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Partial hepatectomy for ruptured hepatocellular carcinoma

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Background: Improvements in surgical technique and perioperative care have made partial hepatectomy a safe and effective treatment for hepatocellular carcinoma (HCC), even in the event of spontaneous HCC rupture.

Methods: A consecutive cohort of patients who underwent partial hepatectomy for HCC between 2000 and 2009 was divided into a ruptured group and a non-ruptured group. Patients with ruptured HCC were further divided into emergency and staged hepatectomy subgroups. Mortality and morbidity, overall survival and recurrence-free survival (RFS) were compared. Prognostic factors for overall survival and RFS were identified by univariable and multivariable analyses.

Results: A total of 1233 patients underwent partial hepatectomy for HCC, of whom 143 had a ruptured tumour. The morbidity and mortality rates were similar in the ruptured and non-ruptured groups, as well as in the emergency and staged subgroups. In univariable analyses, overall survival and RFS were lower in the ruptured group than in the non-ruptured group (both \( P < 0.001 \)), and also in the emergency subgroup compared with the staged subgroup (\( P = 0.016 \) and \( P = 0.025 \) respectively). In multivariable analysis, spontaneous rupture independently predicted poor overall survival after hepatectomy (hazard ratio 1.54, 95 per cent confidence interval 1.24 to 1.93) and RFS (HR 1.75, 1.39 to 2.22). Overall survival and RFS after hepatectomy for ruptured HCC in the emergency and staged subgroups were not significantly different in multivariable analyses.

Conclusion: Spontaneous rupture predicted poor long-term survival after hepatectomy for HCC, but surgical treatment seems possible, safe and appropriate in selected patients.

Introduction

Hepatocellular carcinoma (HCC) is the sixth most prevalent cancer and the third most frequent cause of cancer-related death, and is especially common in South-East Asia and Africa1. Spontaneous rupture of HCC is considered a life-threatening condition, and about 10–15 per cent of patients with HCC develop this complication2–5.

Surgical resection (partial hepatectomy) is considered the preferred treatment for HCC, and has become safer and more effective in recent years owing to improvements in surgical technique and perioperative care. When technically feasible, partial hepatectomy, carried out as either an emergency or a staged operation (embolization or other conservative procedures to achieve haemostasis, followed by surgery), is an effective treatment for spontaneously ruptured HCC, and long-term survival can be achieved in selected patients5–10. However, it remains unclear how short- and long-term outcomes of partial hepatectomy are affected by spontaneous rupture of HCC1. In addition, whether emergency hepatectomy and staged hepatectomy for ruptured HCC affect perioperative and long-term outcomes differently has rarely been investigated.

The present study reviewed a 9-year experience of partial hepatectomy in patients with HCC, with the aim of evaluating the effects of spontaneous rupture of HCC on short- and long-term outcomes, and identifying prognostic factors in patients with ruptured HCC undergoing partial hepatectomy.

Methods

This was a retrospective study of consecutive patients who underwent partial hepatectomy for HCC between
February 2000 and February 2009 at the Fifth Department of Hepatic Surgery, Eastern Hepatobiliary Surgery Hospital, Shanghai, China. Data were collected in a prospectively maintained computer database and then analysed retrospectively. Additional data were obtained by reviewing medical records. Patients were divided into two groups, according to whether the HCC had ruptured. The research protocol was approved by the Clinical Research Ethics Committee of the Eastern Hepatobiliary Surgery Hospital. Informed consent was obtained from all patients.

Preoperative care, surgical procedures and follow-up
Routine preoperative investigations included complete blood counts, liver and renal function tests, electrocardiography, measurement of serum α-fetoprotein (AFP) and serological markers for hepatitis B and C, coagulation profile and chest X-ray. Tumour resectability was assessed by computed tomography (CT) and/or magnetic resonance imaging (MRI). Child–Pugh grade C classification was considered an absolute contraindication to partial hepatectomy. The criteria used for resection remained identical over the study period.

