Hepatic Resection for Hepatocellular Carcinoma

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KEYWORDS

• Hepatocellular carcinoma • Hepatic resection • Milan criteria

KEY POINTS

- Over the past 2 decades, the landscape of hepatocellular carcinoma (HCC) epidemiology has undergone significant shifts, influenced by changes in risk factors, disease burden, and healthcare practices.
- Resection criteria for HCC vary globally, determined by factors such as tumor size, liver function, and available treatment options.
- Developments in technology, as well as the changing demographics of HCC have led to an increasing role for locoregional therapy, particularly in the neoadjuvant setting.
- Current efforts focus on extending immunotherapy to patients with lower tumor burdens to facilitate curative surgery and reduce recurrence rates.
- Treatment options for recurrent HCC are diverse, with long-term survival achievable in select patients, especially those with favorable tumor biology and candidates for curative treatments like repeat hepatectomy or salvage transplantation.

INTRODUCTION

In 2020, liver cancer was the sixth most common malignancy and third most common cause of cancer-related death worldwide.[1] The number of new cases seen annually has risen by 70% since 1990.[1]

Although survival varies based on stage at presentation, the 5-year overall survival for all patients presenting with hepatocellular carcinoma (HCC) is 22% in the United States (US).[2] Eligibility criteria for HCC resection vary globally based on tumor extent, liver function, and alternative therapy availability, with more stringent guidelines in Europe and the US compared to Asia.[3] Candidate selection and exploring neoadjuvant therapies like transarterial radioembolization (TARE) and immunotherapy aim to potentially improve outcomes in cirrhotic patients.

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Recent advances in immunotherapeutic and targeted approaches have revolutionized HCC treatment.[4–6] Efforts are now focused on extending immunotherapy to patients with lower tumor burden to facilitate curative surgery and reduce recurrence rates.[4–6]

Recurrence rates after HCC resection range between 50% and 70% at 5 years.[7] Treatment options for recurrent HCC are diverse with long-term survival achievable in select patients, particularly those with favorable tumor biology and suitable for curative treatments like repeat hepatectomy or salvage transplantation (SLT).[3,7]

This review focuses on the latest advancements in the treatment of HCC.

Epidemiology and Changes in Hepatocellular Carcinoma over the Past 2 Decades

Over the past 2 decades, the landscape of HCC epidemiology has undergone significant shifts, reflecting changes in risk factors, disease burden, and healthcare practices. Viral hepatitis is the most common underlying cause; Hepatitis B virus (HBV) contributes to 54% of cases, mostly in Asia and Africa, with Hepatitis C virus (HCV) accounting for 31% predominantly in the Western world.[1,2] The incidence of HCV-related HCC has decelerated in recent years, largely due to advancements in antiviral therapeutics.[1,2] However, the impact of metabolic-associated fatty liver disease and resultant steatohepatitis (MAFLD/MASH) is currently the fastest-growing etiology of HCC.

Unlike viral hepatitis, MAFLD is just a manifestation of a systemic disorder, metabolic syndrome, that also underlies the various manifestations of cardiovascular disease that are the leading causes of ill health and death globally.[8] Patients with MAFLD-related HCC are older at diagnosis, with higher body mass index (BMI) and more comorbidities than patients with HCC due to other etiologies.[3,8] Around one-third of MAFLD-related HCC develops in the absence of cirrhosis, where the denominator is huge and there is no guideline for screening/surveillance.[4,8] MAFLD-HCC is therefore more commonly found at a more advanced stage than with other etiologies. As a result of all of these factors, patients with MAFLD/HCC are as a group less likely than patients with viral hepatitis to be suitable candidates for surgery.

The incidence of alcohol-related liver disease (ALD)-related HCC has been increasing for the past several decades with a 109% increase from 1990 to 2015. Patients with alcoholic cirrhosis have a high rate of related comorbidities including malnutrition, cardiomyopathy, myopathy, and neurologic manifestations that, like patients with MAFLD-HCC, commonly render them suboptimal candidate for hepatic resection.[9]

Patient Selection for Resection

Resection criteria for HCC vary worldwide, influenced by factors such as tumor size, liver function, and treatment options (**Fig. 1**).[10] Asian guidelines typically allow broader resection criteria compared to stricter European and US standards, resulting in varied survival rates from 50% in China to 70% in Europe over 5 y (**Table 1**).[3,11–14]

Liver function is typically better preserved in HBV-related HCC compared to other etiologies, with approximately 20% of patients having noncirrhotic disease. This encourages more aggressive surgical approaches in Asia, despite potential perioperative complications like liver decompensations (~20%) and up to 5% mortality rates.[4] Some Asian countries, such as Japan and Korea, are moving toward more restrictive practices similar to the West.

