Introduction

Worldwide, hepatocellular carcinoma (HCC) is the sixth most common cancer and the second leading cause of cancer-related deaths (1,2). In 2017, there were 953,000 incident cases of liver cancer and 819,000 deaths globally (3). Most commonly occurring in the setting of chronic liver disease, HCC represents the leading cause of death in patients diagnosed with cirrhosis (4). Factors determining outcome following HCC diagnosis are complex and heterogeneous in nature, dependent on not only tumor burden and biology, but on patient performance status and underlying liver function as well. These complexities require maintaining a tenuous balance between tumor-related and patient-related factors with decisions regarding treatment best made in the context of a multidisciplinary team approach (5).

Surgical resection if one of the mainstays of curative HCC treatment and has been associated with a median overall survival (OS) of >60 months with 5-year OS rates approaching 60% (6-8). Clinical practice guidelines have recommended the use of surgical resection in early stage HCC (9). However, due to heterogeneity of the patient population and underutilization of HCC screening, in the past only 10–37% of patients were eligible for surgical resection at the time of initial HCC diagnosis. With recent implementation of HCC screening programs resulting in earlier diagnosis, the number of patients that might be candidates for curative surgical resection has increased. Factors determining outcome following HCC diagnosis are complex and heterogenous in nature and treatment decisions should be based on both tumor- and patient-related factors. Tumor characteristics including tumor size, macrovascular invasion (MVI), and multifocality must be balanced against measures of liver dysfunction including portal hypertension, liver function, and future liver remnant (FLR) to assess the applicability of hepatic resection in patients newly diagnosed with HCC. The aim of this article is to review the indications for curative HCC surgical resection as it pertains to underlying tumor- and patient-related factors. We also discuss adjunctive therapies that may allow for an increased role for hepatic resection in HCC patients with early stage disease who are ineligible for upfront resection due to small liver remnant size.

Keywords: Hepatocellular carcinoma (HCC); liver function; liver resection; remnant liver volume; Model for End-Stage Liver Disease score (MELD score)
Resection at the time of initial HCC diagnosis (10-12). With recent implementation of HCC screening programs resulting in earlier diagnosis, the number of patients that might be candidates for curative surgical resection has increased (13). In this article, we review the indications for curative HCC surgical resection as it pertains to underlying tumor- and patient-related factors.

**Indications for surgical resection**

Deciding to proceed with surgical resection requires careful consideration of tumor biology, including the number of tumor nodules, tumor size, and presence of vascular involvement, as well as underlying liver dysfunction and overall patient performance status. A multidisciplinary approach with input from surgical oncology, transplant hepatology, medical oncology, transplant surgery, radiation oncology, and both diagnostic and interventional radiology should be utilized. This approach has been associated with improved patient outcomes following HCC diagnosis (5). The existence of a multitude of HCC staging systems exemplifies the complexities present in evaluating a newly diagnosed HCC patient for curative surgical resection. Based on the Barcelona Clinic Liver Cancer (BCLC) system which is endorsed by the American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL), early stage (0/A) disease is recommended for consideration of surgical resection. BCLC stage 0 is defined as patients with a single nodule ≤2 cm in size with preserved liver function, while BCLC stage A represents a solitary nodule or up to 3 nodules ≤3 cm in size with preserved liver function and good patient performance status (14,15). The ultimate goal of hepatic resection for HCC is achieving an appropriate oncological margin while maintaining a functional liver remnant.

**Tumor-related factors**

**Tumor size**

Within the initially described BCLC staging system, a solitary HCC tumor greater than 5 cm was considered intermediate stage (BCLC B) and loco-regional therapy consisting of intraarterial therapies was recommend (16). Within the updated BCLC staging guidelines, tumor size in a solitary nodule is no longer a criterion. While tumor size by itself is not an independent predictor of HCC recurrence following surgery, increasing tumor size is associated with increasing incidence of microvascular invasion and distant metastases, factors portending increased recurrence and worse OS (17).