All operations were carried out by experienced surgeons. The Pringle manoeuvre was routinely used with cycles of clamp/unclamp times of 15/5 min. Transection of hepatic parenchyma was performed using the clamp-crushing technique, and haemostasis was secured using sutures and an argon beam coagulator. Anatomical resections were preferred, but non-anatomical resections were used for tumours situated at the junction of several liver segments, for peripherally located tumours and in patients with serious cirrhosis. Major hepatectomy was defined as resection of three or more Couinaud liver segments, and minor hepatectomy as resection of fewer than three segments. Cirrhosis was confirmed by histopathological examination.

R0 resection was defined as complete resection of all microscopic and macroscopic tumours. A complication was defined as the occurrence of postoperative hepatic failure, biliary complications, sepsis of any aetiology, pulmonary, renal, cardiac and wound complications. Ascites and pleural effusion that required diuretics or paracentesis was good. In all other patients, surgical haemostatic procedures, including plication, suturing, alcohol injection, and haemostatic measures, including correction of coagulopathy, were instituted in haemodynamically unstable patients; the patients were monitored closely in the ward or the intensive care unit. The bleeding stopped spontaneously with initial conservative treatment in the majority of patients. If bleeding continued, emergency transcatheter arterial embolization (TAE) was used. Some patients underwent these non-surgical treatments before transfer to the authors’ hospital for further treatment.

Emergency laparotomy was carried out when bleeding could not be controlled by non-surgical treatments. During emergency operation, partial hepatectomy was undertaken only in patients in whom the tumour was resectable, liver functional reserves were adequate, and general condition was good. In all other patients, surgical haemostatic procedures, including plication, suturing, alcohol injection, packing or hepatic artery ligation, were used to stop active bleeding at the site of rupture.

During emergency partial hepatectomy, the Pringle manoeuvre or occlusion of the hepatic artery proper was used. After removal of clots from the peritoneal cavity, the tumour was reassessed for resectability. A resection margin of more than 1 cm was aimed for. After partial hepatectomy, peritoneal lavage was performed with distilled water (5000–10 000 ml), and 5-fluorouracil (500 mg) was left in the abdominal cavity at the end of the operation.

For patients with resectable HCC whose bleeding had stopped either spontaneously or at laparotomy, staged partial hepatectomy was carried out 2–6 weeks after the episode of spontaneous rupture, when the patient had recovered fully.

Special procedures for ruptured hepatocellular carcinoma
In the majority of patients, the diagnosis of ruptured HCC was based on symptoms and signs on hospital admission, and confirmed by bedside ultrasonography. Active resuscitation with intravascular fluid and supportive measures, including correction of coagulopathy, were instituted in haemodynamically unstable patients; the patients were monitored closely in the ward or the intensive care unit. The bleeding stopped spontaneously with initial conservative treatment in the majority of patients. If bleeding continued, emergency transcatheter arterial embolization (TAE) was used. Some patients underwent these non-surgical treatments before transfer to the authors’ hospital for further treatment.

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Statistical analysis

For analysis, patients with ruptured HCC were divided into two groups: those who had an emergency hepatectomy and those who had a staged procedure. Hospital mortality was defined as death during the hospital stay or within 60 days of surgery. Overall survival was defined as the interval from the date of surgery to the date of death or last follow-up. Recurrence-free survival (RFS) was defined as the interval between the date of surgery and the date when recurrence was diagnosed after R0 resection. If recurrence was not diagnosed, the patients were censored on the date of last follow-up.

The distribution of continuous data was tested using kolmogoro – smirnov test; values are shown as mean(s.d.,) if distributed normally and as median (range) otherwise. These data were analysed by means of the independent-samples t test and Wilcoxon rank sum (Mann–Whitney U) test respectively. Categorical variables were compared between groups using the χ² test with Yates’ correction or Fisher’s exact test, as appropriate. Survival curves were prepared according to the Kaplan–Meier method, with the date of operation as the starting date, and were compared using the log rank test. To identify factors predictive of survival, univariable and multivariable analyses were carried out, using the log rank test and Cox proportional hazards model respectively. P < 0·050 was considered statistically significant. All statistical analyses were performed with SPSS® version 12.0 (IBM, Armonk, New York, USA).