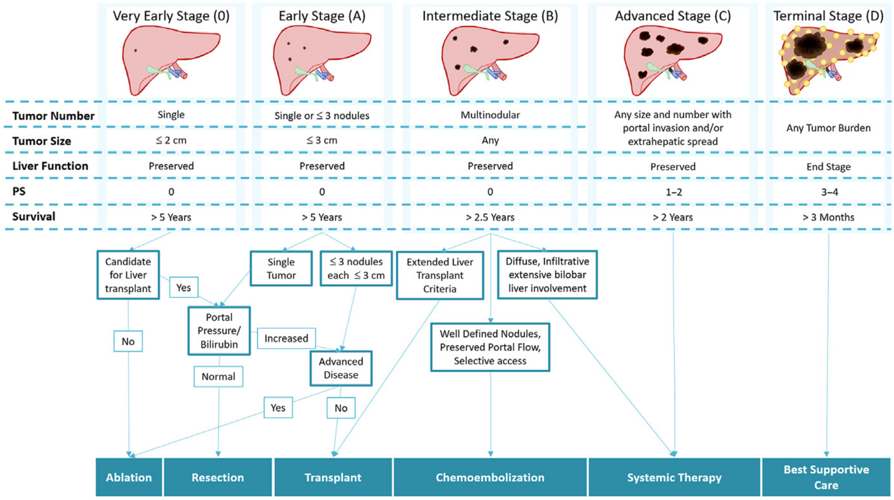

Fig. 1. Clinical algorithm for treating patients with hepatocellular carcinoma (HCC) based on the Barcelona Clinic Liver Cancer (BCLC) staging system with classification and predicted survival. (*Adapted from* Llovet JM, Kelley RK, Villanueva A, et al. Hepatocellular carcinoma. Nat Rev Dis Primers. Jan 21 2021;7(1):6. https://doi.org/10.1038/s41572-020-00240-3.)

In Western nations where HCV, ALD, and MAFLD commonly cause HCC leading to cirrhosis, surgeons lean toward conservative resection strategies. They prioritize candidates with a single tumor, well-maintained liver function (Child–Pugh class A), and no significant portal hypertension.[3,10]

Selecting appropriate candidates for resection among cirrhotic patients requires careful consideration of both liver functional reserve and tumor extension. Child-Pugh class serves as a common measure for estimating hepatic reserve, while portal hypertension, estimated through platelet count or by direct hepatic venous pressure gradient measurement, emerges as a crucial prognostic factor in HCC treatment.[10,15,16] Anatomic resection has been advocated based on a belief that retrograde spread of HCC through portal branches contributes importantly to outcome, but this idea has been largely abandoned; resection should be limited in cirrhotic patients, sparing unaffected parenchyma to the extent possible, with local resection with a margin preferred over extensive resections like right hepatectomy.[17]

Barcelona Clinic Liver Cancer (BCLC) guidelines recommend resection for patients with single tumors and no evidence of vascular invasion on imaging (see **Fig. 1**).[10] Larger tumors correlate with poorer outcomes prompting interest in alternative therapies as tumor size increases, though many patients with well-contained large tumors achieve long-term survival.[16]

Despite its efficacy, resection has limitations. Current research emphasizes refining patient selection and exploring neoadjuvant therapies such as TARE or immunotherapy to enhance outcomes.[18,19]

Patients with HCC invading portal or hepatic vein branches are classified as advanced stage (BCLC C) and typically receive systemic therapy as per guidelines.[10] In Asia, surgeons often consider resection for select patients with branch portal invasion, achieving promising long-term survival rates in certain cohorts.[20] Ongoing studies investigate neoadjuvant therapy to optimize outcomes by selecting patients likely to benefit most from surgery.

