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REVIEW

Parenchymal-sparing liver surgery in patients with colorectal carcinoma liver metastases

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Abstract

Liver resection is the treatment of choice for patients with colorectal liver metastases (CLM). However, major resections are often required to achieve R0 resection, which are associated with substantial rates of morbidity and mortality. Maximizing the amount of residual liver gained increasing significance in modern liver surgery due to the high incidence of chemotherapy-associated parenchymal injury. This fact, along with the progressive expansion of resectability criteria, has led to the development of a surgical philosophy known as "parenchymal-sparing liver surgery" (PSLS). This philosophy includes a variety of resection strategies, either performed alone or in combination with ablative therapies. A profound knowledge of liver anatomy and expert intraoperative ultrasound skills are required to perform PSLS appropriately and safely. There is a clear trend toward PSLS in hepatobiliary centers worldwide as current evidence indicates that tumor biology is the most important predictor of intrahepatic recurrence and survival, rather than the extent of a negative resection margin. Tumor removal avoiding the unnecessary sacrifice of functional parenchyma has been associated with less surgical stress, fewer postoperative complications, uncompromised cancer-related outcomes and higher feasibility of future resections. The increasing evidence supporting PSLS prompts its consideration as the gold-standard surgical approach for CLM.

Key words: Colorectal liver metastases; Parenchymal-sparing hepatectomy; Ultrasound; Liver failure; Resection margins; Complications; Ablative therapies

Core tip: This review provides a profound insight into parenchymal-sparing liver surgery, including the oncological rationality for this approach, the different anatomical and technical aspects as well as its present role and future perspective in modern liver surgery.

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INTRODUCTION

Colorectal carcinoma is the third most frequent cancer in the world, with nearly 1.23 million new cases diagnosed each year[1,2]. About half of these patients will develop liver metastases during the course of the disease, causing two thirds of deaths[3]. In terms of treatment, liver resection is the treatment of choice to prolong survival and offer a chance of cure to patients with colorectal liver metastases (CLM)[3,4]. However, resection is not always feasible due to tumor location, contact with major vascular elements, bilaterality, insufficient liver remnant or patient comorbidities. Although not long ago the majority of patients with CLM (70%-80%) were considered unsuitable for resection at diagnosis, nowadays a greater number of patients finally undergo surgery thanks to the significant improvements in imaging modalities, surgical techniques, anesthesia, chemotherapy regimens and the expansion of resectability criteria among surgeons[4].

Over the years, hepatobiliary surgeons have been constantly pushing the frontiers of resectability in patients with malignant liver tumors. The paradigm of resectability in modern liver surgery has shifted from "what is resected" to "what remains after resection"[5]. Surgeons performing oncological liver surgery must balance two conflicting objectives that might jeopardize each other whenever extensive disease is present: (1) to achieve a complete tumor resection with curative intent (negative margins); and (2) to preserve as much liver parenchyma as possible to avoid liver failure. However, major hepatectomies are often required to achieve an *R*0 resection and these are associated with substantial rates of morbidity and mortality[6]. Posthepatectomy liver failure (PLF) is the main cause of death after major hepatectomy and it is strictly related to the volume and quality of the future liver remnant (FLR)[7]. Several strategies have been developed to minimize the risk of PLF and expand resectability. These strategies could be grouped into those that tend to reduce the tumor size (*e.g.*, conversion chemotherapy, endovascular procedures) and those that tend to preserve or increase the amount of liver remnant (*e.g.*, local ablation techniques, preoperative portal vein embolization, two-stage procedures). These developments led to the successful removal of multiple, often bilateral, liver lesions otherwise considered unresectable. Yet, when using classical approaches of portal vein occlusion (either ligation or embolization) to increase the amount of FLR, up to 40% of patients never become eligible for tumor resection either because of insufficient hypertrophy or disease progression during the long interval periods (6-12 wk) usually required to achieve hypertrophy[8,9]. Moreover, patients who fail to complete the second stage have worse survival than those treated with chemotherapy alone[10].

Although maximizing the amount of residual liver parenchyma has always been a matter of concern among surgeons, it has become a major issue to modern liver surgery due to the high incidence of parenchymal injury associated with downsizing chemotherapy (*i.e.*, steatohepatitis, sinusoidal obstruction syndrome), where the extent of resection critically determines postoperative risk. The need of preserving non-tumor parenchyma as well as the progressive expansion of resectability criteria for CLM, mainly related to the significant reduction of what was considered a sufficient tumor margin, has led to the development of a surgical concept known as "parenchymal-sparing liver surgery" (PSLS). This philosophy gathers various surgical strategies aiming to offer the minimum sufficient margins in order to preserve as much liver parenchyma as possible, where preoperative planning and intraoperative ultrasound (US) are key factors for success. PSLS, which intends to avoid major liver resections and eventually the need of using techniques to induce FLR hypertrophy, has recently been associated with equal or better perioperative and long-term outcomes than non-PSLS[11-13].

This review aims to critically analyze the literature available to date regarding PSLS in the treatment of patients with CLM.

HISTORICAL PERSPECTIVE AND ONCOLOGICAL BASIS

Over the years, there has been an increasing trend towards PSLS for patients with stage Ⅳ colorectal cancer in most specialized centers around the world. This has been clearly reflected by the group from Memorial Sloan-Kettering Cancer Center (MSKCC), demonstrating that the techniques used to deal with bilateral CLM changed uniformly over a 20-year period in favor of wedge resections and ablations to spare uninvolved surrounding liver instead of major hepatectomies[12]. From an oncological perspective, there are mainly two factors closely associated with this phenomenon: (1) The evolution of the concept of resectability; and (2) The increased knowledge on tumor biology.

Tumor resectability

The concept of tumor resectability in CLM has evolved greatly in the past three decades. In the 1970s, most surgeons considered resection only in patients with single liver metastasis. In 1984, Adson *et al*[14] reported similar 5-year survival rates between patients with solitary metastases and those with multiple lesions (25% and 18%, respectively). Two years later, Ekberg *et al*[15] identified a series of poor prognostic factors associated with surgical resection and proposed to contraindicate surgery in patients with any of the following characteristics: More than four lesions, bilobar compromise, impossibility to achieve a margin of at least 1 cm and presence of extrahepatic disease. These were known as the "Ekberg criteria" and were welcomed by various authors up to the late 1980s. During the 1990s, this concept evolved again due to the increased use of chemotherapy and more aggressive surgical treatments with favorable outcomes were performed in patients presenting the characteristics traditionally considered contraindications[16]. Probably the most important breakthrough with regards to tumor margins was accomplished by Pawlik *et al*[17] in 2005, who demonstrated that the width of a negative surgical margin did not affect survival, recurrence risk, or site of recurrence. In this study, which included 557 patients undergoing liver resection for CLM, negative margins had similar overall recurrence rates (1-4 mm: 38.7%; 5-9 mm: 41.2%; ⩾ 10 mm: 39.2%, P = 0.32) and 5-year overall survival (OS) rates (1-4 mm: 62.3%; 5-9 mm: 71.1%; ⩾ 10 mm: 63.0%, P = 0.63). This was later supported by many authors, including a recent propensity score-matched analysis in 2715 patients demonstrating that the disease-free survival (DFS) was not significantly different between patients with more than 1 mm margin (1-4.9 mm *vs* 5-9.9 mm *vs* ⩾ 10 mm), and showed that a 1 mm cancer-free margin was sufficient to achieve 33% 5-year DFS[18]. Moreover, unfortunately around 70%-80% of patients with bilateral CLM recur within five years of surgery, most of them with disease at an extrahepatic site as a component of a recurrence pattern in which a wide resection margin would not really make any difference[12,19,20].