Results

During the study period, 6955 patients attended the authors’ unit for treatment of HCC, and 409 (5·9 per cent) presented with ruptured HCC. Of 1233 patients who underwent partial hepatectomy for HCC, the tumour ruptured spontaneously before surgery in 143 (11·6 per cent) (Fig. 1). The patients were thus divided into ruptured (143) and non-ruptured (1090) groups. A total of 279 patients with ruptured HCC did not receive hepatectomy because they had unresectable HCC (160, 57·3 per cent), insufficient liver functional reserve (53, 19·0 per cent), were in poor general condition (30, 10·8 per cent), refused surgery (10, 3·6 per cent), an intraoperative decision was made not to carry out hepatectomy (7, 2·5 per cent), or for unknown reasons (19, 6·8 per cent).

There were no significant differences between the two groups in sex, age, seropositivity for hepatitis B and C virus, liver function tests and Child–Pugh grades (Table S1, supporting information). Patients were usually men and around 50 years old. However, there were significantly more patients with symptomatic presentation and fewer patients with cirrhosis in the ruptured group than in the non-ruptured group. Furthermore, patients in the ruptured group had a lower haemoglobin concentration, a shorter prothrombin time, a higher serum AFP level and worse tumour characteristics (including size, macroscopic vascular invasion, differentiation, multiple/diffuse tumour type and extrahepatic spread).

Characteristics of ruptured HCC

The 143 patients with ruptured HCC were referred from elsewhere to the authors’ unit. Sudden epigastric or right hypochondriac pain was present in 137 patients (95·8 per cent), haemorrhagic shock in 32, signs of peritonitis or abdominal distension in 27 and haemodynamic instability in 14 patients at the time of hospital admission. Haemodynamic stability was restored after a short period of resuscitation in the latter patients.

All 143 patients underwent hepatic CT or MRI before operation. The definitive diagnosis of ruptured HCC was made before partial hepatectomy in 134 patients (93·7 per cent). Haemoperitoneum (free rupture) was found in 138 patients, with a median intra-abdominal blood loss of 400 (range 30–3500) ml. Eleven patients were diagnosed with intraperitoneal metastasis before or during operation, and seven underwent complete resection of metastasis in addition to partial hepatectomy.

Emergency TAE for haemostasis was performed in 13 patients before partial hepatectomy but failed in two. Bleeding stopped with conservative treatment in 104 patients before operation. Emergency partial hepatectomy was carried out in 28 patients (19·6 per cent) and staged partial hepatectomy in the remaining 115 (80·4 per cent). R0 resection was achieved in 116 (81·1 per cent).

Perioperative outcomes

Patients with ruptured HCC had more intraoperative blood loss, more intraoperative red blood cell transfusion and a longer duration of operation than those with non-ruptured HCC. In addition, there was a lower R0 resection rate in the ruptured group (81·1 versus 87·9 per cent). More patients with ruptured HCC underwent non-anatomical partial hepatectomy. There was no statistically significant difference in morbidity and mortality rates (according to the Clavien classification of surgical complications17) between the ruptured and non-ruptured groups (Table 1). There were four hospital deaths in the ruptured group, from hepatic failure (2), postoperative intra-abdominal bleeding (1) and pulmonary infection (1).
Fig. 1 Study flow chart. HCC, hepatocellular carcinoma

Long-term survival outcomes

Follow-up ranged from 1 to 135 (median 41) months. Among the 1215 surviving patients, 139 patients were in the ruptured group and 1076 in the non-ruptured group. The 1-, 3- and 5-year overall survival rates for all 1215 patients were 81·8, 56·8 and 46·9 per cent respectively, with a median overall survival of 51 months. The 1-, 3- and 5-year RFS rates for the 1074 survivors who had an R0 resection were 69·3, 49·3 and 40·7 per cent respectively, with a median of 35 months.

