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Technical Note

Reappraisal of anatomical liver resection for hepatoblastoma in children

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ABSTRACT

Background: The principle of hepatoblastoma (HB) treatment is complete resection. The removal of tumor-bearing section(s) or hemiliver is widely accepted. However, neither the standardized anterior approach for right hepatectomy nor parenchymal sparing anatomical liver resection has been described for HB.
Methods: We retrospectively reviewed the clinical course of two pediatric HB patients who underwent extended right hepatectomy using the anterior approach with the liver hanging maneuver and one who underwent parenchymal sparing anatomical liver resection of S4 apical+S8 ventral/dorsal+S7. The critical aspects of surgical techniques are described in detail.
Results: In all three patients, R0 resection was achieved without complications and are currently alive without recurrence after an average follow-up of 23 months. Intraoperative cardiac hemodynamics were stable, even in a trisomy 18 patient with cardiac disease.
Conclusions: Our findings suggest that these innovative techniques established in adults are safe and feasible for HB in children. These techniques also allow optimal anatomical liver resection to accomplish curative surgery while maintaining the functional reserve of the remnant liver.

Introduction

Hepatoblastoma (HB) is the most common primary liver malignancy in children, and radical surgical resection is the only potentially curative treatment [1]. In adults, the anterior approach with the liver hanging maneuver (LHM) was established for hepatocellular carcinoma (HCC) to reduce several critical risks caused by liver mobilization during hepatectomy (i.e., bleeding, tumor rupture, dissemination of the tumor, and hemodynamic changes) [2–7]. An improved understanding of anatomical borders and segmentation of the liver led to the "cone unit" concept, which is the smallest resectable anatomical part of the liver [8,9]. A novel technique called parenchymal sparing anatomical liver resection was implemented, and it involves less invasive surgery and oncological benefits in patients with HCC and colorectal liver metastases [10–12]. Avoiding remnant liver ischemia, which is associated with decreased survival, is crucial [13,14]. However, data are scarce regarding hepatectomy for HB in children using these innovative techniques [15,16]. Mochizuki et al. reported three cases of liver resection for HB using the LHM, but when performing right lobectomy, the right liver was mobilized prior to liver transection to ensure safety [17]. Chowdappa et al. also presented a unique case of central hepatectomy with double LHM in a child with HB [18], and it is indispensable to accumulate evidence to standardize liver resection in the pediatric population.

We report extended right hepatectomy using the anterior approach with the LHM and parenchymal sparing anatomical liver resection for HB in children and validate their safety and rationality.

Methods

In this study, we retrospectively reviewed the medical records of

Abbreviations: HB, hepatoblastoma; LHM, liver hanging maneuver; HCC, hepatocellular carcinoma; PRETEXT, pretreatment extent of disease; AFP, α-fetoprotein; MHV, middle hepatic vein; RHV, right hepatic vein; LHV, left hepatic vein; CT, computed tomography.