Table 1
Selection criteria for resection and ablation by region

	Liver Function	Region	Candidate	Tumor Characteristics	5-y Overall Survival
Resection	Preserved	Europe and North America[3,11]	Optimal	Single lesion of any size	60%–70% in Patients with HCC ≤ 5 cm and no portal hypertension
			Suboptimal	2–3 Nodules < 3 cm or presence of portal hypertension	
	Child-Pugh A	Korea[12]	Optimal	Single lesion of any size	69%
	Child-Pugh A/B		Suboptimal	Single lesion with vascular or bile duct invasion or 2–3 nodules of any size	
		Japan[13]	Optimal	≤ 3 nodules ≤ 3 cm, single lesion ≤ 5 cm, 1–3 nodules > 3 cm or Vp1/2, Vv1/2	70% for patients meeting optimal criteria
			Suboptimal	≥ 4 nodules of any size, portal hypertension, Vp3/4, Vv3/4 or single lesion > 5 cm	67% for Child-Pugh A/B and Portal hypertension
		China[14]	Optimal	Single lesion or 2–3 nodules of any size	~50%
			Suboptimal	≥ 4 nodules or portal vein invasion	
Ablation	Preserved	Europe and North America[3,11]	Optimal	BCLC 0 or BCLC A	60%–70% (with RFA, PEI, or MWA)
			Suboptimal	NA	
	Child-Pugh A/B	Korea[12]	Optimal	≤ 3 nodules ≤ 3 cm	65%
			Suboptimal	Single lesion ≤ 5 cm	
		Japan[13]	Optimal	≤ 3 nodules ≤ 3 cm	71%
			Suboptimal	Single lesion ≤ 5 cm or > 4 nodules of any size	62%
		China[14]	Optimal	Single lesion ≤ 5 cm or 2–3 nodules ≤ 3 cm	45%
			Suboptimal	Single lesion > 5 cm or 2–3 nodules > 3 cm	

Surgical Resection Versus Liver Transplant

Liver transplantation (LT) has become the primary treatment for early hepatocellular carcinoma that cannot be resected ever since the introduction of the Milan Criteria (MC) by Mazzaferro in 1996.[21] These criteria define early HCC as either a single tumor less than or equal to 5 cm or 2 to 3 tumors each less than or equal to 3 cm, without vascular invasion, showing outcomes similar to non-HCC transplant patients (**Tables 2** and **3**).[21–34] However, the definition of unresectable varies across centers, with some considering cirrhosis itself a reason not to perform surgery. In cases of multiple tumors meeting MC, transplantation is generally preferred. Patients with symptomatic cirrhosis and a solitary tumor within MC can use the tumor to qualify for a transplant that would otherwise be unattainable. For patients who meet resection criteria, resection (or increasingly, nonsurgical therapies) serves well as definitive treatment, with long-term survival similar to transplant in comparable patients. Over the past 15 years, the US organ allocation system has progressively deprioritized HCC patients.[11]

Patients with metabolic syndrome-associated HCC are typically older with more comorbidities than those with viral-related HCC, often making them poor candidates for surgery.[8] While LT offers a comprehensive approach to managing chronic disease, it comes with upfront risks and long-term complications, leading to reduced life expectancy compared to healthy individuals. Nonsurgical treatments are advantageous as they prioritize patients for transplant and can potentially prevent early recurrence.[18,19] However, for clinically stable patients without active tumors, a watchful waiting approach is often recommended. Treating HCC tumors smaller than 2 cm upon discovery is crucial, as treatment success rates decline as tumors grow larger.[35]

LT involves waiting due to organ scarcity, prompting the treatment of HCC in listed patients to prevent progression and maintain eligibility using nonsurgical methods.[36] Resection is generally avoided if LT is planned, but patients with recurring tumors

Table 2
Milan criteria and other proposed criteria for transplantation in patients with hepatocellular carcinoma with overall survival and recurrence free survival