After partial hepatectomy, 110 (79·1 per cent) of 139 patients in the ruptured group and 576 (53·5 per cent) of 1076 in the non-ruptured group died during follow-up. Of 650 patients with tumour recurrence after R0 resection, 93 (80·2 per cent) of 116 had a ruptured HCC and 557 (58·1 per cent) of 958 had a non-ruptured tumour. Patterns of tumour recurrence after R0 resection are shown in Table S2 (supporting information). Peritoneal dissemination developed in 90 (8·4 per cent) of 1074 patients after R0 resection, and occurred more often in the ruptured group: 38 (32·8 per cent) of 116 versus 52 (5·4 per cent) of 958 (P < 0·001).

Some 279 patients with ruptured HCC did not undergo partial hepatectomy but had emergency TAE or other conservative treatment during the present study interval (Fig. 1). Fifty-four of these patients died in hospital, and the 1-, 3- and 5-year overall survival rates for the 279 patients were 16·8, 3·4 and 0 per cent respectively, with a median of 5 months. Overall survival was lower than for patients with ruptured HCC who underwent partial hepatectomy (P < 0·001) (Fig. S1, supporting information).

Impact of spontaneous tumour rupture on survival

The ruptured HCC group had significantly lower overall survival rates (66·2, 25·1 and 16·8 per cent at 1, 3 and 5 years respectively) than the non-ruptured HCC group (83·8, 61·0 and 50·5 per cent) (P < 0·001) (Fig. 2a). There was also a significant difference in RFS between the ruptured (40·5, 25·8 and 14·8 per cent at 1, 3 and 5 years respectively) and non-ruptured (72·8, 52·5 and 43·7 per cent) groups (P < 0·001).

Both univariable and multivariable analyses showed that spontaneous tumour rupture was independently associated with poorer overall survival (hazard ratio 1·54, 95 per cent confidence interval 1·24 to 1·93) and RFS (hazard ratio 1·75, 1·39 to 2·22) after partial hepatectomy for HCC (Tables S3 and S4, supporting information).

Impact of emergency and staged hepatectomy on outcomes of ruptured HCC

Perioperative and long-term outcomes in patients undergoing emergency hepatectomy were compared with
Table 1  Perioperative outcomes

<table>
<thead>
<tr>
<th></th>
<th>All patients (n = 1233)</th>
<th>Non-ruptured (n = 1090)</th>
<th>Ruptured (n = 143)</th>
<th>P‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood loss (ml)*</td>
<td>380 (30–8200)</td>
<td>350 (30–8200)</td>
<td>500 (100–5400)</td>
<td>0.032§</td>
</tr>
</tbody>
</table>
| Intraoperative red blood cell transfusion | 339 (27.5)             | 274 (25.1)              | 65 (45.5)         | <0.001
| Duration of operation (min)†  | 132(52)                 | 131(52)                 | 143(44)           | 0.007¶ |
| Pringle manoeuvre             | 1099 (89.1)             | 967 (88.7)              | 132 (92.3)        | 0.194
| Duration of clamping (min)‡   | 20(10)                  | 20(10)                  | 21(8)             | 0.672¶ |
| Local surgical resection margin |                        |                         |                   |    |
| R0                             | 1074 (87.1)             | 958 (87.9)              | 116 (81.1)        | 0.025
| R1                             | 94 (7.6)                | 81 (7.4)                | 13 (9.1)          |      |
| R2                             | 65 (5.3)                | 51 (4.7)                | 14 (9.8)          |      |
| Type of hepatectomy            |                         |                         |                   |    |
| Anatomical                     | 803 (65.1)              | 723 (66.3)              | 80 (55.9)         | 0.014
| Non-anatomical                 | 430 (34.9)              | 367 (33.7)              | 63 (44.1)         |      |
| Extent of hepatectomy          |                         |                         |                   |    |
| Major                          | 395 (32.0)              | 343 (31.5)              | 52 (36.4)         | 0.238
| Minor                          | 838 (68.0)              | 747 (68.5)              | 91 (63.6)         |      |
| Hospital death                 | 18 (1.5)                | 14 (1.3)                | 4 (2.8)           | 0.156
| Morbidity                      |                         |                         |                   |    |
| Clavien grade I                | 319 (25.9)              | 283 (26.0)              | 36 (25.2)         | 0.840
| Clavien grade II               | 32 (2.6)                | 28 (2.6)                | 4 (2.8)           | 0.552# |
| Clavien grade III              | 153 (12.4)              | 135 (12.4)              | 18 (12.6)         |      |
| Clavien grade IV               | 95 (7.7)                | 87 (8.0)                | 8 (5.6)           |      |
| Clavien grade V                | 21 (1.7)                | 19 (1.7)                | 2 (1.4)           |      |