Along with the finding that the width of surgical margin did not correlate with liver recurrence, several surgeons started favoring limited liver resections over major hepatectomies. This laid the foundations for the development of sophisticated techniques to spare liver parenchyma. However, there are special situations where achieving a negative margin might require scarifying more parenchyma than expected by preoperative and intraoperative evaluation. Mentha *et al*[21] found a dangerous halo of re-growing tumor occurring at the periphery of the metastasis when chemotherapy was interrupted before surgery in patients undergoing two-staged liver resections, regardless of previous response. Therefore, a resection margin wider than 1 mm might be especially advisable when chemotherapy is interrupted for a long time before surgery.

Although securing a margin larger than 1 mm should be considered the standard of care, recent evidence suggests that in the era of modern chemotherapy, even patients with microscopic positive margins (R1) may benefit from resection because survival is similar to that of R0 resection and better than chemotherapy alone[22,23]. Moreover it has been demonstrated that the negative impact of positive margins is mainly restricted to patients with suboptimal response to preoperative chemotherapy[24]. Nowadays the paradigm of resectability considers that CLM should be resected regardless of size and number, provided resection is complete (negative margins), the remaining parenchyma is sufficient to prevent PLF and there is no unresectable extrahepatic disease[25].

Tumor biology

There are two known mechanisms for intrahepatic spread of CLM: Metastasis from the primary site and remetastasis from other existing metastases. Most liver metastases arise from circulating tumor cells that have shed into the bloodstream from the primary tumor[26,27]. Given that the distribution of such deposits is random, the presence of a high density of micrometastases in the immediate vicinity of the main tumor indicates that the majority of such micrometastases might have derived from the closest main tumor[27,28]. Contrarily to hepatocellular carcinoma, tumor cells from CLM do not migrate into intrahepatic portal branches to form intrahepatic secondary metastases. Instead, intrahepatic lymphatic invasion is in fact the main responsible for "remetastasis" from liver metastases[28,29]. The incidence and distribution of intrahepatic micrometastases (IHM), defined as any microscopic lesions separated from the gross tumor by a rim of non-neoplastic parenchyma, remains controversial in the literature. Kokudo *et al*[27] demonstrated an incidence of histological IHM of 24%. However, the incidence of genetically confirmed IHM in the study was 2% and they were located within 4 mm of the tumor border. In contrast, Wakai *et al*[28] found in a more recent study an incidence of IHM of 58%, 95% of them located in the close zone (< 1 cm). The differences found in these studies might have been related to different patient populations, IHM detection methods and variable use of chemotherapy, as recent evidence demonstrated that neoadjuvant chemotherapy in CLM reduces the incidence of IHM[30]. Despite the differences found in terms of IHM incidence and location, both studies recognized a 2 mm margin as the acceptable minimum requirement based on survival analysis and margin recurrence[27,28]. Moreover, a recent retrospective study evaluating intrahepatic mechanisms of invasion on patients undergoing resection of CLM demonstrated that lymphatic vascular invasion rather than blood vascular, biliary, or sinusoidal invasion is the key prognostic marker of aggressiveness and spread of CLM, and this feature was evident only within 2 mm from the tumor edge[31].

Segmental resections including tumor-bearing portal branches and the corresponding liver parenchyma in CLM do not appear justified at least from a theoretical point of view. On the other hand, while previous authors have advocated anatomic hepatectomies on the basis of a reduced likelihood of margin involvement, a recent meta-analysis including 1662 patients contradicted this data demonstrating that the incidence of a positive surgical margin was equal in both anatomic resection (AR) and non-anatomic resection (NAR) groups (OR = 0.64; 95%CI: 0.31-1.32; *P* = 0.23)[13]. Moreover, most studies evaluating long-term oncological outcomes have demonstrated that there is no benefit of AR over NAR in terms of 5-year OS and DFS in patients with similar tumor characteristics[13,32]. Other studies have looked specifically at differences between major AR *vs* restricted NAR in patients with limited resectable disease (one or two lesions). Kokudo *et al*[33] demonstrated that prophylactic large resections were useless in preventing intra- or extra-hepatic recurrence in the majority of patients, since ipsilateral recurrence developed in only 19.6% of patients undergoing limited NAR and 90% of such recurrences could undergo second hepatectomy, compared to only 20% in the AR group. In this study, equivalent 5-year OS was reported between major AR *vs* limited NAR (45.7% *vs* 40.4%). More recently, the MD Anderson group[11] found that patients with a solitary tumor of less than 30 mm in size who underwent partial wedge resection instead of right hepatectomy, left hepatectomy or left lateral sectionectomy (LLS) had similar liver-only recurrence rates (14% *vs* 17%, *P* = 0.44) and significantly improved survival due to higher salvageability (68% *vs* 24%, *P* < 0.01). Taken together, this evidence clearly demonstrates that a combination of a first limited NAR followed by repeated hepatectomy in case of recurrence offers equivalent or even more benefits than major hepatectomy in patients with few unilobar metastases and should probably be considered now on the standard of care approach[11,33]. Moreover, although the prognostic significance of micrometastases is still controversial, it should be taken into account that the greater the amount of liver parenchyma resected, the more likely to accelerate the growth of occult intra or extrahepatic disease as a response to growth factors and cytokines produced to stimulate liver regeneration[11,34-36]. This fact might be especially important in patients with aggressive disease behavior. Tanaka *et al*[37] found that the prognosis of patients having 6 or more metastases was poorer after major resection than after multiple minor resections, perhaps due to a more accelerated growth of micrometastases after a massive hepatectomy. Current evidence indicates that the hypothetical benefit of prophylactically resecting more "at-risk" parenchyma where metastases could seed does not really reduce disease recurrence and is counteracted in the clinical setting by increased patient risk, more tumor stimulation and less chances of future repeated resection. Thus, it seems to be that tumor biology (as expressed by primary tumor stage, preoperative CEA level, number and size of metastatic tumors, time from primary tumor treatment to hepatic metastases, preexisting occult metastases and the presence of extrahepatic disease) rather than the number of millimeters present at a negative surgical margin, is the most important factor determining survival in patients with CLM.

PREOPERATIVE ASSESSMENT AND PATIENT SELECTION

All patients with CLM should be discussed at a multidisciplinary tumor board and considered eligible for surgery with curative intent on a case-by-case basis. Either patients with single or multiple liver metastases are potentially eligible for a parenchymal-sparing type of surgery as has been demonstrated by several authors[11-13,33,37]. Preoperative staging should include a multislice computed tomographic (CT) scan of the abdomen and chest, as well as an abdominal magnetic resonance imaging (MRI) for a better assessment of patients with small lesions, a fatty liver or preoperative chemotherapy[38]. Positron emission tomography (PET) scan should be considered in case of tumor recurrence in patients with a previous liver resection or suspected distant metastasis.

Eligibility for surgery should be determined taking into account three aspects: (1) risk perspective; (2) technical resectability; and (3) oncological rationality. With regards to risk perspective, medical fitness for general anesthesia and major abdominal surgery (anesthesiological risk and patient fragility) has to be carefully evaluated preoperatively. In certain cases, this includes the evaluation of the underlying parenchymal status and function. Surgeons should be especially careful with obese patients and those who have undergone long-course chemotherapy regimens, consequently adjusting the volume of the predicted FLR to its respecting quality. For patients with normal hepatic function, a FLR of approximately 25% of total liver volume is considered sufficient to maintain liver function after resection[39]. On the other hand, in patients with hepatic dysfunction or liver injury (*e.g.*, because of chemotherapy) a FLR of at least 40% of total liver volume is highly recommended[40]. The surgical indication should therefore be tailored according to the existence of both patient and liver-related operative risks. PSLS might be particularly beneficial for patients with a high operative risk for major resection, who would otherwise not be candidates for resection. From a technical perspective, the availability of state-of-the-art abdominal imaging is crucial to define resectability and to plan the optimal surgical procedure. However, given the widely varying concept of resectability among surgeons, as evidenced by the literature[41], surgical exploration should be undertaken at specialized centers only when the surgical team strongly believes that a potentially curative operation will be feasible. Even though resection with negative margins of every CLM is the preferred treatment option, it has to be remarked that when selecting candidates for PSLS, the combination of resection of most lesions with radiofrequency ablation of those unfavorably located could be considered for certain patients in order to offer the best possible survival[12,42]. From an oncological perspective, evaluation of extrahepatic disease and its resectability, as well as the response to pre-operative systemic therapy in patients with dismal prognostic factors are main considerations, as they are the most likely to benefit from this approach. Thus, associating an acceptable patient risk with a safe technical proposal and a reasonable oncological indication should be the goal of liver surgeons when selecting candidates for PSLS. As in any type of liver resection, unresectable extrahepatic metastases or unresectable primary tumor, prohibitive anesthesiological risk and medical contraindications to hepatectomy still constitute contraindications for resection.

