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Successful management and technical aspects of major liver resection in children
A retrospective cohort study

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Abstract

Optimal treatment of patients with various types of liver tumors or certain liver diseases frequently demands major liver resection, which remains a clinical challenge especially in children.

Eighty seven consecutive pediatric liver resections including 51 (59%) major resections (resection of 3 or more hepatic segments) and 36 (41%) minor resections (resection of 1 or 2 segments) were analyzed. All patients were treated between January 2010 and March 2018. Perioperative outcomes were compared between major and minor hepatic resections.

The male to female ratio was 1.72:1. The median age at operation was 20 months (range, 0.33–150 months). There was no significant difference in demographics including age, weight, ASA class, and underlying pathology. The surgical management included functional assessment of the future liver remnant, critical perioperative management, enhanced understanding of hepatic segmental anatomy, and bleeding control, as well as refined surgical techniques. The median estimated blood loss was 40 ml in the minor liver resection group, and 90 ml in major liver resection group ($P < .001$). Children undergoing major liver resection had a significantly longer median operative time (80 vs 140 minutes), anesthesia time (140 vs 205 minutes), as well as higher median intraoperative total fluid input (255 vs 450 ml) ($P < .001$ for all). Fourteen (16.1%) patients had postoperative complications. By Clavien-Dindo classification, there were 8 grade I, 4 grade II, and 2 grade III-a complications. There were no significant differences in complication rates between groups ($P = .902$). Time to clear liquid diet ($P = .381$) and general diet ($P = .473$) was not significantly different. There was no difference in hospital length of stay (7 vs 7 days, $P = .450$). There were no 90-day readmissions or mortalities.

Major liver resection in children is not associated with an increased incidence of postoperative complications or prolonged postoperative hospital stay compared to minor liver resection. Techniques employed in this study offered good perioperative outcomes for children undergoing major liver resections.

Abbreviations: ALPPS = associating liver partition and portal vein ligation for staged hepatectomy, FLR = future liver remnant, FNH = focal nodular hyperplasia, HBL = hepatoblastoma, ISGLS = International Study Group of Liver Surgery, MH = mesenchymal hamartoma, PHLF = posthepatectomy liver failure, PPCs = postoperative pulmonary complications, THVE = total hepatic vascular exclusion.

Keywords: future liver remnant, hepatectomy, hepatoblastoma, pediatric, total hepatic vascular exclusion

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1. Introduction

Optimal treatment of patients with various types of liver tumors or certain liver diseases frequently demands major liver resection, which remains a clinical challenge especially in children. Although refinement in surgical technology and perioperative management of liver resection over the past years has led to enormous improvements in patients' outcomes, hepatic resection remains morbid overall. Even at high volume centers, in-hospital mortality is as high as 3%, while morbidity ranges from 8.3% to 31% in recent studies.[1] Major hepatic resection, defined as resection of 3nine or more segments, poses an even more difficult clinical challenge with operative mortality historically reported at 8.6% to 14.7% and more recent series describing a 3.1% to 8.7% mortality rate.[2]

The risk of posthepatectomy liver failure (PHLF), which is in line with postoperative morbidity and mortality, remains an important concern following major liver resection[3] (see Definitions). Many factors associated with PHLF have been observed, including preoperative liver function, remnant liver volume, nd amount of blood lost during operation.[4] In adults, there have been significant advances in preoperative assessment of PHLF risk as well as refinement of surgical technique. In children, however, hepatic resection is relatively uncommon. As a

result, there are very limited studies available on techniques and outcomes for major liver resection in children. Therefore, with the overarching aim to prevent postoperative clinical sequelae, we conducted a retrospective study to investigate the safety and technical aspects of major liver resection in children.

2. Methods

2.1. Patients

Between January 2010 and March 2018, all children admitted to our hospital for benign or malignant liver disease and contemplated for curative liver resection were consecutively recruited and retrospectively analyzed. The data were collected from patient chart review of electronic medical records at West China Hospital of Sichuan University. We included patients who underwent liver resection at 16 years of age or younger. We excluded patients with hepatic hydatid cysts who underwent endocystectomy, patients who underwent liver biopsy and those with missing data. The patients were divided into 2 groups according to 2 different surgical approaches: minor liver resection and major liver resection. Minor resection was defined as resection of 1 or 2 segments. Major liver resection was defined as resection of 3 or more hepatic segments.[5,6] Data were collected on demographic data, preoperative, and intraoperative characteristics, as well as postoperative outcomes. Clinical records were independently reviewed by 2 authors. This study was approved by the Regional Ethics Committee of our hospital, and due to its retrospective nature, informed consent was waived.

2.2. Preoperative assessment and operative technique

All patients underwent routine preoperative assessment. Preoperative diagnosis and etiology were based on Doppler ultrasound, triple-phase enhanced computed tomography angiography and three-dimensional reconstruction system or magnetic resonance imaging (MRI). Child-Pugh (CP) score and indocyanine green (ICG)-15 test (in patients with liver cirrhosis) were checked preoperatively. ALBI grade was implemented for hepatic reserve estimation in children (a model to identify patients at risk for adverse outcomes after hepatectomy, see Definitions). Future liver remnant (FLR) was calculated by computed tomography (CT) volumetric analysis (IQQA-liver, EDDA technology, Princeton, NJ, USA) when developing operative strategies for complicated cases (Fig. 1).