System	Criteria	OS (%)	RFS (%)
Milan[21]	Single tumor $\leq$ 5 cm or $\leq$ 3 tumors $\leq$ 3 cm	85	92
Seoul Criteria[22]	Assigns points based on tumor size [$\leq$3 cm (1), 3.1–5 cm (2), 5.1–6.5 cm (3), > 6.5 cm (4)], tumor number [1–2 (1), 3–4 (2), 5–6 (3), > 6 (4)], and AFP [$\leq$20 (1), 20.1–200 (2), 200.1–1000 (3), > 1000 (4)] with scores of 3–6 considered transplantable.	79	87
UCSF[23]	Tumor $\leq$ 6.5 cm, or $\leq$ 3 nodules with the largest $\leq$ 4.5 cm and a total tumor $\leq$ 8 cm	75.2	None
ASAN[24]	Tumor $\leq$ 5 cm, $\leq$ 6 nodules, no gross vascular invasion	81.6	None
Total Tumor Volume (TTV)[25]	Total tumor volume < 115 cm^3	74	78
Up-to-7[26]	Sum of the tumor number and size of the largest tumor $\leq$ 7	71.2	None
Hangzhou Criteria[27]	Total tumor diameter $\leq$ 8 cm, > 8 cm with grade I or II tumors and AFP $\leq$ 400	73.8	73.3

Monomorphic Criteria.

Table 3
Downstaging criteria proposed from selected sources with overall survival and recurrence frees survival or recurrence rate

System	Parameters	OS (%)	RFS (%)
Tumor Size			
Ravaioli et al,[28] 2008	DS from single HCC 5–6 cm or 2 HCCs $\leq$ 5 cm or < 6 HCCs $\leq$ 4 cm and sum diameter $\leq$ 12 cm	56	71
	Within Milan Criteria	62.8	71
Sinha et al,[29] 2019	DS from UCSF criteria	78.5	86.1
	All comers	50	40
AFP			
Soin et al,[30] 2020	Preoperative AFP > 100 in patients with PVTT undergoing LDLT	3.57 (HR)	4.46 (HR)
Mehta et al,[31] 2019	AFP > 1000	49	35 (RR)
	AFP 101–499	67	13.3 (RR)
	AFP $\leq$ 100	88	7.2 (RR)
Assalino et al,[32] 2020	Macrovascular invasion with DS in patients with AFP < 10	83	72
	Macrovascular invasion with DS in patients with AFP $\geq$ 10	27	33
Wait Time for Downstaging			
Halazun et al,[33] 2014	Short Wait-Listing Region	67	
	Long Wait-Listing Region	75	
Mehta et al,[34] 2020	Short Wait-Listing Regions (<3 mo)	79	
	Mid Wait-Listing Regions (3–9 mo)	73	
	Long Wait-Listing Regions (>9 mo)	92	

or declining liver function post-resection may qualify for "salvage transplantation" or SLT.[36,37] A recent meta-analysis of 11,275 patients found SLT had slightly higher perioperative mortality (6.31%) compared to primary liver transplant (4.47%), but demonstrated superior overall and recurrence-free survival rates. Despite challenges, SLT remains a viable option for patients unfit for repeat resection.[37]

Surgery Versus Other Locoregional Therapies

Developments in technology, as well as the changing demographics of HCC have led to an increasing role for locoregional therapy vis-à-vis resection, a trend that is likely to continue. MAFLD-related HCC patients as a group are older with high BMI and more comorbidities that make them less-suitable for resection, and nonsurgical alternatives that can provide a high rate of local control (which, after all, is all that resection can offer) have increased appeal; a marginally higher rate of local recurrence can be counterbalanced by a substantially lower treatment-related risk.[8]

Improved imaging and guidance systems have enabled thermal ablation (microwave having largely replaced radiofrequency) to claim a place in guidelines as the preferred first-line treatment for HCC less than 2 cm, and the size of tumors that can be reliably destroyed is increasing with technological advances.[35]

Transarterial chemoembolization (TACE) is recommended under BCLC guidelines as the preferred treatment for multifocal HCC outside of MC but confined to the liver and without macrovascular invasion (BCLC B).[10] However, there is an extensive literature, primarily from China, demonstrating benefit of TACE administered adjuvantly after resection in patients where pathology shows microvascular invasion, and this is widely practiced in Asia.[38]

Radioembolization has come to have a significant role both as an alternative and an adjunct to resection. In a prospective trial involving 29 patients with single HCC less than or equal to 3 cm, Kim and colleagues demonstrated 90% sustained complete response.[18] Radiation segmentectomy is increasingly being employed in suboptimal resection candidates in lieu of thermal ablation when tumor location makes percutaneous access difficult.[39] Radioembolization can also be employed prior to resection to increase the size and function of the future remnant liver by treating the portion of the liver to be resected (usually the right lobe). Portal vein embolization (PVE) has classically been employed for this purpose but is associated with accelerated progression of tumor during the period between PVE and surgery. Radioembolization, by contrast, while it works more slowly, both induces contralateral hypertrophy and treats the tumor.[40] This approach is particularly applicable in cases where segmental portal invasion is present; the time it takes for the liver to hypertrophy provides a window to observe for a period and identify patients who are destined to develop early evidence of tumor spread.