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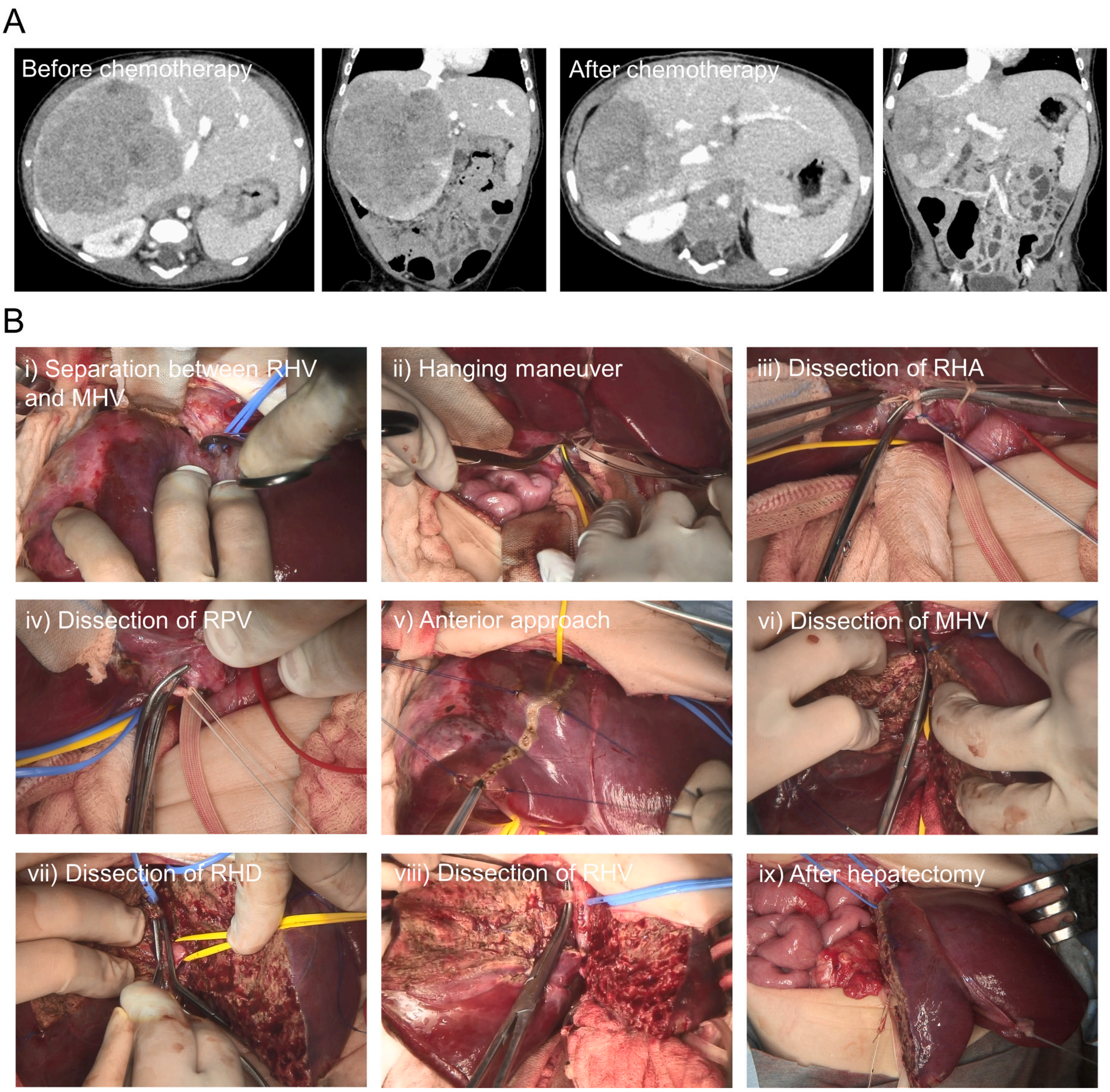

Fig. 1. Extended right hepatectomy using the anterior approach and liver hanging maneuver for HB (patient 1). (A) CT images of HB before and after chemotherapy. (B) Intraoperative findings of extended right hepatectomy using the anterior approach and the liver hanging maneuver.

three pediatric HB patients who underwent extended right hepatectomy using the anterior approach with the LHM or parenchymal sparing anatomical liver resection at Kumamoto University (patients 1 and 3) and Tokyo Metropolitan Children's Medical Center (patient 2) between December 2019 and October 2022. Preoperative factors including age at surgery, sex, body weight, pretreatment extent of disease (PRETEXT), α-fetoprotein (AFP) at diagnosis, details of surgery including operative time and estimated blood loss, postoperative complications, and oncological outcomes were reviewed. This study was performed in accordance with the Declaration of Helsinki and the Ethical Guidelines for Medical and Biological Research Involving Human Subjects of the Ministry of Health, Labour and Welfare of Japan. The institutional review board of Kumamoto University (CRB7200002) waived the need for ethical approval for this case report since all data presented were collected as part of routine clinical management and not for research purposes.