We approached all cases with either conventional (complete mobilization of the hepatic lobe and transection of liver attachments and ligaments before liver resection) or anterior (with no dissection of liver attachments or ligaments before liver resection) method via a right subcostal incision and upper median extension to the xiphoid process. For patients with large masses, we performed bilateral subcostal incisions to obtain improved visualization. In patients with suspected malignancy, formal anatomic resection according to Couinaud classification was performed. Intraoperative ultrasound was performed to identify any additional nodules, vascular anatomy, and the transection plane. The dissection of the hilum was started with or without cholecystectomy. Briefly, our technique for right hepatectomy, involved mobilizing the right lobe of liver from the inferior vena cava (IVC) by dividing the ipsilateral short hepatic veins, then advancing cephalad. The right hepatic vein was cautiously

dissected and occluded when necessary. For left hepatectomies, we exposed the junction of the left hepatic vein and IVC after division of the peritoneal reflection above Spiegel lobe and the ligamentum venosum. For inflow control, we employed an intermittent Pringle maneuver (15 minutes of ischemia followed by 5 minutes of reperfusion, without hepatic ischemic preconditioning), hemihepatic or segmental vascular occlusion (using an intra-Glissonean or extra-Glissonean approach) or total hepatic vascular exclusion (THVE) (in patients with significant bleeding).[7] The liver was meticulously transected using Cavitro Ultrasonic Surgical Aspirator (CUSA), Hydrojet, or traditional clamp crushing technique. The liver hanging maneuver was applied in general to avoid injury of IVC and hepatic veins. We aimed for a histologic margin of >1 cm in patients with known or suspected malignant tumors. Polypropylene suture and titanium clips were used for hemostasis and bile leakage. We placed 1 or 2 drains in the subphrenic space. We aimed for intraoperative fluid input of 1.0 to 2.0 ml/kg/hour and adjusted accordingly when central venous pressure (CVP) remained above 5 cm H_2O during parenchymal transection. If the CVP exceeded 10 cm H_2O despite the administration of furosemide, we did not make further efforts to reduce the CVP with intravenous nitroglycerin or morphine.[8]

2.3. Definitions

The American Society of Anesthesiologists (ASA) score was used to assess surgical risk. Baseline ALBI score was calculated according to the following equation [ALBI score= $-0.085 \times$ (albumin g/L) +0.66 log10 (Tbil umol/L)]. ALBI grades were inductively defined as follows: grade $1 \leq -2.60$, grade $2 > -2.60$ to ≤ -1.39 and grade $3 > -1.39$.[9] Ascites was clinically defined as abdominal drainage exceeding 10 ml/kg on postoperative day (POD) 5.[7] Bile leak was defined as drain bilirubin >3-fold serum concentration on POD 3 or after.[10] PHLF was defined as increased international normalized ratio (INR) and concomitant hyperbilirubinemia on POD 5 or after according to the International Study Group of Liver Surgery (ISGLS).[11] The 50–50 criteria, which was defined as threshold values of 50% for PT and 50 μmol/L for total bilirubin on POD 5, was also used for estimating postoperative liver function.[12] Postoperative complications were graded by the Clavien-Dindo classification.[13] Death within 90 days after liver resection was considered postoperative mortality. The Ishak staging system was used for assessing hepatic fibrosis.[14]

2.4. Postoperative care and follow-up

During the postoperative hospital stay, blood samples were obtained and analyzed on POD 1, 3, 5, 7. Postoperative Doppler ultrasound was performed routinely, and chest radiographs were used when considered necessary for example, symptoms of pulmonary infiltrates or pleural effusions. After discharge, the patients were seen biweekly during the first month, and monthly during a 3-month interval, and then every 3 months regularly for the first year.