IMAGING TECHNIQUES AND OPERATIVE PLANNING

Operative planning is the key for successful treatment in patients with CLM. As mentioned before, a parenchymal-sparing approach should be preferred whenever possible. Hepatic surgery has evolved greatly in the last 20 years and advances in complementary imaging studies have played a key role in this development.

Imaging techniques

Operative planning is essentially based on imaging techniques, both pre- and intra-operatively, since the type of surgical procedure will be personalized to each patient according to the size, location and number of tumors. In the preoperative setting, multislice CT-scan utilizing tri-phase contrasted acquisitions is still the standard imaging modality for the liver, and while it is principally used for the evaluation of liver tumors, it also provides useful information about the quality of liver parenchyma, vascular distribution, total and partial liver volumes, *etc.*[43]. Nowadays multislice CT angiography with three-dimensional (3D) reconstruction has replaced hepatic angiography for the preoperative study of vascular liver anatomy. Regarding specifically CLM evaluation, recent evidence suggests that MRI offers superior sensitivity and specificity compared with CT-scan, particularly for the detection of lesions measuring less than 1 cm[38]. Diffusion-weighted imaging techniques of MRI improves the diagnostic accuracy because of the differences in proton diffusion between benign and malignant tissue, the last showing in general a more restricted diffusion. Furthermore, the recent introduction of new liver-specific MRI contrast agents has further improved the capacity of MRI for detecting and characterizing small lesions[38].

With regards to the intraoperative scenario, ultrasonography deserves a particular mention since it stands out as the most important imaging aid to the surgeon and PSLS is essentially an ultrasonographically-guided surgical approach[44,45]. After being described by M. Makuuchi in 1977, intraoperative ultrasound (IOUS) exploration of the liver has gained increasing protagonism and is nowadays a fundamental component of modern liver surgery. IOUS guidance is crucial to fulfill the objective of PSLS, which is essentially to minimize resection margins while keeping the oncological radicality, reducing the rate of major hepatectomies and whenever possible avoiding the need for strict anatomic approaches. IOUS should be the first step of any liver surgery and has to be always carried out personally by the surgeon in charge rather than an assistant, radiologist or technician. It allows to confirm the findings of preoperative images, evaluate vascular anatomy, study the tumor-vessel relationships, assess the direction of portal flow and to guide the planned type of resection or ablation. Therefore, state-of-the-art color Doppler ultrasonography equipment with standard convex, microconvex and T-shaped probes should be present in the operative room. The liver is usually evaluated at 5 and 7.5 MHz[44,45]. The preferred probes to obtain the best images without artifacts are those that can be sterilized and then stay in direct contact with the liver surface. If available, contrast-enhanced IOUS (CE-IOUS) may help intraoperative staging and assessment of tumor relation with the liver vascular structures. This seems to be especially important in patients who received preoperative chemotherapy, scenario in which Ruzzenente *et al*[46] found that CE-IOUS allowed detecting additional lesions in 14% of patients and changing the operative management in 18% of patients, therefore improving both the sensitivity of IOUS to detect CLM and the R0 resection rate.

Although standard IOUS provides real-time visualization of anatomic structures, limitations may arise from the 2D nature of the images. Recent technological advances have enabled operation planning using 3D image-processing software for both CT and US[47,48]. Detailed 3D anatomical information could facilitate complete tumor removal while preserving a sufficient amount of functional liver tissue especially in complex liver surgery and interventional treatments. Those who favor navigation in liver surgery argue that this technology is not only useful for guiding surgical instruments during resection or ablation, but also for the treatment of patients who have received chemotherapy prior to liver resection or who have steatosis, where liver parenchyma is often difficult to evaluate with conventional US. However, despite several efforts to make real-time navigation feasible, some limitations continue to hamper its clinical application. Lack of millimetric accuracy, deformation of the liver parenchyma during resection, and breathing movements are some of the most important criticisms of this method. Recent preliminary studies using navigation systems that integrate IOUS, preoperative CT imaging and 3D anatomic models on a single display have shown promising results[49]. Real-time navigation systems might become in the near future an important adjunct for safe liver resections, although its actual applicability for PSLS has not been consistently proven yet.

Operative planning

The final technical strategy should be decided upon

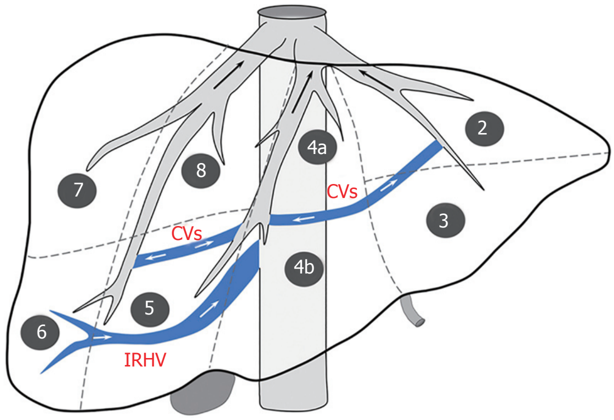

Figure 1 Diagram of liver segmentation and the anatomical variations of hepatic outflow important for parenchymal-sparing liver resections. CVs: Communicating hepatic veins; IRHV: Inferior right hepatic vein.

completion of IOUS assessment, based on the following: Unexpected discovery of new lesions or invasion of vascular structures, FLR volume, chemo-related liver toxicity and the need to perform simultaneous resection of the primary tumor or adjacent organs. Atypical resections can be used for peripheral lesions, but some tumors might require larger and eventually anatomical resections only because they are located centrally or in the vicinity of major portal pedicles or hepatic veins (HVs). With specific regards to the feasibility of PSLS related to vascular proximity, Torzilli *et al*[50] proposed certain criteria to define operative strategy. Whenever a tumor is near a HV close to the hepato-caval confluence and either of the following is present: (1) the tumor is not separated by a thin layer of liver parenchyma; (2) there is vessel wall discontinuation; or (3) the contact exceeds 1/3 of the vessel diameter; the vessel has to be sacrificed and AR of the segment/s (S) is many times necessary to avoid the risk of congestion if certain vascular variations are not present. In this scenario, after HV resection, the drained liver can't be spared and if the FLR is not sufficient to allow major resection, HV reconstruction could represent the only surgical option[51]. Similarly, when a tumor is near a Glissonean pedicle and contact exceeds 2/3 of the diameter or a distal bile duct dilatation is present, it is mandatory to sacrifice the corresponding anatomic territory[52].

Anatomical principles

The vascular anatomy of the liver should be thoroughly assessed with imaging methods before PSLS. Hepatic venous variants, as well as the pattern of venous drainage into the inferior vena cava (IVC) need to be specially investigated[53]. This is particularly important when en-block resection of a HV and part or the entire adjacent liver segment/s needs to be performed for tumors involving HVs at the hepato-caval confluence.

