World Journal of Hepatology

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DOI: 10.4254/wjh.v7.i20.2292

World J Hepatol 2015 September 18; 7(20): 2292-2302
ISSN 1948-5182 (online)

REVIEW

Management before hepatectomy for hepatocellular carcinoma with cirrhosis

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Author contributions: Both authors contributed to this work.

Supported by A Grant-in-Aid for Scientific Research (C) 25350856 from the Ministry of Education, Culture, Sports, Science and Technology (MEXT), Japan.

Conflict-of-interest statement: The authors declare no conflict of interest.

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Received: May 18, 2015
Peer-review started: May 19, 2015
First decision: July 6, 2015
Revised: August 4, 2015
Accepted: August 30, 2015
Article in press: August 31, 2015
Published online: September 18, 2015

Abstract

The global distribution of hepatocellular carcinoma (HCC) varies markedly among regions, and patients in East Asia and Central Africa account for about 80% of all cases. The risk factors are hepatitis B, hepatitis C, alcohol, and *etc.* The risk of carcinogenesis further increases with progression to hepatic cirrhosis in all liver disorders. Radical treatment of HCC by liver resection without causing liver failure has been established as a safe approach through selection of an appropriate range of resection of the damaged liver. This background indicates that both evaluation of hepatic functional reserve and measures against concomitant diseases such as thrombocytopenia accompanying portal hypertension, prevention of rupture of esophageal varices, reliable control of ascites, and improvement of hypoalbuminemia are important issues in liver resection in patients with hepatic cirrhosis. We review the latest information on perioperative management of liver resection in HCC patients with hepatic cirrhosis.

Key words: Hepatocellular carcinoma; Liver resection; Liver cirrhosis; Portal hypertension

Core tip: Radical treatment of hepatocellular carcinoma (HCC) by liver resection without causing liver failure has been established as a safe approach through selection of an appropriate range of resection of the damaged liver. This background indicates that both evaluation of hepatic functional reserve and measures against concomitant diseases such as thrombocytopenia accompanying portal hypertension, prevention of rupture of esophageal varices, reliable control of ascites, and improvement of hypoalbuminemia are important issues in liver resection in patients with hepatic cirrhosis. The latest information on perioperative management of liver resection in HCC patients with hepatic cirrhosis was reviewed.

Nakayama H, Takayama T. Management before hepatectomy for hepatocellular carcinoma with cirrhosis. *World J Hepatol* 2015; 7(20): 2292-2302 Available from: URL: http://www.

wjgnet.com/1948-5182/full/v7/i20/2292.htm DOI: http://dx.doi.org/10.4254/wjh.v7.i20.2292

INTRODUCTION

The global distribution of hepatocellular carcinoma (HCC) varies markedly among regions, and patients in East Asia and Central Africa account for about 80% of all cases[1,2]. The risk factors are hepatitis B and aflatoxin in these regions[3], whereas hepatitis C and alcohol are risk factors in North America, Europe and Japan[4,5]. The risk of carcinogenesis further increases with progression to hepatic cirrhosis in all liver disorders. Hepatic cirrhosis is an irreversible pathological change and inhibition of disease progression has previously been considered difficult. However, advances in antiviral therapy now permit eradication or inhibition of replication of viruses[6].

Radical treatment of HCC by liver resection without causing liver failure has been established as a safe approach through selection of an appropriate range of resection of the damaged liver[7,8]. In the HCC practice guidelines of the Barcelona Clinic Liver Cancer (BCLC) staging system, liver resection is not recommended for patients with portal hypertension[9], and radiofrequency ablation (RFA) and transcatheter arterial chemoembolization are selected in many countries. In Japan, liver resection using appropriate preoperative management has been found to be safe and to improve the prognosis for patients with portal hypertension[10].

This background indicates that both evaluation of hepatic functional reserve[11] and measures against concomitant diseases such as thrombocytopenia accompanying portal hypertension, prevention of rupture of esophageal varices, reliable control of ascites, and improvement of hypoalbuminemia are important issues in liver resection in patients with hepatic cirrhosis[12]. In this report, we review the latest information on perioperative management of liver resection in HCC patients with hepatic cirrhosis.

