Perioperative and Long-term Outcome of Major Hepatic Resection for Small Solitary Hepatocellular Carcinoma in Patients With Cirrhosis

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Hypothesis: Major hepatic resection is safe and provides favorable long-term survival for cirrhotic patients with a small solitary hepatocellular carcinoma.

Design: Retrospective case series.

Setting: Tertiary referral center.

Patients: From January 1, 1989, to December 31, 2001, 218 cirrhotic patients with a solitary hepatocellular carcinoma 5 cm or less in diameter underwent either a major hepatic resection (n=84) or a minor hepatic resection (n=134).

Major Outcome Measures: Perioperative morbidity and mortality, and long-term survival rates.

Results: The major resection group had significantly larger tumors (median, 3.5 vs 2.5 cm; $P<.001$) and better liver function (median indocyanine green retention at 15 minutes, 9.3% vs 12.9%; $P<.001$) than the minor resection group. Postoperative morbidity (46.4% vs 39.6%) and mortality (8.3% vs 3.0%) were higher in the major resection group than in the minor resection group, but the differences did not reach statistical significance ($P=.32$ and $P=.11$, respectively). The median overall survival did not differ significantly between the 2 groups (102.0 vs 72.3 months; $P=.25$). However, the median disease-free survival in the major resection group was significantly better than that in the minor resection group (59.0 vs 29.5 months; $P=.03$). On further subgroup analysis, both disease-free and overall survival rates were significantly better in the major hepatic resection group for tumors of 3 to 5 cm.

Conclusion: In well-selected cirrhotic patients with a small, solitary hepatocellular carcinoma, major hepatic resection is safe and may offer a better long-term survival over minor hepatic resection for patients with tumors of 3 to 5 cm.

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IN PATIENTS with cirrhosis, hepatocellular carcinomas (HCCs) are often detected while they are relatively early and small.[1,2] This may be related to the success of screening programs for cirrhotic patients.[3,4] For HCC in the setting of cirrhosis, hepatic resection remains the most viable curative treatment option.[5,6] For tumors larger than 5 cm in diameter, major hepatic resection in the form of hemihepatectomy or extended hepatectomy is generally the preferred type of resection to allow removal of the entire tumor with an adequate resection margin.[6] Because a large portion of the resected hemiliver is usually already occupied by the tumor itself, the loss of functional liver parenchyma is relatively small compared with hemihepatectomy for a small tumor. Hence, major hepatic resection may not necessarily lead to a significant compromise in the existing liver function in cases of large HCCs.

On the other hand, for tumors smaller than 5 cm, the preferred type of resection is more controversial. The extent of resection can be variable and often depends on a number of factors such as the location of the tumor, liver functional reserve, and the surgeon's preference. For a peripherally located HCC, a minor hepatic resection in the form of a segmentectomy or nonanatomic wedge resection has generally been advocated, as it preserves the surrounding nontumorous functional liver.[7-9] However, for a small HCC centrally located in one lobe or situated close to a major portal vein or hepatic vein branch, resection may entail a major hepatectomy and require the removal of a large bulk of nontumorous functional liver. In the presence of cirrhosis, this could lead to postoperative liver failure[10,11] and may also jeopardize the long-term survival outcome.[12,13] With the availability of alternative effective treat-

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ment options such as liver transplantation[14,15] and local ablative therapy[16] for cirrhotic patients with HCCs of 5 cm or less, the role of major hepatic resection for a small HCC in a cirrhotic liver has become even more debatable.

To our knowledge, no study has specifically evaluated the operative risk and long-term survival outcome of major hepatic resection with hemihepatectomy or extended hepatectomy in patients with small HCC and cirrhosis. Although some recent studies have shown that a larger hepatic resection may translate into a better long-term survival outcome for small HCCs,[17-19] these studies were mainly concerned with comparing segmentectomy or the so-called anatomic resection with nonanatomic resection. This study aimed to evaluate the perioperative and long-term survival outcome of major hepatic resection in patients with a small solitary HCC of 5 cm or less and cirrhosis.