More frequently, the right HV (RHV) drains S5, 6, 7 and 8; the middle HV (MHV) drains S4, 5 and 8; and the left HV (LHV) drains S2, 3 and 4. However, S6 may have an independent drainage directly into the IVC[53]. Although this accessory HV is present in most patients (86%-100%), it is larger than 0.5 cm in less than a quarter of them, representing a variant know as inferior right HV (IRHV)[53,54]. Another important anatomical variation is the presence of communicating veins (CVs), which connect adjacent HVs, and have been demonstrated using IOUS in up to 80% of patients with CLM at the hepato-caval confluence[55]. The detection of the IRHV or CVs between adjacent HVs in cases with hepato-caval confluence compromise may enable safe conservative hepatectomies instead of major resections or complex vascular reconstructions (Figure 1)[45,51]. However, to guarantee the safety of the procedure, a HV should be resected only after intraoperatively testing the proper function of these variants. As proposed by Torzilli[52], the feeding portal branch of the segment to be spared must preserve hepatopetal blood flow (rather than hepatofugal) on Doppler US when the HV/s is occluded by using a clamp or just the fingers. Systematically using this method, these authors observed that only 2 out of 22 patients with involvement of HVs needed a major hepatectomy, and none underwent vessel reconstruction[45].

SURGICAL TECHNIQUES

Once the feasibility of PSLS has been determined pre- and intra-operatively, resection can be carried out. Different kinds of resections have been proposed in order to maximize the amount of liver parenchyma after resection. The consideration of a certain technique as parenchymal-sparing depends on each patient. Almost any type of hepatic resection could be considered as sparing whenever it involves the willing of performing a certain procedure over another that compromises more liver parenchyma (*e.g.*, a major central hepatectomy may be excessive for a peripheral lesion involving both S5 and 4b, but it becomes a parenchymal-sparing approach if used instead of a hemi-hepatectomy right or left for a patient with a large centrally located tumor).

From a technical point of view and for the purpose of this review, PSLS could be considered as every type of liver resection not conforming an AR of a hemiliver or extended resections as defined by the standardized Brisbane 2000 nomenclature, proposed by the International Hepato-Pancreato-Biliary Association[56]. The sole exception to these rule would be LLS, because the left lateral liver accounts for more than 20% of total liver volume in one out of every four patients, and its preservation is always desired to increase future salvageability[11,57]. PSLS includes both segment-oriented and non-segment-oriented variants, either as isolated procedures or in combination. The different proposals reported in the literature are summarized in Table 1. In general, segment-oriented resections are reserved for patients with multiple tumors within a single anatomic segment or those in whom the tumor is located centrally and invading the major portal pedicle or HV to an anatomic segment/s[58]. In theses cases transection

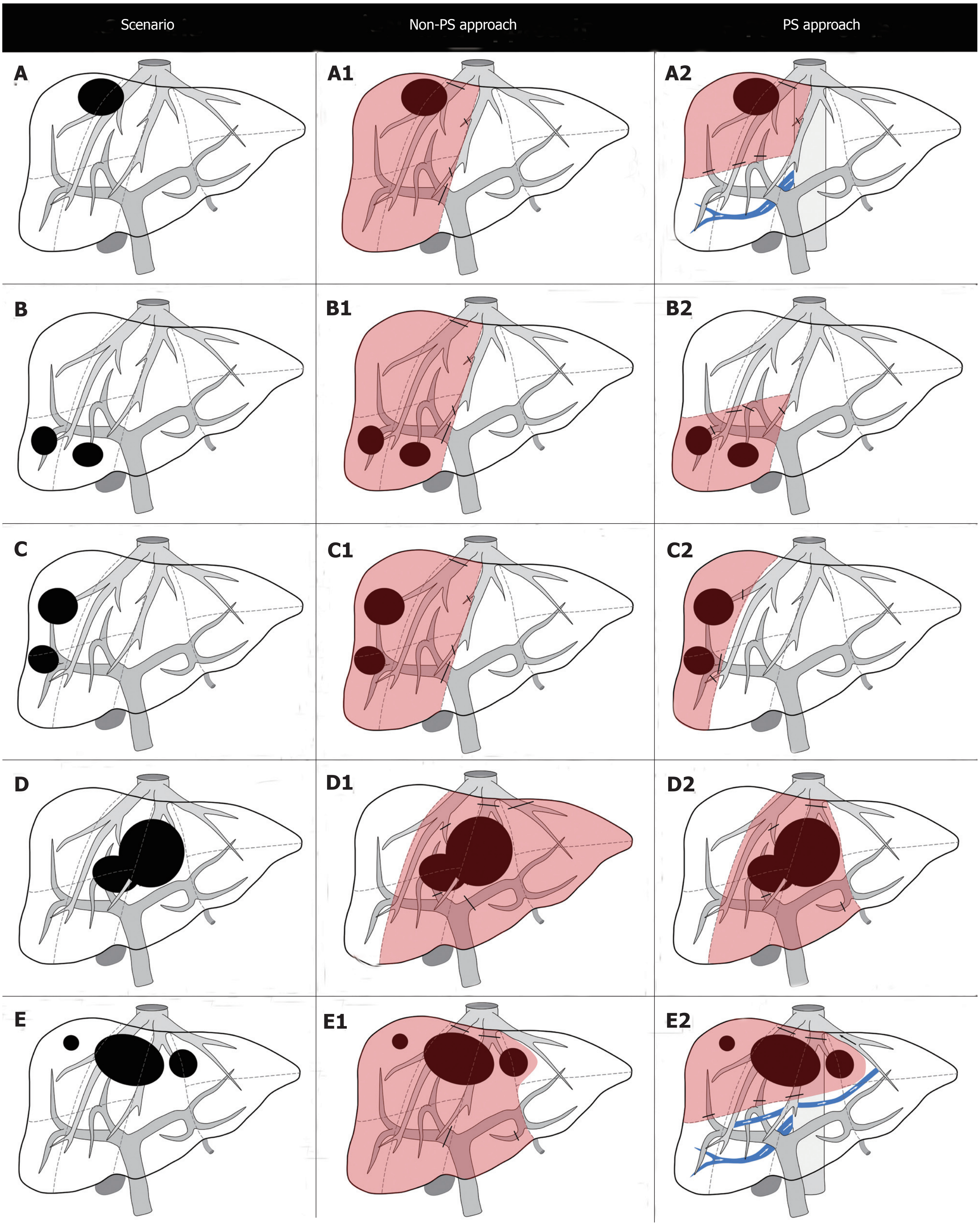

Figure 2 Diagram of segment-oriented parenchymal-sparing resections according to different surgical scenarios. A: Metastatic lesion infiltrating the RHV; A1: Right hepatectomy; A2: Bisegmentectomy 7-8 is possible due to the presence of an IRHV; B: Metastatic lesions located in S5-6; B1: Right hepatectomy; B2: Bisegmentectomy 5-6; C: Metastatic lesions in right posterior section; C1: Right hepatectomy; C2: Right posterior sectionectomy; D: Large central tumors invading the MHV; D1: Left trisectionectomy; D2: Central hepatectomy; E: Metastatic lesions invading the RHV and the MHV; E1: Right trisectionectomy extended to S2; E2: Upper transversal hepatectomy is possible due to the presence of an IRHV and communicating hepatic veins. PS: Parenchymal-sparing; RHV: Right hepatic vein; IRHV: Inferior right hepatic vein; MHV: Middle hepatic vein.

lines are based on the combination of external anatomic landmarks, selective devascularization by clamping