Despite the increased preponderance of risk factors associated with the likelihood of worse prognostic features, surgical resection of large HCC tumors (>5 cm in size) is associated with both similar surgical complication rates and long-term oncological outcomes compared to resections done of smaller tumors. With improvements in patient selection and perioperative management, morbidity rates range from 30–40% with post-operative mortality rates ranging from 3% to 5% in patients undergoing surgical resections for tumors >5 cm in size (18,19). Similarly, oncological outcomes following resection of solitary HCC tumors >5 cm in size support the role of resection versus non-curate therapies in this patient cohort, with 5-year OS rates ranging from 27% to 53% (18,20-24).

Intra-arterial therapy for large HCC tumors including trans-arterial chemoembolization (TACE) or trans-arterial radioembolization (TARE) is the non-curative treatment option recommended by the updated BCLC guidelines (17). A recent propensity score analysis comparing outcomes of patients with solitary HCC tumors >5 cm in size undergoing hepatic resection versus TACE demonstrate improved outcomes with resection. Five-year OS in the resection group was 41.3% vs. 18.5% in the TACE group (P=0.007) (25). Given the safety and efficacy of surgical resection combined with the lack of effective alternative curative treatment options, tumor size of a solitary HCC tumor should not preclude hepatic resection given patient-related factors including liver function, liver volume and performance status are considered acceptable.

**Multifocality of tumors**

Indications for hepatic resection in the face of multifocal HCC tumors is controversial and generally limited to patients who lack liver transplantation options, as multifocality is an independent risk factor associated with tumor recurrence following resection (26,27). Multiple published studies have demonstrated that surgical resection in patients with multifocal HCC, but still within the Milan criteria (≤3 tumors ≤3 cm in size), have 5-year OS rates ranging from 46% to 69% (19,22,28). Outcome measures in patients undergoing hepatic resection for multifocal HCC tumors outside of the Milan Criteria are not as favorable, with 5-year OS rates ranging from 12% to 24%
The major limitation of these surgical series are their retrospective nature with multifocality determined on pathology results from surgical resections rather than a priori based on pre-operative imaging studies. Given the lack of conclusive data demonstrating an oncological benefit in multifocal HCC tumors, liver resection should be reserved for circumstances where liver transplantation is not available and only non-curative therapies including TACE, TARE, or systemic therapy are an option.

**Presence of macrovascular invasion (MVI)**

The presence of MVI, either in the form of portal venous tumor thrombus (PVTT) or hepatic venous tumor thrombus (HVTT), is a poor prognostic factor following HCC diagnosis and is seen as a harbinger of systemic metastatic spread (30). Patients presenting with HCC tumors demonstrating MVI are classified as BCLC C stage (advanced) and are most commonly treated with systemic therapy with median OS times ranging from 6.5 to 13.6 months in the first-line setting (31-33).

Although 5-year OS rates after hepatic resection for HCC in the presence of MVI are dismal, ranging from 10% to 40% in retrospective series, careful patient selection based on extent of MVI and subsequent extent of hepatectomy have slightly improved outcome measures (21,22,34-38). Based on a classification scheme developed by the Liver Cancer Study Group of Japan (39), PVTT can be divided into five grades: Vp0, no tumor thrombus in the portal vein; Vp1, presence of a tumor thrombus in the second-order branches of the portal vein; Vp3, presence of a tumor thrombus in the first-order branches of the portal vein; and Vp4, presence of a tumor thrombus in the main trunk of the portal vein or a portal vein branch contralateral to the primarily involved lobe (or both). A large Japanese retrospective study using propensity score matching demonstrated that liver resection in the presence of PVTT had significantly prolonged median survival times compared to non-liver resection therapy (locoregional or systemic therapy (2.5 vs. 1.6 years, P<0.001). In the liver resection cohort, this survival benefit was only demonstrated in patients with Vp1–3 and not Vp4 PVTT. Ninety-day mortality following liver resection was also significantly higher in the Vp4 vs. Vp1–3 cohort (40). Given the lack of relative efficacious therapy compared to hepatic resection, patients presenting with MVI in the form of PVTT (Vp1–3) can be safely considered for liver resection following a multidisciplinary discussion in high volume centers. There is no current published literature supporting hepatic resection in patients presenting with Vp4 PVTT or HVVT.