METHODS

From January 1, 1989, to December 31, 2001, 638 patients underwent hepatic resection of HCC with macroscopically complete removal of the tumor at Queen Mary Hospital, University of Hong Kong Medical Centre, Hong Kong. Among them, 218 patients had liver cirrhosis and a solitary HCC with a maximum diameter of 5 cm. Both liver cirrhosis and HCC were confirmed histologically in each case. Of the 218 patients, 84 patients (38.5%) underwent a major hepatic resection, either hemihepatectomy or extended hepatectomy, and 134 patients (61.5%) underwent either a segmentectomy of 1 or 2 segments or nonanatomic wedge resection. The perioperative and long-term outcomes of the major hepatic resection group were compared with those of the minor hepatic resection group. Details of preoperative investigations, operative techniques, and perioperative management have been reported elsewhere.[20] After the operation, all patients underwent daily liver function testing for at least 7 days. For each patient, an indocyanine green (ICG) clearance test was performed before operation and repeated at postoperative day 7. Postoperative liver failure was defined as the appearance of hepatic encephalopathy, progressively worsening hyperbilirubinemia, and decreasing activity of blood coagulation as assessed by the prothrombin time.[21]

TYPES OF HEPATIC RESECTION

The types of hepatic resection were defined according to a recent consensus classification.[22] Right hepatectomy, left hepatectomy, extended right hepatectomy, and extended left hepatectomy were considered major hepatic resection (3 segments or more), whereas segmentectomy of 1 or 2 segments and nonanatomic wedge resection were classified as minor hepatic resection (2 segments or fewer).

For each patient, the decision whether to perform a major or minor hepatic resection was made preoperatively on the basis of the radiologic location of the tumor on computed tomographic scan, the patient's liver function including the result of the ICG clearance test,[23] and the likelihood of achieving an adequate resection margin. Previously we used an ICG retention at 15 minutes (ICG-R15) of less than 14% as the safety limit for major hepatic resection,[23] but in recent years we have performed major hepatic resection in patients with ICG-R15 up to 20%.[24] The operating surgeon might have changed the decision regarding the extent of resection during the operation if there were discrepancies between the preoperative assessment and intraoperative findings, such as the presence of ascites, gross severity of cirrhosis, and the size of the liver remnant. In general, minor hepatic resection was the preferred procedure if macroscopic tumor clearance could be achieved, but major hepatic resections were performed quite liberally for patients with more centrally located tumors close to a major portal vein or hepatic vein, provided their liver function reserve was considered adequate.

COLLECTION OF CLINICOPATHOLOGIC AND FOLLOW-UP DATA

Since January 1989, a computerized database has been in place to collect all clinical, laboratory, histopathologic, intraoperative, and postoperative data prospectively from patients who underwent hepatic resection in our center. Hospital morbidity and mortality were defined as events occurring during the same admission as operation.

All patients were regularly followed up at our outpatient clinic and were prospectively monitored for recurrence by serum α-fetoprotein level monthly and an ultrasound or contrast computed tomographic scan, together with chest x-ray film, every 3 months. Suspected intrahepatic recurrence was confirmed by computed tomographic scan, hepatic angiography, and, if necessary, post-Lipiodol (Lipiodol Ultrafluide; Laboratoire Guerbet, Aulnay-sous-Bois, France) computed tomographic scan or percutaneous needle biopsy. Recurrent tumors were treated by reresection if possible, or otherwise by transarterial chemoembolization or local ablation.[25] By the time of data analysis (June 30, 2002), all patients had been followed up for at least 6 months.

STATISTICAL ANALYSIS

Statistical analysis was performed by the χ^2 test or the Fisher exact test to compare discrete variables, and the Mann-Whitney test to compare continuous variables between groups. Survival analysis, including cumulative overall survival and disease-free survival, was estimated by the Kaplan-Meier method. Hospital deaths were included in the overall survival analysis, but were excluded from the disease-free survival analysis. Statistical comparison of survival distributions was analyzed by the log-rank test. Multivariate analysis by the Cox proportional hazard regression model was used to identify independent prognostic factors in predicting disease-free and overall cumulative survival. A *P* value less than .05 was considered to indicate statistical significance. Statistical analyses were performed with SPSS for Windows 10.0 computer software (SPSS Inc, Chicago, Ill).