2.5. Statistical analyses

All statistical analysis was performed using SPSS for Mac version 24.0 (SPSS Inc., Chicago, IL). Continuous variables were expressed as the mean ± SD, or as median (range) for continuous
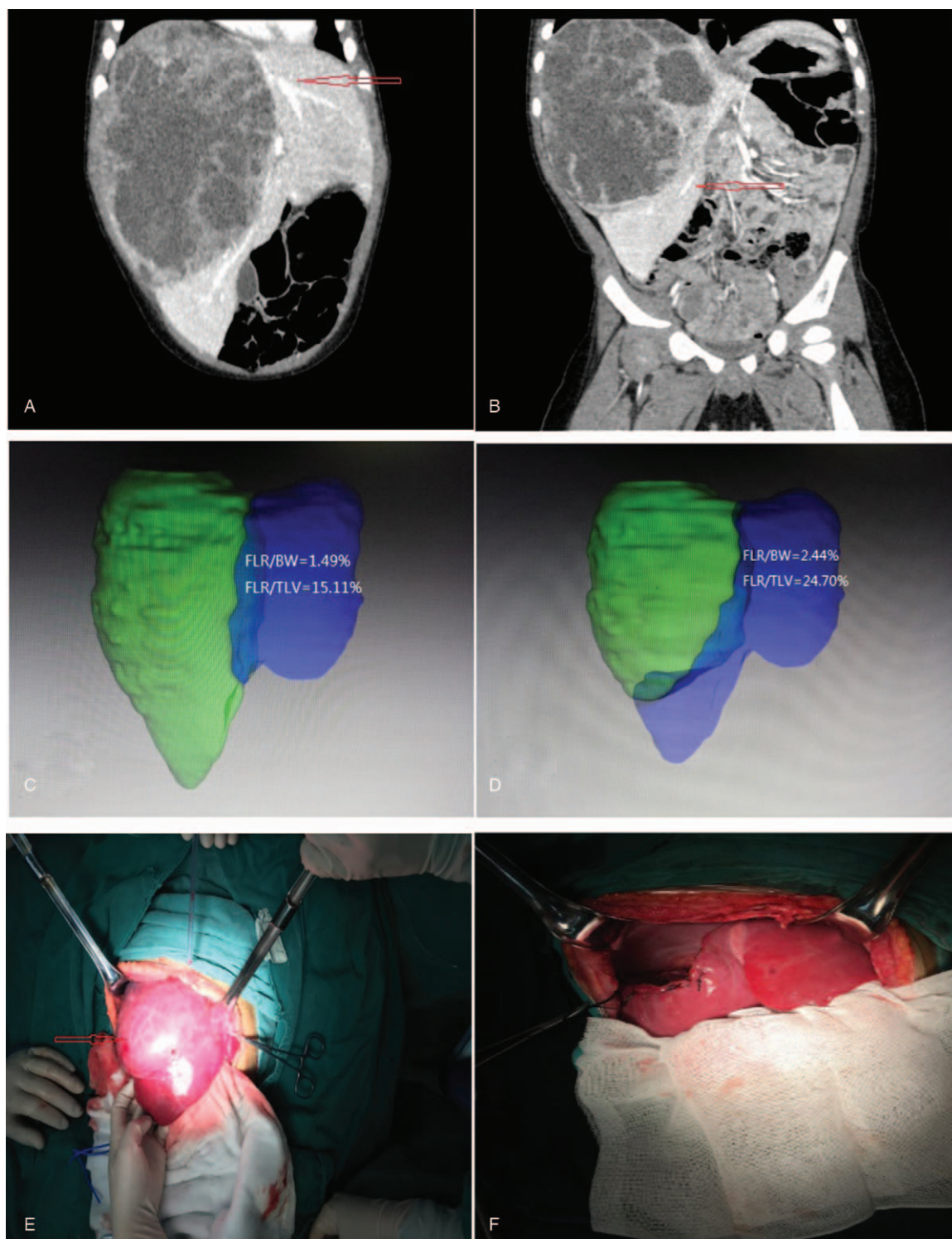
Figure 1. Future liver remnant (FLR) and total liver volume (TLV) estimation by CT volumetric analysis. A 20-month old boy, body weight (BW) 12.5 kg, diagnosed with mesenchymal hamartoma (MH). 1A and 1B display CT scan of the tumor. The arrow in 1A identifies the left hepatic vein. The arrow in 1B illustrates the inferior right hepatic vein. 1C displays the predicted FLR/BW ratio for trisegmentectomy (anatomic resection), estimated FLR/BW = 1.49%, estimated FLR/TLV = 15.11%. 1D demonstrates the predicted FLR/BW ratio for wedge resection (nonanatomic resection), estimated FLR/BW = 2.44%, estimated FLR/TLV = 24.70%. The arrow in 1E identifies the tumor. 1F displays liver remnant with adequate blood perfusion after wedge resection (preserving inferior right hepatic vein).

variables with a non-normal distribution. Intergroup comparisons were analyzed using student t test or Mann–Whitney U test, as appropriate. Categorical data were reported as counts (percentage) and compared using the Chi-Squared test or Fisher exact test. Calculated P values were 2-sided, and a P value $<.05$ was considered statistically significant.

3. Results

3.1. Demographic characteristics

Between January 2010 and March 2018, 139 children with various liver diseases were screened for eligibility. After exclusion of 8 unresectable liver diseases, 1 hepatic trauma which was repaired rather than resected, 15 liver abscesses, 21 hepatic hydatid cysts undergoing endocystectomy, 4 liver biopsies, and 3 patients with significant missing data, a total of 87 children were enrolled in this study (Fig. 2), including 36 minor liver resections and 51 major liver resections. No patient was lost to follow-up. Characteristics of the study population were described in Table 1. The male to female ratio was 1.72:1. The median age at operation was 20 months (range, 0.33–150 months). The median weight was 20 kg (range, 3.7–50.0 kg). Forty two (48.3%) children had an ASA score >2. Four (4.6%) children were positive by HBV-DNA test. Four (4.6%) children had liver fibrosis in the biopsy specimen, which was scored 1 to 3 according to the Ishak staging system. There were 8 (9.2%) children with ALBI grade 2 and none with grade 3 in our study. Pathologic specimens included 32 hepatoblastoma (HBL), 3 hepatocellular carcinoma (HCC), 12 hemangioendothelioma, 9 focal nodular hyperplasia (FNH), 7 mesenchymal hamartoma (MH), 2 alveolar echinococcosis (AE), 4 liver traumatic injuries, and 18 others. There were no significant differences in demographic characteristics and baseline liver function parameters between patients undergoing minor or major hepatic resection (Table 1).

