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REVIEW ARTICLE

A contemporary view on vascular resections and reconstruction during hepatectomies

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Abstract

Oncological hepatic surgery carries the possibility to perform vascular reconstructions for advanced tumours with vessel invasion since surgery often represents the only potentially curative approach for these tumours. An extended review was conducted in an attempt to understand and clarify the latest trends in hepatectomies with vascular resections. We searched bibliographic databases including PubMed, Scopus, references from bibliographies and Cochrane Library. Information and outcomes from worldwide clinical trials were collected from qualified institutions performing hepatectomies with vascular resection and reconstruction. Careful patient selection and thorough preoperative imaging remain crucial for correct and safe surgical planning. A literature analysis shows that vascular resections carry different indications in different diseases. Despite significant advances made in imaging techniques and technical skills, reports of hepatectomies with vascular resections are still associated with high postoperative morbidity and mortality. The trend of complex liver resection with vascular resection is constantly on the increase, but more profound knowledge as well as further trials are required. Recent technological developments in multiple fields could surely provide novel approaches and enhance a new era of digital imaging and intelligent hepatic surgery.

Keywords Liver malignancy · Vascular resection · Vascular reconstruction · Hepatectomy · Review

Introduction

The incidence of liver tumours, including hepatocellular carcinoma (HCC), cholangiocarcinoma (CCA), and metastatic liver malignancies is rising in most European countries and the USA [1–3].

Whenever technically feasible and oncologically appropriate, surgical treatment represents the gold standard for several liver malignancies, providing the best chance of curative treatment. For a long time, the vascular involvement of the portal vein (PV), hepatic artery (HA), hepatic veins (HV), hepatocaval confluence, or inferior vena cava (IVC), was considered a contraindication to liver resection due to the poor prognosis and high risk of morbidity and mortality. Nowadays, advances in oncological therapy, novel technology and techniques of vascular anastomosis, mostly derived from liver transplantation surgery, allowed specialised centres to perform complex liver resections and contextual vascular resections and reconstruction (VR) for hepatic malignancies [4]. These complex operations are indicated as far as free margins and remnant liver perfusion can be guaranteed. As a result, more patients, otherwise considered unresectable, could be operated on, thus increasing their long-term survival.

However, since these resections can be challenging and burdened by higher morbidity and mortality, careful patient selection is crucial to achieve satisfactory outcomes. Adequate preoperative planning with a perfect understanding of the vascular anatomy is mandatory and the introduction in the clinical practise of the 3D reconstruction technology can be helpful. Anatomical variations of the PV can be easily encountered [5], anatomical variants of the HA could be found in almost 50% of the population [6], and some of the most common anatomical variations of the HV include a prominent inferior HV draining segment 6 and 7, a branch of the middle HV draining segment 8 (up to 9% of patients), and a variant vein of segment 3 draining in the middle HV

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[7]. Finally, since the risk of infection is particularly dreadful in patients undergoing VR with a synthetic prosthesis, the preoperative placement of drains or biliary stents needs to be carefully evaluated in patients with cholestasis.

Primary VR, defined as direct vessel repair without synthetic or biological prosthesis, is to be preferred whenever possible. Larger vessels defects benefit from autologous peritoneal patches (PP), or vascular grafts. Sometimes, mostly when the hepatocaval confluence is involved, a more complex technique including the total vascular exclusion of the liver (TVE, i.e. PV, HA, and IVC clamping, above and below the HVs) with or without hypothermic perfusion or in situ, ante situm, or ex situ hepatic resections, may be required [7–9].

This review aims to provide a thorough overview of the indications for VR and of the outcomes after liver resections combined with VR.

Methods

"Vascular invasion", "vascular resection", "vascular reconstruction", "liver surgery", "liver resection" and the combination of these keywords were used to perform extended research on PubMed, Cochrane Library, Scopus, and from references in the bibliography of articles dealing with VR. Duplicated manuscripts were excluded from our analysis. Manuscripts in English and Italian were included, whilst other languages were discarded.