Values in parentheses are percentages unless indicated otherwise; values are *median (range) and †mean(s.d.). ‡χ² test with Yates’ correction, except §Wilcoxon rank sum test, ¶independent-samples t test and #Fisher’s exact test.

Fig. 2  a Overall and b recurrence-free survival after hepatectomy for ruptured and non-ruptured hepatocellular carcinoma. a, b P < 0.001 (log rank test)
Table 2 Patient characteristics, perioperative and long-term outcomes for patients who had emergency or staged hepatectomy for ruptured hepatocellular carcinoma

<table>
<thead>
<tr>
<th></th>
<th>Emergency hepatectomy (n = 28)</th>
<th>Staged hepatectomy (n = 115)</th>
<th>P‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)*</td>
<td>49(10)</td>
<td>49(11)</td>
<td>0.917$\dagger$</td>
</tr>
<tr>
<td>Sex ratio (M : F)</td>
<td>222 : 6</td>
<td>105 : 10</td>
<td>0.055</td>
</tr>
<tr>
<td>Haemorrhagic shock</td>
<td>18 (64)</td>
<td>14 (12.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sudden onset of abdominal pain</td>
<td>28 (100)</td>
<td>109 (94.8)</td>
<td>0.478</td>
</tr>
<tr>
<td>Preoperative emergency TAE</td>
<td>2 (7)</td>
<td>11 (9.6)</td>
<td>0.689</td>
</tr>
<tr>
<td>Haemostasis achieved before operation</td>
<td>14 (50)</td>
<td>115 (100)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Haemoglobin (g/l)*</td>
<td>123(30)</td>
<td>129(22)</td>
<td>0.309$\dagger$</td>
</tr>
<tr>
<td>Child–Pugh grade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>24 (86)</td>
<td>108 (93.9)</td>
<td>0.287$\ddagger$</td>
</tr>
<tr>
<td>B</td>
<td>4 (14)</td>
<td>7 (6.1)</td>
<td></td>
</tr>
<tr>
<td>Peritoneal dissemination before operation</td>
<td>0 (0)</td>
<td>11 (9.6)</td>
<td>0.191$\ddagger$</td>
</tr>
<tr>
<td>Estimated intraperitoneal bleeding (ml)†</td>
<td>1200 (300–5000)</td>
<td>300 (50–2200)</td>
<td>&lt;0.001$#$</td>
</tr>
<tr>
<td>Blood loss (ml)†</td>
<td>650 (100–5400)</td>
<td>400 (100–3500)</td>
<td>0.083$#$</td>
</tr>
<tr>
<td>Intraoperative RBC transfusion</td>
<td>23 (82)</td>
<td>42 (36.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of operation (min)*</td>
<td>164(52)</td>
<td>138(41)</td>
<td>0.021$\ddagger$</td>
</tr>
<tr>
<td>Type of resection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R0</td>
<td>22 (79)</td>
<td>94 (81.7)</td>
<td>0.701</td>
</tr>
<tr>
<td>R1 + R2</td>
<td>6 (21)</td>
<td>21 (18.3)</td>
<td></td>
</tr>
<tr>
<td>Hospital death</td>
<td>2 (17)</td>
<td>2 (1.7)</td>
<td>0.360$\ddagger$</td>
</tr>
<tr>
<td>Morbidity</td>
<td>7 (25)</td>
<td>29 (25.2)</td>
<td>0.981</td>
</tr>
<tr>
<td>Clavien grade I–II</td>
<td>3 (11)</td>
<td>19 (16.5)</td>
<td>0.502$\ddagger$</td>
</tr>
<tr>
<td>Clavien grade III–IV</td>
<td>4 (14)</td>
<td>10 (8.7)</td>
<td></td>
</tr>
<tr>
<td>Status at last follow-up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alive without disease</td>
<td>3 (12)</td>
<td>23 (20.4)</td>
<td>0.286$\ddagger$</td>
</tr>
<tr>
<td>Alive with disease</td>
<td>0 (0)</td>
<td>5 (4.4)</td>
<td></td>
</tr>
<tr>
<td>Dead</td>
<td>23 (88)</td>
<td>85 (75.2)</td>
<td></td>
</tr>
</tbody>
</table>

