Liver Transplantation Is Highly Effective in Children With Irresectable Hepatoblastoma

Simon Moosburner  
Charité Universitätsmedizin Berlin: Charite Universitätsmedizin Berlin

Moritz Schmelze  
Charité Universitätsmedizin Berlin: Charite Universitätsmedizin Berlin

Brigitta Globke  
Charité Universitätsmedizin Berlin: Charite Universitätsmedizin Berlin

Wenzel Schöning  
Charité Universitätsmedizin Berlin: Charite Universitätsmedizin Berlin

Angelika Eggert  
Charité Universitätsmedizin Berlin: Charite Universitätsmedizin Berlin

Philippa Seika  
Charité Universitätsmedizin Berlin: Charite Universitätsmedizin Berlin

Anika Kästner  
Universitätsmedizin Greifswald: Universitätsmedizin Greifswald

Johann Pratschke  
Charité Universitätsmedizin Berlin: Charite Universitätsmedizin Berlin

Robert Öllinger  
Charité Universitätsmedizin Berlin: Charite Universitätsmedizin Berlin

Safak Gül-Klein (✉ safak.guel@charite.de)  
Charité Universitätsmedizin Berlin: Charite Universitätsmedizin Berlin  https://orcid.org/0000-0003-1013-7126

Research

Keywords: Hepatoblastoma, Pediatric Liver Transplantation, Pediatric Liver Resection, Survival, Postoperative Complications

DOI: https://doi.org/10.21203/rs.3.rs-473238/v1

License: ☕️ This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

Introduction

In children, hepatoblastoma preferentially is managed by liver resection (LR). However, in irresectable cases, liver transplantation (LT) is required. Aim of our study was to compare short- and long-term results after LR and LT for the curative treatment of hepatoblastoma.

Materials and methods

Retrospective analysis of all patients treated surgically for hepatoblastoma from January 2000 till December 2019. Demographic and clinical data were collected before and after surgery. Primary endpoints were disease free survival and patient survival.

Results

In total, 38 patients were included into our analysis (n=28 for LR, n=10 for LT) with a median follow up of 5 years. 36 patients received chemotherapy prior to surgery. Total hospital stay and intensive care unit (ICU) stay were significantly longer within the LT vs. the LR group (ICU 23 vs. 4 days, hospital stay 34 vs. 16 days, respectively; p < 0.001). Surgical complications (≤ Clavien-Dindo 3a) were equally distributed in both groups (60% vs. 57%; p = 1.00). Severe complications (≥ Clavien-Dindo 3a) were more frequent after LT (50% vs. 21.4%; p = 0.11). Recurrence rates were 7% for LR and 0% for LT at 5 years after resection or transplantation (p=. Overall, 5-year survival was 90% for LT and 96% for LR (p = 0.44).

Conclusion

In unresectable cases, liver transplantation reveals excellent outcomes in children with hepatoblastoma with an acceptable number of perioperative complications.

Introduction

Primary hepatic tumors in children account for about 1% of all childhood malignancies. Hepatoblastoma is the most common malignant hepatic tumor with 90%. Despite hepatoblastoma remaining a relatively rare disease, hepatoblastoma has shown an annual increase in incidence of 4.3% in children under the age of 19, especially in countries with a high human development index.

Patients generally remain asymptomatic and are diagnosed in a progressed state of the disease, requiring a multimodal treatment strategy of chemotherapy (CTx) and surgery. Staging is performed through the PRE-Treatment EXTent of disease (PRETEXT) system, a radiological score for risk stratification prior to neoadjuvant chemotherapy influencing the method of surgical treatment.

Over the past three decades, several multicenter study groups have introduced effective risk-based chemotherapeutic regimens, which in combination with more aggressive surgical approaches, including
liver transplantation (LT), have resulted in significant improvements in outcomes\textsuperscript{7−12}. Nevertheless, Hiyama et al., for the Japanese Study Group for Pediatric Liver Tumors, recently showed that neoadjuvant and adjuvant CTx with cisplatin-tetrahydropyranyl-adriamycin (pirarubicin; CITA) was effective for resectable hepatoblastoma, but remained unsatisfactory for unresectable and metastatic hepatoblastoma patients\textsuperscript{12}. After CTx, surgical completion through LR or LT, if hepatoblastoma remains unresectable, in the following phase can lead to a completely curative treatment\textsuperscript{13}.

Primary resectability implies radical surgical resection as a first-line therapy. Nevertheless, curative LR after successful tumor reduction remains a challenge, especially in cases of extensive liver resection. LT is in turn the treatment of choice for unresectable tumors (bilobar localization, vascular infiltration) and in cases of expected excessive parenchymal loss by radical resection\textsuperscript{14,15,16,17}. Overall, an improvement in survival rates, with 5-year survival rates as high as 90\%, has been observed over the past four decades\textsuperscript{18,19}. Advanced hepatoblastoma requires a decision to be made between a complex and radical LR or alternatively a LT, which is also known as a complex procedure - especially in infants. LT as well as extended resections for metastatic and locally advanced hepatoblastoma after neoadjuvant chemotherapy require referral to centers with expertise in both pediatric transplantation and hepatobiliary surgery. Preoperative imaging may identify hepatoblastomas as presumptively inoperable and subvert surgical exploration. Synchronous pulmonary metastases are seen in approximately 20\% of cases and, per se, are no contraindication for a radical surgical approach, however, this is an ongoing matter of discussion\textsuperscript{20}.