RESULTS

COMPARISON OF CLINICOPATHOLOGIC AND OPERATIVE DATA

Comparisons of the clinical and laboratory data between the major and minor hepatic resection groups are shown in **Table 1**. Sex distribution and age were comparable between the 2 groups. In both groups, more than 80% of the HCCs were related to hepatitis B infection. The minor hepatic resection group tended to be suffering from a greater degree of cirrhosis, as reflected by the significantly lower platelet count, longer prothrombin time, and worse ICG-R15. Major hepatic resections took longer to perform, but the operative blood loss and blood transfusion were not significantly greater than those in minor hepatic resections (**Table 2**).

Table 1. Clinical and Laboratory Data*

Variable	Major Resection (n = 84)	Minor Resection (n = 134)	P Value
Sex, No. (%) M	69 (82.1)	110 (82.1)	.99
Age, y	54 (19-82)	56.5 (7-86)	.53
HbsAg positive, No. (%)	73 (86.9)	111 (82.8)	.49
AFP, ng/mL	90 (2-32 843)	100 (2-16 800)	.68
Albumin, g/L	42 (23-50)	40 (24-52)	.07
Total bilirubin, mg/dL	0.64 (0.23-1.87)	0.70 (0.18-3.39)	.07
AST, U/L	35.5 (15-393)	40.5 (19-219)	.04
Hemoglobin, g/dL	14.2 (8.4-16.5)	14.2 (7.9-16.7)	.34
Platelets, $\times 10^3$/uL	160 (27-502)	126 (27-566)	<.001
Prothrombin time, s	12.2 (9.5-15.7)	12.8 (10-21.4)	<.001
ICG-R15, %	9.3 (2.2-28.5)	12.9 (1.2-63.0)	<.001
Child-Pugh classification, No. (%)			
A	82 (97.6)	12.4 (92.5)	.14
B	2 (2.4)	10 (7.5)	

Abbreviations: AFP, α-fetoprotein; AST, aspartate aminotransferase; HbsAg, hepatitis B surface antigen; ICG-R15, indocyanine green retention at 15 minutes.

SI conversion factor: To convert bilirubin to micromoles per liter, multiply by 17.1.

*Continuous data are expressed as median with range in parentheses, unless otherwise indicated.

Table 2. Operative and Pathologic Data*

Variable	Major Resection (n = 84)	Minor Resection (n = 134)	P Value
Blood loss, L	1.0 (0.1-5.0)	0.8 (0.05-5.6)	.12
Blood transfusion, L	0.0 (0.0-3.7)	0.0 (0.0-9.0)	.31
No. (%) of patients with transfusion	17 (20.2)	36 (26.9)	.26
Ascites, L	0.0 (0-2.0)	0.0 (0-3.0)	.05
Operating time, min	402.5 (200-708)	285 (70-750)	<.001
Tumor size, cm	3.5 (1.0-5.0)	2.5 (0.5-5.0)	<.001
<, No. (%)	28 (33.3)	89 (66.4)	<.001
3-5, No. (%)	56 (66.7)	45 (33.6)	<.001
Tumor-free resection margin, cm	1.5 (0-7.0)	0.8 (0-4.0)	<.001
Positive microscopic resection margin, No. (%)	2 (2.4)	6 (4.5)	.49
Resection margin width, No. (%)			
≤1 cm	31 (36.9)	82 (61.2)	<.001
>1 cm	53 (63.1)	42 (38.8)	
Venous infiltration, No. (%)	29 (34.5)	29 (21.6)	.03
Pathologic TNM staging, No. (%)			
Stage I	7 (8.3)	36 (27.0)	.002
Stage II	47 (56.0)	71 (53.0)	
Stage III	23 (27.4)	18 (13.4)	
Stage IVA	7 (8.3)	9 (6.7)	

*Continuous data are expressed as median with range in parentheses, unless otherwise indicated.

