Liver resection for hepatocellular carcinoma in patients with clinically significant portal hypertension

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Background & Aims: Liver resection (LR) in patients with hepatocellular carcinoma (HCC) and clinically significant portal hypertension (CSPH) defined as a hepatic venous pressure gradient (HVPG) ≥10 mmHg is not encouraged. Here, we reappraised the outcomes of patients with cirrhosis and CSPH who underwent LR for HCC in highly specialised liver centres.

Methods: This was a retrospective multicentre study from 1999 to 2019. Predictors for postoperative liver decompensation and textbook outcomes were identified.

Results: In total, 79 patients with a median age of 65 years were included. The Child-Pugh grade was A in 99% of patients, and the median model for end-stage liver disease (MELD) score was 8. The median HVPG was 12 mmHg. Major hepatectomies and laparoscopies were performed in 28% and 34% of patients, respectively. Ninety-day mortality and severe morbidity rates were 6% and 27%, respectively. Postoperative and persistent liver decompensation occurred in 35% and 10% of patients at 3 months. Predictors of liver decompensation included increased preoperative HVPG (p = 0.004), increased serum total bilirubin (p = 0.02), and open approach (p = 0.03). Of the patients, 34% achieved a textbook outcome, of which the laparoscopic approach was the sole predictor (p = 0.004). The 5-year overall survival and recurrence-free survival rates were 55% and 43%, respectively.

Conclusions: Patients with cirrhosis, HCC and HVPG ≥10 mmHg can undergo LR with acceptable mortality, morbidity, and liver decompensation rates. The laparoscopic approach was the sole predictor of a textbook outcome.

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Keywords: Hepatectomy; Hepatic venous pressure gradient; Clinically significant portal hypertension; Postoperative liver decompensation; Textbook outcome.

Materials and methods

Study design

The study population included all consecutive patients with cirrhosis and preoperative CSPH, as assessed by HVPG.
measurement, who underwent LR for HCC between November 1999 and March 2019 in three Western liver centres (Henri Mondor Hospital, Créteil, France; Universitari Dr Josep Trueta Hospital, Girona, Spain; and Universitari de Bellvitge Hospital, Barcelona, Spain).

The primary endpoint was to assess the safety of LR in patients with preoperative CSPH, evaluated as 90-day mortality and morbidity. Secondary endpoints included the occurrence of postoperative liver decompensation, a textbook outcome, and long-term oncological outcomes. The study protocol was designed according to the ethical guidelines of the 1975 Declaration of Helsinki and approved by the institutional review boards of the three centres.

Study population
The diagnosis of HCC relied on the acknowledged diagnostic criteria of HCC. First, to be considered potential candidates for LR, patients had to fulfil the following criteria: no previous history of ascites, variceal rupture, or spontaneous encephalopathy; no prohibitive comorbidities; Child-Pugh class A liver function or class B, provided this was because of biliary obstruction; and a plan for a complete macroscopic resection combined with a sufficient future remnant liver volume upon preoperative computed tomography (CT) volumetric assessment [following percutaneous portal vein embolisation (PVE) whenever needed]. The alpha-fetoprotein (AFP) level was not considered in the decision for surgery. Second, all of the above-selected patients underwent preoperative PHT assessment, including transjugular HVPG measurement complying with technical recommendations. CT and upper gastrointestinal endoscopy. Briefly, within the 2 weeks before surgery, HVPG measurements were performed in fasting conditions under local anaesthesia. The right jugular vein was canalised under ultrasonographic guidance. A 7-French balloon-tipped catheter (‘Fogarty’ Edwards Lifesciences LLC, Irvine, CA, USA) was guided into the main right or middle hepatic vein for measurements of wedged and free HVPs to calculate the HVPG. All measurements were performed in triplicate and averaged to obtain the baseline HVPG. HVPG $\geq$10 mmHg indicated the presence of CSPH regardless of the presence of oesophageal varices, thrombopoenia, or splenomegaly.

The presence of oesophageal varices or the coexistence of a platelet count $<10^9$/L and splenomegaly $>120$ mm in diameter were considered surrogates of CSPH. At this stage, patients with HVPG $\geq$30 mmHg were arbitrarily excluded from resection. The indications for surgery, planned resection, and the chosen approach were homogeneous across centres (see later) and decided during board meetings at each liver centre.