Assessment of vascular involvement and technical resectability

Vascular involvement includes direct vascular invasion by the tumour or vascular thrombosis. The two scenarios are different and usually require different approaches: a VR in the first and a hepatectomy plus thrombectomy in the latter.

Preoperative workup defines the relationship between the tumour and the surrounding structures. Radiological imaging includes triphasic contrast-enhanced multidetector high-resolution computed tomography (MDCT), magnetic resonance imaging (MRI), magnetic resonance cholangiopancreatography (MRCP), cholangiography, and endoscopic retrograde cholangiopancreatography, whenever needed.

Vascular involvement is suspected in the presence of vessel occlusion, stenosis, irregularity or encasement of more than half of the vessel circumference [10]. However, the accuracy of MDCT and MRI in detecting vascular involvement is 77–93% and 73–80%, respectively [11]. Furthermore, contrast-enhanced CT could differentiate portal non-tumoural thrombosis, frequently found in cirrhotic patients, from tumoural portal invasion with a high grade of accuracy [12].

The most frequently used classification was proposed by the Liver Cancer Study Group of Japan where Vp_1 indicates tumour embolus distal to the second-order branch, Vp_2 refers to the second-order branch involvement, Vp_3 implies first-order branch invasion, and Vp_4 portal vein trunk involvement. Involvement of a branch of an HV, thrombus in an HV, or the vena cava are indicated as Vv_1, Vv_2, and Vv_3, respectively [13].

When planning a liver resection, especially if vascular involvement is presumed, an adequate future liver remnant (FLR) volume should be ensured together with a preserved hepatic artery and portal inflow, venous outflow, and the biliary drainage of the remnant liver as well [7, 14].

The volume of the FLR must be carefully measured from MDCT [15]. A percentage ranging between 20 and 40% of FLR is required to prevent postoperative liver failure or the "small for size" syndrome depending on the liver function [16]. In cases of low percentage of FLR volume at planned hepatectomies, the induction of preoperative FLR growth is mandatory remembering that liver hypertrophy and regeneration are reduced by cholestasis [7, 17].

Recently, three-dimensional (3D) reconstructions with the visualisation of the intrahepatic structures, anatomical variations, and their spatial relationship with cancer facilitate the assessment of vascular involvement. Indeed, 3D models have been widely accepted for liver surgical planning, including the reconstruction of infiltrated vessels, and computing liver volumes [18]. Furthermore, 3D reconstruction amplifies virtual immersion and, together with 3D-printed models, intends to reduce the gap between traditional imaging techniques and the real operating scenario [19, 20].

Wang et al. in a well-designed study reported data prospectively collected on 305 patients, who underwent both a 2D and 3D hepatic rendering for hepatic resections. When compared with the 2D techniques, the 3D reconstruction proved to be significantly more useful in establishing correct preoperative planning in those patients undergoing more complex resection suggesting a different plan in the 37.4% of the patients of this subgroup. Furthermore, a higher number of patients were judged resectable after evaluating the 3D imaging (287 patients vs. 272 patients evaluated with the 2D technique, 5% more of the general population or 11.5% patients more when considering the complex subgroup) [21]. Comparable results have been successively reported [22–24].

Finally, preoperative planning should always be confirmed intraoperatively after the intraoperative ultrasound (IOUS) evaluation. Since the middle of the Fifties, the presence of communicating veins (CVs) between adjacent HVs has been reported [25]. For tumours located at the hepatocaval confluence, the presence of CVs allows the avoidance

of HV reconstruction, otherwise required to preserve liver parenchyma. In 2010, Torzilli et al. reported the results of the use of the new e-flow IOUS modality for the detection of CVs. In almost all the patients requiring HV resection (11 out of 12, 80% of the cohort analysed), CVs were found, major/extended hepatectomies were never required, and only minor complications were observed. This new IOUS modality showed higher sensitivity and allowed the visualisation of the CVs without the necessity of hepatic vein compression [26].