Stereotactic body radiotherapy (SBRT) delivers high dose radiation to focal tumors under image guidance.[41] Although SBRT is not incorporated in the 2022 BCLC guidelines, it has been recommended for patients with HCC who are unsuitable for surgery or ablation including patients with portal vein tumor thrombosis (PVTT).[42] For HCC less than 3 cm, SBRT offers a high rate of local control, demonstrated to be noninferior to thermal ablation.[35] For larger tumors, combining SBRT with TACE has been shown to yield a high rate of sustained complete response, providing an alternative to resection in patients who are questionable resection candidates based on their liver function and functional status.[42]

Rather than an either/or approach, therapies may be sequenced with resection performed to remove remaining viable tumor after treatment; in the case of complete response to nonsurgical management, it remains to be seen whether resection will have a role.

Neoadjuvant and Adjuvant Immunotherapy

Recent advances in immunotherapeutic and targeted approaches have transformed therapeutic protocols for HCC.[4–6]

Efforts have shifted toward extending immunotherapy to patients with lower tumor burden.[5] The goal is to facilitate curative surgery by identifying effective immunotherapeutic and combination strategies to reduce historically high recurrence rates and/or to serve as downstaging therapy.

Over the last decade, the concept of ’conversion’ surgery has grown. Initially applied utilizing LRT’s such as TACE, hepatic arterial infusion pump, or TARE, these interventions aimed to reduce tumor burden and enhance resection rates.[43] However, their application has yielded unclear survival benefit.

Considering successful immunotherapeutic schemes in other malignancies, several randomized phase III trials have been undertaken assessing the impact of immunotherapy in the adjuvant setting.[44]

This section will be discussed in depth in another article.

Post-Surgical Complications (Including Liver Failure and Management)

Liver surgery has advanced to the point where perioperative mortality should be a rarity—no more than 1 to 2%—and complications should be infrequent.[4,7] Achieving and maintaining near-zero mortality and low complications rates requires the dedicated efforts of an experienced multidisciplinary team comprising surgeons, anesthesiologists, intensivists, interventional radiologists and gastroenterologists, and the support of medical consultants such as is typically found in referral centers. Complications can be divided broadly into those that are the result of technical problems, and those that are due to errors in judgement.

Technical complications

Bleeding is usually the first complication of liver resection that comes to mind, but in experienced hands, significant bleeding is unusual, with the need for transfusion only in exceptional cases. Maintaining a near-bloodless field during liver transection is crucial because it allows for good visibility and identification of intrahepatic structures. The anesthesiologist plays a key role in minimizing bleeding, which largely comes from hepatic veins, by maintaining a low central venous pressure.[45] Insertion of a central line is not necessarily required; minimizing fluid administration and using pressors to manage blood pressure dips is generally adequate. However, adequate large-bore intravenous access is mandatory for major resections.

Inflow occlusion by clamping the hepatoduodenal ligament (Pringle maneuver) is an important technique that facilitates near-bloodless transection and is routinely employed by many surgeons. Total vascular isolation, combining hilar occlusion with clamping of the vena cava above and below the liver, is rarely used but important for resecting large tumors adjacent to the cava and hepatic veins.

The liver's texture is very relevant: cirrhosis makes it harder to identify small blood vessels, and steatotic livers tend to ooze more.[46] Various techniques are used to divide the liver, and surgeons typically have a preferred method.[47] The classic crush-clamp technique is tried-and-true, enabling precise dissection and identification of key anatomic structures. Ultrasonic or hydrojet dissectors are widely used and facilitate the identification of intrahepatic structures, especially near structures that must be preserved or near tumors. These devices can be used without hilar occlusion, but using them with occlusion speeds up the process and helps control oozing. Energy devices are useful for minor resections but can lead to bleeding from hepatic veins when used deep in the liver. Stapling devices are useful for transecting major vessels, particularly during minimally invasive resection, but often cause bleeding when used blindly to transect the liver.