Compared with the minor resection group, the major resection group had significantly larger tumors (median, 3.5 vs 2.5 cm; $P<.001$) and more frequent venous infiltration by tumor (34.5% vs 21.6%; $P=.03$) (Table 2). The major resection group had a lower proportion of stage I tumors and a higher proportion of stage III tumors ($P=.002$) by pathologic TNM staging.[26] A wider resection margin (1.5 vs 0.8 cm; $P<.001$) was achieved in major hepatic resections, but the proportion of histologically positive resection margin in the major resection group was not significantly different from that in the minor resection group.

The types of hepatectomy for each resection group are shown in **Table 3**. In the major hepatic resection group, the majority of patients (77.4%) underwent right hepatectomy or extended right hepatectomy. In the minor hepatic resection group, about half of the patients (53.0%) had bisegmentectomy or segmentectomy, and the other patients (47.0%) had nonanatomic wedge resection.

POSTOPERATIVE MORBIDITY AND MORTALITY

Although the major resection group had better baseline liver function measures, the impairment in liver function after resection was more evident after a major hepatic resection, as indicated by a significantly higher postoperative bilirubin level and ICG-R15 (**Table 4**). However, the overall postoperative complication rates were comparable in both groups (46.4% vs 39.6%; $P=.32$). The postoperative liver failure rates were also comparable in both groups (8.3% vs 3.0%; $P=.17$). The major resection group had a slightly higher hospital mortality than the minor resection group (8.3% vs 3.0%), but the difference was not statistically significant ($P=.11$). The causes of hospital mortality in the major hepatic resection group were liver failure (n=2), intra-abdominal sepsis (n=2), congestive heart failure (n=1), chest infection (n=1), and intra-abdominal bleeding (n=1), whereas the hospital mortality in the minor resection group was ascribed to liver failure (n=2), intra-abdominal sepsis (n=1), and chest infection (n=1).

LONG-TERM SURVIVAL OUTCOME

By the time of data analysis, the major resection group had a significantly lower intrahepatic recurrence rate than the minor resection group (31.0% vs 44.8%; $P=.04$), whereas extrahepatic recurrence rates were comparable between the 2 groups (7.1% vs 8.2%; $P=.78$). **Figure 1** shows the cumulative disease-free survival curves of cirrhotic patients who had undergone either a major or minor resection for HCCs of 5 cm or smaller. The median disease-free survival in the major hepatic resection group was 59.0 months, which was significantly better than that of the minor hepatic resection group (29.5 months; $P=.03$). The 5-year disease-free survival rate was 48.8% in the major resection group and 34.6% in the minor resection group, respectively. **Figure 2** shows the cumulative overall survival curves of cirrhotic patients who had undergone either a major or minor resection. The overall median survival in the major hepatic resection group was better than that of the minor hepatic resection group (102.0 vs 72.3 months), although it was not statistically significant ($P=.25$). The 5-year overall cumulative survival rate was 72.5% in the major resection group and 60.3% in the minor resection group, respectively.

Table 3. Type of Hepatectomy

Hepatectomy	No. (%)
Major Resection (n = 84)	
Right hepatectomy	49 (58.3)
Right hepatectomy + caudate lobectomy	2 (2.4)
Extended right hepatectomy	13 (15.5)
Extended right hepatectomy + caudate lobectomy	1 (1.2)
Left hepatectomy	11 (13.1)
Extended left hepatectomy	7 (8.3)
Extended left hepatectomy + caudate lobectomy	1 (1.2)
Minor Resection (n = 134)	
Bisegmentectomy	19 (14.2)
Segmentectomy	52 (38.8)
Nonanatomic resection	63 (47.0)