Results

Patient 1 was an 8-month-old male infant (weight, 6960 g) who was diagnosed with HB that occupied the right liver and extended to the left medial section (PRETEXT III) (Fig. 1A). After two courses of cisplatin-based chemotherapy, the tumor showed regression, but the middle hepatic vein (MHV) remained involved. Extended right hepatectomy using the anterior approach with the LHM was planned. Careful dissection between the right hepatic vein (RHV) and MHV exposed the suprahepatic avascular plane at the 10- to 11-o'clock position of the inferior vena cava (Fig. 1B, Supplementary Video 1). This avascular plane was then developed from the infrahepatic space and in the cranial direction up to the space between the RHV and MHV. A tape was passed through the retrohepatic space for the LHM. The right hepatic artery and portal vein were divided individually. After parenchymal transection between the caudate process and the Spiegel lobe, the LHM tape was repositioned above the hilar plate. Parenchymal transection was performed while elevating the LHM tape. After the transection, the right hepatic duct, MHV, and RHV were divided. Subsequently, the hepatocaval ligament

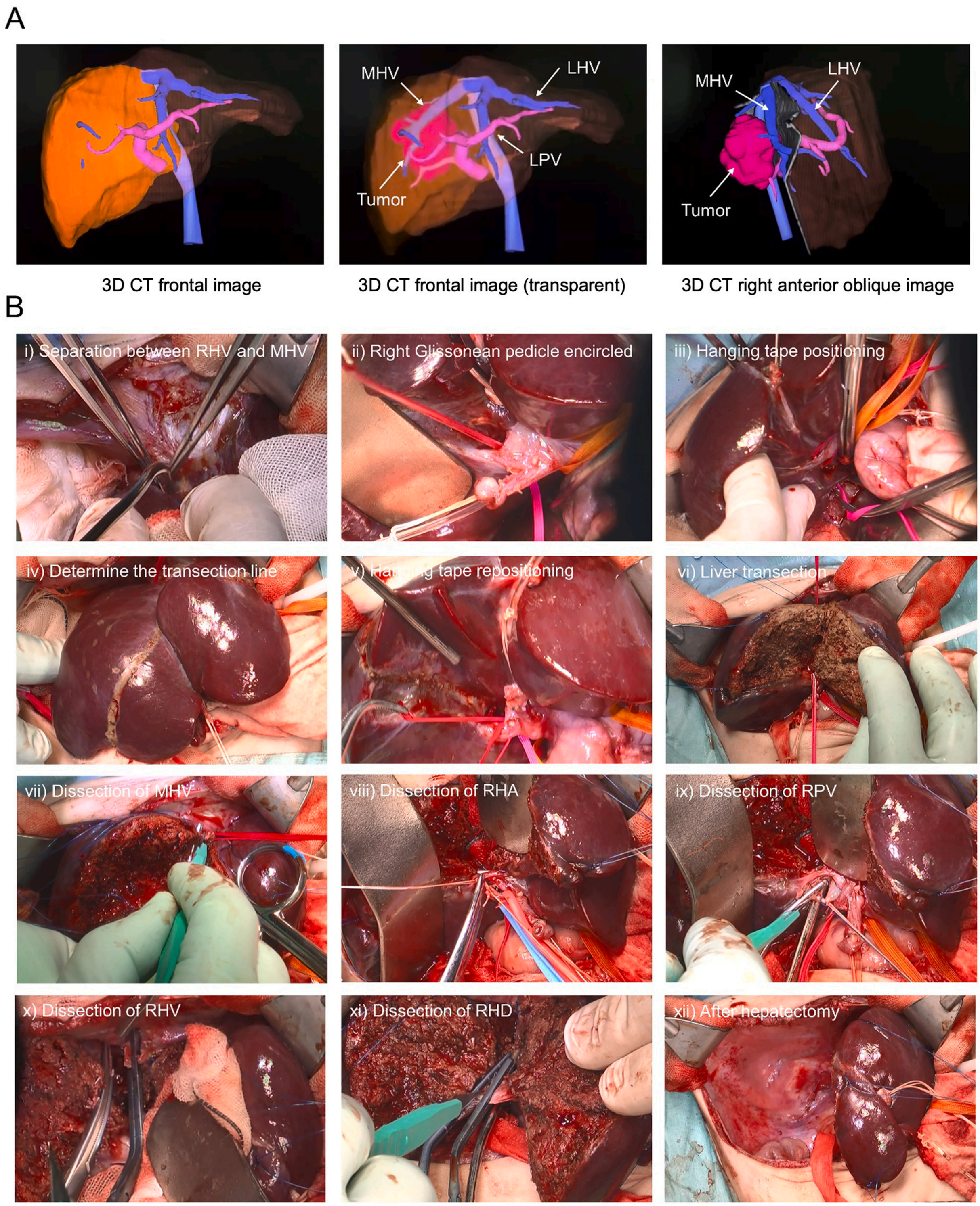

Fig. 2. Extended right hepatectomy using the anterior approach and liver hanging maneuver with the extrahepatic Glissonean approach for HB (patient 2). (A) 3D CT images of HB after chemotherapy. (B) Intraoperative findings of extended right hepatectomy using the anterior approach and the liver hanging maneuver with the extrahepatic Glissonean approach.

and all short hepatic veins were dissected. Finally, the right liver was dissected from the bare area, and a specimen was retrieved (operation time, 476 min; blood loss, 277 g). After two courses of adjuvant chemotherapy, the patient is alive without recurrence for 27 months after the operation.

Patient 2 was a male infant with trisomy 18 who was born at 34 weeks' gestation and underwent gastrostomy for esophageal atresia (Gross A). The patient then underwent pulmonary artery banding for a large ventricular septal defect followed by tracheostomy. Furthermore, he was diagnosed with HB that occupied the right anterior/posterior and left medial sections of the liver (PRETEXT III) at 1 year and 3 months of age. Although the tumor showed regression after four courses of cisplatin-based chemotherapy, MHV abutment remained unchanged and extended right hepatectomy was considered necessary (Fig. 2A).