Table 1 Different parenchymal-sparing operative procedures

Type of resection	Segment/s resected
Segment-oriented	
Monosegmentectomy	Any isolated segment
Bisegmentectomy	Two contiguous segments
Right posterior sectionectomy	S6 and 7
Right anterior sectionectomy	S5 and 8
Right inferior bisegmentectomy	S5 and 6
Right superior bisegmentectomy	S7 and 8
Central anterior bisegmentectomy	S4b and 5
Central posterior bisegmentectomy	S4a and 8
Left medial sectionectomy	S4a and 4b
Central hepatectomy	S4, 5 and 8
Upper Transversal Hepatectomy	S7, 8, 4a and 2 + RHV and MHV
Non-segment-oriented	
Corkscrew technique	Any segment
Mini-mesohepatectomy	Partial S8 and 4a + MHV
Mini upper-transversal hepatectomy	Partial S7, 8 + RHV
Hepatic Vein-Sparing Hepatectomy	Partial S7, 8, and 4a ± 1 paracaval
Systematic extended right posterior sectionectomy	Complete S6-7 + partial S5 and/or S8 (en-block)
Liver tunnel	Partial S4a, 8 and 1
Lower inferior hepatectomy	S3, 4b, 5, 6 and 7
Local ablation[1]	Any

[1]Combined with other surgical resection. MHV: Middle hepatic vein; RHV: Right hepatic vein.

to create ischemic margins and intraoperative US. Segment-oriented operative procedures for PSLS are depicted in Figure 2. Non-segment-oriented resections (also referred as atypical or wedge resections) are usually applied for lesions smaller than 5 cm and located near the liver surface. Since anatomical boundaries are not respected, the use IOUS to guide this type of resection is paramount to clearly identify all the bile ducts and vascular branches. For non-large atypical resections, the "corkscrew technique" proposed by de Santibañes *et al*[59] is especially useful. In this particular technique, the liver surface is marked with electrocautery and stiches are placed surrounding the lesion in order to easily achieve traction and countertraction of the liver, thus facilitating the identification of biliary ducts and vascular branches. Non-segment-oriented operative procedures for PSLS are depicted in Figure 3.

Even though most patients treated by PSLS are usually approached by a J-shaped or bilateral subcostal incision with upper midline extension, Torzilli *et al*[44] recommends a J-shaped thoracophrenolaparotomy for cases with tumors involving S1, 4a, 7, and 8 close to the HV confluence into the IVC. Regarding parenchymal transection, no study has consistently demonstrated significant differences among the various existing techniques up to date. However, it is strongly recommend to use the cavitron ultrasonic surgical aspirator (CUSA) for PSLS since it facilitates a meticulous transection and provides an additional margin beyond that examined by the pathologist. This has been recently associated with an advantage in case of limited margins[18,60,61].

There are some especially sophisticated IOUS-guided variants of PSLS that deserve to be addressed independently.

Bisegmentectomy 7-8 or right superior bisegmentectomy

Metastatic lesions located in S7-8 that infiltrate the RHV have been traditionally treated with a right hepatectomy given that the right hemiliver is theoretically drained totally (S6, 7) or partially (S5, 8) by the RHV (Figure 2A). The presence of an IRHV, allowed Makuuchi *et al*[62] in 1987 to report the first resection of S7-8 en-block with the RHV sparing S5 and S6 without congestion. Although the presence of IRHV is paramount when considering the possibility of sacrificing the RHV, Machado *et al*[63] and Capussotti *et al*[54] described the feasibility of resecting S7-8 and the RHV without an IRHV. These experiences were based on the anatomical assumption that S6 has several venous anastomoses with S5 and the latter drains into the MHV. The presence of these CVs was later confirmed by Torzilli *et al*[55] using high-frequency IOUS. In summary, a 7-8 bisegmentectomy with RHV resection can be performed safely when: (1) an IRHV is present; (2) CVs connecting the RHV with MHV are recognized; and/or (3) hepatopetal rather than hepatofugal blood flow is maintained in the feeding portal branch by color Doppler IOUS after clamping the RHV.

Mesohepatectomy or central hepatectomy

When a tumor invades the MHV at the confluence with the IVC or large central tumors are present, formal anatomic extended hepatectomies are performed by most surgeons (Figure 2D). The resection of central hepatic segments (Couinaud's S4, 5, and 8), was first proposed by McBride *et al*[64] in 1972 and later validated by others as a conservative alternative, preserving more functioning liver tissue than either left or right trisectionectomy[65,66]. Central resection could also be less extensive; either including S4b and S5 (anterior central) or S4a and S8 (posterior central). Despite being a technically demanding major resection, mesohepatectomy represents a valuable alternative to extended hepatectomy since its complication rate, postoperative recovery, and preserved liver tissue compare favorably with extended hepatic resections.

Mini-mesohepatectomy

In order to avoid major resection, mini-mesohepatectomy (MMH) has been designed by Torzilli *et al*[67] specifically for non-large tumors (< 5 cm) invading more than 2/3 of the circumference of the MHV close to the hepato-caval confluence (within 4 cm) (Figure 3B). It is defined as the partial removal of S8 and/or S4a including the involved tract of MHV[68]. To carry out this technique, as for RHV ligation, at least one of these 3 criteria must be present when the surgeon fingertips compress the MHV: (1) reversed flow direction in the peripheral portion of the MHV, which suggests drainage through collateral circulation in adjacent HVs or IVC;