**Patient-related factors**

Although perioperative mortality following hepatic resection for HCC has decreased over the past three decades (41,42), as indications for resection continue to expand, careful preoperative assessment of the degree of functional impairment of the liver is crucial to ensuring that oncological benefit outweigh the risks of post-hepatectomy liver failure (PHLF). PHLF, defined by the International Study Group of Liver Surgery as an increased prothrombin time and concomitant hyperbilirubinemia on or after postoperative day 5, is associated with perioperative mortality rates of more than 50% (43).

**Pre-operative assessment: clinical and blood tests**

Multiple validated tools exist and are used to stratify patients based on pre-resection liver function to determine both feasibility of resection and the extent of resection tolerability. In the West, the three most utilized prognostic tools are the Child-Pugh (CP) classification, the Model for End-Stage Liver Disease (MELD) score, and the Albumin-Bilirubin (ALBI) score.

In 1964, Child and Turcotte developed a classification based on total bilirubin, serum albumin, and prothrombin time, as well as the presence and grade of hepatic encephalopathy and ascites, to predict short-term mortality following portacaval shunt surgery (44). Although widely used to stratify patients for hepatic resection for HCC, neither the original CP score nor the Pugh modification was designed specifically for this purpose (45). Nevertheless, the CP score remains widely utilized for surgical decision making. In the West, liver resection for HCC is limited to CP A patients, with CP C status universally accepted as a contraindication to resection.

A critique of the CP classification is that it relies on the use of subjective variables (severity of ascites and encephalopathy). In response to these concerns, Johnson et al. proposed a grading system based only on the serum ALBI as an alternative system (46). Similar to CP classification, the ALBI score was not intended to serve as a predictive biomarker for PHLF following liver resection for HCC. However, investigators have reported the ALBI grade more accurately predicts PHLF than CP score (47).

Currently, the AASLD/EASL guidelines recommend that
liver resection for HCC only be performed in patients with a serum total bilirubin of \( \leq 1 \) mg/dL. In some Asian centers, a cutoff of \( \leq 2 \) mg/dL is widely used (48). Given that liver resection for HCC is usually limited to patients with normal bilirubin levels, the usefulness of the ALBI grade in determining surgical candidacy may be based simply on the albumin level alone.

The MELD score, based on serum total bilirubin, international normalized ratio (INR), and creatinine, was first reported to predict early death after elective transjugular intrahepatic portosystemic shunt placement but is now used primarily for allocation of organs for liver transplantation (49). Multiple studies have suggested MELD score might be associated with PHLF following hepatectomy for HCC in cirrhotic patients. Teh et al. demonstrated that cirrhotic patients with cirrhosis and a MELD score of \( < 9 \) have generally low morbidity of around 8% and negligible mortality from PHLF (50). Patients with a MELD score \( \geq 9 \) have been shown to have greater risk of post-operative liver failure and peri-operative mortality (51,52). Originally designed as a continuous score in patients with poor underlying liver function, the use of MELD as a discrete variable with an a priori cut-off point to determine PHLF might limit its usefulness.

Pre-operative assessment: portal hypertension

The presence of portal hypertension, defined as a hepatic venous pressure gradient (HVPG) \( \geq 10 \) mmHg, is defined by both AASLD and EASL guidelines as a contraindication to hepatic resection for HCC (14,17). These recommendations were based on a study by Bruix et al. in 1996 in 29 patients undergoing liver resection for HCC. In their study, elevated HVPG and thrombocytopenia was associated with decompensation following hepatic resection in Child A cirrhotic patients (53). Twenty-three of the 29 study patients underwent at least a major hepatectomy (sectionectomy or greater), calling into question the applicability of their findings in operations involving less liver parenchyma. In contrast, several other studies have demonstrated that resections for HCC can be safely performed in patients with portal hypertension with resultant low perioperative mortality rates and clear oncologic benefits (28,54,55).