3.2. Intraoperative characteristics according to surgical approach

Of the 36 minor liver resections, 11 were 1 segment resections (including 5 caudate lobe resections), and 25 had 2 segment resections. Major liver resections consisted of 18 right hepatec-tomies, 8 left hepatectomies, 5 central hepatectomies, 8 extended right/left hepatectomies, 5 trisegmentectomies, and 7 others. In the major liver resection group, 8 were 3 segment resections, 23 were 4 segments, and 20 were 5 or more segments resected (Table 2). Children in the major liver resection group had a higher incidence of biliary reconstruction (0 vs 6, $P = .040$) and vascular reconstruction (1 vs 9, $P = .041$). Two children in major liver group had concomitant diaphragm resection without a mesh repair due to tumor involvement. According to pathology results, all children underwent R0 resection with absence of tumor at the resection margin. As regards to vascular occlusions, there were significant differences between 2 groups on Pringle maneuver (0 vs 18 cases, $P < .001$), hemihepatic vascular occlusion (6 vs 26 cases, $P = .001$), and segmental vascular occlusion (6 vs 0 case, $P = .004$), respectively. There was 1 THVE in the minor liver resection group (Fig. 3). Pringle maneuver ischemia time ranged from 15 to 60 minutes. The median estimated blood loss was 40 ml (range, 15–200 ml) in the minor liver resection group, and 90 ml (range, 30–400 ml) in major liver resection group ($P < .001$). Correspondingly, transfusion rates were higher in major liver resection group (6 vs 20 cases, $P = .024$). Children undergoing major liver resection had a significantly longer median operative time (80 (range 40–170) vs 140 (range 90–230) minutes), median anesthesia time (140 (range 100–240) vs 205 (range 160–300) minutes), as well as higher median intraoperative fluid input (255 (range 100–700) vs 450 (range 200–1300) ml) and median urine output (70 (range 30–300) vs 130 (range 40–390) ml) (Table 2, $P < .001$ for all).

3.3. Postoperative complications and recovery course according to surgical approach

The complications encountered and postoperative recovery course are displayed in Table 3. Of the 87 children evaluated,
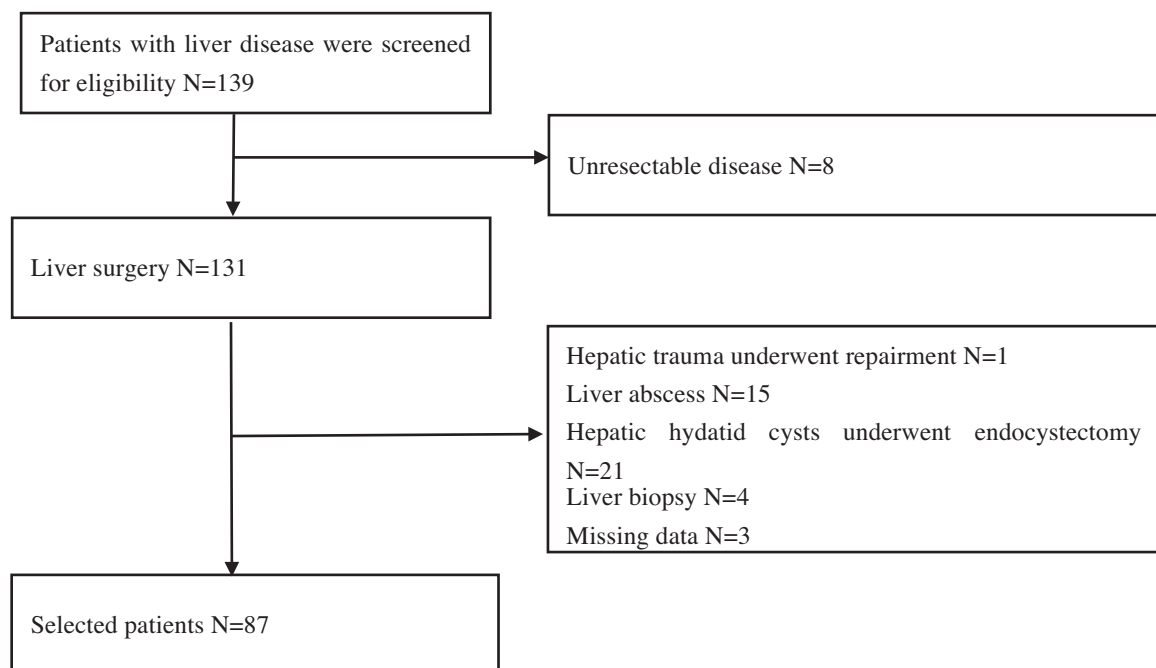

Figure 2. Study flow of pediatric liver resections.

Table 1

Preoperative and operative characteristics of patients undergoing hepatectomy according to surgical approach.