Table 4. Postoperative Data*

Postoperative Data	Major Resection (n = 84)	Minor Resection (n = 134)	*P* Value
Total bilirubin on postoperative day 7, mg/dL	1.7 (0.4-24.7)	1.6 (0.3-21.2)	<.001
Maximum postoperative bilirubin, mg/dL	3.2 (1.1-51.5)	2.0 (0.5-33.2)	<.001
Platelets on postoperative day 7, $\times 10^3$/L	129 (17-399)	157 (44-693)	.02
Maximum postoperative creatinine level, mg/dL	1.1 (0.7-5.6)	1.1 (0.2-12.0)	.72
ICG-R15 on postoperative day 7, %	59.3 (20.1-75.2)	44.3 (16.4-70.3)	.01
Postoperative liver failure, No. (%)	7 (8.3)	4 (3.0)	.17
Postoperative complications, No. (%)	39 (46.4)	53 (39.6)	.32
Hospital mortality, No. (%)	7 (8.3)	4 (3.0)	.11

Abbreviation: ICG-R15, indocyanine green retention at 15 minutes.
SI conversion factors: To convert bilirubin to micromoles per liter, multiply by 17.1; creatinine to micromoles per liter, multiply by 88.4.
*Continuous data are expressed as median with range in parentheses, unless otherwise indicated.

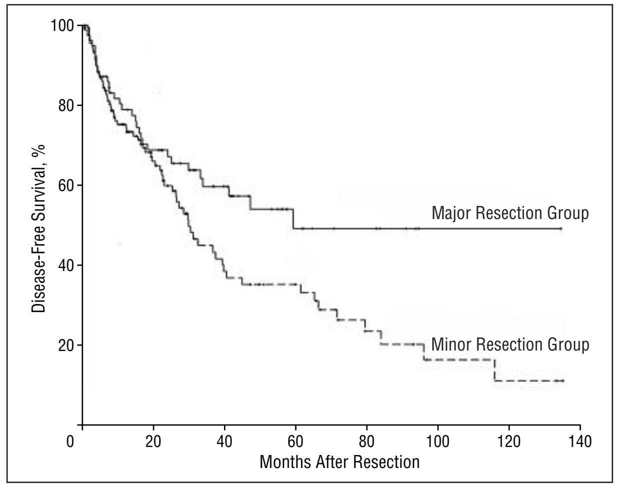

Figure 1. Cumulative disease-free survival curves of the major resection group (n=77) and the minor resection group (n=130) (*P*=.03).

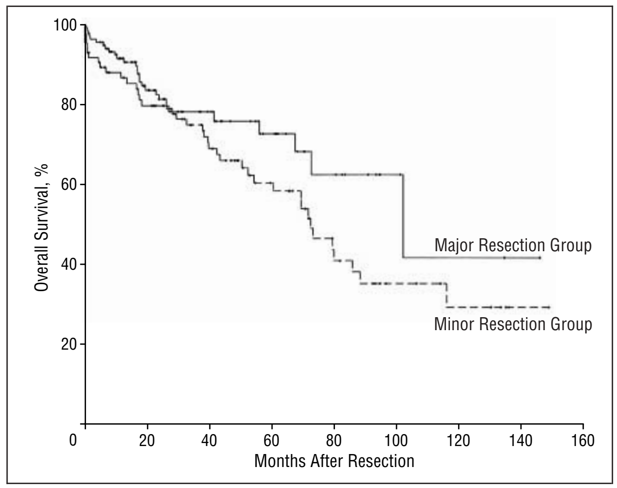

Figure 2. Cumulative overall survival curves of the major resection group (n=84) and the minor resection group (n=134) (*P*=.25).

When survival outcome of the major hepatic resection group was compared with that of patients who had undergone bisegmentectomy or segmentectomy, there were no significant differences in the disease-free survival (median, 59.0 vs 30.0 months; *P*=.12) or the overall cumulative survival (median, 102.0 vs 85.7 months; *P*=.86). However, when survival outcome of major hepatic resection was compared with that of nonanatomic resections, there was a significant difference in both the disease-free survival (median, 59.0 vs 29.5 months; *P*=.03) and the overall cumulative survival (median, 102.0 vs 54.1 months; *P*=.04).