The aim of our study was to evaluate patients after LR and after LT in the postoperative course with respect to early and late complications and recurrence of hepatoblastoma.

Materials And Methods

Study Design and Participants

All patients with hepatoblastoma presenting at the Surgical Department, Campus Charité Mitte and Campus Virchow-Klinikum at Charité – Universitätsmedizin Berlin from 1990 to 2019 were included in the study.

Demographic and clinical data before and after surgery, i.e. age at presentation, gender, tumor size, presence of distant metastasis, values of alpha-fetoprotein (AFP), chemotherapy, type of surgery, postoperative complications, complication management, tumor recurrence/disease free survival and mortality for both groups were collected. Patients were followed up at regular time intervals through routine follow-up examinations. In addition, all unplanned inpatient stays were considered for both groups, with special attention given to readmissions that entailed re-operations or were associated with complications in general. PRETEXT staging was performed by our radiologists at the time of diagnosis according to standardized criteria\textsuperscript{6}. Postoperative complications were classified after Clavien-Dindo. Cancer recurrence was defined as local recurrence or distant metastasis.
Immunosuppression was administered based on individualized protocols including calcineurin inhibitors, mycophenolate mofetil (MMF), mTOR inhibitors and steroids.

Patients who underwent LR before LT were included in the LT group. The study was approved by the institutional ethics board (EA2/267/20).

**Surgical Technique**

LT from deceased donors were donations after brain death only (DBD) due to regulations in Germany. DBD donors were chosen based on donor age, size of the donor organ, cause of death, laboratory values at time of organ donation, perspective cold ischemia time and frozen cut section analysis, if available. Living donors for partial living donor liver transplantation (LDLT) were carefully evaluated, including the ethics board of the German federal medical association ("Bundesärztekammer") and underwent S2/3 sectionectomy using a small median laparotomy. Full size organs were transplanted orthotopically whereas split grafts and grafts form living donors were placed in a modified piggy-back technique, using the recipients unified left and middle hepatic vein for venous anastomosis. Portal vein and arterial anastomoses were all performed in an end-to-end fashion using loupes or a microscope for magnification. Biliary anastomosis was performed in side-to-side technique with the addition of a T-Drain. If duct-to-duct anastomosis was not feasible a hepaticojejunostomy was performed with intraoperative placement of a Polyvinyl-drainage.

LR was performed as open surgery with a right subcostal incision and upper midline extension to the xiphoid. Intraoperative ultrasound was used to identify a dissection plane. Pringle’s maneuver was prepared for use if needed. Parenchymal dissection was carried out using ultrasound dissection.

**Statistical Analysis**

Statistical analysis was performed using the software solutions R (version 4.0.3) and R Studio (version 1.25) for macOS (both: R Foundation for Statistical computing, Vienna, Austria). Graphs were plotted using GraphPad PRISM version 8.2 for macOS (GraphPad Software, La Jolla, CA, USA). Survival was analyzed using the Kaplan-Meier curves and compared with the log rank method. Data was tested for normality using the Shapiro-Wilk test and analyzed with a student’s t-test or Mann-Whitney-U test accordingly. Data, unless otherwise stated, is reported as mean and standard deviation (SD) or median and interquartile range (IQR).

**Results**

**Patient characteristics**

During the analysis period 42 patients with suspected hepatoblastoma were surgically treated in the Charité – Universitätsmedizin Berlin. Of those 42 patients, 4 were excluded from our analysis due to final histopathology showing no hepatoblastoma (n = 2) or patients being lost to follow-up (n = 2). Median age
at time of presentation was 2 years (IQR 1 year). Median follow-up was 64 months for LR and 170 months for LT patients respectively.

Ten patients (26%) underwent LT for hepatoblastoma. Within these 10 patients, 5 patients received a graft from a living donor, the remaining 5 patients either a segment II/III split graft (n = 3) or a full-size graft (n = 2) from a deceased donor (supplemental table 2). For three patients, LT was a rescue procedure due to recurrent disease, small for size syndrome or cirrhosis in the remnant liver. Immunosuppression in the 10 LT patients was carried out as mono-therapy with tacrolimus (tac) in 5 patients, while 3 patients had dual-therapy (Tacrolimus and plus Mycophenolate mofetil). One patient received mono-therapy with Everolimus. A total of 28 patients underwent LR, amongst them 1 patient with a segment II resection, 3 patients with atypical resections including > 2 segments, 4 patients left-lateral hepatectomy (SII and III), 4 patients left hemihepatectomy, 7 patients right hemihepatectomy, 5 patients extended right hemihepatectomy and 4 patients extended left hemihepatectomy (supplemental table 2).