Surgical approach and complexity of liver resection
Laparoscopic approach, repeat hepatectomy, or anatomical resection were performed whenever possible. The laparoscopic approach was chosen according to the guidelines of the World Consensus Conference on Laparoscopic Surgery. The technical difficulty of each procedure was evaluated based on a 3-level classification validated for both the laparoscopic and open approaches. Briefly, this comprised three levels of technical difficulty [low, wedge resection and left lateral sectionectomy; moderate, anterolateral sectionectomy (from segments II to VI) and left hepatectomy; and high: posterolateral segmentectomy (segments VII, VIII, and I), right and extended right heptectomy, right posterior sectionectomy, central heptectomy, and extended left heptectomy].

Major resection was defined as resection $\geq$3 contiguous Couinaud’s segments. Morbidity was evaluated according to the comprehensive complication index described by Slankamenac et al. (available at www.assesssurgery.com/calculator_single/). Severe morbidity was defined by a Comprehensive Complication Index (CCI) $\geq$26.2, which refers to 1 complication of Clavien-Dindo grade IIIa.

Liver complications (grade A or higher) included liver failure, bile leakage, and haemorrhage as defined by the International Study Group on Liver Surgery. Postoperative ascites and encephalopathy were defined based on the definition of Moore et al. and Vilstrup et al. respectively. Non-liver complications included cardiopulmonary and infectious complications and acute kidney injury.

Three binary composite endpoints were used: postoperative liver decompensation; persistent liver decompensation at 3 months; and textbook outcome. Postoperative liver decompensation was defined as present when at least 1 of the following complications occurred within 3 months after resection: liver failure; ascites; or encephalopathy. Persistent liver decompensation was defined as present when at least 1 of the following liver complications occurred at 3 months after resection: jaundice and/or ascites and/or encephalopathy. A textbook outcome was achieved when all 6 of the following criteria were met: no perioperative transfusion; no major postoperative complications (CCI <26.2); no mortality within 90 days or during the hospital stay; hospital stay $<$90th percentile of the total cohort ($\leq$8 days); R0 resection ($\geq$1 mm), and no readmission.

Postoperative mortality included any death within 90 days or during hospitalisation for LR. Readmission included any hospitalisation occurring after discharge within 90 days following LR.

Follow-up
Patients were followed up every 4 months for the first 2 years and every 6 months thereafter. Tumour recurrence and liver status were monitored, and patients were treated according to disease presentation. HCC recurrence, persistent liver decompensation, or death were recorded as major impact events. Follow-up for this study was completed on 11 April 2020.

Statistical analysis
Continuous variables were expressed as the median and 25–75th IQR. Categorical variables were expressed as numbers and percentages. Student’s t test, the Mann-Whitney U test and Fisher’s exact test were used as appropriate.

Overall survival was defined as the period between the date of hepatectomy and the date of death or last follow-up. Recurrence-free survival was defined as the period between the date of hepatectomy and the date of first recurrence or death.

Two multivariate regression logistic analyses were performed to identify the independent predictors of: (1) postoperative liver decompensation; and (2) textbook outcome. All pre- and intraoperative variables associated with these two latter composite endpoints in the univariable analysis ($p <0.1$) were included in the multivariate analysis. Statistical analysis was performed using Statview version 5.0 (SAS Institute, Inc., Cary, NC, USA). The present study complied with RECORD guidelines.
Results

Study population

During the study period, a total of 375 consecutive patients with HCC and liver cirrhosis who had LRIs underwent HVPG assessment before surgery. The study population comprised 79 (21%) patients with preoperative CSPH, namely, those with HVPG ≥10 mmHg. The baseline characteristics of the study population are shown in Table 1. Viral infection (63%) was the most common cause of cirrhosis. The Child-Pugh grade of 78 (99%) patients was A, and the median MELD score was 8 (IQR: 6–9). The median HVPG was 12 mmHg (IQR: 11–15, range 10–26 mmHg). Indirect signs of CSPH were observed in 31 (39%) patients: oesophageal varices were present in 26 (33%) and splenomegaly and thrombopenia in 12 (15%). Only 7 (9%) patients met all the surrogate criteria for CSPH, and 28 (35%) patients had none of them. Tumours presented as a single nodule in 66 patients (84%), and the median size of the largest nodule was 27 (IQR: 18–35) mm.