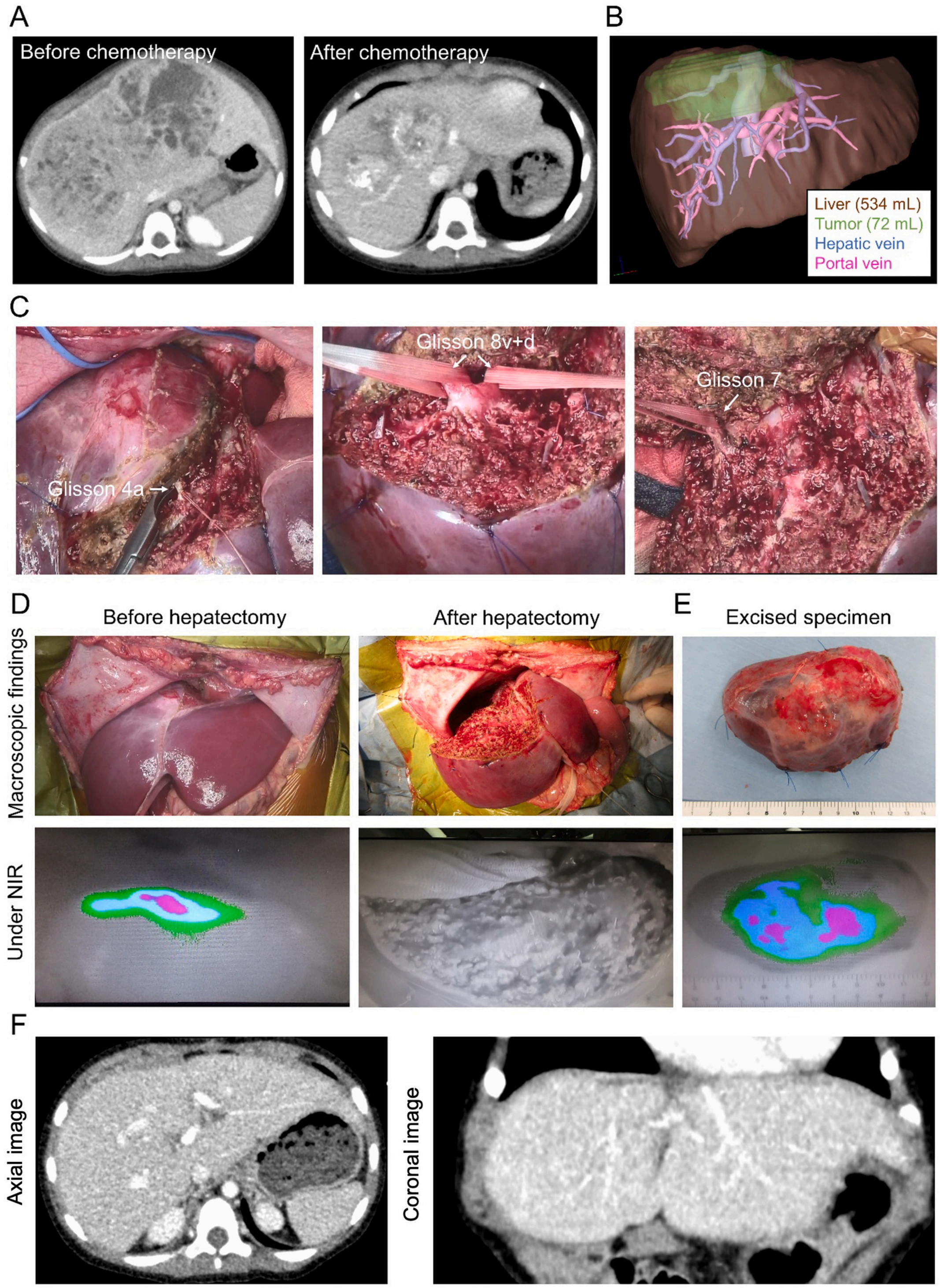

Fig. 3. Parenchymal sparing anatomical liver resection (S4a + S8v/d + S7) for HB (patient 3). (A) CT images of HB before and after chemotherapy. (B) Virtual three-dimensional imaging of the liver anatomy was reconstructed using Vincent software. HB is visualized in green, indicating its relationship with the portal veins (red) and hepatic veins (blue). (C) Intraoperative findings of parenchymal sparing anatomical liver resection (left: Glissonean pedicle 4a; middle: Glissonean pedicle 8v and 8d; right: Glissonean pedicle 7). (D) Fluorescence of indocyanine green under near-infrared (NIR) shows the tumor during hepatectomy. (E) Fluorescence in the excised specimen. Green indicates HB. (F) Postoperative dynamic CT images show a well-perfused parenchyma without remnant liver ischemia. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Preoperative cardiac function was preserved with no signs of pulmonary hypertension. At 1 year and 9 months of age with a weight of 3212 g, he underwent hepatectomy using the anterior approach with the LHM almost in the same manner as that in patient 1 (operation time, 469 min; blood loss, 24 g). The only difference was that the right Glissonean pedicle was controlled by the extrahepatic Glissonean approach [19] because the tumor was not in the close vicinity of the hilar structures (Fig. 2B). Briefly, by maintaining ventral retraction of the tape around the hepatoduodenal ligament, the right Glissonean pedicle is gently and bluntly dissected off the liver surface preserving the Laennec's capsule from the dorsal side of the hepatic hilum toward the cranial edge of the hilar plate. Next, the tape around the hepatoduodenal ligament is pulled

Table 1
Clinical characteristics of three children with hepatoblastoma resected by extended right hepatectomy with anterior approach or parenchymal sparing anatomical liver resection.