Characteristic	Minor liver resection (n = 36)	Major liver resection (n = 51)	P value
Sex, n (%)			.312
Male	25 (28.7)	30 (34.5)	
Female	11 (12.6)	21 (24.1)	
Age, month, median (range)	12 (0.33-144)	24 (1–150)	.168
Weight, Kg, median (range)	11.0 (3.7–50.0)	13.2 (3.8–45.0)	.216
ASA score > 2, n (%)	21 (24.1)	21 (24.1)	.115
HBV-DNA, n (%)	3 (3.4)	1 (1.1)	.302
Fibrosis, n (%)	1 (1.1)	3 (3.4)	.639
NASH, n (%)	0	0	
SOS, n (%)	0	0	
Baseline liver function			
Platelet count, × 10^9/dL, mean (SD)	220.7 (72.1)	252.7 (81.6)	.062
INR, mean (SD)	1.06 (0.06)	1.04 (0.07)	.158
Albumin, g/L, mean (SD)	44.9 (4.4)	44.4 (3.3)	.543
TBIL, μmol/L, median (range)	11.6 (5.3–30.8)	11.9 (5.8–29.5)	.365
ALBI grade, n (%)			.267
1	31 (35.6)	48 (55.2)	
2	5 (5.7)	3 (3.4)	
Pathology, n (%)			.136
Malignant disease	15 (17.2)	29 (33.3)	.195
HBL	10 (11.5)	22 (25.3)	
PRETEXT I-II	10 (11.5)	11 (12.6)	
PRETEXT III	0	11 (12.6)	
HCC	2 (2.3)	1 (1.1)	
other	3 (3.4)	6 (6.9)	
Benign disease	21 (24.1)	22 (25.3)	
hemangioendothelioma	7 (8.0)	5 (5.7)	
FNH	3 (3.4)	6 (6.9)	
MH	3 (3.4)	4 (4.6)	
AE	1 (1.1)	1 (1.1)	
Liver injury	0	4 (4.6)	
other	7 (8.0)	2 (2.3)	

AE = alveolar echinococcosis, FNH = focal nodular hyperplasia, HBL = hepatoblastoma, HCC = hepatocellular carcinoma, INR = international normalized ratio, MH = mesenchymal hamartoma, NASH = non-alcoholic fatty liver disease, SOS = sinusoidal obstruction syndrome, TBIL = total bilirubin.

14 (16.1%) had postoperative complications. By Clavien-Dindo classification: 8 were grade I, 4 were grade II, and 2 were III-a. There were no Clavien-Dindo III-b, IV, or V complications. Complications included 3 children with ascites, 3 bile leaks (resolved with delayed removal of surgical drain for 7–9 days, ISGLS Grade A[15]), 1 surgical site infection (SSI), 4 mild postoperative respiratory infections, 3 mild to moderate pleural effusions (2 required pleural drainage with a 7F central venous catheter, 1 treated with diuretics). There were no patients with postoperative haemorrhage, confusion, PHLF, meeting 50–50 criteria, renal failure or reoperations. There were no significant differences in Clavien-Dindo classification (P = .902) between major and minor resections. The median time to clear liquid diet was 3 days (range, 1–3 days) vs 3 days (range, 1–4 days) (P = .381), and 3 days (range, 1–4 days) vs 3 days (range, 2–5 days) (P = .473) for general diet, respectively. Children in the major liver resection group had a higher postoperative morphine sulphate equivalents dose (1.05 ± 0.10 vs 1.11 ± 0.12 mg/kg, P = .03), and longer intensive care unit (ICU) stay (median 23 vs 40 hours, P < .001). The median postoperative hospital stay was 7 days for children undergoing minor resection (range, 4–15 days) and major resection (range, 4–12 days) (P = .450). All 87 children were eventually discharged and made uneventful

recoveries. There were no 90-day readmissions or postoperative mortalities.

4. Discussion

Although the feasibility and safety of major liver resections in adults has long been investigated, our knowledge about the approach in children remains quite limited. In comparison to adult patients, most pediatric patients with liver lesions have normal liver function and the oncologic nature of the tumor tends to be the most important factor in their prognosis. However, due to the lack of liver donors, major liver resection remains the only curative option available for substantial numbers of liver lesions. Our study showed that in pediatric patients, 51 cases (59%) need major liver resection.

For patients with large tumor burden, it has been widely demonstrated that portal vein embolization (PVE), portal and hepatic vein embolization (biembolization, BE), associating liver partition and portal vein ligation for staged hepatectomy (ALPPS), and alternative techniques have contributed to extending the indications for liver resection and improved surgical outcomes in patients who would otherwise not be hepatectomy candidates. However, in some cases, liver resection

Table 2

Intraoperative characteristics of patients undergoing hepatectomy according to surgical approach.