Table 2 shows the detailed intraoperative events. The open approach was used in 52 (66%) patients, and the laparoscopic approach was used in 27 (34%) patients, with 1 case (4%) of conversion to the open approach. The latter was evaluated in the laparoscopic group on an intent-to-treat basis. Minor LR was performed in 72% (n = 65) of patients. Eleven (14%) patients needed intraoperative blood transfusion. Overall, the 90-day mortality rate was 6% (n = 5; Table 3); 3 and 2 patients had major and minor resections, respectively. All patients had postoperative liver decompensation, and 3 had persistent liver decompensation at 3 months. Causes of death included persistent liver decompensation in 3 patients (liver failure in 2 patients and ascites in 1 patient), new onset of ascites in 1 patient, and post-operative diffuse portal vein thrombosis in 1 patient.

The details of postoperative complications are shown in Table 3. Overall, 53 of 79 patients developed postoperative complications (morbidity rate = 67%) with a median CCI of 8.7 (0–30). Major complications (CCI ≥26.2) occurred in 21 (27%) patients.

Postoperative ascites, liver failure, haemorrhage, and bile leakage occurred in 25 (3%), 6 (8%), 6 (8%), and 3 (4%) patients, respectively. The median hospital stay was 14 (IQR: 8–19) days. Nine (10%) patients needed readmission.

Postoperative liver decompensation

Overall, 28 (35%) patients developed at least 1 sign of postoperative liver decompensation, including ascites in 25 patients, jaundice in 6, and encephalopathy in 3. Among them, 5 (18%, 5/28) died within 90 days of surgery (see later). An increased preoperative HVPG value (p = 0.004; odds ratio (OR) = 1.1; 95% CI = 1.1–1.9), increased elevated preoperative serum total bilirubin (p = 0.02; OR = 1.1; 95% CI = 1.0–1.3), and open approach (p = 0.03; OR = 8.7; 95% CI = 1.2–63.9) were independent predictors of postoperative liver decompensation (Table 4).

At 3 months following resection, 8 (10%) patients had persistent liver decompensation: 5 had refractory ascites, 2 had jaundice and ascites, and 1 had encephalopathy. Four (50%, 4/8) of them died within 12 months following surgery.

Table 1. Baseline clinical, laboratory and tumour characteristics of the study population.

| Variables                 | Study population (79 patients) |
|---------------------------|--------------------------------|
| Age (years)               | 65 (59–70)                     |
| Male gender, yes          | 65 (82)                        |
| Body mass index (kg/m²)   | 29 (25–31)                     |
| ASA score >2              | 38 (48)                        |
| Previous treatment before resection | 18 (23)                     |
| Hepatectomy               | 2 (3)                          |
| Local resection           | 2 (3)                          |
| TACE                      | 12 (15)                        |
| Sorafenib                 | 2 (3)                          |
| Child-Pugh class (A/B)    | 78 (99)/11 (1)                 |
| HVPG (mmHg)               | 12 (11–15)                     |
| Surrogate criteria of CSPH| 31 (39)                        |
| Oesophageal varices        | 26 (33)                        |
| Splenomegaly and thrombopenia* | 12 (15)                     |
| Viral infection           | 50 (63)                        |
| MELD score                | 8 (6–9)                        |

Pre-resection blood tests

| Variable                  | Study population (79 patients) |
|---------------------------|--------------------------------|
| Serum albumin (g/L)       | 40 (37–43)                     |
| Serum total bilirubin (µmol/L) | 12 (8–18)                 |
| Platelet (/10⁹/ml)        | 133 (101–167)                  |
| Serum creatinine (µmol/L) | 83 (67–92)                     |
| AFP (ng/ml)               | 8 (4–38)                       |
| Multiple nodules          | 13 (16)                        |
| Maximum tumour size (mm)  | 27 (18–35)                     |
| Resection margin (mm)     | 5 (2–10)                       |
| Satellite nodules         | 9 (11)                         |
| Macrovascular invasion    | 3 (4)                          |
| Microvascular invasion    | 25 (32)                        |
| Poor differentiated nodules | 5 (6)                          |

Results are presented as median (IQR) or n (%).