Patient	Sex	Age, mo	PRE TEXT	POST-TEXT	Initial AFP, ng/mL	NATx	Comorbidity	Liver resection	Prognosis
1	M	8	III	III	616,400	Cisplatin × 2	None	Extended RHx with anterior approach and the LHM	NED, 27 mo
2	M	15	III	II	110,000	Cisplatin × 7	Trisomy 18, EA, VSD	Extended RHx with anterior approach and the LHM	NED, 13 mo
3	F	14	III	III	260,537	Cisplatin and doxorubicin × 4	None	Parenchymal sparing anatomical resection of S4a + S8v/d + S7	NED, 45 mo

PRETEXT, pretreatment extent of disease; POST-TEXT, post-treatment extent of disease; AFP, α-fetoprotein; NATx, neoadjuvant treatment; RHx, right hepatectomy; LHM, liver hanging maneuver; NED, no evidence of disease; EA, esophageal atresia; VSD, ventricular septal defect.

caudally and the right Glissonean pedicle is fully dissected off the liver surface from the ventral side of the hepatic hilum and the Glissonean pedicle is encircled by a tape [20]. Intraoperative central venous pressure was maintained at 5–8 mmHg, and circulatory dynamics remained stable during hepatectomy. The patient received adjuvant chemotherapy and is alive without recurrence for 13 months after the operation.

Patient 3 was a 1-year-old female infant (weight, 9200 g) who presented with PRETEXT III HB that strongly compressed the confluence of the three major hepatic veins (Fig. 3A). Although the tumor showed regression after four courses of cisplatin/doxorubicin-based chemotherapy, the tumor remained in segments 4a (apical), 7, and 8 ventral (v)/dorsal (d) (POST-TEXT III). Additionally, left hepatic vein (LHV) abutment was evident. Furthermore, the RHV and MHV were completely encased by the tumor. Computed tomography (CT) volumetry showed that the estimated future liver remnant after right trisectionectomy would be less than 30 % of the whole liver. To avoid posthepatectomy liver failure, parenchymal sparing anatomical liver resection was indicated. Before the surgery, three-dimensional reconstruction of CT images was performed (Fig. 3B), and indocyanine green (0.5 mg/kg) was injected intravenously 72 h before surgery. After encircling the RHV and MHV/LHV, liver transection started from the root side of the LHV (Supplementary Video 2). The tumor was safely detached from the LHV, and the transection continued along the umbilical fissure vein (hepatic vein-guided cranio-ventral approach) [19]. The S4a Glissonean pedicle was then divided, and the transection continued along the demarcation line between S4a and S4b. After dividing the MHV distal to the point of tumor involvement, the tumor-bearing Glissonean pedicles of S8v, S8d, and S7 that emerged on the transection plane were divided in this order while securing an adequate surgical margin. The transection plane was developed cautiously along the demarcation line that appeared after division of each Glissonean pedicle (Fig. 3C). The RHV and MHV were divided at their roots and the specimen was retrieved (operation time, 498 min; blood loss, 57 g). The lateral branch of S8 and the inferior right hepatic vein were preserved. Intraoperative fluorescence indocyanine green imaging confirmed no residual tumor in the remnant liver (Fig. 3D, E). The patient received adjuvant chemotherapy and is alive without recurrence for 45 months after the operation. A postoperative dynamic CT showed well-perfused parenchyma with no remnant liver ischemia (Fig. 3F).

The clinical characteristics of the three patients are summarized in Table 1. All three patients demonstrated uneventful recovery and R0 resection was confirmed pathologically. They are alive without recurrence for an average of 28 months postoperatively.