Vascular involvement: when vascular resection is oncologically appropriate

Different liver malignancies could present with different rates of vascular involvement that have a dissimilar impact on the patient's prognosis (Table 1).

All hepatic structures could potentially be resected but the more reconstructions performed, the higher the risks of morbidity and mortality in patients are reported [7]. Nevertheless, even if resectable, vascular invasion is a negative prognostic factor and neoadjuvant and/or adjuvant treatments represent a chance to prevent tumour progression and to improve long-term oncological outcomes (Table 2).

Moreover, neoadjuvant treatment (NT) might obtain early neutralisation of micrometastasis, reduce the tumour burden and consequently the vascular invasion expanding the number of patients who were previously considered non-resectable, allowing greater chances to detach the tumour from the vessels and increasing the possibilities of executing less technically difficult surgical interventions with less VR [27–29].

Hepatocellular carcinoma

HCC is a common cancer worldwide and a leading cause of tumour-related death [30]. HCC has a particular tropism for glissonean vessels with an expansive growth pattern described as "infiltrative" into the liver parenchyma rather than into the glissonean structures and pedicles [31]. This behaviour determines a higher probability of generating tumour thrombi in the PV and its branches, or, less frequently, in the HVs than vessel infiltration [32].

Although it is possible to consider a tumour thrombectomy in the context of an HCC liver resection, the presence of neoplastic portal vein thrombus represents a negative factor for long-term survival after liver resection [33]. In both Eastern and Western series long survival has been reported after resection of HCC with portal or HV involvement [34,

Table 1 Frequency of presentation and estimated 5-year outcomes of liver malignancies with vascular resection and reconstruction

	PV	HA	IVC	HV
HCC	Uncommon Acceptable outcomes	Rare Poor outcomes	Common Acceptable outcomes	Common Dubious outcomes
CRLM	Uncommon Acceptable outcomes	Rare Poor outcomes	Common Acceptable outcomes	Common Acceptable outcomes
pCCA	Common Dubious outcomes	Uncommon Poor outcomes	Common Dubious outcomes	Uncommon Poor outcomes
iCCA	Uncommon Poor outcomes	Uncommon Poor outcomes	Uncommon Dubious outcomes	Uncommon Poor outcomes
Tumour thrombi	Common Dubious outcomes	Rare Poor Outcomes	Common Dubious outcomes	Common Dubious outcomes

HCC hepatocarcinoma, *CRLM* colo-rectal liver metastasis, *pCCA* perihilar cholangiocarcinoma, *iCCA* intrahepatic cholangiocarcinoma; *PV* portal vein; *HA* hepatic artery; *IVC* inferior vena cava; *HV* hepatic vein

Table 2 Treatment recommendations according to liver malignancy

	Neoadjuvant therapy	Surgery	Adjuvant therapy
HCC	Not available	Gold standard	Not available as a standard
CRLM	Tumours with high-risk factors	Upfront surgery if no high-risk factors	Recommended
pCCA	Not available as a standard	Gold standard	Six months (low evidence)
iCCA	Not available	Gold standard	Six months (low evidence)

HCC hepatocarcinoma, *CRLM* colo-rectal liver metastasis, *pCCA* perihilar cholangiocarcinoma, *iCCA* intrahepatic cholangiocarcinoma

35]. Kokudo et al. reported the data from a nationwide survey including almost 6500 Child A patient with portal vein tumour thrombosis treated between 2000 and 2007. After a propensity score-matched analysis, resected patients with portal involvement (excluding those with main trunk or controlateral invasion) had longer survival compared to those receiving non-surgical treatments [36]. Pesi et al. showed a survival benefit of resection with thrombectomy in a retrospective multicentric analysis of 62 patients with a portal or HV thrombosis [37]. Moreover, the association of TARE with capecitabine determined survival benefits with low-morbidity rates in Child B patients with portal vein involvement [38].