As HVPG is an invasive procedure requiring institutional expertise, clinical parameters including splenomegaly \( > 12 \) cm, clinical signs of collateralization such as a recanalized periumblical vein, and thrombocytopenia \( < 100/nL \) are surrogate markers for clinically significant portal hypertension. The decision to perform hepatic resection in a patient with clinically significant portal hypertension must be weighed in the context of possible alternative curative therapies including liver transplantation and ablation.

Pre-operative assessment: functional imaging

Quantitative assessment by indocyanine green (ICG) clearance is the most often utilized pre-operative test in the East. ICG is a water-soluble fluorescent cyanine dye that is exclusively excreted by the liver into the bile without metabolism or enterohepatic circulation and its retention, measured as percentage serum retention at 15 minutes (R15), is an indirect assessment of functional hepatic blood flow (56). A surgical decision algorithm based on R15 was first reported by Makuuchi et al in 1993 and is now widely used in many Eastern centers (57).

A recent multi-center Japanese study developed the ALICE grading system, a system utilizing serum albumin and ICG R15 evaluation (58). Like ALBI, ALICE has predictive power comparable with CP classification, but allows further stratification of CP A patients. These results were validated in a retrospective European cohort (59). However, the use of ICG clearance over other functional tests is still under debate and is seldom utilized in the US (Table 1).

Assessing future liver remnant (FLR) volume

Knowledge of standard liver volume proportion is necessary to determine the if extent of surgical resection will result in an appreciable decline in remnant functional liver volume. Generally, the right liver (segments V–VIII) contributes two-thirds of the total liver volume and the left liver (segments II–IV) contributes one-third of the liver volume (60). The optimal method for calculating the FLR is heavily debated and relies on formulas involving body surface area and radiographic imaging (61,62).Computed tomography with 3D reconstruction or volumetric MRI traces the hepatic segmental contours and multiplies the surface area by slice thickness to calculate the total liver volume (63). To calculate the FLR, the following formula is used: (resected volume-tumor volume)/(total liver volume-tumor volume) (64,65). The minimum FLR considered to be safe following liver resection is based on the function and underlying disease status of the liver. Patients with HCC and cirrhosis necessitate a greater FLR than non-cirrhotic patients, with liver remnants of 40% needed. Small liver remnant volume is
associated with higher rates of PHLF and other perioperative complications following hepatic resection (66,67).

### Techniques for increasing FLR size

**Portal vein embolization (PVE)**

In patients with inadequate or borderline standardized FLR (sFLR), selective PVE can successfully increase remnant size. PVE is an image-guided procedure that induces hypertrophy of the FLR by redirecting portal blood flow away from the liver segments to be resected toward the non-tumor-bearing liver. PVE can decrease postoperative morbidity and increase the number of HCC patients eligible for curative intent resection when utilized appropriately. In patients without liver dysfunction, PVE is indicated when sFLR is <20%, which is often the case when extended right hepatectomy is required (68). In cirrhotic patients with HCC, PVE is indicated when sFLR is <40%. Using ICG criteria, PVE can be considered for FLR ≤40% when ICG R15 is ≤20% and for FLR ≤50% when ICG R15 is between 10–20% (68).

PVE is absolutely contraindicated in cases with extensive ipsilateral tumor thrombus or clinically evident portal hypertension. When extensive ipsilateral tumor thrombus exists, PVE is contraindicated as most of the portal blood flow has already been diverted, and safe delivery of an embolic agent is difficult (69). As clinically evident portal hypertension is a contraindication to hepatectomy, PVE is not indicated in this setting.