Survival analysis was also repeated with further stratification of the patients according to tumor size less than 3 cm and tumor size 3 to 5 cm. In the subgroup analysis, for tumors smaller than 3 cm, both disease-free and overall cumulative survival were not significantly different between the 2 resection groups (*P*=.61 and *P*=.82, respectively). However, as depicted in **Figure 3** and **Figure 4**, for tumors of 3 to 5 cm, both disease-free and overall cumulative survival were significantly better in the major resection group.

To test whether major hepatic resection was an independent favorable prognostic factor of disease-free survival of the whole cohort of 218 patients, a multivariate analysis was performed. Clinicopathologic variables that might affect the disease-free survival of the patients in this study, including Child-Pugh classification, ICG-R15, intraoperative blood loss volume, blood transfusion volume, resection margin, tumor size (<3 cm or ≥3 cm), pathologic TNM staging, venous infiltration by HCC, and major hepatic resection were subjected to Cox regression analysis. The result showed that early pathologic TNM staging and major hepatic resection were the independent favorable prognostic factors of cumulative disease-free survival (**Table 5**).

COMMENT

The role of major hepatic resection for small HCCs in cirrhotic patients remains controversial because of sev-

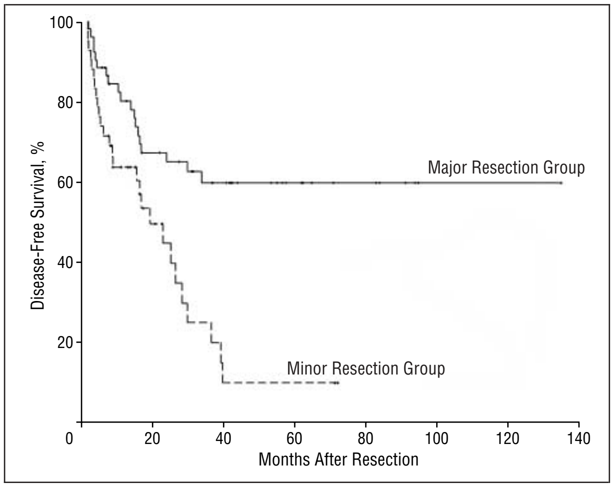

Figure 3. Cumulative disease-free survival curves for tumors 3 cm or larger in the major resection group (n=53) and the minor resection group (n=43) ($P<.001$).

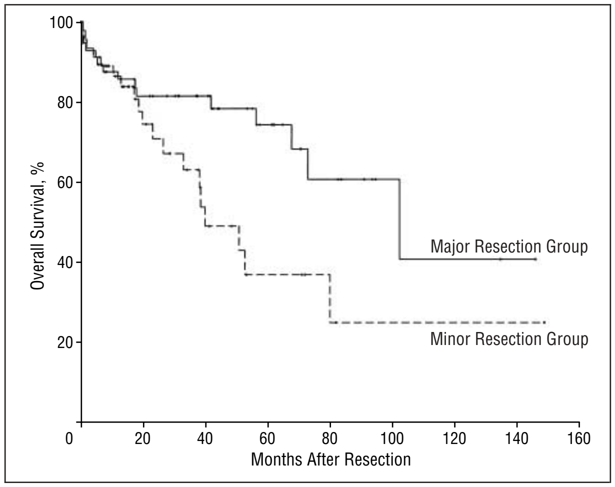

Figure 4. Cumulative overall survival curves for tumors 3 cm or larger in the major resection group (n=56) and the minor resection group (n=45) ($P=.02$).

