aimed to induce a the more rapid and robust hypertrophy of the FRL. In the present series one patient with multiple colorectal LM located in the right hemiliver and segment 4 was treated successfully using this procedure, with no recurrence at 9 months after surgery. The role of IOUS was significant in this case, as it discovered several new nodules, including the ones in segment 4, and guided the liver transection plane in such way to exclude the nodules and to preserve as much as possible of segment 4 in the FRL. This proved very useful, as the without postoperative complications maximum hypertrophy obtained after 21 days was borderline (26%). However, the limitations of this technique are related to the increased rates of major morbidity (up to 40%) and mortality (up to 12%) (101). Indeed, our case had a late wound evisceration that required surgery.
- Multiple liver resections as an alternative to the two stage hepatectomy (102,103), especially in patients with bilobar liver tumors, that were encountered in a significant proportion of our series (40.9%). The strategy consisted in avoidance of major LRs, replacing them with multiple non-anatomical resections, or segmental oriented minor LR associated with limited non-anatomical resections (*fig. 9*). The main criticism is represented by narrow resection margins and even a higher incidence of R1 resections, but, as recently proved, tumor exposure when in contact with major vessels is a safe approach (6).
- Replacement of major anatomical hepatectomies with non-anatomical limited LRs. Thus, hemi-hepatectomy associated with partial resection of the adjacent section was preferred instead of a trisectionectomy, and right posterior sectionectomy associated with partial resection of the anterior section replaced the right hepatectomy (64). For centrally located tumors (segments 4, 5 and 8), an alternative to the central hepatectomy (trisegmentectomy 4, 5, 8) was a non-anatomical LRs of the tumors located in these segments (*fig. 10*). The performance of such a hepatectomy, which

Figure 9. Non-anatomical multiple IOUS guided liver resection for multiple bilobar colorectal liver metastases (9 lesions)

Figure 10 - Non-anatomical IOUS guided liver resection of segments 4, 5 and 8, preserving the P8 and P8d pedicles, for a centrally located hepatocellular carcinoma on Child A liver cirrhosis

involves segmental resection of the middle HV, requires IOUS to detect the presence of compensatory collateral venous circulation towards the right HV and left HV (34,65). By these techniques, as much as possible liver parenchyma is preserved, enabling LR in some patients considered unresectable by conventional LR techniques.

- LR associated with in-situ ablation of less than 2 cm tumors located in the FRL.

Postoperative outcome

LR has been associated with high morbidity and mortality. The reported morbidity has ranged from 16.2% to 47.7% (104,105). This large range is partially due to the heterogeneity of the published series, with major differences in indication, extension of hepatic resection, patients with cirrhosis, and criteria for post-operative complication. In our experience, the overall and major complication rates were 46.5% and 7.6%, respectively, which is in accordance with the published data. Among all liver-related complications, cut surface collection was the most frequent (11.6%), but in only 2 cases (1%) this was a major complication as percutaneous drainage was needed. Of note, the patient with liver failure after LR was transplanted with a whole liver graft, but he died due to neurological complications.

The mortality rate after LR varies from 1.5-3.5% in high-volume centers, to 8-24% in low-volume ones (106,107). In our experience, the 90-day mortality rate was 2%, which is similar to other high-volume centers.

CONCLUSION

Despite substantial advancements in preoperative imaging, IOUS remains an essential diagnostic tool

during surgery, often leading to changes in surgical planning and patient management due to new FLLs not detected preoperatively or more advanced presentation of the preoperatively known FLLs. Accurate evaluation of liver anatomy, precise FLLs localization, characterization, differential diagnosis and local staging, as well as background liver evaluation (steatosis, fibrosis, cirrhosis) are common indication for IOUS. Moreover, real-time guidance of LR and/or ablation techniques, and control of post procedural results, leading to low morbidity and mortality, makes IOUS an essential part of surgical techniques, and therefore should be a standard procedure in liver surgery. Finally, IOUS guidance, integrated in specific policies, insures resectability in patients who otherwise would be submitted to conventional but riskier or incomplete surgery, or would be excluded from curative surgery.

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