However, there is a lack of prospective studies and the level of evidence, often derived from highly selected patients in small series and/or in a wide period, is quite low. Consequently, the recently updated BCLC and EASL guidelines consider this situation a contraindication to perform a hepatectomy or a transarterial treatment and suggest systemic treatment except within clinical trials [39, 40].

Similarly, although not recommended, some case series showed that neoadjuvant [41], postoperative adjuvant hepatic artery infusion chemotherapy [42], or neoadjuvant RT [43] could provide a significant survival benefit in resected patients with macrovascular involvement. Some ongoing trials are evaluating different regimens of neoadjuvant systemic therapies for HCC [44]. Whilst there is still scarce evidence of the use of Atezolizumab plus Bevacizumab in the neoadjuvant setting, a recently published interim analysis from the randomised, multicenter, phase 3 trial (IMbrave050), compared the adjuvant treatment with these drugs and active surveillance in high-risk HCC treated (resected or ablated) with curative intent. This study was the first to demonstrate a longer recurrence-free survival in the patients receiving the therapy [45].

Colorectal liver metastasis

Colorectal liver metastasis (CRLM) behaves in different and unpredictable manners, and in some cases also infiltrates major vessels [46]. Whilst portal invasion and tumour thrombi are quite rare with CRLM, the major number of liver resections combined with retrohepatic IVC resections reported in the literature were performed for CRLMs [47]. However, some CRLMs present with an expansive growth pattern, favouring a safe detachment of the tumour from vascular structures. This concept was reported by Torzilli et al., who described that R1 resection obtained by detaching the tumour from major intrahepatic vessels (R1Vasc) in liver resections for CRLM obtains a local disease control equivalent to R0 resections in terms of survival [48]. These data were successively confirmed in other series [49].

Chemotherapy (ChT) represents an essential tool in reducing the dimension of CRLMs before performing surgery, especially in patients affected by high operative risk factors, borderline and unresectable disease [50, 51]. Tumour shrinkage after ChT might favour CRLM detachment from the hepatic structures, allowing vessel- and parenchymal-sparing resections, thus increasing their overall resectability ("conversion therapy" for initially unresectable patients) [50, 51]. The great majority of the regimens are platinum-based with or without the association of an anti-EGFR (cetuximab, panitumumab)/anti-VEGF (bevacizumab), according to the presence of KRAS and BRAF mutations [50, 51].

A recent study by Viganò et al. reported data on 75 patients with tumour vascular extension (128 CRLMs: 89 in contact with an HV and 39 with the portal pedicle) who received six cycles of neoadjuvant ChT. 45% of the tumours shrank and 36 CRLMs showed a reduction below 90° of their vascular encasement. According to imaging reports, only 24 CRLMs, out of the 36 CRLMs with regression, (18.7% out of the total) confirmed their regression during surgery. For the remaining 12 CRLMs CT scan overestimated tumour response and VR was needed [28]. These data were concordant with results from other previous studies, where only around 20% of subjects confirmed a tumour shrinkage with a reduction of the tumour-vessel contact and one-quarter of radiological cases of regression were not confirmed intraoperatively [52, 52].

Cholangiocarcinoma

CCA is the second most common primary liver cancer after HCC, and its incidence is rising in several Western countries [27, 54]. CCA is biologically characterised by a predominant infiltrative pattern, due to its spread through the lymphatics surrounding intra- and extrahepatic vessels [55].

In the past, any vascular involvement caused by these malignancies would have represented a contraindication for surgery [40]. However, advances in liver surgical techniques and aggressive policies of resection of these malignancies improved patient survival, especially for pCCA. Tumour clearance and negative margins were the targets to achieve any beneficial effects of PVR for pCCA, as reported in the first Western porto-portal reconstruction performed by Hadjis et al. in 1990 [56]. Klempnauer et al. reported the first extended right hepatectomy with PVR [57]. This experience inspired Neuhaus et al. to develop the no-touch en bloc technique resecting the portal bifurcation together with the tumour. This approach improved the rate of local radicality with negative margins and minimised the tumoral dissemination for pCCA determining an encouraging 5-year survival rate of 58% [58]. A recent meta-analysis confirmed that PVR in pCCA is no longer a significant adverse prognostic factor for long-term survival, despite being usually performed in

patients with advanced disease [59]. The R1Vasc proposed by Torzilli et al. failed to demonstrate evident long-term survival benefits when performed for CCA [60, 61]. In conclusion, despite PVR in pCCA is nowadays offering encouraging results and for these patients, the prognosis could be better than for those considered unresectable, it is still not worldwide considered a standard procedure [14, 58, 59].