DEFINITION OF HEPATIC CIRRHOSIS

Hepatic cirrhosis is the terminal stage of chronic liver disease, in which fibrous tissue accumulation due to necrotizing inflammatory reactions makes the liver surface rough and irregular[12]. Histologically, lobular structure remodeling and pseudolobule formation are observed; *i.e.*, hepatic cirrhosis is a morphologically defined disease[13].

Classification

Hepatic cirrhosis is classified based on: (1) cause; (2) function and clinical stage; and (3) node size-based morphology (World Health Organization classification). In (2), hepatic cirrhosis is classified into compensated and decompensated phases, and by the Child-Pugh classification, as described below. In (3), hepatic cirrhosis is classified into three types: micro-nodular type, with nodes < 3 mm, macro-nodular type, with nodes ⩾ 3 mm, and mixed nodular type, in which both nodules are mixed.

Cause

Persistent hepatitis virus B and C infections and excessive alcohol intake are the causes in many patients. The specific types are primary biliary hepatic cirrhosis; autoimmune hepatitis; non-alcoholic steatohepatitis; and metabolic (Wilson disease, hemochromatosis), congestive (Budd-Chiari syndrome), parasitic, and drug-induced types[12].

Diagnosis

Hepatic cirrhosis is definitively diagnosed by histological confirmation of lobular structure remodeling and pseudolobule formation on liver biopsy. However, liver biopsy is not optimal because performance of this procedure before liver resection has a risk of complications. Thus, it is desirable to evaluate the presence of hepatic cirrhosis based on blood chemistry and diagnostic imaging. Several formulas for this purpose using blood tests have been reported[14-17] (Table 1). The aspartate aminotransferase (AST) to platelet ratio index (APRI index) is based on the AST level and platelet count. The diagnostic performance for hepatic cirrhosis C using a cut-off of 1.0 is about 77% sensitivity and 75% specificity[16].

In imaging diagnosis, transient elastography (FibroScan™) can be used for noninvasive measurement of liver stiffness (stiffness), in which liver elasticity is determined by measuring the velocity of transmission in the liver of a single shear wave emitted from a specific probe of an ultrasonic diagnostic device[18,19]. A strong correlation between liver elasticity and fibrosis stage has been reported[20].

Staging

The most common hepatic cirrhosis classification is the Child-Pugh classification, in which 5 factors are scored: encephalopathy, ascites, serum bilirubin level, serum albumin level, and prothrombin activity[21,22]. However, diagnoses of encephalopathy and ascites are subjective, and evaluation of liver function is determined specifically at the time of the test, which are disadvantages in evaluation of hepatic functional reserve for liver resection. In planning for liver resection, the liver damage classification is more appropriate, particularly for HCC[23]. This classification uses the indocyanine green retention rate at 15 min (ICG-R_{15}), instead of encephalopathy in the Child-Pugh classification, and stricter measurements of serum albumin and prothrombin levels. This classification is particularly useful for preoperative selection of patients with favorable hepatic functional reserve[24].

The prognosis of HCC depends on the hepatic functional reserve and tumor stage. These variables are integrated in staging systems including the model for

Table 1 Prediction formula and discriminating factors for hepatic cirrhosis

Year	Ref.	Formula
2000	Ikeda *et al*[14]	Z = (0.124) × [γ globulin (%)] + (0.001) × hyaluronic acid (ng/mL) + (0.075) × platelet count (10^4/μL) + (-0.413) × gender (male = 1, female = 2) + (-2.005) The condition is hepatic cirrhosis when Z is positive, and chronic hepatitis when Z is negative
2007	Koda *et al*[15]	Fibroindex = (1.738) + (-0.064) × platelet count (10^4/μL) + (0.005) × AST (IU/L) + (0.463) × [γ globulin (g/dL)] The fibroindex value corresponds to fibrosis stage
2003	Wai *et al*[16]	APRI = 100 × [AST level/(upper limit of normal AST)/platelet count (× 10^9/L)]
2006	Sterling *et al*[17]	FIB-4 = [age × AST (U/L)]/[platelet count (× 10^9/L) × ALT (U/L)$^{1/2}$]

APRI: AST to platelet ratio index; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; FIB-4: Fibroindex-4.