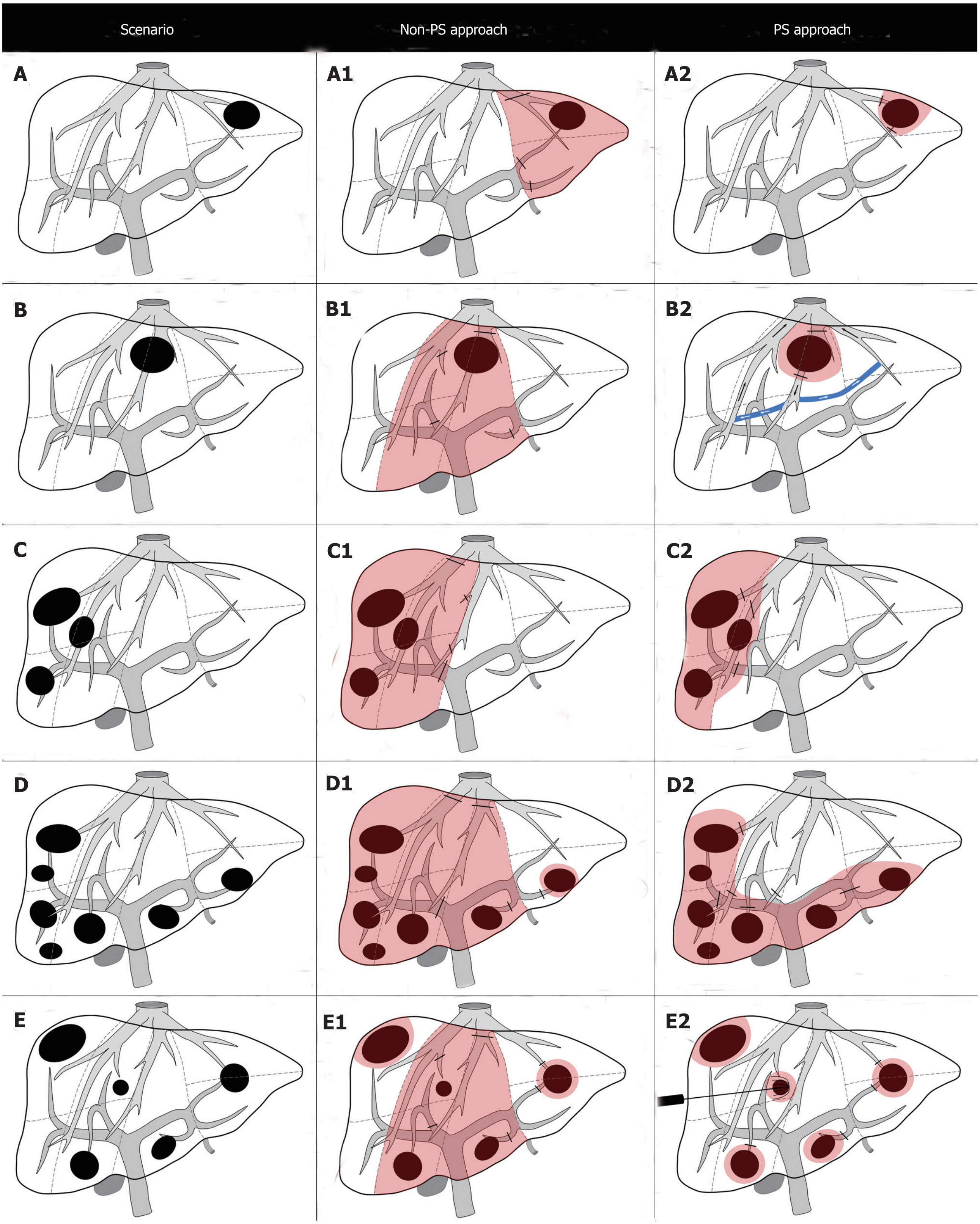

Figure 3 Diagram of non-segment-oriented parenchymal-sparing resections according to different surgical scenarios. A: Metastatic lesion in S2; A1: Left lateral sectionectomy; A2: Atypical resection of S2; B: Metastatic lesion infiltrating the MHV close to the hepato-caval confluence; B1: Central hepatectomy; B2: Mini-mesohepatectomy is possible due to the presence of communicating hepatic veins; C: Metastatic lesions in right posterior section invading the RHV and tumor in proximity of right anterior portal branch; C1: Right hepatectomy; C2: Systematic extended right posterior sectionectomy; D: Liver metastases peripherally located in S3, 4b, 5, 6 and 7; D1: Right trisectionectomy; D2: Lower inferior hepatectomy; E: Multiple bilateral metastases; E1: Atypical resections combined with central hepatectomy; E2: Multiple atypical resections combined with radiofrequency ablation. PS: Parenchymal-sparing; RHV: Right hepatic vein; MHV: Middle hepatic vein.

(2) detectable shunting collaterals between MHV and RHV or LHV; and (3) hepatopetal flow in S5, 8 and/or

S4b portal branches. The posterior wall of the MHV or of the tumor itself is used as the deepest landmark of the resection area. A crucial point is to delineate a transection plane that does not interrupt CVs. This is obtained by dividing the MHV the closest possible to its point of infiltration using IOUS guidance, preserving its distal portion for collateral circulation. Even though this interesting surgical proposal provides an alternative to limit the use or even replace central hepatectomy in certain cases, further validation of its efficacy and safety is awaited before expanding its application.

Upper transversal hepatectomy

This type of parenchymal-sparing resection, proposed by Torzilli *et al*[69], is specifically useful for tumors involving the RHV and MHV, or even all HVs at the hepato-caval confluence (Figure 2E). These cases are considered irresectable by most surgeons. However, a major hepatectomy with vascular reconstruction represents the only option offered by others. This last can be avoided when CVs between adjacent HVs are detected intraoperatively with US[69]. Upper transversal hepatectomy involves total or partial resection of the superior liver segments (S7, 8, 4a and 2) accompanied by the RHV and MHV or even all HVs. It can be performed only when an IRHV is present simultaneously with CVs connecting the IRHV with the MHV and the MHV with the LHV. After checking the function of the complete inter-venous circuit by IOUS and certifying the absence of macroscopic congestion, resection is IOUS-guided preserving the CVs. More recently, an even more conservative variant of this approach has been proposed also by Torzilli *et al*[70], denominated "mini upper-transversal hepatectomy".

HV-sparing hepatectomy

This approach has been recently introduced by Torzilli *et al*[71] for metastases located in S8, 4a involving both the RHV and MHV at the hepato-caval confluence but neither the IRHV nor CVs are present at imaging. In such cases, when vascular invasion comprises 1/3 of their circumference or less, partial resection of S7, 8, and 4a ± 1 paracaval can be performed sparing both RHV and MHV by partial resection and reconstruction by running suture. This approach has been proposed as an effective alternative to major resection performed immediately or in a staged perspective[71].

Systematic extended right posterior sectionectomy

In case of vascular invasion of the RHV with multiple tumors in the right posterior section, and/or invasion of the right posterior portal branch (P6, 7) with tumor in close adjacency (< 5 mm) with right anterior portal branch (P5, 8), right hepatectomy is traditionally performed (Figure 3C). Systematic extended right posterior sectionectomy (SERPS) has been proposed by Torzilli *et al*[72] as an alternative approach, performing a right posterior sectionectomy with a tailored extension to the right anterior section, either the right part of segment 8 ± the RHV and/or the right part of S5 exposing but not dividing the pedicle of S5, 8 on the cut surface just enough to guarantee complete tumor removal. In all the aforementioned conditions, portal blood flow at color-Doppler IOUS in the pedicle of S5, 8 (right anterior glissonean sheath) has to be hepatopetal once RHV is clamped for carrying out SERPS. SERPS serves also as an alternative to right hepatectomy when bisegmentectomy 7-8 is not possible (in cases where there is vascular invasion of the RHV but without tumor involving S6) because there is not a proper outflow for S6 once RHV is divided (absence of IRHV and hepatofugal portal blood flow at Doppler IOUS in P6 when RHV is clamped). IOUS-guided SERPS has proven to be feasible, safe and effective[72]. Preserving the majority of the right anterior section (S5, 8) is utmost important, as the right anterior section of the liver is most relevant in terms of volume[73,74]. In a previous prospective series including 201 patients, SERPS was performed more frequently than right or extended right hepatectomy (10% *vs* 9%), avoiding such major resections[72].

Other types of parenchymal sparing resections

There have been anecdotal reports of exceptional strategies of PSLS[52]. The so-called "liver tunnel" represents an extension of the MMH in patients with central tumors compromising the MHV but extending from S8 vertically to S1 and the "lower inferior hepatectomy" represents the atypical en-block resection of S3, 4b, 5, 6 and 7 for liver metastases peripherally located in these segments (Figure 3D). These particularly challenging approaches deserve further validation in larger series of patients before expanding its application.

Combination of resection with local ablation

As the indications for surgical treatment of CLM have broadened, the use of multimodal therapies has become more common. Nowadays, the use of interstitial treatments (radiofrequency or microwaves) to compliment resectional strategies has proven to be a useful and rationale approach to treat patients with multiple lesions when complete resection of all metastases is not possible, therefore extending the limits of surgical treatment[12]. In this combined approach, hepatectomy addresses the main tumor mass and the residual tumor that cannot be resected is treated with local tumor-ablative therapy (Figure 3E). Ideally, lesions treated with RFA should be less than 25 mm in size, since technically successful ablation is possible in more than 90% of the cases[74]. However, a recent retrospective study evaluating recurrence patterns of CLM treated with ablation, found that ablation was more effective for metastases of size equal to or smaller than 10 mm[75]. This combined approach has not been associated with a compromise in disease-specific survival[12], while demonstrated a reduction in the need of major resections and two-stage procedures, offering the possibility of repeated treatments for recurrences with reduced morbidity[42,50].