Values in parentheses are percentages unless indicated otherwise; values are*mean(s.d.) and †median (range). TAE, transcatheter arterial embolization; RBC, red blood cell. $\chi^2$ test with Yates’ correction, except §independent-samples $t$ test, $\ddagger$Fisher’s exact test and $\#$Wilcoxon rank sum test.

Fig. 3 a Overall and b recurrence-free survival after emergency and staged hepatectomy for ruptured hepatocellular carcinoma. 
a $P = 0.016$, b $P = 0.025$ (log rank test)
those in patients who underwent staged hepatectomy for ruptured HCC (Table 2, Fig. 3). Operative morbidity and mortality rates were comparable after emergency and staged procedures. Although univariable analyses showed that overall survival and RFS after emergency hepatectomy were poorer than after staged hepatectomy ($P = 0.016$ and $P = 0.025$ respectively), the differences were not significant in multivariable analyses (Tables S5 and S6, supporting information).

**Discussion**

Although it is generally assumed that spontaneous tumour rupture is a risk factor influencing the prognosis of patients with HCC undergoing partial hepatectomy, there are still controversies over this issue$^{6,7,16,17}$. The present study has confirmed in a large patient cohort that spontaneous rupture of HCC is an independent predictor of survival after hepatectomy. Overall survival and RFS in the ruptured group were significantly worse than in the non-ruptured group. Perioperative morbidity and mortality rates were comparable between the two groups, indicating that partial hepatectomy does not increase the perioperative risk for ruptured HCC, as long as patients are selected carefully and operations carried out by experienced surgeons.

This study also showed that tumour characteristics (including size, macroscopic vascular invasion and differentiation) were poorer in the ruptured group, indicating that the risk of tumour rupture increases when HCC progresses. Relatively high tension in large tumours, intrahepatic infiltration and the occurrence of vascular invasion are possible mechanisms associated with spontaneous tumour rupture$^{18–21}$. In addition to the tumours being more advanced in the ruptured group, the R0 resection rate was significantly lower than in the non-ruptured group (81·1 versus 87·9 per cent). In some patients with ruptured HCC, the intraoperative extent of tumour was more advanced than on preoperative assessment, with intraperitoneal seeding being detected at operation. Finally, peritoneal secondaries were more often found on follow-up in the ruptured group after R0 resection.