Table 2 Definitions of the cancer of the liver Italian program score[27]

Variable	Score		
	0	1	2
Child-Pugh stage	A	B	C
Tumor morphology	Uninodular and extension ⩽ 50%	Multinodular and extension ⩽ 50%	Massive or extension > 50%
AFP (ng/mL)	< 400	⩾ 400	
Portal vein thrombosis	No	Yes	

AFP: Alpha-fetoprotein.

Table 3 Definitions of the Japan integrated staging score[28]

Variable	0	1	2	3
Child-Pugh stage	A	B	C	
TNM stage[1]	I	II	III	IV

[1]By liver cancer study group of Japan.

end-stage liver disease[25], OKUDA[26], cancer of the liver Italian program (CLIP) (Table 2)[27], Japan integrated staging (JIS) score (Table 3)[28], modified-JIS score[29], and the Tokyo score[30], all of which are useful predictors of outcomes. Kudo *et al*[28] proposed the JIS score, in which the TNM stage and Child-Pugh classification are integrated. This score has advantages over the CLIP score (integration of the Child-Pugh classification, tumor morphology, alpha-fetoprotein, and portal vein tumor thrombosis) because (1) stratification of scores is distinct; (2) the prognosis of score-0 liver cancer is favorable; and (3) there is a definitive JIS score for cases with a poor prognosis. Integrated staging is useful for prediction of outcomes, but inappropriate for selection and comparison of treatment methods[31].

TREATMENT OF THROMBOCYTOPENIA

A reduced platelet count is an indicator of hepatic cirrhosis, and liver resection requires measures against thrombocytopenia to reduce the risk of hemorrhage[12]. Low preoperative platelet count is independently associated with increased major complications, post-operative liver insufficiency, and mortality after resection of HCC[32].

Partial splenic embolization is performed to improve hypersplenism through partially necrotizing the spleen by embolization of the splenic artery with a gelatin sponge or metal coil[33,34]. Long-term maintenance of the increased platelet count requires extensive splenic embolization of about 80% (splenic volumes ⩽ 700 mL)[35], but this treatment is accompanied by risks of complications such as abdominal pain (82.4%), fever (94.1%), and splenic abscess (1.2%)[36]. A short-term minimum effect of embolization is believed to be sufficient to prevent hemorrhage after liver resection[37].

Splenectomy reliably improves portal hypertension and hypersplenism. In HCC accompanied by hepatic cirrhosis, splenectomy improves the serum bilirubin, albumin, and prothrombin levels, and splenectomy performed before liver resection has a significant benefit[38]. In contrast, splenectomy before brain dead liver transplantation causes an increase in infection, decrease in survival rate, and high mortality[39,40]. Thus, it has been suggested that cases should be carefully selected for splenectomy. Also, since immune function is reduced in patients with hepatic cirrhosis, overwhelming post-splenectomy infection syndrome (OPSI) is a concern[41]. OPSI is a complication that develops rapidly regardless of the time after surgery and has a poor prognosis and high mortality (50%-70%)[42-44]. Pneumococcus is the causative bacteria in 80% of cases and a pneumococcus vaccine is recommended for splenectomized patients. Interferon administration following splenectomy may also induce OPSI; thus, antiviral therapy should be performed carefully. The incidences of portal vein thrombosis after splenectomy are 9%-29% and 1.6%-8.0% in patients with and without concomitant spleen enlargement, respectively[45-48]. Doppler ultrasonography and contrast CT are useful for early diagnosis of portal vein thrombosis following splenectomy. The timing of splenectomy varies among institutions (Table 4). Sugawara *et al*[49] recommended simultaneous splenectomy for readily resectable HCC

Table 4 Reports on liver resection and splenectomy for hepatocellular carcinoma complicated by hepatic cirrhosis accompanied by hypersplenism