Discussion

We showed that the anterior approach with the LHM (patients 1, 2) with/without the extrahepatic Glissonean approach was effective for right hepatectomy in children with HB. To date, it has been reported that this approach prevented intraoperative bleeding, systemic tumor dissemination, and hemodynamic instability induced by twisting and compression of the IVC in adult HCC patients [2,3]. We have also reported that Glissonean approach and the LHM reduces bile leakage from the hepatic hilum in living donor hepatectomy [20]. Indeed, despite the relatively challenging liver resection, the surgical outcomes were comparable to the conventional standard hepatectomy in pediatric patients with HB performed at our institution (data not shown). It is also worth noting that this approach may be beneficial particularly for patients with trisomy 18 and pulmonary hypertension to prevent elevation of central venous pressure [21]. Long-term survivors of trisomy 18 have a high risk of developing HB, and less invasive surgery should be selected while managing comorbidities [22]. Moreover, the hepatic vein-guided approach was an indispensable technique to control tumor-bearing Glissonean pedicles enabling parenchymal sparing anatomical hepatectomy to achieve R0 resection (patient 3) [19].

In the Tokyo 2020 Terminology, anatomical liver resection was defined as “the complete removal of the liver parenchyma confined within the responsible portal territory” [23]. If the tumor occupies multiple subsegments (or cone units), only the tumor-bearing cone units, not all affected Couinaud's segments, should be removed. In HCC, anatomical resection reduces local recurrence compared with non-anatomical resection [24]. Furthermore, remnant liver ischemia was recently reported to be associated with poor oncological outcomes for HCC and colorectal liver metastases [13,14]. These principles and observations should also apply for HB in children. Of note, this is the first study describing standardized implementation of innovative techniques established in adults (anterior approach combined with the LHM and parenchymal-sparing anatomical hepatectomy) to pediatric patients with HB. We also reported for the first time the safe and effective adoption of the concept of precision anatomy for minimally invasive hepatobiliary pancreatic surgery and Tokyo 2020 terminology of liver anatomy to pediatric liver resection [19,23].

The limitations of the present study include its retrospective nature and a small patient population. However, all liver resections for pediatric patients with HB in this study were performed by a collaborative team of board-certified instructors of pediatric surgery (M. H. and N. S.) and an expert surgeon of hepato-biliary-pancreatic surgery (T. H.) [25]. Therefore, all the surgical techniques demonstrated in this study are considered reproducible in specialized centers. Future multicenter prospective studies, eventually in an international framework, are critical to validate the safety and feasibility of our novel surgical approach.

In conclusion, the anterior approach with the LHM for right hepatectomy and parenchymal sparing anatomical resection are safe and feasible for HB in children. These strategies should be introduced judiciously in children to allow optimal anatomical liver resection and accomplish curative surgery, while maintaining the functional reserve of the remnant liver.

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CRediT authorship contribution statement

Masaki Honda: Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Writing – original draft, Visualization. **Kaori Isono:** Data curation, Writing – review & editing. **Kazuya Hirukawa:** Data curation, Writing – review & editing. **Masahiro Tomita:** Data curation, Writing – review & editing. **Hiroki Hirao:** Data curation, Writing – review & editing. **Kazuki Hirohara:** Data curation, Writing – review & editing. **Yuto Sakurai:** Data curation, Writing – review & editing. **Tomoaki Irie:** Data curation, Writing – review & editing. **Teizaburo Mori:** Data curation, Writing – review & editing. **Keita Shimata:** Data curation, Writing – review & editing. **Naoki Shimojima:** Data curation, Writing – review & editing. **Yasuhiko Sugawara:** Data curation, Writing – review & editing. **Taizo Hibi:** Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Writing – original draft, Visualization, Supervision, Project administration.

Declaration of competing interest

All authors have no related conflict of interest to disclose.

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Ethics approval

This study was performed in accordance with the Declaration of Helsinki and the Ethical Guidelines for Medical and Biological Research Involving Human Subjects of the Ministry of Health, Labour and Welfare of Japan. The institutional review board of Kumamoto University (CRB7200002) waived the need for ethical approval for this case report since all data presented were collected as part of routine clinical management and not for research purposes.

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