Peritoneal dissemination is common after curative resection of ruptured HCC$^{22}$. In an attempt to combat peritoneal dissemination, large amounts of distilled water were used to irrigate the peritoneal cavity and intraperitoneal 5-fluorouracil was administered. However, long-term survival remained disappointing despite these efforts.

Haemostasis is the prime objective in the initial treatment of ruptured HCC. However, some surgeons advocate emergency partial hepatectomy when the patient’s condition permits$^{8,21,24}$. Emergency hepatectomy accounted for a fifth of partial hepatectomies for spontaneous tumour rupture in the present series. The hospital mortality rate associated with emergency partial hepatectomy for ruptured HCC was 7 per cent. Partial hepatectomy was staged in patients whose bleeding stopped spontaneously or after TAE, although there is a risk of tumour progression during the interval until the second procedure in staged partial hepatectomy$^{25}$. Early resection of ruptured tumour and clearance of intraperitoneal haematoma may reduce the occurrence of peritoneal dissemination$^{26}$.

The present study was carried out in the largest hepatobiliary surgical centre in China, and all surgeons had extensive operating experience of hepatectomies for HCC. When patients with ruptured HCC were admitted to the department, partial hepatectomy, either an emergency or staged operation, was considered first. Partial hepatectomy was performed if the HCC was resectable, liver functional reserve was adequate and the patient fit enough. As a consequence, the rate of hepatectomy for ruptured HCC in the present cohort was much higher than in previous series$^{1,3,6,8,23}$. The 1-, 3- and 5-year overall survival and RFS rates after hepatectomy for ruptured HCC were comparable with those reported elsewhere$^{6,7,16,22–25}$.

The decision to undertake emergency or staged hepatectomy was made on an individual basis, depending on the vital signs after rupture, the effectiveness of haemostasis and liver function. Operation for ruptured HCC should be carried out as soon as possible, even by staged hepatectomy. In the present study, among patients with ruptured HCC who underwent staged hepatectomy, approximately 10 per cent had peritoneal dissemination during operation, and one-third suffered from peritoneal dissemination during follow-up. On the other hand, none of the patients was found to have peritoneal dissemination during emergency hepatectomy, and a fifth suffered from peritoneal dissemination during follow-up. Thus, it could be argued that peritoneal dissemination was reduced if hepatectomy and peritoneal lavage were carried out as early as possible.

Anatomical resection was the preferred procedure in this study, but non-anatomical resection was used for tumours situated at the junction of several liver segments, small or peripherally located tumours, or in patients with severe cirrhosis. There were no significant differences in overall survival and DFS between anatomical and non-anatomical resection, as reported previously$^{27,28}$. On the other hand, anatomical resections have been reported to have better outcomes than non-anatomical resections, especially for single HCC$^{29,30}$, T1–T2 HCC$^{31}$ and patients without cirrhosis$^{32}$.
The present study has some limitations. First, although the data were collected prospectively, this is actually a retrospective cohort study with all its inherent shortcomings. Second, most of the patients in this study had hepatitis B virus-related HCC, which is different from that seen in patient populations in Western countries.

**Acknowledgements**

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**Disclosure:** The authors declare no conflict of interest.

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**Supporting information**

Additional supporting information may be found in the online version of this article:

- **Fig. S1** Overall survival curves for non-surgically treated and surgically treated patients with ruptured hepatocellular carcinoma (Word document)
- **Table S1** Patient characteristics (Word document)
- **Table S2** Patterns of tumour recurrence after R0 resection (Word document)
- **Table S3** Univariable and multivariable analyses of overall survival in 1215 patients with hepatocellular carcinoma (Word document)
- **Table S4** Univariable and multivariable analyses of recurrence-free survival in 1074 patients with hepatocellular carcinoma (Word document)
- **Table S5** Univariable and multivariable analyses of overall survival in 139 patients with ruptured hepatocellular carcinoma (Word document)
- **Table S6** Univariable and multivariable analyses of recurrence-free survival in 116 patients with ruptured hepatocellular carcinoma (Word document)