eral issues. First, in addition to the already increased operative risk in patients with cirrhosis, major hepatic resection has generally been associated with a higher perioperative morbidity and mortality than minor hepatic resection. Some authors have reported a 30-day mortality of up to 20% after major hepatic resections.[27] The increase in operative risk associated with major hepatic resection may be related to the longer operating time, the smaller functional reserve of the liver remnant,[28] and the increased amount of intraoperative blood loss.[9,29] Liver failure remains a common complication, with a high risk of death after major hepatic resections in patients with cirrhosis.[30] Second, a cirrhotic liver has a more limited regenerating growth capacity than a normal liver after hepatic resection.[28] A major hepatic resection may have an adverse impact not only on the immediate postoperative outcome but also on the long-term prognosis. Removing a large bulk of nontumorous functioning liver could potentially lead to postoperative liver failure[10,11] and also a poorer long-term survival outcome.[13] Preserving liver function appears to be an important long-term prognostic factor for patients with both HCC and cirrhosis.[31] Third, a cirrhotic liver is prone to multicentric hepatocarcinogenesis. Even after an apparently curative resection, consistently more than 50% of patients will experience intrahepatic recurrences within 5 years of resection, and the majority of these recurrences are multicentric in location and distant from the resection margin.[32-34] This would imply that even a wider resection margin or a larger hepatic resection may not prevent these recurrences.[35] As a result, preservation of liver function is often considered a priority.

The additional increase in operative risk associated with major hepatic resection as documented in the literature and also the potential adverse influence of extensive hepatic resection on long-term prognosis have made some surgeons refrain from performing major hepatic resection for HCC in cirrhotic patients. This is particularly true for small HCCs (≤5 cm) because hemihepatectomy or extended hepatectomy for small tumors sacrifices a large volume of functional liver parenchyma. Furthermore, with the availability of effective alternative treatment such as radiofrequency ablation[36,37] and liver transplantation for HCCs 5 cm or smaller in cirrhotic patients,[14,15] the role of major hepatic resection for small HCCs in cirrhotic patients has become even more debatable. In some recent series of hepatic resection for HCC in cirrhotic patients, most patients had minor hepatic resections, and only 5% to 12% of the patients had major hepatic resections.[38-40] This illustrates a generally conservative attitude among surgeons toward major hepatic resection in cirrhotic patients. Our center adopts a more aggressive approach in offering major hepatic resection to cirrhotic patients with small HCCs, especially for centrally located tumors. This is reflected by the relatively high proportion (38.5%) of major hepatic resections for small HCCs in this series.

Table 5. Factors Affecting Disease-Free Survival

Independent Factors	Risk Ratio	95% Confidence Interval	*P* Value
Pathologic TNM staging	2.22	1.60-3.08	<.001
Major hepatic resection	0.39	0.23-0.64	<.001

Our results showed that major hepatic resection was a relatively safe procedure, with a hospital mortality rate of around 8%, a rate that was not significantly different from that of minor hepatic resection. Of course, this is in part attributable to the careful case selection when major hepatic resection is considered in cirrhotic patients, as reflected by the better preoperative liver function in this group of patients. The amount of blood loss and blood transfusion was also not significantly higher after major hepatic resection. Although the liver mass removed in a major hepatic resection was larger, the transection area might actually have been smaller than that in some segmentectomies or nonanatomic resections. Hence, there may not have been a significantly higher risk of operative bleeding. Postoperative liver failure did not occur frequently after major hepatic resection, and the postoperative complication rate was comparable to that of minor hepatic resection. Our results illustrated that, with appropriate case selection, meticulous operative techniques, and careful perioperative management, major hepatic resection could be performed as safely as minor hepatic resection in cirrhotic patients with small HCCs. Although major resection had a more severe impact on the patient's postoperative liver function, as reflected by the significant rise in bilirubin level and ICG-R15, it did not translate into a higher liver failure rate or poorer long-term survival outcome. In fact, major hepatic resection resulted in a better disease-free survival in the long term.