Characteristic	Minor liver resection (n = 36)	Major liver resection (n = 51)	P value
Type of liver resection, n (%)			
Right hepatectomy	0	18 (20.7)	
Left hepatectomy	0	8 (9.2)	
Central resection	0	5 (5.7)	
Caudate lobe resection	5 (5.7)	0	
Extended right hepatectomy	0	6 (6.9)	
Extended left hepatectomy	0	2 (2.3)	
Trisegmentectomy	0	5 (5.7)	
other	31 (35.6)	7 (8.0)	
Biliary reconstruction, n (%)	0	6 (6.9)	.040
Vascular reconstruction, n (%)	1 (1.1)	9 (10.3)	.041
Diaphragm resection, n (%)	0	2 (2.3)	.509
No. of resected segments, n (%)			
1	11 (12.6)	0	
2	25 (28.7)	0	
3	0	8 (9.2)	
4	0	23 (26.4)	
≥5	0	20 (23.0)	
Surgical margin R1/R2, n (%)	0	0	
Pringle maneuver, n (%)	0	18 (20.7)	<.001
Hemihepatic vascular occlusion, n (%)	6 (6.9)	26 (29.9)	.001
Segmental vascular occlusion, n (%)	6 (6.9)	0	.004
THVE, n (%)	1 (1.1)	0	.414
Operation time, min, median (range)	80 (40–170)	140 (90–230)	<.001
Anesthesia time, min, median (range)	140 (100–240)	205 (160–300)	<.001
Total fluid input, ml, median (range)	255 (100–700)	450 (200–1300)	<.001
Total Urine output, ml, median (range)	70 (30–300)	130 (40–390)	<.001
Estimated blood loss, ml, median (range)	40 (15–200)	90 (30–400)	<.001
Transfusion rate, n (%)	6 (6.9)	20 (23.0)	.024

THVE = total hepatic vascular exclusion.

remains contraindicated because of insufficient augmentation of the FLR or insidious tumor progression while awaiting liver growth.[16,17] Julio and colleagues reported a rapid growth of the remnant livers in pediatric patients. The increase ratio of future liver remnant/total liver volume (FLR/TLV) ranged from 62% to 102% in 4 patients, but 1 girl only showed a 13% increase even though her FLR (left lateral segment) had grown from 750 ml to 910 ml after 11 days of ALPPS.[18] Regarding ALPPS, it may occasionally place patients at higher risk of poor outcomes or even deaths.[16]

Other contraindications to liver resection are dependent on both the underlying pathology and other patient factors. The radiographic pretreatment extent of disease (PRETEXT) system designed by consensus of the North American Children's Oncology Group (COG) and the International Childhood Liver Tumor Strategy Group (SIOPEL) includes extensive guidance regarding the indications for neoadjuvant chemotherapy, transplantation, and resection in hepatoblastoma patients, the largest pathologic cohort in our study and the most common liver malignancy in children.[19,20]

When major liver resection is appropriate, assessment of baseline liver function and FLR is very significant part of the therapeutic decision-making process. The ALBI score, a recently qualified prognostic nomogram, shows promise as a preoperative risk-assessment model to identify patients at risk for adverse outcomes after hepatectomy.[21–23] The ALBI grade could further classify patients with CP grade A disease into 2 distinct overall

survival cohorts - overall survival rates in the group with poorer outcomes were more in line with those in majority of patients with CP grade B disease.[24] In our article, the nomogram was firstly implemented in children for assessment of liver function. We observed that 8 (9.2%) children were ALBI grade 2, and as shown here, no PHLF or postoperative mortalities were recorded.

Preoperative risk stratification based on those factors is useful in the evaluation of a patient's eligibility for liver resection, however, the prediction of morbidity and mortality based on postoperative factors may be more accurate. Therefore, several postoperative risk scores were established previously. Two of the more practical risk scores include the 50–50 criteria, and a score recently proposed by ISGLS (ISGLS criteria).[25] The 50–50 criteria have been recommended as a prediction of nearly 100% morbidity rate and 50% mortality rate.[12] As a study on 835 patients indicating, the perioperative mortality of patients with PHLF grades (ISGLS criteria) A, B, and C were 0%, 12%, and 54%, respectively.[11] However, based on encouraging recovery in this study, no child met either of the criteria.