In patients with pCCA, conflicting results have been reported in the literature about the outcomes of HAR which is a rare event often performed together with PVR. According to Miyazaki et al. after performing nine combined PVR and HAR, there were no benefits in survival (17% and 0% after 1 and 3 years, respectively), with a significant rise in operative mortality (36%) and morbidity (78%). Consequently, combined resection seemed not justifiable [60]. Further case series confirmed these results [59, 63]. On the contrary, other institutions reported promising outcomes [7, 62, 64, 65]. Mizuno et al. reported a wide case series of patients receiving a combined VR and showed a significant survival benefit for these patients when compared to the unresected patients with acceptable postoperative complications [66]. More recently published meta-analyses reported an undoubtful higher rate of postoperative complications of HAR/combined HAR-PVR but whether HAR is worthy in terms of patient prognosis is still to be demonstrated [59, 67]. Probably, despite the quite good quality of the evaluated studies, bias (mostly the selection bias) could not be completely excluded, and no definitive conclusions could be drawn until prospective/randomised studies were available.

In patients with iCCA, vascular involvement is reported in up to 50% of the patients. PV thrombosis/encasement is more frequent than HVs involvement and the confirmation of segmental/lobar atrophy should suggest PV involvement. VR could provide a survival benefit for these patients. However, an effort to provide a multimodal treatment to the patients is still required to achieve fewer dismal results [68].

There is no evidence concerning the benefit of NT for resectable CCA and vascular invasion does not preclude resectability. However, attempts to downstage borderline resectable and locally advanced malignancies (including those with vascular invasion) with NT regimens based on gemcitabine alone or in combination with cisplatin and S-1, seem to improve R0 resections and to provide a better prognosis in selected patients [69]. Trials such as the TRANSPHIL French trial (NCT02232932, non-disseminated unresectable CCA) and the first report from the ongoing phase II NACRAC study tried to establish whether radio-chemotherapy with or without LT could provide better results than liver resections alone. However, despite some presented data showed a promising role of targeted therapies, including Durvalumab (for example, the ongoing DEBATE trial [70]), the literature on this topic is still inconclusive [71–73]. On the contrary, adjuvant regimens are often administered [74], mostly capecitabine-based, the role of Durvalumab is mainly analysed in the setting of advanced disease [75]. However, CCA is strongly resistant to systemic chemotherapeutic agents and its long-term prognosis remains dismal, having a 5-year survival of about 10% [27].

Hepatic veins and vena cava involvement

Extensive HVs involvement has also been long considered a contraindication to surgery being related to a poor prognosis.

HCC can present with a tumour thrombus in the IVC. Potential complications may include thrombus migration into the right atrium and a consequent risk of heart failure, outflow obstruction, embolism, and sudden death [26, 76]. In these rare cases (1–4%) of cardiac involvement, the prognosis is unfavourable [77].

Despite poor long-term survival from multiple other studies, surgery still offers more encouraging outcomes than in subjects who are considered unresectable, with a long-term survival rate ranging from 11 to 27% [7, 78].

Vascular involvement: how vascular resections could be performed and postoperative outcomes

Primary anastomosis is to be preferred whenever possible, whilst autologous patches and grafts are requested in more complex cases. Preoperative planning involves the evaluation of whether it is possible to perform VR with autologous vessels. A Doppler ultrasonography of the greater saphenous veins and jugular veins should be obtained before performing the surgical procedure. Other vessels that could be used include the splenic vein, the gonadal vein, and the left renal vein [7, 79]. Sometimes, the retrieval of vessels from the resected liver portion could represent another possibility of performing an autologous graft. More recently, autologous parietal PPs were successfully introduced to perform VR [8, 79]. PP are easily retrievable and can be modelled according to the need of the surgeon. Moreover, PP avoids additional surgical fields and the sacrifice of other vessels.