Despite a higher proportion of more aggressive tumors in terms of venous invasion and advanced pathologic TNM staging in the major resection group, the lower recurrence rate and better long-term disease-free survival suggest an important role of major hepatic resection in the management of small HCCs. This finding was reinforced by the multivariate analysis, which showed that major hepatic resection was a significant independent factor in predicting favorable disease-free survival. The overall survival also appeared to be better in the major resection group, although the difference as compared with the minor resection group was not significant. One possible explanation for the lower intrahepatic recurrence rate and the better disease-free survival after major hepatic resection may be attributed to the propensity of HCC to disseminate into the portal venous system at an early stage, even while the tumor was still small.[41,42] This is, in fact, the very argument against nonanatomic resections for small HCCs because these types of resection do not encompass the portal venous drainage of the tumor, thus providing a less optimal surgical clearance.[17-19,43] A possible advantage of major hepatic resection is the removal of the entire unilobar portal venous drainage of the involved lobe of the liver. This disease-free survival advantage of major hepatic resection was more significant when compared with that of patients who underwent nonanatomic resection. On the other hand, for those who underwent segmentectomies, the disease-free and overall cumulative survival rates were not significantly different from those with major hepatic resections. Hence, our results suggest that segmentectomy is still advisable for small tumors located peripherally that can be completely resected without a major resection. However, for tumors located in a position where segmentectomy is not feasible, a major hepatic resection is justified and is preferred over nonanatomic resections.

A subgroup analysis was also performed to assess the survival benefit of major hepatic resection in relation to tumor size. For this purpose, we subdivided the tumors into those smaller than 3 cm and those 3 cm or larger.[18] For tumors smaller than 3 cm, both the disease-free and overall cumulative survival rates were comparable between the 2 resection groups. However, for tumors 3 cm or larger, major hepatic resection provided significantly better disease-free and overall cumulative survival rates. The particular survival benefit of major hepatic resection for this group may be related to the higher propensity for larger tumors to have portal venous infiltration,[44] for which major hepatic resection may provide better oncologic clearance.

Another possible explanation for the better survival outcome in the major hepatic resection group is a wider resection margin in this group. However, the role of resection margin in the long-term survival after resection of HCC remains controversial. While some authors advocated a resection margin of 1 cm or even 2 to 3 cm,[45,46] other studies found no correlation between the width of resection margin and long-term survival outcome.[47,48] As both multicentric tumors and metastatic lesions disseminated via the portal vein tend to occur at sites distant from the resection margin, the role of a wider resection margin is probably not as important as the encompassment of the entire portal venous drainage area in major hepatic resection. Hepatocellular carcinoma is characterized by its tendency to invade into the portal vein, and a previous literature review by our group found that venous invasion is the most commonly reported risk factor for postoperative recurrence after hepatic resection.[44] The ability of a resection to clear the portal venous drainage area of the tumor is likely to be an important factor in reducing recurrence.

The results of segmentectomies and nonanatomic resections were comparable to those reported by other authors.[18,19] Thus, the difference in survival outcome between the major and minor resection group was not owing to a set of particularly poor outcomes in the latter group. The excellent survival outcome in the major resection group, with a 5-year survival rate of 72.5%, is comparable to the respectable results of liver transplantation for small HCCs ($\leq$5 cm).[14,49] The 5-year disease-free survival of 48.8% is also quite satisfactory. Our data may pose a challenge to the view of some authors who recommend liver transplantation as the first treatment of choice even for patients with Child A cirrhosis and preserved liver function.[15,50]

Despite these encouraging results, we emphasize the presence of selection bias in this retrospective study that needs to be taken into account when our data are interpreted. The major and minor resection groups were not exactly comparable, with more advanced tumors but more favorable liver function being present in the former group. This could have some confounding effect on the results of a comparison between the 2 groups in the perioperative and long-term outcomes. In an attempt to reduce some of the possible influence of confounding factors that may differ between the 2 groups, we evaluated the role of major hepatic resection in the long-term disease-free survival result in a multivariate analysis, which showed a benefit associated with major resection. However, a prospective randomized trial is necessary to clearly demonstrate the benefit of major hepatic resection in reducing postoperative recurrence. Similarly, the role of hepatic resection compared with other treatments such as liver transplantation in cirrhotic patients with a solitary small HCC also needs to be evaluated in the setting of a prospective randomized trial.

In conclusion, our study shows that major hepatic resection can be safely performed for a well-selected group of cirrhotic patients with small, solitary HCCs. Furthermore, it may offer a survival benefit over less extensive hepatic resection especially for tumors in the size range of 3 to 5 cm.

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