Year	Ref.	Simultaneous splenectomy, 2-stage (No. of patients)	Platelet count ($\times 10^4/\mu L$)	Child-Pugh (A/B/C)	Mortality	Morbidity	Survival rate	Effect
1989	Takayama *et al*[38]	Simultaneous (12), 2-stage (8)	4.6	N	N	N	N	Expansion of indication of liver resection
1999	Lin *et al*[94]	Simultaneous (11)	5.2 ± 1.5	5/6/0	9.1%	27.3%	5 yr recurrence-free 66.7%	Improvement of serum bilirubin level
2000	Sugawara *et al*[49]	Simultaneous (35), 2-stage (13)	4.7 ± 0.3	N	0	47.9	3/5 yr survival rate: 72.3%/38.9%	Improvement of safety
2000	Shimada *et al*[95]	2-stage (6)	5.2 ± 1.5	1/4/1	0	17	N	Improvement of platelet count, albumin level, and Child classification
2003	Oh *et al*[96]	Simultaneous (12), no sp (6)	5.5 ± 1.5	10/8/0	11.1	66.7	N	Expansion of indication of liver resection
2004	Wu *et al*[97]	Simultaneous (41), no sp (485)	3.8 ± 2.1	419/85/23	1.5	20.5	N	Improvement of recurrence-free survival rate
2005	Chen *et al*[98]	Simultaneous (94), no sp (110)	6.2	125/79/0	N	15.2	5 yr survival 56%, recurrence-free survival 35%	Improvement of recurrence-free survival rate
2008	Sugimachi *et al*[99]	Simultaneous (4), no sp (11)	4.2 ± 0.8	9/6/0	6.7	47	N	3-yr survival rate equivalent to that after conventional liver resection
2015	Zhang *et al*[100]	Simultaneous (84), no sp (84)	6.1 ± 4.2	84/0/0	0	39.3	1/3/5 yr survival: 90%/78%/66%	Improvement of recurrence-free survival rate

N: Details unknown.

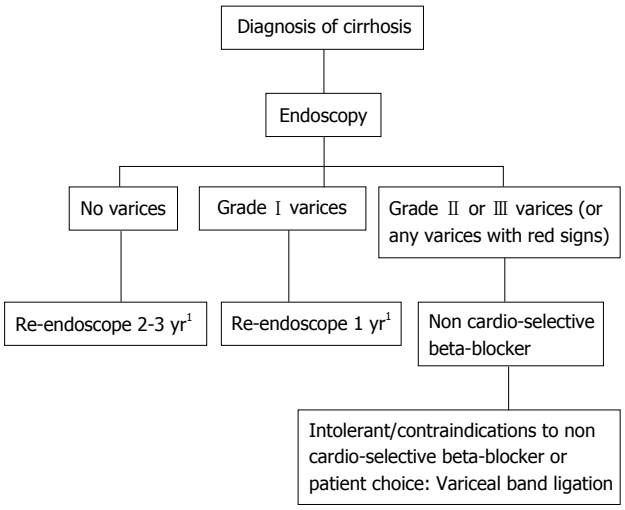


Figure 1 United Kingdom guidelines. Algorithm for surveillance of varices and primary prophylaxis in cirrhosis. [1]If there is clear evidence of disease progression this interval can be modified by clinician. Endoscopy should also be offered at time of decompensation[51].

in cases with favorable liver function and general conditions, and earlier splenectomy if these criteria are not met.

TREATMENT OF ESOPHAGEAL VARIX

The prognosis for patients with cirrhosis primarily depends on the occurrence of hemorrhage from esophageal varices and gastropathy. General rules for recording endoscopic findings of esophagogastric varices is formatted with location, form, color, red color signs, bleeding sings and mucosal findings (Table 5)[50]. According to the United Kingdom guide lines, esophageal varices are classified into 3 grades based on the size of varices[51]. Grade Ⅱ/Ⅲ varices (large) are indicated to beta-blocker or variceal ligation (Figure 1). McCormack classification is useful to definite of portal hypertensive gastropathy (Table 6)[52]. Thus, endoscopy should be performed before liver resection to avoid overlooking esophageal varices because the portal blood pressure rises after liver resection and this may aggravate varices. For patients with a history of hemorrhage from a varix, treatment of the varix before liver resection is required. For patients with a large (F2 or larger) varix accompanied by red color sign based on above general rules, preventive treatment is indicated[53].