When autologous tissues are not available, vessels from tissue banks could be requested. Some institutions are provided with their tissue bank. On the other hand, animal-derived tissues and synthetic materials offer alternative solutions for VR, with bovine pericardium and polyethylenterephtalat (PTE) or polytetrafluoroethylene (PTFE) grafts [80, 81].

Overall, autologous tissues are preferred due to their reduced risk of graft infection and thrombosis compared to synthetic components [82]. On the other hand, PTFE rings

guarantee better structural stability, which is required, for example, in larger retrohepatic IVC reconstructions.

Postoperative use of anticoagulants/antiaggregants is still largely debated.

Hepatic inflow: portal vein

Portal vein resection and reconstruction are performed when malignancies directly involve the PV or when there is a peritumoral fibrotic reaction surrounding the main PV and/or its right/left branches at the bifurcation. Perihilar cholangiocarcinoma (pCCA) and gallbladder cancer represent the main indications of PVR, followed by centrally located HCC.

Over the recent years, encouraging results after PVR during liver resection have been reported and PVR has become the most performed additional procedure in hepatic surgery [14, 83]. However, a crucial issue regarding major liver resections with VR remains postoperative morbidity, ranging from 40 to 100% [7]. The complications after PVR are bleeding, thrombosis, stenosis, and kinking, which require prompt treatment. In the case of portal thrombosis, a higher chance of portal flow restoration was reported to be achieved with reoperation within 3 days. The percentage of thrombosis varies according to the kind of reconstruction performed and the pathology requiring the operation ranging between 0 and 40% [84].

Hepatic resection with PVR for HCC has been reported to be feasible with longer operative time and acceptable morbidity rates [85].

Early case series with few patients undergoing PVR for pCCA, reported mortality rates from 8 to 33% [60, 86]. The main cause was PV thrombosis leading to progressive liver failure. However, in the last few decades specialised high-volume centres registered mortality rates lower than 5% after PVR or combined resections, like major hepatectomies with no VR [14, 64]. Lee reported a perioperative mortality rate of 0% in patients resected between 2005 and 2008, whilst patients operated between 1989 and 2005 had a mortality rate of 9.8% [87]. The combination of different factors, such as better patient selection, the progression of microvascular techniques, greater surgical expertise, and preoperative remnant biliary drainage seems to be responsible for these favourable registered outcomes.

Hepatic inflow: hepatic artery

The main indications for HA resection and reconstruction (HAR) are again represented by gallbladder cancer and pCCA infiltrating the common HA, the proper HA or its first division branches. Before performing a HAR, the presence of a tumour-free margin should be assessed.

End-to-end reconstructions represent the first choice. The common HA can be anastomosed with the left or right hepatic artery or with the common HA itself. The anastomosis with sectoral branches, the right posterior HA after an extended left hemihepatectomy or the artery of segments 2–3 after an extended right hepatectomy is more demanding. The left gastric artery and the gastroduodenal artery may be transposed when required to guarantee a tension-free end-to-end anastomosis [7, 86]. Reconstructions using autologous grafts of the splenic artery, the inferior mesenteric artery, the radial artery, or the saphenous vein are other possible techniques derived from the liver transplantation field [7]. Finally, portal vein arterialization (PVA) is a salvage procedure performed when arterial anastomoses are not technically possible. In this case, an end-to-side anastomosis of the HA to the PV is performed [88]. Biliary complications and haemorrhage could be mentioned amongst the list of complications following PVA, due to induced portal hypertension. Literature reports only a few studies where PVA was performed, and the largest series of PVA accounts for 16 patients, with a 60% success rate, due to the high risk of complications [88].