When bleeding is encountered, the first step is to control it with pressure, assure adequate exposure, and have adequate assistance. Identifying the precise source of bleeding and achieving precise hemostasis are critical, as blind attempts to suture, clip, or staple often fail and can cause further injury. Communication with the anesthesiologist is essential, and keeping up with blood loss is very important; administration of plasma and platelets is necessary to maintain normal coagulation when multiple units of packed red blood cells have been transfused.

Bile leak

The risk of bile leak after hepatic resection ranges from 3.6% to 10%.[48] Leakage occurs when a branch of the biliary tree is cut during transection and goes unrecognized. Ideally, bile ducts should not be encountered during anatomic resection except in the portal pedicle of the resected segment(s), but nonanatomic resections are common. Unlike bleeding, bile leaks from small ducts can go undetected during surgery and only be recognized postoperatively. Placing a white gauze sponge next to the cut liver edge and inspecting it for bile staining can help detect leaks before closing the abdomen. While studies show that leaving drains after liver resection does not provide benefit, many surgeons use them to identify bile leaks and prevent bile collections.

Often, small bile leaks resolve spontaneously with drains in place, avoiding further procedures.

Bile ducts run through the liver within Glissonian sheaths with hepatic artery and portal vein branches. Even in nonanatomic resections with good visibility and precise technique, bile leaks are rare. Common sites of leaks include ducts draining the caudate and small ducts near the hilar plate during major resections. Early identification and repair of significant bile leaks are crucial. Unrepaired leaks resulting in collections can often be managed by percutaneous drainage and endoscopic stenting or, in some cases, by percutaneous occlusion of the leaking duct with glue.

Injury of hilar structures

Injury to hilar structures is rare with a risk of 2% to 6% for portal vein thrombosis and 3% to 9% for hepatic artery thrombosis after transplant with no such rates reported for resection.[49] When performing resections that require dissection in the hepatic hilum, it is possible to injure the portal vein, hepatic artery, or bile duct, but apart from cases where concomitant liver and vascular resection is required such injuries are uncommon. It is important to review imaging preoperatively to identify any anatomic variations that require attention. It is possible to cause narrowing of the biliary or portal bifurcation by dividing the structure too close to the branching point, resulting in stricture. If recognized early, return to the operating room for repair should be considered; stenting, endoscopic or in radiology, can often treat such strictures when found late. Clamping of the hepatic hilum or, if dissected individually the hepatic artery, can cause arterial dissection.[49] If recognized immediately, repair can be performed; stenting in radiology can often deal with dissections that are identified late.

Impaired venous outflow

When performing left hepatectomy it must be decided, based on the situation of the tumor, whether to preserve the middle hepatic vein with the right lobe or to divide it leaving its confluence with the left hepatic vein with the resected left lobe. In the latter instance, the venous drainage of segments 5 and 8 can be impaired leading to congestion of those segments.[50] This issue has been well-studied in regard to living donor liver transplantation where right donor hepatectomy without the middle hepatic vein is routine; congestion of segments 5 and 8 resulting poor early graft function in the early experience has led to the current practice of reconstructing the segment 5 and 8 branches in the recipient. When the right lobe remains in situ after left lobe resection congestion may be evident based on the appearance of segments 5 and 8 but reconstruction is not usually required, though in cases with less-than-perfect baseline liver function this could become an issue.