Currently, endoscopic treatment is the standard for esophageal varices, using endoscopic injection sclerotherapy and endoscopic variceal ligation[54]. Balloon-occluded retrograde transvenous obliteration (BRTO) improves the varix and ICG-R_{15} value in patients with a gastric varix[55], but there is no evidence that BRTO improves the safety of liver resection. The endoscopic F factor (large varices) rating of bleeding esophageal varices can be a significant predictive factor for HCC[56]. So the screening of HCC is required after the treatment

Table 5 General rules for recording endoscopic findings of esophagogastric varices[50]

Category	Code subcategory
Location (L)	Ls: Locus superior
	Lm: Locus medialis
	Li: Locus inferior
	Lg-c: Adjacent to the cardiac orifice
	Lg-cf: Extension from the cardiac orifice to the fornix
	Lg-f: Isolated in the fornix
	Lg-b: Located in the gastric body
	Lg-a: Located in the gastric antrum
Form (F)	F0: No varicose appearance
	F1: Straight, small-caliber varices
	F2: Moderately enlarged, beady varices
	F3: Markedly enlarged, nodular or tumor-shaped varices
Color (C)	Cw: White varices
	Cb: Blue varices
	Cw-Th: Thrombosed white varices
	Cb-Th: Thrombosed blue varices
Red color signs (RC)	RWM: Red wale markings
	CRS: Cherry red spots
	HCS: Hematocystic spots
	Esophageal varices: RC0, RC1, RC2, RC3
	Gastric varices: RC0, RC1
	Te: Telangiectasia
Bleeding signs	Gushing bleeding
	Spurting bleeding
	Oozing bleeding
	Red plug
	White plug
Mucosal findings	E: Erosion
	Ul: Ulcer
	S: Scar

of large varices.

CONTROL OF ASCITES

Ascites accompanying hepatic cirrhosis involves interactions among various factors, including enhancement of liver lymph production with elevation of the portal blood pressure, enhancement of intra-abdominal portal permeability, reduction of the effective circulating blood volume, and enhancement of the sympathetic nervous system[12]. Treatment of fluid retention, which manifests as ascites, includes restriction of salts and water, administration of diuretics, and transfusion of an albumin preparation. If no effect is obtained in a short time, the patient is at high risk of liver or multiple organ failure, and liver resection should be avoided[57]. Selection of the smallest possible range of resection in patients with relatively favorable liver function and early resolution of ascites is the key to safe and successful liver resection[11].

IMPROVEMENT OF NUTRITIONAL STATUS

The association between preoperative sarcopenia and postoperative morbidity/mortality has been reported for various types of surgeries. Preoperative sarcopenia increased the morbidity rate including the rate of liver failure, in patients who underwent major hepatectomy with extrahepatic bile duct resection[58]. European Society for Parenteral and Enteral Nutrition guidelines recommended an energy intake of 35-40 kcal/kgBW per day (147-168 kJ/kgBW per day) and a protein intake of 1.2-1.5 g/kgBW per day for cirrhotic patients perioperatively[59].