AFP: α-fetoprotein; ASA, American Society of Anesthesiologists; CSPH, clinically significant portal hypertension; HVPG, hepatic venous pressure gradient; MELD, Model for End-Stage Liver Disease; LLR, laparoscopic liver resection; TACE, transarterial chemoembolisation.

* Splenomegaly >120 mm in diameter and platelet count <100,000/ml.

Results are presented as median (IQR) or n (%), unless indicated otherwise.

1 Defined as any type of systematic resection of the portal areas based on Couinaud classification.
2 Major hepatectomy defined by resection ≥3 Couinaud segments.
3 Associated procedures included partial hepatectomy (3 patients), local destruction (2 patients), portal thrombectomy (1 patient), opening of the diaphragm (1 patient), portal thrombectomy, and opening of the diaphragm (1 patient).

Results are presented as median (IQR) or n (%), unless indicated otherwise.

Table 2. Surgical procedures and intraoperative characteristics.

| Variable                      | Study population (79 patients) |
|-------------------------------|--------------------------------|
| Portal vein embolisation     | 5 (6)                          |
| Repeat hepatectomy           | 2 (3)                          |
| Laparoscopic hepatectomy     | 27 (34)                        |
| Anatomical resection*         | 45 (57)                        |
| Type of surgical procedure   |                                |
| Wedge resection              | 34 (43)                        |
| Segmentectomy                | 17 (22)                        |
| Bisegmentectomy              | 14 (18)                        |
| Major hepatectomy†           | 14 (18)                        |
| Left-sided hepatectomy       | 5 (6)                          |
| Right-sided hepatectomy      | 9 (11)                         |
| Multiple hepatectomies       | 6 (8)                          |
| Associated procedures‡       | 8 (10)                         |
| Technical difficulty grade   |                                |
| (low/moderate/high)          | 44 (56)/14 (18)/21 (27)        |
| Inflow clamping              | 66 (84)                        |
| Duration of inflow clamping (min) | 30 (10–48)                  |
| Duration of operation (min)  | 240 (180–300)                  |
| Blood loss (ml)              | 200 (110–611)                  |
| Blood transfusion            | 11 (14)                        |
| Red blood cell units (mean ± SD) | 1.3 ± 0.8                   |
| Intraoperative mortality     | 0 (0)                          |

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Ninety-day mortality and morbidity

Overall, the 90-day mortality rate was 6% (n = 5; Table 3); 3 and 2 patients had major and minor resections, respectively. All patients had postoperative liver decompensation, and 3 had persistent liver decompensation at 3 months. Causes of death included persistent liver decompensation in 3 patients (liver failure in 2 patients and ascites in 1 patient), new onset of ascites in 1 patient, and post-operative diffuse portal vein thrombosis in 1 patient.

The details of postoperative complications are shown in Table 3. Overall, 53 of 79 patients developed postoperative complications (morbidity rate = 67%) with a median CCI of 8.7 (0–30). Major complications (CCI ≥26.2) occurred in 21 (27%) patients.

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At 3 months following resection, 8 (10%) patients had persistent liver decompensation: 5 had refractory ascites, 2 had jaundice and ascites, and 1 had encephalopathy. Four (50%, 4/8) of them died within 12 months following surgery.

Textbook outcomes

A textbook outcome was achieved in 27 (34%) patients. The distributions of each textbook outcome criterion are shown in
Curative treatment included transplantation, surgery and local destruction, respectively (Table 2). A textbook outcome was achieved in 56%, 37%, 0%, and 0% of patients with tumours of different grade, respectively. The most effective treatment was retained when a multimodal management was compared with the HVPG measurement10,11,35,36 and >50% of compensated cirrhosis and actual CSPH, as assessed by HVPG measurement, was performed with acceptable results not only in terms of standard medical-centered outcomes, including 90-day mortality (6%), overall morbidity (67%), and 5-year overall survival (55%), but also in terms of patient-centered outcomes, with textbook outcomes achieved in one-third of patients across the various technical difficulty and BCLC grades. In addition, our selection criteria increased the number of LRs for HCC by 21%.