Major resection of the liver is substantially restricted to the remnant liver volume, referred to as FLR. It is well known that FLR should be at least 25% to 30% of the total liver volume (TLV) of healthy livers, and approximately 40% of the TLV in patients with cirrhosis or previous chemotherapy.[18] Due to the impressive liver regenerative capabilities in children, 75% to 85% of the liver parenchyma can be safely resected.[26,27] Ribero and colleagues suggested that TLV measured by CT was highly
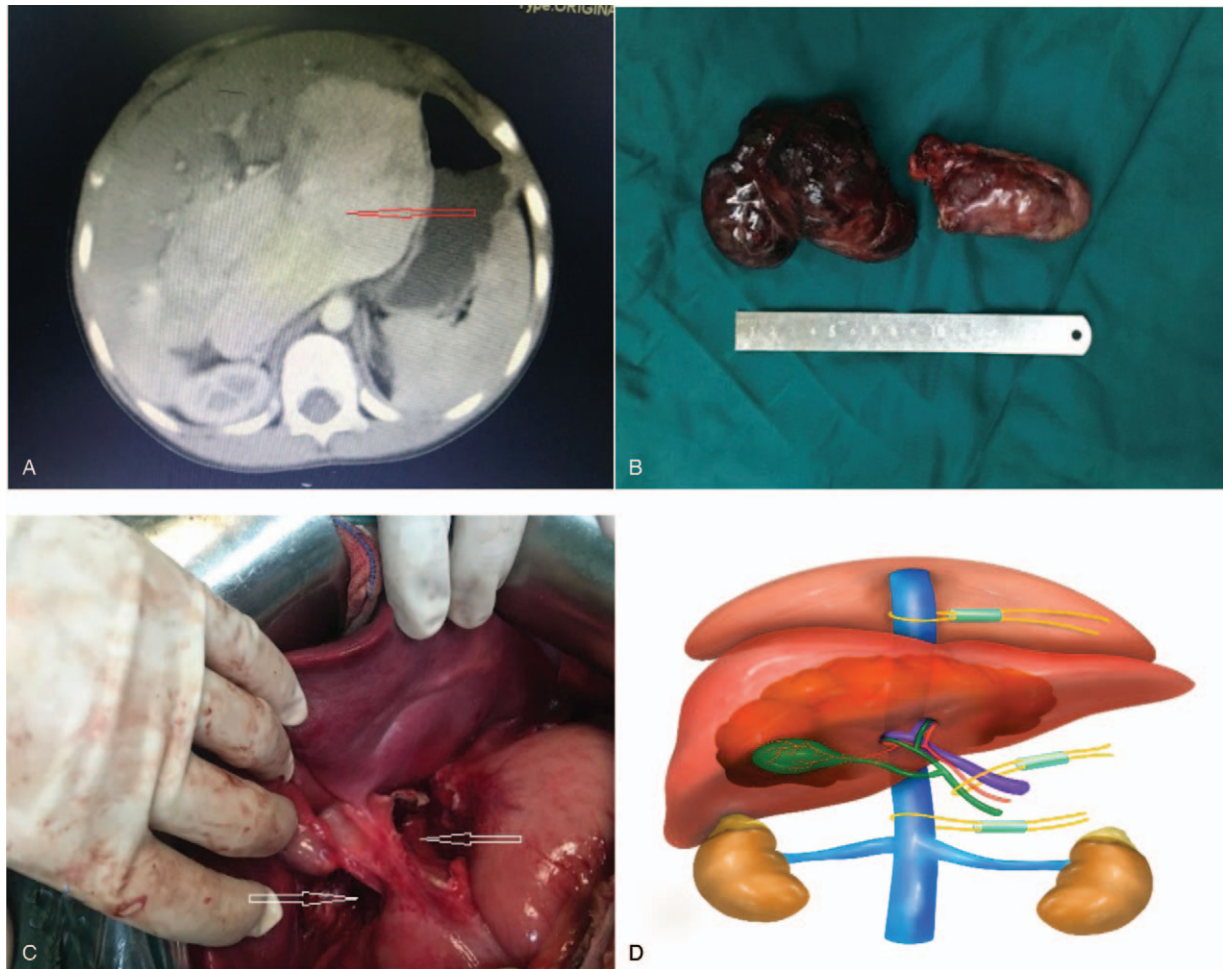
Figure 3. Complete caudate lobectomy (right- and left-sided approaches) for large focal nodular hyperplasia (FNH) with 20 minutes of total hepatic vascular exclusion (THVE). The arrow in 3A identifies a large FNH with extensively caudate lobe invasion. 3B displays the resected tumor. The arrows in 3C show the space between liver, hepatoduodenal ligament and vena cava after tumor had been removed. 3D shows the THVE technique used in this patient.

variable compared with TLV estimated on the correlation existing with the body surface area.[28] However, there is no widely - accepted estimation formula for children, thus we suggest use future liver remnant/body weight (FLR/BW) as an alternative instrument according to a minimal graft-recipient weight ratio (GRWR) of 0.8% employed in liver transplantation. As Figure 1 shows, if we performed trisegmentectomy (anatomic resection) for the child, the estimated FLR/BW =1.49%, and estimated FLR/TLV =15.11%, or if we performed wedge resection (nonanatomic resection), the estimated FLR/BW = 2.44%, and estimated FLR/TLV =24.70% (FLR and TLV were calculated by IQQA-liver, EDDA technology, Princeton, NJ, USA). Ultimately, the wedge resection (preserving inferior right hepatic vein) for this child was an optimal strategy due to the benign nature of disease and more adequate FLR (FLR/BW = 2.44%, FLR/TLV =24.70%).

Although major liver resection without vascular clamping is feasible and safe, the Pringle maneuver and other vascular occlusions are frequently applied in combination with low central venous pressure to minimize blood loss, which is an important factor associated with poor outcomes and may be responsible for impaired survival.[29] In this study, our team shared the same conviction that the risk of detriment to the liver parenchyma caused by clamping is outweighed by the benefits of reduced blood loss. The Pringle maneuver ($P < .001$) and hemihepatic vascular occlusion ($P = .001$) rates were employed more frequently in the major resection group, however we found no correlation between these maneuvers and short-term postoperative complications ($P = .902$). In select circumstances, our group employed THVE. Figure 3 demonstrates a complete caudate lobectomy (right- and left-sided approaches) for very large FNH with 20 minutes of THVE, achieving safety and radicality in this child (Fig. 3).