HAR remains a challenge since the rates of success could be hampered by complications such as stenosis, thrombosis, or occlusion, with poor results in the long term. Early series of HAR with or without PVR reported mortality rates up to 55.6%. Results from Yamanaka et al. also reported similar results, with a postoperative mortality rate of 8.8% after performing 25 major hepatectomies for pCCA and 10 HARs [89]. A 4% of perioperative mortality was reported by Berumen and Hemming in 2016, after performing HARs in a cohort of patients with CCA and gallbladder cancer [78]. These results were attributed to the newest available microsurgical techniques, that allowed to perform more precise arterial anastomoses with better technologies. Likewise, the growing reports from living-donor liver transplantations (LDLT) positively influenced the outcomes of HAR.

Hepatic outflow: hepatic veins and inferior vena cava

Metastases, HCC, pCCA, and CRLM often involve the HVs, requiring their resection and reconstruction, with or without the involvement of the IVC. Despite being amongst the most demanding surgical procedures, hepatectomies involving the IVC-HV confluence with IVC reconstruction are nowadays regularly performed in specialised centres.

A recently described technique is the “Liver Tunnel” which could be chosen to resect malignancies involving segments 1, 8 and eventually 4a, with or without invasion of the HVs confluence, according to the presence of communicating veins [90]. When all the HVs are infiltrated, the presence of a sufficient intrahepatic tumour-free tract of the HV should be assessed [91].

A direct re-implantation of the HV within the IVC should be chosen as the first choice to minimise the risk of anastomotic kinking. Unfortunately, most of the cases require the interposition of an autologous or synthetic patch or graft, since primary closures of the wall defects could lead to a significant stenosis of the HVs [7]. Autologous PP are used to perform reconstruction of either the HVs or the IVC [8, 92].

Postoperative morbidity after HV resection is reported to occur in up to 50% of the patients [53]. Air embolism could be a dreadful complication.

Tangential or segmental resections of the IVC can be performed. The hepatic outflow could be preserved with a partial IVC clamping to repair defects of about 2 cm or with a circumferential involvement inferior to 30% [7]. Autologous or bovine patches of the parietal peritoneum could be used to reconstruct an IVC defect involving more than 30% of the wall or when it is bigger than 2 cm [86, 93]. When a longer tract of the IVC is infiltrated by the tumour, segmental resection of the IVC is required. Synthetic PTFE grafts could also be used and multiple experiences from several institutions report different outcomes with both autologous patches and ringed PTFE grafts [7, 94]. Recently published results from an international multicentric retrospective cohort study showed the feasibility of vena cava resection and replacement associated with major hepatectomy in skilled hepatobiliary centres. Although considering the small number of patients enrolled, 36, median ICU and length of hospital stay were 4 and 15 days, respectively, post-hepatectomy liver failure rate was 12%, 90-day mortality rate was 14%, the estimated 5-year overall and disease-free survival was 48% and 55%, respectively. In this setting in which patients were previously deemed unresectable, these results should be considered satisfactory compared to those achievable with non-surgical treatments [95].

The most challenging liver resections are represented by large tumours infiltrating the IVC-HV confluence when TVE could be necessary. The main issue of TVE remains warm liver ischaemia, whose tolerance varies from 30 to 120 min, depending on the patient [7, 9]. TVE with caval flow preservation avoids the hemodynamical drawbacks of classical TVE [96]. This technique is used in patients affected by liver malignancies with synchronous involvement of the IVC and any of the hepatocaval confluences, with at least one HV free from tumour involvement, and could be applied intermittently or partially [97].

In situ liver resections with cold perfusion represent a viable option if liver resection requires TVE for periods exceeding one hour allowing easier visualisation of the anatomical structures in a bloodless field. It was first performed by Fortner et al. after systemic heparin application and perfusing the liver with a cool (4 °C) Ringer solution through a catheter inserted into the PV after TVE [98]. Since in situ cold perfusion does not enable satisfying access to the HVs, *ante situm* or ex situ techniques were further developed.