Table 3. Short and long-term outcomes.

| Outcome | N =79 | 95% CI |
|---------|-------|--------|
| Any perioperative morbidity | 53 (67) |
| CCI | 8.7 (0–28) |
| Severe morbidity (CCI ≥26.2) | 21 (27) |
| Combined medical, surgical and/or liver-related complications | 16 (20) |
| Medical complications only | 14 (18) |
| Infection | 14 (18) |
| Cardiac and respiratory | 14 (18) |
| Acute kidney injury | 4 (5) |
| Surgical complication only | 7 (9) |
| Wound complications | 3 (4) |
| Haemorrhage | 6 (8) |
| Fluid collections requiring percutaneous drainage | 10 (13) |
| Surgical reintervention | 2 (3) |
| Liver-related complications only | 16 (20) |
| Ascites | 25 (3) |
| Biliary fistula | 3 (4) |
| Encephalopathy | 3 (4) |
| Liver failure | 6 (8) |
| Postoperative liver decompensation | 28 (35) |
| Persistent liver decompensation at 3 months | 8 (10) |
| Jaundice and ascites | 2 (3) |
| Ascites | 5 (6) |
| Encephalopathy | 1 (1) |
| Postoperative hospital stay (days) | 8 (6–15) |
| Mortality | |
| 90-day mortality | 5 (6) |
| 1-year mortality | 9 (11) |
| HCC recurrence | 36 (46) |
| Timing (months following resection) | 22 (1–43) |
| Intrahepatic/extrahepatic/both recurrence | 33 (92)/2 (6)/1 (2) |
| Curative treatment† | 14 (19) |
| Treatment type† | |
| Liver transplantation | 3 (8) |
| Re-hepatectomy | 2 (6) |
| Local destruction | 9 (25) |
| TACE | 10 (28) |
| Combination local destruction and chemotherapy | 1 (3) |
| Best supportive care | 11 (31) |
| Postoperative follow-up (months) | 39 (18–56) |

Results are presented as median (IQR) or n (%).

CCI Comprehensive Complication Index; TACE, transarterial chemoembolisation.

† The most effective treatment was retained when a multimodal management was implemented.

In the present series, LR for HCC in selected patients with cirrhosis and actual CSPH, as assessed by HVPG measurement, was performed with acceptable results not only in terms of standard medical-centered outcomes, including 90-day mortality (6%), overall morbidity (67%), and 5-year overall survival (55%), but also in terms of patient-centered outcomes, with textbook outcomes achieved in one-third of patients across the various technical difficulty and BCLC grades. In addition, our selection criteria increased the number of LRs for HCC by 21%.

The updated EASL guidelines endorse a risk algorithm for postoperative decompenesation following LR for HCC, which includes the hierarchical interaction of three variables in the following order: presence of PHT; extent of resection; and MELD score. In these guidelines, CSPH is no longer a formal contraindication for the resection of HCC in patients with cirrhosis, provided that this is balanced by the extent of LR and liver function. Importantly, the above-mentioned algorithm was developed from a series of surgeries all performed with an open approach, in which CSPH was defined by the presence of indirect signs for this condition; however, the laparoscopic approach per se is acknowledged to decrease the risk of liver surgery, and surrogates of CSPH lack sensitivity and specificity compared with the HVPG measurement and >50% of compensated patients, as in our study population, with HVPG ≥10 mmHg might have no varices and normal or almost normal platelet count. In this subset of well-selected patients with HVPG ≥10 mmHg, some centres, following the guidelines, reported reasonable surgical and acceptable long-term oncological outcomes, with postoperative liver decompensation ranging from 6% to 33% and 3-year survival ranging from 72% to 79%.

Clearly, the present series only included selected patients with good general condition [52% with American Society of Anesthesiologists (ASA) score <2], a preserved liver condition [99% with Child-Pugh A, median MELD score of 8], and favourable tumour biology [84% with single nodules, median tumour size of 27 mm, median AFP level = 8 ng/ml]. Nevertheless, it comprised a full spectrum of the three aspects of tumours across the BCLC classification, of the magnitude of surgical procedures from non-anatomical to major resections, and of technical complexity. The mortality and morbidity rates as well as the postoperative liver decompensation incidence achieved here do not require further comment, because they were concordant with those reported by other series including patients with CSPH defined by HVPG ≥10 mmHg. We consider that the comparison of these results to those obtained when the criteria per the guidelines to proceed for surgery are met, is at least debatable, if even clinically sound, because these guidelines target both the best perioperative outcome and longest survival time possible following surgery for the ideal surgical candidates. We acknowledge the value of guideline recommendations and expected results, but we also consider it meaningful to clinicians and patients to provide a comparison between surgical management and the best non-surgical management for clinical use.