The goal of PVE is complete portal occlusion of targeted

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Table 1 Classification systems for evaluating liver function

<table>
<thead>
<tr>
<th>Classification system</th>
<th>Variables</th>
<th>Points</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child-Pugh</td>
<td>Encephalopathy</td>
<td>None</td>
<td>Mild or moderate (grade 1–2)</td>
</tr>
<tr>
<td></td>
<td>Ascites</td>
<td>None</td>
<td>Mild or moderate (diuretic responsive)</td>
</tr>
<tr>
<td></td>
<td>Bilirubin (mg/dL)</td>
<td>&lt;2</td>
<td>2–3</td>
</tr>
<tr>
<td></td>
<td>Albumin (g/dL)</td>
<td>&gt;3.5</td>
<td>2.8–3.5</td>
</tr>
<tr>
<td></td>
<td>PT/INR</td>
<td>&lt;1.7</td>
<td>1.7–2.3</td>
</tr>
<tr>
<td>ALBI</td>
<td>Bilirubin (µmol/L)</td>
<td>Calculated as ALBI = [log10(bilirubin) × 0.66] + (albumin × –0.085)</td>
<td>Grade 1: ≤–2.60; Grade 2: –2.60 to ≤–1.39; Grade 3: &gt;–1.39</td>
</tr>
<tr>
<td></td>
<td>Albumin (g/L)</td>
<td></td>
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<tr>
<td>MELD</td>
<td>Bilirubin (mg/dL)</td>
<td>Calculated as MELD = 3.8 × loge(serum bilirubin) + 11.2 × loge(INR) + 9.6 × loge(serum creatinine) + 6.4</td>
<td>Ranges from 6 to 40, with higher numbers correlating to more severe liver dysfunction</td>
</tr>
<tr>
<td></td>
<td>INR</td>
<td></td>
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<tr>
<td></td>
<td>Serum creatinine (mg/dL)</td>
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<td></td>
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<tr>
<td></td>
<td>Did the patient receive dialysis at least twice in the past week, or received 24 hours of CVVHD within the prior week? (Yes/No)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Serum sodium (mmol/L)</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>ALICE</td>
<td>ICG R15 (%)</td>
<td>Calculated as ALICE= 0.663 × log10(ICG R15) – 0.0718 × albumin</td>
<td>Grade 1: ≤2.20; Grade 2a: –2.20 to ≤–1.88; Grade 2b: &gt;–1.88 to ≤–1.39; Grade 3: &gt;–1.39</td>
</tr>
<tr>
<td></td>
<td>Albumin (g/L)</td>
<td></td>
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</tr>
</tbody>
</table>

*, In January 2016, the MELD score was updated to include serum sodium as a factor in calculating the MELD score (known as MELD-Na) for patients with a MELD of ≥12. Calculated as MELD-Na = MELD + 1.32 × (137-Na) – [0.033 × MELD × (137-Na)]. INR, international normalized ratio; ALBI, Albumin-Bilirubin; MELD, Model for End-Stage Liver Disease; ICG, indocyanine green; R15, retention at 15 minutes.
liver segments. Embolizing the entire portal tree, including distal branches, is critical to prevent portoportal shunts, as well as to maximize hypertrophy of the FLR and prevent hypertrophy of segments planned for resection. Multiple embolic agents have been described for PVE including fibrin glue, n-butyl cyanoacrylate (NBCA), ethanol, ethiodized oil, and microparticles such as trisacryl gelatin or polyvinyl alcohol. No randomized trials have been conducted comparing the various agents, but retrospective studies show similar efficacy (69).

The degree of hypertrophy after PVE depends on the presence/absence and severity of underlying liver disease. Patients with normal livers can be expected to regenerate at 2 weeks post-procedure at rates of 12–21 vs. 9 cm$^3$/day in patients with cirrhosis. In non-cirrhotic patients, sufficient hypertrophy usually occurs within 2–4 weeks, while sufficient hypertrophy in cirrhotic patients can take up to 4 weeks or more (70). Additionally, 10–20% of cirrhotic patients do not achieve adequate contralateral hypertrophy after undergoing PVE due to diminished liver regenerative capacity (71).