USE OF LAPAROSCOPY IN PARENCHYMAL SPARING RESECTIONS

The advantages of laparoscopic hepatic resection *vs* open surgery in the perioperative period (*e.g.*, less blood loss, fewer complications, and shorter duration of hospitalization) as well as favorable cosmetic results have been well recognized in the literature[76]. In addition, there is an increase body of evidence indicating that laparoscopic approach does not compromise oncological principles in selected patients[76,77]. Traditionally, laparoscopy has been mostly used for small and subcapsular liver lesions located in peripheral liver segments (S2, 3, 4b, and 5). With regards to laparoscopic PSLS, from the beginning of laparoscopic liver surgery a parenchymal-sparing philosophy has been applied and limited NAR of accessible segments dominated the scene. Along with increasing experience in laparoscopic liver surgery, more complex laparoscopic liver resections are being practiced to treat central liver lesions or those ill located in posterior and superior segments. Recent evidence presented by experienced surgical teams demonstrates that segment-oriented parenchymal-sparing variants can be performed safely using laparoscopy[78]. A recent retrospective study concluded that laparoscopic liver resection with a parenchymal-sparing approach does not worsen oncological outcome, allowing a higher percentage of repeat hepatectomy[79]. Montalti *et al*[80] showed that the laparoscopic parenchyma-preserving approach with the CUSA is possible and that R1 margins are a risk factor for tumor recurrence but not for OS. A major limitation for this technique was the presence of multiple lesions since it was identified as the only independent risk factor for R1 margins[80]. More recently, robot-assisted liver surgery has been introduced as a minimally invasive alternative to facilitate the parenchymal-sparing treatment of lesions located in the posterosuperior segments or when portal triad dissection is necessary, suggesting the potential of robotics to resemble techniques and outcome of open PSLS[81]. The routine use of laparoscopic IOUS is as important as in the open approach and have also been highlighted in the literature[82].

During the 2nd international consensus conference for laparoscopic liver resection held in Morioka (Japan) in 2014[76], it was noted as a concern that larger procedures resecting more liver parenchyma are sometimes favored if the procedure is done laparoscopically because a smaller parenchyma-sparing operation may be more complex laparoscopically. As well, there has been a tendency towards more LLS instead of atypical resections to facilitate laparoscopic treatment of single or few small sized metastases located in the left lateral segment. However, recent data in patients with single lesions supports atypical resection over LLS, demonstrating increased future salvageability and survival[11]. Therefore, in light of this new evidence, LLS should be discouraged from now on, for lesions amenable to atypical resection even when performing laparoscopic surgery.

SHORT AND LONG-TERM OUTCOMES

As mentioned previously, PSLS encompasses a wide variety of surgical alternatives for a heterogeneous population of patients, therefore outcome analysis can be very complex. In terms of comparative studies, Torzilli *et al*[72] compared SERPS with right hepatectomy in patients matched for age, tumor size and number. They found that SERPS resulted in significantly less blood loos, less transfusions, less portal pedicle clamping with similar operative length, hospital stay and safety profile. Similarly, Ferrero *et al*[83] demonstrated that bisegmentectomy instead of right hepatectomy improves postoperative outcomes, offering similar survival results and increasing the opportunity to re-resection in patients with CLM of ≤ 10 cm located in the right liver lobe. Despite these few reports, for the purpose of the present review, probably the most practical way to evaluate outcomes would be to consider PSLS as the philosophy of saving parenchyma and compare it against a non-saving parenchyma philosophy, rather than each different technical variant evaluated separately. The comparison that most resembles this scenario, and even gave rise to the debate, is that of AR *vs* NAR in patients with CLM. There have been many studies in the literature aiming to compare the outcomes of these opposite approaches with similar results (Table 2).

Operative results and complications

From the short-term perioperative results perspective, several groups have experienced better perioperative outcomes with the increased use of a parenchymal-sparing policy[11-13]. This association correlates well with findings from large series demonstrating that the number of segments resected is an important determinant of outcomes[84,85]. In 2008 the MSKCC group evaluated a series of 440 patients operated on for bilateral CLM from 1992 to 2003, dividing the study in four time-periods with the purpose of determining trends over time[12]. They found a significant trend away from large resections in favor of multiple smaller resections despite patient and tumor variables did not change over time. A significant drop in 90-d mortality (from 6.3% to 1.2%, P = 0.02); operative blood loss (from 950 to 490 mL, P < 0.001) and length of hospital stay (from 12 to 9 d, P < 0.001) was observed occurring simultaneously with the increased application of parenchymal-sparing techniques[12]. In a retrospective

Table 2 Overview of the different comparative studies involving non-anatomic resection in patients with colorectal liver metastases

Ref.	Year	Groups (*n*)	Hospital stay (d)	Morbidity (%)	Mortality (%)	Operative time (min)	Blood loss (mL)	Margin + (%)	5-year DFS (%)	5-year OS (%)	Matching[2]
Mise *et al*[11]	2015	AR (144) *vs* NAR (156)	NA	36 *vs* 36	1 *vs* 0	128 *vs* 150	200 *vs* 100[3]	5 *vs* 2	NS	NS	1-8, 10
Von Heesen *et al*[89]	2012	AR (47) *vs* NAR (61)	NA	NA	NA	In favor of NAR[3]	In favor of NAR[3]	NA	37 *vs* 27	37 *vs* 48	NA
Lalmahomed *et al*[32]	2011	AR (88) *vs* NAR (113)	8 *vs* 7[3]	27 *vs* 23	2 *vs* 1	NA	NA	9 *vs* 11	30 *vs* 32	49 *vs* 39	1-4, 6-10
Sarpel *et al*[86]	2009	AR 94 *vs* NAR 89	8 *vs* 6[3]	NA	3 *vs* 0	NA	NA	1 *vs* 6	NS	NS	1, 2, 6, 9
Guzzetti *et al*[88]	2008	AR 102 *vs* NAR 106	9 *vs* 8	8.8 *vs* 16	0 *vs* 0	300 *vs* 240[3]	700 *vs* 500[3]	20 *vs* 11	NS	27 *vs* 29	1-8, 10
Finch *et al*[61]	2007	AR 280 *vs* NAR 96	NA	29 *vs* 15	4.4 *vs* 0	NA	NA	25 *vs* 33	35 *vs* 24	50 *vs* 54	1, 2, 8, 9
Zorzi *et al*[87]	2006	AR 181 *vs* NAR 72	7 *vs* 7	23 *vs* 28	1.1 *vs* 1.4	NA	NA	8.3 *vs* 8.3	NA	60 *vs* 61	1-3, 6-9
Kokudo *et al*[33]	2001	AR 96 *vs* NAR 78	NA	12 *vs* 6.4	2.1 *vs* 0	315 *vs* 259[3]	1489 *vs* 895[3]	27 *vs* 20[1]	NA	46 *vs* 40	1-4, 6
DeMatteo *et al*[90]	2000	AR 148 *vs* NAR 119	8 *vs* 9	20 *vs* 13	0.8 *vs* 0.4	198 *vs* 189	531 *vs* 456	2 *vs* 16[3]	NA	49 *vs* 37[3]	1-3, 6-8

[1]Margins < 2 mm; [2]Matching: 1 = age; 2 = gender, 3 = number of tumors; 4 = tumor distribution; 5 = tumor size; 6 = primary tumor site; 7 = node positive primary; 8 = preoperative carcinoembryonic antigen level; 9 = synchronous disease; 10 = disease-free interval. [3]Statistically significant difference ($P < 0.05$). NAR: Non-anatomic resection; NA: Not-available; NS: Not-stated in the original article because of non-significant difference; DFS: Disease-free survival; OS: Overall survival. AR: Anatomic resection.