Improvement in surgical management and better recognition of liver anatomy and functional FLR have contributed to decreased incidence of PHLF and perioperative blood transfusion needs. These improvements, however, have not been linked to a decrease in the rate of postoperative bile leakage, which remains "the Achilles' heel" in liver surgery and a major cause of postoperative morbidity. Data suggest that the frequency of bile leaks over time parallels the increased complexity of hepatectomies, rising from 3.7% before 2006 to 5.9% after 2006.[30] The biliary complications rates after liver resection in children are not well estimated. Institutional experiences have reported biliary com-

Table 3

Comparison of postoperative complications and recovery course of patients undergoing hepatectomy according to surgical approach.

Characteristic	Minor liver resection (n = 36)	Major liver resection (n = 51)	P value
Clavien-Dindo grade, n (%)	6 (6.9)	8 (9.2)	.902
I	2 (2.3)	6 (6.9)	.461
II	3 (3.4)	1 (1.1)	.302
III-a	1 (1.1)	1 (1.1)	1.000
III-b/IV-a, b/V	0	0	
Haemorrhage, n (%)	0	0	
Ascites, n (%)	1 (1.1)	2 (2.3)	
PHLF, n (%)	0	0	
Confusion, n (%)	0	0	
The 50–50 criteria, n (%)	0	0	
Biliary leakage, n (%)	0	3 (3.4)	
SSI, n (%)	1 (1.1)	0	
Respiratory infections, n (%)	3 (3.4)	1 (1.1)	
Pleural effusion, n (%)	1 (1.1)	2 (2.3)	
Renal failure, n (%)	0	0	
Reoperation, n (%)	0	0	
Time to clear liquid diet, d, median (range)	3 (1–3)	3 (1–4)	.381
Time to general diet, d, median (range)	3 (1–4)	3 (2–5)	.473
MS equiv. used, mg/kg, mean (SD)	1.05 (0.10)	1.11 (0.12)	.03
ICU stay, hour, mean (SD)	23 (0–70)	40 (19–80)	<.001
Postoperative hospital stay, d, mean (SD)	7 (4–15)	7 (4–12)	.450
Readmission within 90 days, n (%)	0	0	
Postoperative mortality, n (%)	0	0	

PHLF = posthepatectomy liver failure, SSI = surgical site infection, PPCs = postoperative pulmonary complications, MS equiv = morphine sulphate equivalents, ICU = intensive care unit.

plication rates ranging from 5% to 29%.[31] Odaiyappan and colleagues reported a bile leak rate of 7% with their experience of more than 100 liver resections of HBL.[32] In our own experience, although the major liver resection group had a higher incidence of biliary reconstructions (P =.040), there were just 3 (3.4%) cases of postoperative biliary leakage (Grade A). These all were detected and settled spontaneously with prolonged drainage of 7 to 9 days. No additional surgical interventions were needed for biliary complications.

In the present series, postoperative pulmonary complications (PPCs) were among the most common presenting complications after liver surgery. While these complications occur in 20% to 50% of adults, to our knowledge, no reports focus on this complication in children.[33–35] Transection of the abdominal muscles and prolonged retraction of the right hemidiaphragm, caused by extended right subcostal incisions or bisubcostal incisions with vertical midline superior extension, may be risk factors for PPCs. These incisions may cause painful limitation of thoracic cage excursion and have been shown to decrease 50% to 60% of vital capacity and 30% of functional residual capacity. Additionally, the modification of diaphragmatic lymphatic vessel drainage following dissection in close vicinity to the diaphragm may increase the risk of chyle leak and associated thoracic complications.[34] The incidence of PPCs was 8.0% in our study, including 4 mild pneumonias and 3 pleural effusions. Therefore, we suggest close monitoring for respiratory complications postoperatively in children undergoing hepatectomy. Adequate postoperative analgesia with morphine or other opioids should be routinely used to address postoperative pain and prevent splinting.

Taken together, our study indicates that major liver resection in children is not associated with an increase incidence of postoperative complications compared to minor liver resection.

Both groups had similar recovery courses based on advancement of diet, and postoperative hospital length of stay. Postoperative outcomes in this study had a favorable performance as compared to adult studies' data and data from other geographical regions. We attribute this to our use of functional assessment of the FLR, critical perioperative management, enhanced understanding of hepatic segmental anatomy and intraoperative bleeding control, as well as refined surgical techniques.[36] The use of these strategies can allow for safe major liver resection and potentially expand the eligibility criteria for liver resection in children.

The current study has several limitations. Despite inclusion of all consecutive patients between January 2010 and March 2018, the retrospective study design is prone to selection bias. This study is also limited by a relatively small sample size and low complication rates, which may underpower the analysis of complications comparing major and minor liver resections in this series. While this is one of the largest series of major liver resection in children to date, the absolute sample size remains relatively small. This, in turn, restricts subset analyses. The third limitation is a paucity of information on oncological outcomes after resection. We plan to examine long term outcomes and oncologic outcomes in this population in the foreseeable future.

5. Conclusions

Major liver resection in children is not associated with an increase incidence of postoperative complications and prolonged postoperative hospital stay compared to minor liver resection. The surgical approaches employed in this study offered good results in pediatric patients requiring major liver resection. With the application of these techniques, major liver resection could be performed more widely and safely in children.

Author contributions

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