The *ante situm* technique was described by Hannoun et al. in 1991 [99]. *Ante situm* is required in difficult IVC and HVs resections when better access to the IVC-HV confluence is required, keeping the liver vascularized via the hilar structures (PV, HA, main bile duct).

The ex situ technique necessitates the removal of the liver from the abdomen and it is generally performed with no veno-venous bypass since most of the patients keep an adequate volume load after IVC clamping [7, 86]. This technique is particularly indicated in the case of simultaneous involvement of the IVC, HVs, and portal structures.

Perfusion machines could have a role in these cases in the next future [100]. The main current limitations of these machines are their cost and their complex management [94, 101, 102].

Finally, the removal of a thrombus extending to the atrium could require a cardiopulmonary bypass with a sternotomy in collaboration with cardiovascular surgeons [77].

Hemming et al. described the results from 16 patients (9 HCC, 5 CRLM, 1 CCA and 1 hepatoblastoma) who underwent major liver surgery [103]. Eight cases received a primary end-to-end anastomosis between the HV and the IVC, in four patients a synthetic interposition graft was used, whilst four patients needed a combined resection and reconstruction of both the HV and IVC. Two patients (12%) died within 3 months from surgery, but thrombosis or further vascular events were not reported in the series. The reported 3-year survival rate was 50%.

The complete closure of the retrohepatic IVC with the removal of the infiltrated wall is rarely required but could be performed (e.g. chronic infection of a synthetic IVC replacement, end-stage hepatic echinococcosis, or to control bleeding in tumours involving the HV confluence). In these cases, patients develop lumbar venous collaterals that bring blood from the lower extremities and the abdomen to the superior vena cava [104].

The postoperative morbidity and mortality rates after HVs-IVC confluent reported in the literature range around 25–64% and 0–12%, respectively. Interestingly, the patency of synthetic IVC reconstruction in the long term varies around 89–100% [7], whilst a case series by Pulitanò et al. reported autologous graft patency of 100% after IVC reconstruction [93].

To date, Hemming et al. provided data on one of the largest series of hepatectomies and IVC resections for cancer, accounting for 60 patients over 16 years. All vascular anastomoses were patented after a 10-year follow-up, including 5 ex vivo resections and 8 cases necessitating in situ cold perfusion. The perioperative mortality was 8%, whilst the 1- and 5-year survival was 89 and 35%, respectively [105].

Malde et al. provided data on 35 patients who needed TVE, *ante situm* (3 patients), ex vivo (6 patients) and cold perfusion (13 patients). Overall, 23 patients underwent primary or PP IVC repair, whilst the remaining patients required an interposition graft. Morbidity was 40% and mortality was 11.4%, whilst the cumulative survival was 37.7% at 5 years. R0 resections were possible in 51% of cases (18 patients) [106].

Conclusions and future perspectives

The management of vascular invasion in hepatic malignancies represents a major challenge. Achieving R0 margins with an adequate FLR remains the main goal in terms of survival and tertiary referring centres no longer consider liver malignancies infiltrating vascular structures as a contraindication for surgery. However, careful patient selection and exhaustive preoperative imaging are fundamental in minimising the onset of perioperative complications in such delicate patients. Recent advances in the promising fields of regenerative medicine and 3D technology could surely provide novel approaches to reconstructing anatomical segments and enhance a new era of digital imaging and intelligent hepatic surgery.

Currently, NT regimens do not represent a satisfying option for patients with vascular invasion from hepatic tumours Hence, the VR of PV, HA, IVC, and HVs combined with liver resection actually represent the best option to reach a potentially curative approach in patients otherwise considered untreatable.

Vascular involvement in liver surgery still remains a passionately discussed topic amongst surgeons dedicated to these kinds of procedures which results remain questionable and dubitative. This review does not provide a conclusive statement on this demanding surgical act which ultimately remains a fundamental and essential weapon in hepato-biliary surgeon's armamentarium.

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