**Combination arterial and portal embolization**

Interest has developed in applying TACE sequentially with PVE before performing resection for HCC. In theory, this combination of TACE + PVE offers several benefits. Firstly, the liver necrosis that is typically seen after TACE may lead to increased regeneration rates. Secondly, hepatic arterial flow within the embolized segment increases after PVE, which can lead to increased tumor growth as HCC tumors preferentially derive blood supply from the hepatic artery. TACE therefore might provide local control of tumors in the interval between PVE and hepatectomy. Lastly, the formation of arterioportal shunts has been associated with HCC. These shunts can diminish the efficacy of PVE, which is usually performed upstream of these shunts. TACE targets these shunts and may render PVE more effective.

A French study compared 36 HCC patients with cirrhosis treated between 1998–2004, half (n=18) underwent TACE + PVE while the remaining half underwent PVE alone prior to right hepatectomy. The TACE + PVE treated patients experienced significantly higher mean increases in FLR volume compared to the PVE alone group. Operative blood loss, liver failure, and mortality were comparable between groups. The TACE + PVE group was significantly more likely to have complete tumor necrosis and had higher 5-year disease-free survival (37% vs. 19%) (72). A more recent Korean study published in 2011 of 135 patients undergoing TACE+PVE or PVE alone prior to right hepatectomy found similar results, with patients receiving combination therapy experiencing higher mean increase in sFLR and improved overall and disease-free survival compared with PVE alone (73). While there is a growing experience with TACE + PVE, including a randomized controlled trial currently ongoing in China, this procedure is still considered experimental and is not widely utilized in the US.

**Associated liver partition with portal vein ligation for staged hepatectomy (ALPPS)**

ALPPS is a novel, alternate method to PVE which has been utilized for FLR hypertrophy in patients with extensive colorectal liver metastasis (CRLM) undergoing extended right hepatectomy. In this technique, portal vein ligation and in situ splitting of the liver along the falciform ligament is performed to induce rapid hypertrophy of the left lateral section. After a short median interval of 9 days, patients undergo completion hepatectomy. Recently, ALPPS has been attempted in HCC patients. A retrospective review of 35 patients in the ALPPS registry from 2010–2015 with HCC found rapid and extensive FLR hypertrophy; however, this was significantly lower than for CRLM patients (47% vs. 76%) (74). The degree of hypertrophy was negatively correlated with the severity of liver fibrosis. The 90-day perioperative mortality was high at 31% (compared to 7% for CRLM) and the long-term oncologic outcomes are unknown. This procedure is still experimental and PVE remains the preferred technique to induce FLR hypertrophy prior to hepatectomy in HCC patients. There may be a limited role for ALPPS in younger, healthy non-cirrhotic patients who are not candidates for liver transplant and for whom the operative risks are deemed acceptable.

**Stem cell infusion**

A growing interest has developed in infusing stem cells into the FLR during PVE to improve hepatic regeneration. Small phase II trials have shown promising initial results, with stem cell-treated patients experiencing significant increases in hepatic growth volume compared with PVE-only patients, as well as improvements in underlying liver function (75,76). Further studies are needed to determine
whether stem cell infusion positively impacts surgical outcomes and survival.

Conclusions
Most HCC patients are not candidates for resection at diagnosis, often due to underlying liver dysfunction, inadequate FLR, or tumor characteristics. The perioperative risks of hepatic resection in cirrhotic patients with HCC must be balanced against the oncological benefits. Tumor characteristics including large tumor size, vascular invasion, and multifocality are not absolute contraindications to hepatic resection in well-compensated patients with a lack of alternative curative options. Underlying liver dysfunction must be carefully assessed, accounting for the degree of dysfunction, extent of planned liver resection, and alternative curative therapies including liver transplantation and ablation. Adjuncts such as PVE or ALPPS may allow an increased role for hepatic resection in HCC patients with small FLR.

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References
10. Fong Y, Sun RL, Jarnagin W, Blumgart LH. An analysis of 412 cases of hepatocellular carcinoma at a Western center.


61. Ribero D, Chun YS, Vauth ey JN. Standardized liver volumetry for portal vein embolization. Semin Intervent


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