study comparing major AR *vs* minor NAR in 174 patients, Kokudo *et al*[33] found that the mean operating time and operative blood loss were significantly greater during AR. These findings are in accordance with those of Sarpel *et al*[86], who reported significantly more blood transfusions in patients who underwent AR compared to NAR (44% *vs* 16%, $P < 0.001$), despite Pringle time was similar between groups (11 ± 7 min *vs* 10 ± 7 min, $P = 0.313$). Even though several more recent series have confirmed a significant advantage in terms of operating time and blood loss during NAR[11], in most studies this was not translated into a significant difference in morbidity or mortality, probably owing to an insufficient number of patients studied and the retrospective nature of the analyses[32,33,86-88]. A recent meta-analysis of non-randomized studies was designed as an attempt to overcome these limitations[13]. Among 1662 subjects with CLM, 989 underwent AR and 673 underwent NAR. The meta-analysis demonstrated that NAR reduced the operation time and blood transfusions, whereas it confirmed that overall morbidity (22.1% AR *vs* 16.6% NAR, $P = 0.32$) and mortality were similar between the two groups (0.9% AR *vs* 0.7% NAR, $P = 0.68$). However, it has to be taken into account that significant heterogeneity across studies was present for some of these variables. In a recent comparative study of patients matched for clinical characteristics and tumor size, the MD Anderson group found that parenchymal-sparing resection was associated with significantly reduced blood loss but equal morbidity (23% *vs* 26%, $P = 0.54$), major complications (3% *vs* 6%, $P = 0.21$) and 90-d mortality (0% *vs* 1%, $P = 0.23$) compared to non-parenchymal-sparing resection[11]. Conversely, when analyzing specifically liver-related morbidity, Gold *et al*[12] showed that AR were independently associated with higher liver-related complications as opposed to wedge resections. Moreover, von Heesen *et al*[89] found that AR had a significant higher incidence of pleural effusions requiring interventional drainage than NAR and combined resections.

Oncological results

In terms of oncological long-term results, one of the main concerns regarding PSLS has been the specimen margin status and the fact of leaving more at-risk liver parenchyma behind where liver metastasis could seed, with their potential negative impact in patient survival. So far, none of these concerns has found a solid scientific background in the current clinical field.

Among the few authors who advocated non-parenchymal-sparing resections for CLM during the 1990s, DeMatteo *et al*[90] presented one of the most controversial evidence in 2000. In their series of 267 patients, AR resection had a significantly lower rate of positive margins compared to NAR (2% *vs* 16%, $P < 0.001$) resulting in longer survival for AR on univariate analysis (53 mo *vs* 38 mo, $P = 0.015$). In a larger study published 8 years later, the same group found that although the width of negative margin using wedge resection was significantly less than when wedge resection was not used (mean 0.5 cm *vs* 0.8 cm, $P = 0.02$), margin positivity did not correlate with the use of a wedge resection ($P = 0.40$)[12]. More recent studies involving modern approaches reported that the incidence of a positive surgical margin was equal for AR and NAR either with single or multiple liver lesions[11,32,61,86-88]. A recent meta-analysis confirmed these results[13].

With regards to recurrence and survival, the majority of reports have found no significant differences according to the type of hepatectomy performed. The study published in 2009 from the Mount Sinai Medical Center found that the type of resection was not associated with significant differences in recurrence or survival even when adjusted for differences in preoperative risk[86]. Another study by Lalmahomed *et al*[32] reported comparable median time to recurrence between AR and NAR (9 mo *vs* 10 mo, *P* = 0.802) in 201 patients with single or multiple liver metastases. In addition, the pattern of recurrence in terms of location and 3-year intrahepatic recurrence rate did not differ between the two groups[32]. The 5-year DFS and OS were also similar for AR and NAR (30% *vs* 32%, *P* = 0.599; 49% *vs* 39%, *P* = 0.989). These findings were later confirmed by the meta-analysis by Sui *et al*[13], where 5-year OS was not significantly different between the two groups (OR = 1.13; 95%CI: 0.92-1.39, *P* = 0.24). Regarding 5-year DFS, even though no significant difference was shown between the groups, the marked heterogeneity between studies raises questions about the validity of this data. In order to overcome the effects of differences in the number of liver tumors that might influence patient survival between types of resections, some authors individualized patients with multiple metastases and analyzed them separately. In this regard, in the study presented by Tanaka *et al*[37], from Yokohama city in 2008, among the subgroup of patients with six or more metastases, the overall survival of those who had a major resection was significantly poorer than those who had minor resections (*P* = 0.028), although the clinical characteristics were comparable between the two groups. On the other hand, in the MSKCC study from the same year regarding the unique subgroup of patients with multiple bilateral lesions, the use of wedge resection independently correlated with worse liver recurrence-free survival but not disease-specific survival[12]. Additionally, they found that in the era of modern multimodal tactics, disease-specific survival or liver recurrence-free survival did not change over time despite modifying the technical approach.

It has been hypothesized that in the specific subgroup of patients with multiple CLM, local failure in the liver after wedge resection may not be as critical to survival as for patients with solitary metastases. Thus suggesting that patients with a less aggressive disease behavior should probably not undergo parenchymal-sparing procedures. However, different studies have not supported this proposal. In a retrospective study by Kokudo *et al*[33] a subset analysis of patients with unilobar single or double tumors demonstrated that intrahepatic recurrence did not differ significantly between those who underwent major AR *vs* minor NAR (31.3% *vs* 41.2%, *P* > 0.05), and nor did patient survival. Interestingly, only 19.6% of patients in the NAR group developed ipsilateral recurrence and 90% were resected, compared to 20% of recurrences resected in the AR group[33]. Almost fifteen years later a similar study from the MD Anderson group[11], but focused in patients matched for clinical characteristics and with solitary metastases equal or less than 3 cm, reported even more interesting results in the era of modern chemotherapy. They retrospectively compared 156 patients who underwent a parenchymal-sparing hepatectomy (excluding concomitant RFA) with 144 patients who underwent non-parenchymal-sparing hepatectomy, and found that no significant differences were found in OS, recurrence-free survival, and liver-only recurrence-free survival[11]. However, a subanalysis of patients who had liver-only recurrence revealed a significantly improved 5-year OS from initial hepatectomy (72.4% *vs* 47.2%, *P* = 0.047) and from liver recurrence (73.6% *vs* 30.1%, *P* = 0.018) in the parenchymal-sparing hepatectomy group[11]. This was explained by the fact that salvage hepatectomy for liver-only recurrence was performed significantly more often in the parenchymal-sparing hepatectomy group compared to the non- parenchymal-sparing hepatectomy group (68% *vs* 24%, *P* < 0.01). In this study, multivariate analysis revealed that non-PSH was a risk of noncandidacy for repeat hepatectomy[11].

All reports addressing PSLS are retrospective in nature and most compare heterogeneous groups of patients, thus making the interpretation of data problematic. Given that results may be biased by different patient selection criteria for either approach among centers and surgeons, definitive conclusions in terms of oncological results cannot be drawn. However, the presence of an increasing body of evidence with consistent data among different centers, strongly suggests that PSLS does not compromise oncological outcome and in certain occasions long-term survival might be even better than non-parenchymal approaches in current days. Randomized controlled data is best desired to confirm these findings. However, such a study seems unfeasible from a practical and ethical point of view, given that surgical risk of anatomical major resection is greater and surgeons would be unwilling to choose an unnecessary major hepatectomy for small single tumors near the liver surface.

CONCLUSION

There is a clear trend toward a parenchymal-sparing philosophy in HPB centers worldwide. Parenchymal-sparing strategies, either by resection alone or complemented with ablative therapies, have become an essential part of modern liver surgery and every liver surgeon should be aware of their existence and feasibility. A profound knowledge of liver anatomy as well as expert IOUS skills are necessary to perform PSLS appropriately and safely. Current evidence indicates that tumor biology is the most important predictor for intrahepatic recurrence and survival rather than the amount of millimeters at a negative resection margin. Complete tumor removal avoiding the unnecessary sacrifice of functional parenchyma has been associated with less surgical stress, fewer postoperative complications, uncompromised cancer-related outcomes and higher feasibility of future resections. The increasing evidence supporting PSLS prompts its consideration as the gold-standard surgical approach for patients bearing liver metastases from colorectal cancer.

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