Long-term oncological outcomes

During the follow-up period, recurrence occurred in 36 (46%) patients with a median delay of 22 months (IQR: 1–43). The first recurrence was intrahepatic in most cases (33 patients, 92%). Curative treatment could be applied in 14 (39%) patients, including liver transplantation, rehapatectomy, and local destruction in 8%, 6%, and 25% of patients, respectively. The 1-, 3-, and 5-year overall survival rates were 89%, 73%, and 55%, respectively (Figure 2). The 1-, 3-, and 5-year recurrence-free survival rates were 82%, 62%, and 43%, respectively (Figure 2).

Discussion

In the present series, LR for HCC in selected patients with cirrhosis and actual CSPH, as assessed by HVPG measurement, was performed with acceptable results not only in terms of standard medical-centered outcomes, including 90-day mortality (6%), overall morbidity (67%), and 5-year overall survival (55%), but also in terms of patient-centered outcomes, with textbook outcomes achieved in one-third of patients across the various technical difficulty and BCLC grades. In addition, our selection criteria increased the number of LRs for HCC by 21%.

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decision-making and on an intent-to-treat basis. Given the paucity of data published, the natural outcome of patients treated on an intent-to-treat basis is not well known, but median survival has been reported to be <36 months.1

Textbook outcome is a composite endpoint that integrates a paucity of data published, the natural outcome of patients decision-making and on an intent-to-treat basis. Given the ASA, American Society of Anesthesiologists; CSPH, clinically significant portal hypertension; HVPG, hepatic venous pressure gradient; MELD, Model for End-Stage Liver Disease; OR, odds ratio.

Table 4. Uni- and multivariable analysis of variables associated with postoperative liver decompensation.

| Variable                          | Postoperative liver decompensation | Univariate p value | Multivariate p value [OR (95% CI)] |
|-----------------------------------|-----------------------------------|--------------------|------------------------------------|
| Age (years)                       | Yes (n = 28)                      | No (n = 51)        |                                   |
| Male sex                          | 66 (59–70)                        | 65 (58–70)         | 0.90                               |
| BMI (kg/m²)                       | 24 (86)                           | 41 (80)            | 0.55                               |
| ASA score >2                      | 28 (22–31)                        | 29 (25–32)         | 0.24                               |
| Viral aetiology                   | 11 (39)                           | 27 (53)            | 0.25                               |
| Previous treatment                | 21 (75)                           | 29 (57)            | 0.11                               |
| Repeat hepatectomy                | 4 (14)                            | 5 (14)             | 0.62                               |
| Child-Pugh class B                | 5 (18)                            | 7 (14)             | 0.40                               |
| HVPG (mmHg)                       | 14 (12–20)                        | 11 (10–13)         | <0.0001                            |
| Direct signs of CSPH              | 13 (46)                           | 18 (35)            | 0.33                               |
| Oesophageal varices               | 11 (39)                           | 15 (29)            | 0.37                               |
| Splenomegaly and thrombopenia     | 8 (6–10)                          | 6 (6–9)            | 0.93                               |
| Serum albumin (g/L)               | 75 (67–95)                        | 83 (69–92)         | 0.60                               |
| Serum total bilirubin (μmol/L)    | 16 (11–23)                        | 11 (8–15)          | 0.002                              |
| Serum albumin (g/L)               | 37 (34–41)                        | 41 (38–44)         | 0.03                               |
| Platelet (10⁵/mm³)                | 130 (95–164)                      | 135 (104–167)      | 0.36                               |
| Portal vein embolisation          | 4 (14)                            | 1 (2)              | 0.03                               |
| Major resection                   | 9 (32)                            | 5 (10)             | 0.01                               |
| Open approach                     | 23 (82)                           | 29 (57)            | 0.02                               |
| Associated procedures             | 18 (64)                           | 26 (51)            | 0.25                               |
| Inflow clamping                   | 4 (14)                            | 4 (8)              | 0.36                               |
| Operative time (min)              | 230 (184–344)                     | 240 (180–300)      | 0.34                               |
| Blood transfusion                 | 8 (29)                            | 3 (6)              | 0.005                              |
| High grade of technical difficulty| 17 (61)                           | 18 (35)            | 0.03                               |

Results are presented as median (IQR) or n (%). ASA, American Society of Anesthesiologists; CSPH, clinically significant portal hypertension; HVPG, hepatic venous pressure gradient; MELD, Model for End-Stage Liver Disease; OR, odds ratio.