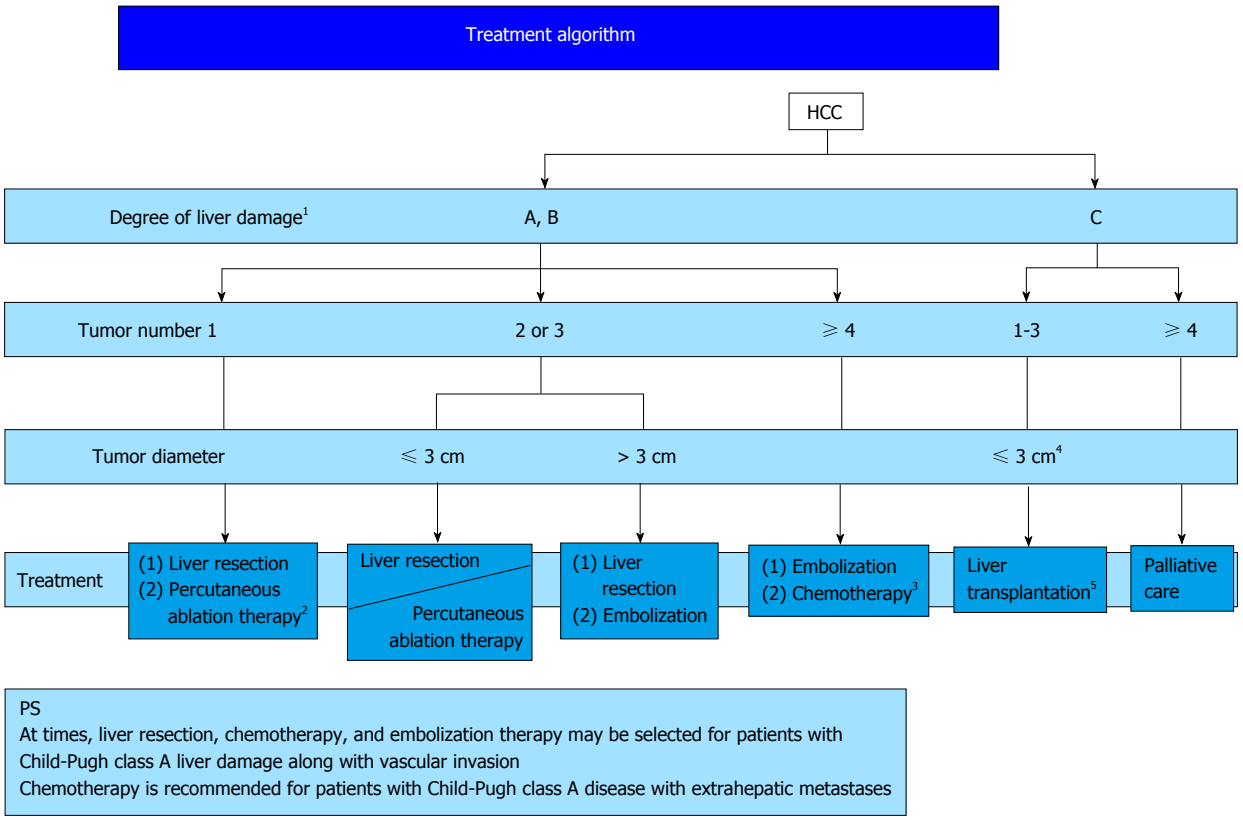
Protein-energy malnutrition (PEM) occurs in 27%-87% of patients with hepatic cirrhosis, and the level of branched-chain amino acids (BCAAs) is markedly reduced[60]. In PEM, hypoalbuminemia is observed and BCAAs are used for processing of ammonia and as an energy source for gluconeogenesis in skeletal muscle. In hepatic cirrhosis, serum albumin and plasma BCAA levels are positively correlated, and the prognosis is significantly poorer when serum albumin is < 3.5 g/dL[61,62]. Oral administration of BCAAs is of interest as a pharmacological and nutritional approach for improvement of hypoalbuminemia and insulin resistance, inhibition of angiogenesis, and activation of immune function[63]. In a randomized controlled trial (RCT) in 646 patients with decompensated hepatic cirrhosis who were divided into groups with and without treatment with oral BCAAs for 2 years, the incidences of death, liver cancer, rupture of esophageal varix, and liver failure were lower in the BCAA group and the prognosis was improved[64].

Table 6 McCormack classification for the presence of portal hypertension and portal hypertensive gastropathy[52]

Mild gastropathy	Fine pink speckling
	Superficial reddening
	Snakeskin (Mosaic-like) appearance
Severe gastropathy	Cherry-red spots
	Diffuse hemorrhagic lesion

SELECTION OF LIVER RESECTION RANGE

In Japan, East Asia and some European countries, ICG-R_{15} is used as an index of hepatic functional reserve. ICG-R_{15} is also a predictor of morbidity and mortality after surgery[65,66] and can be used to determine the acceptable liver resection range. In the therapeutic strategy for HCC, the BCLC staging system recommended by AASLD and EASL is used worldwide[9]. In Japan, the "treatment algorithm" described in the Clinical Guidelines for HCC is widely used to select the optimum treatment based on the liver function and tumor status (Figure 2)[67]. The Japanese treatment algorithm differs markedly from the BCLC system with regard to HCC with concomitant portal hypertension[68]. In the BCLC system, liver resection is not indicated if portal hypertension is present, and liver transplantation and RFA are recommended. In contrast, liver resection is recommended based on the ICG-R_{15} level in the Japanese treatment algorithm, and favorable outcomes