Complications related to errors in judgment

Patients with HCC as a rule have chronic liver disease. Western guidelines limit resection to patients with normal liver tests—Child's class A and no portal hypertension—but is a mistake to consider cirrhotic patients who meet these criteria to have hepatic reserve and regenerative capacity similar to patients without liver disease.[46] These patients can generally undergo limited resections with expectation of a smooth recovery, but performing large resections raises the risk of postoperative liver decompensation. Measurement of remnant liver volume based on 3-dimensional reconstruction of liver images and tests of true liver function such as indocyanine green clearance and mebrofenin scintography are used to try to refine patient selection, but caution remains necessary in cirrhotic patients.[51]

While major resection by convention means resection of 3 or more segments, when operating on cirrhotic patients left hepatectomy is generally better tolerated than right anterior or posterior hepatectomy.[46] Right hepatectomy in cirrhotic patients, unless the right lobe has been replaced by a large tumor and the left lobe has developed compensatory hypertrophy, is a dangerous undertaking regardless of preoperative test findings, and is associated with increased risk of liver decompensation and postoperative ascites, and a perioperative mortality risk above the benchmark 1% to 2%. Techniques to induce hypertrophy of the left lobe prior to resection including right PVE and right lobe radioembolization with yttrium-90 microspheres, can mitigate the risk, though a longer time between treatment and surgery is needed than with a normal liver.[40]

Postoperative liver failure and ascites

Postoperative liver failure is defined as bilirubin greater than 5.0 mg/dL and international normalized ratio less than 50% of the normal range on or after postoperative day 5. Its recent incidence is less than 10%, with mortality rates as high as 70%.[52] There is no specific treatment; gradual recovery can occur if complications are avoided, but some patients never return to baseline liver function. Urgent liver transplantation is an option in rare cases. Major resection reduces the portal circulation's capacitance, possibly causing portal hypertension in patients with previously normal portal pressure. This, along with surgical trauma, lymphatic disruption, and low albumin, can result in postoperative ascites. Ascites is associated with a 90-day mortality of 9.1% compared to 1.9% in patients without it.[52] It is treated like ascites in unoperated cirrhotics, though transjugular intrahepatic portosystemic shunts are rarely used.[46] Minimally invasive liver resection may broaden resection criteria to include patients with mild liver dysfunction or portal hypertension, but the decision requires multidisciplinary evaluation.

Risk of Hepatocellular Carcinoma Recurrence Following Surgical Resection and Treatment

The management of recurrent HCC after resection requires a multidisciplinary approach to tailor treatment strategies to individual patient needs and optimize outcomes in this challenging setting. Recurrence rates after resection have historically ranged between 50% and 70% at 5 y with various patterns, treatment modalities, and prognostic implications.[16] Recurrence can be the result of either the appearance of metastatic or residual local disease that was undetected at the time of surgery, often referred to as "true recurrence" carrying a poorer prognosis, or the de novo development of HCC (>2 years) in the remaining liver.

Risk factors for true recurrence are related to tumor characteristics including multiple tumor nodules, large tumor size, macrovascular or microvascular invasion, and elevated alpha-fetoprotein (AFP) levels.[16,53] De novo HCC development, on the other hand, is related to the underlying liver disease.

Treatment options for recurrent HCC are diverse and tailored to individual patient characteristics and tumor biology. Treatment of late recurrence is the same as for primary HCC, based on tumor characteristics and liver function.[16] When assessing patients with early, likely metastatic recurrence, considerations include the presence of extrahepatic disease and/or portal vein invasion, lesion size and number, and AFP level.[16] While resection and transplantation are possible, surgery should be approached with caution since the initial appearance of early recurrence may not reflect the full extent of disease present and other sites of metastasis may appear over time.

Repeat hepatic resection (10% – 35%) may be considered for patients with recurrent intrahepatic disease and preserved liver function, particularly in cases of solitary or oligo-recurrent tumors.[16] In a large single center study of 661 patients, median survival post-resection of recurrent HCC stood at 56 mo, with nearly half of the patients surviving at 5 y post-surgery for their recurrent cancer.[16] Percutaneous ablation techniques may be used for treating small recurrent lesions, especially those not amenable to repeat resection.[54] TACE or TARE remains the most widely used treatment modalities for unresectable or multifocal recurrent HCC confined to the liver.[54] Several retrospective studies have reported 1-year survival of 64% to 88% with 5-year survival ranging from 0% to 27%. Systemic therapies are promising options for advanced or unresectable recurrence HCC.[1,6] For select patients meeting eligibility criteria, salvage transplantation may be considered as a curative treatment option[37]; Cherqui and colleagues found that 61% of patients with recurrent HCC after resection had recurrence within transplant eligibility criteria, and that 5-year survival after retransplant was 70%.[55]

DISCLOSURE

None of the authors has any commercial or financial conflict related to the content of this article.

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