Interestingly, the laparoscopic approach was the sole independent predictor of a textbook outcome in the present series of a priori high-risk patients. Unsurprisingly, patients with very/early HCC were more likely to achieve a textbook outcome than were those with more advanced tumour stages (BCLC B/C). Patients with minor and low-difficulty LRs were also more likely to achieve a textbook outcome than were those with major and moderate/high-difficulty LRs. Overall, the textbook rate observed in the present series was lower than that reported in a previous series (62.3%).12 There are several possible reasons for this difference, including the baseline characteristics of the patients (70.1% with ASA score <2, 36.2% with only cirrhosis) and the definition of the textbook outcome itself.

This study was retrospective. However, the data were obtained from a multicentric prospectively maintained database, making this series of LRs in patients with cirrhosis and confirmed CSPH the largest available. Given that the main objective of this study was to reappraise the outcomes in this highly selected group of patients in terms of the effects of the laparoscopic surgery and the assessment of textbook outcome, rather than to confirm what previous studies had already shown in terms of feasibility and safety, we did not compare our study population with patients with HVPG <10 mmHg as controls. The most...
appropriate control group would be patients with HVPG >−10 mmHg who did not undergo surgery. Ideally, a randomised controlled trial comparing resection to non-resection management in the selected population (i.e. in patients with 10 mmHg < HVPG <30 mmHg, good general status and preserved liver and kidney function, and low MELD score) would be performed. However, considering the results obtained here, we are not convinced that this trial would be ethical, if ever feasible, because of the limited number of eligible patients.

Liver transplantation is the best available treatment for patients with HCC and PHT, but the shortage of liver grafts, strict inclusion criteria (e.g. age, comorbidities, and tumour characteristics) together with the risks of dropout from the waiting list because of PHT could preclude access for a large number of candidates. Interestingly, 56% (n = 44) of patients in the present series were initially transplantable based on the acknowledged transplantation criteria.

The low rate of posthepatectomy liver failure (8%, n = 6 in this series) methodologically hampered a sound multivariate analysis to identify the independent predictors of this major complication. This event was rare in this series compared with others, again because of the stringent selection of candidates for surgery. Finally, the number of patients did not allow us to perform a subanalysis regarding a potential effect of centre difference or era difference on outcomes.

Conclusions

Patients with cirrhosis, HCC, and measured CSPH (i.e. HVPG ≥10 mmHg) can be resected with acceptable rates of mortality, morbidity, liver decompensation, and even a textbook outcome. These results can be achieved in selected patients with preserved liver function, good general status, and sufficient remnant liver volume.

Abbreviations

AFP, alpha-fetoprotein; ASA, American Society of Anesthesiologists; BCLC, Barcelona-Clinic Liver Cancer; CCI, Comprehensive Complication Index; CSPH, clinically significant portal hypertension; CT, computed tomography; EASL, European Association for the Study of the Liver; HVPG, hepatic venous pressure gradient; MELD, model for end-stage liver disease; LLR,
laparoscopic liver resection; LR, liver resection; PHT, portal hypertension; PVE, portal vein embolisation; TACE, transarterial chemoembolisation.

Conflict of interest
The authors declare no conflicts of interest that pertain to this work. Please refer to the accompanying ICMJE disclosure forms for further details.

Authors’ contributions
Study concept and design: DA, CL; acquisition, analysis and interpretation of data: all authors; drafting of manuscript: DA, CL, CS; critical revision of manuscript for important intellectual content: ER, MCR, LL, RN, JB, CCF, KM, SLB, JF; final approval of manuscript: all authors.

Data availability
The data that support the findings of this study are available on request from the corresponding author.

Supplementary data
Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhepr.2020.100190.

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