(Caution) 1: The Child-Pugh classification may also be used when non-surgical treatment is considered
2: Can be selected for tumors with a diameter of ⩽ 3 cm
3: Oral administration and/or hepatic arterial infusion are available
4: A single tumor ⩽ 5 cm or 2-3 tumors ⩽ 3 cm in diameter
5: Patients aged ⩽ 65 yr

Figure 2 Algorithm for treatment in Japanese hepatocellular carcinoma guidelines[67]. This algorithm has been simple and easy to memorize, consisting of three factors: (1) degree of liver damage; (2) number of tumors; and (3) tumor diameter. The recommendable treatment options are narrowed down to one or two by referring to this algorithm. HCC: Hepatocellular carcinoma.

have been reported[10].

Liver resection for HCC is chosen based on the balance between tumor status and liver function. Resection exceeding the hepatic functional reserve with the goal of cancer cure may lead to liver failure, whereas insufficient resection of the cancer due to excessive safety concerns may have a high risk of early recurrence. Therefore, it is important to select the optimum surgical procedure based on the tumor advancement and the acceptable liver resection range. Preoperative liver function can be evaluated using a galactose tolerance test, ^{99m}Tc-GSA liver scintigraphy, and an ICG tolerance test. The Makuuchi criteria are particularly useful for chronic hepatitis and hepatic cirrhosis cases (Figure 3)[11]. These criteria use the presence or absence of ascites, serum bilirubin level, and ICG-R$_{15}$ as evaluation items. Surgery is not indicated for cases with persistent ascites despite treatment with diuretics or if the serum bilirubin level is consistently > 2.0 mg/dL. The range of resection is determined based on ICG-R$_{15}$ in patients with a normal bilirubin level of ⩽ 1.0 mg/dL, *i.e.*, procedures can be selected for resection of up to 2/3 of the total liver volume (such as right lobectomy) in patients with normal ICG-R$_{15}$ (< 10%), up to 1/3 of the total liver volume (such as left lobectomy) for patients with ICG-R$_{15}$ of 10%-19%, and up to 1/6 of the total liver volume (Couinaud's segmentectomy) for patients with ICG-R$_{15}$ of 20%-29%. When ICG-R$_{15}$ exceeds 30%, surgery is limited to partial resection or enucleation. In a study in 1056 patients who underwent liver resection based on these criteria, the surgical mortality was 0%[8].

Systematic resection of cancer-containing regions perfused by branches of the portal vein should be performed within the range allowed by the liver function and with consideration of HCC invasion of the portal vein. Systematic subsegmentectomy of the liver was developed to overcome two contradictory goals: cancer curability and conservation of liver function[69]. Since HCC develops in a liver damaged by chronic hepatitis and hepatic cirrhosis in many cases, an insufficient volume of residual liver after major hepatectomy, such as lobectomy, may result in liver failure. To prevent liver failure, portal vein embolization (PE) is applied to the branch of the portal vein perfusing the planned region for resection to induce compensatory hypertrophy of the region remaining after liver resection[70]. PE is indicated for cases with ICG-R$_{15}$ < 10% and a ratio of the non-tumorous parenchymal volume of the resected liver to

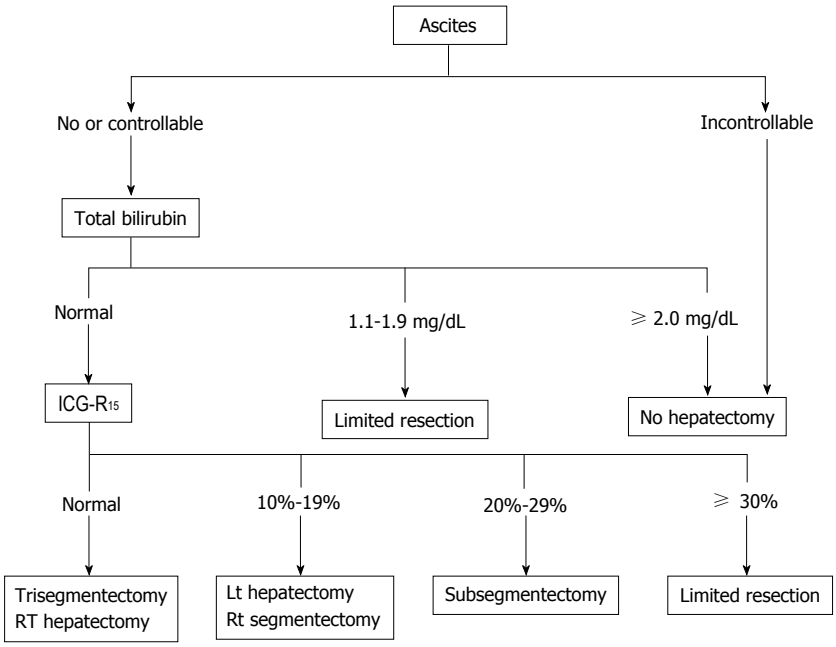


Figure 3 Makuuchi's criteria. Algorithm before proceeding to safety hepatectomy for hepatocellular carcinoma with cirrhotic liver. Makuuchi's criteria include three factors: ascites, total serum bilirubin, and the ICG-R_{15}: indocyanine green 15 min retention rate. This algorithm shows the maximal area for which an operation can be performed safely (modified ref.[11]).

that of the whole liver (R2) of ⩾ 60%, and for cases with ICG-R_{15} ⩾ 10% to < 20% and R2 of 40%-60%[71]. Both degree of liver hypertrophy and growth rate after PE are strong predictors of post-hepatectomy liver failure[72]. Recent introduction of 3-dimensional computed tomography (CT) has enabled simple and accurate determination of the positional relationship between the main vessels and the tumor, the range of resection, and measurement of the residual liver volume[73].

Since 1990, liver resection for HCC has been performed with acceptable blood loss at high-volume medical centers, and centers performing surgery with blood loss of about 500 mL have increased[74-77]. Blood transfusion may promote cancer recurrence and is likely to induce hyperbilirubinemia and liver failure[78]. Since a low hematocrit value is preferable for microcirculation of the liver, perioperative allogeneic transfusion should be avoided as much as possible in liver resection. Autologous blood transfusion is safe and useful for avoidance of allogeneic transfusion without increasing the risk of cancer recurrence[79]. Administration of fresh frozen plasma is recommended to supplement coagulation factors and maintain the effective plasma volume[80], but administration of fresh frozen plasma does not influence the course after liver resection and is not necessary if the serum albumin level 2 d after surgery is ⩾ 2.4 g/dL in Child-Pugh class A cases with intraoperative blood loss of < 1000 mL[81].

The immunosuppressed state after liver resection may lead to progression of liver failure and disseminated intravascular coagulation. In a RCT of steroid administration after liver resection, postoperative liver function was compared between groups treated with and without 500 mg/body hydrocortisone before liver resection. Serum bilirubin significantly decreased 2 d after surgery in the steroid group and there were significant differences in the time-courses of the bilirubin level and the prothrombin activity for 7 d after surgery. These results show the efficacy of steroid administration for liver resection[82].

POSTOPERATIVE ANTIVIRAL TREATMENT FOR HCC

HCC often recurs even after curative liver resection or RFA. It has been believed that controlling hepatitis and ameliorating the symptoms of cirrhosis prevent the recurrence of HCC. Several studies have examined the adjuvant therapies for their ability to prevent recurrence[83]. Eight RCTs were carried out to verify the efficacy of adjuvant interferon therapy for postoperative HCC[84-91]. It is suggested that adjuvant interferon-α reduced HCC recurrence and improved overall survival in patients with hepatitis C virus-infected HCC following curative treatment. The available evidence suggests that antivirus therapy with nucleoside analogs (lamivudine) should be recommended a postoperative preventive therapy for patients with hepatitis B virus-related HCC (> 500 copies of hepatitis B virus DNA/mL)[92,93].

CONCLUSION

Perioperative management is important in liver resection for patients with HCC and hepatic cirrhosis. New methods for evaluation and improvement of liver function are likely to facilitate expansion of the indication for liver resection.

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P- Reviewer: Wang K **S- Editor**: Song XX
L- Editor: A **E- Editor**: Liu SQ

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