**Tumor characteristics**

Histopathological analysis showed the majority of tumors being of fetal origin (54% in LR group, 50% ins LT group) and roughly a third of mixed origin. Macroscopical tumor free resection margins were achieved in all LT and LR patients. In four patients (14.3%) after LR, there was microscopical invasion by tumor cells in the resection margins (R1). Synchronous distant metastases did not differ between groups and affected one third of patients (p = 1.00). There were mostly lung metastases (n = 7) in the LR group and one bone and one spinal cord metastasis. One patient in the LT group had pulmonary metastases and two patients lymphonodal metastases. Almost all (n = 27, 96.4%) patients after LR received adjuvant chemotherapy vs 10% in the patient group after liver transplantation.

**Perioperative Complications**

Surgical complications (≤ Clavien-Dindo 3a) were equally distributed in both groups (60% vs. 57%; p = 1.00). Severe complications ≥ Clavien-Dindo 3a were more frequent in patients after LT (Table 1). Complications after LT were biliary complications (n = 3, 30.0%), hemorrhage (n = 2, 20%) and portal vein thrombosis (n = 2; 20%). After LR, biliary complications were most common (n = 5; 17.9%, vs. 30% for LT; p = 0.41) followed by hemorrhage (n = 3; 10.7%, vs. 20% for LT; p = 0.59) (Table 2).
Table 1
Liver Transplantation and Liver Resection compared

<table>
<thead>
<tr>
<th></th>
<th>Liver Resection</th>
<th>Liver Transplantation</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 28</td>
<td>N = 10</td>
<td></td>
</tr>
<tr>
<td>Sex [f]</td>
<td>10 (35.7%)</td>
<td>7 (70.0%)</td>
<td>0.078</td>
</tr>
<tr>
<td>Age [years]</td>
<td>1.00 [0.00;2.00]</td>
<td>2.00 [2.00;3.00]</td>
<td>0.069</td>
</tr>
<tr>
<td>Age Groups [years]</td>
<td></td>
<td></td>
<td>0.328</td>
</tr>
<tr>
<td>&lt; 1</td>
<td>9 (32.1%)</td>
<td>1 (10.0%)</td>
<td></td>
</tr>
<tr>
<td>1–2</td>
<td>13 (46.4%)</td>
<td>5 (50.0%)</td>
<td></td>
</tr>
<tr>
<td>≥ 3</td>
<td>6 (21.4%)</td>
<td>4 (40.0%)</td>
<td></td>
</tr>
<tr>
<td>PreTEXT</td>
<td></td>
<td></td>
<td>0.002</td>
</tr>
<tr>
<td>1</td>
<td>7 (25.9%)</td>
<td>0 (0.00%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>10 (37.0%)</td>
<td>0 (0.00%)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>9 (33.3%)</td>
<td>5 (55.6%)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1 (3.70%)</td>
<td>4 (44.4%)</td>
<td></td>
</tr>
<tr>
<td>Metastasis</td>
<td>8 (28.6%)</td>
<td>3 (30.0%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Metastasis Localization</td>
<td></td>
<td></td>
<td>0.101</td>
</tr>
<tr>
<td>bone and spinal</td>
<td>1 (3.57%)</td>
<td>0 (0.00%)</td>
<td></td>
</tr>
<tr>
<td>lung</td>
<td>7 (25.0%)</td>
<td>1 (10.0%)</td>
<td></td>
</tr>
<tr>
<td>Operative Time [min]</td>
<td>168 (50.5)</td>
<td>392 (103)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hospital Stay [d]</td>
<td>15.5 [10.0;21.2]</td>
<td>34.0 [28.0;44.0]</td>
<td>0.001</td>
</tr>
<tr>
<td>Intensive Care Unit [d]</td>
<td>3.50 [2.00;6.00]</td>
<td>23.0 [19.0;29.0]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Complications</td>
<td>16 (57.1%)</td>
<td>6 (60.0%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Clavien-Dindo</td>
<td></td>
<td></td>
<td>0.087</td>
</tr>
<tr>
<td>0</td>
<td>12 (42.9%)</td>
<td>4 (40.0%)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2 (7.14%)</td>
<td>0 (0.00%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>8 (28.6%)</td>
<td>1 (10.0%)</td>
<td></td>
</tr>
<tr>
<td>3a</td>
<td>1 (3.57%)</td>
<td>0 (0.00%)</td>
<td></td>
</tr>
<tr>
<td>3b</td>
<td>2 (7.14%)</td>
<td>5 (50.0%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Liver Resection</td>
<td>Liver Transplantation</td>
<td></td>
</tr>
<tr>
<td>------------------------------</td>
<td>-----------------</td>
<td>-----------------------</td>
<td>----</td>
</tr>
<tr>
<td>4a</td>
<td>3 (10.7%)</td>
<td>0 (0.00%)</td>
<td></td>
</tr>
<tr>
<td>Follow-up in Days</td>
<td>1876 [947;2608]</td>
<td>5168 [1486;6805]</td>
<td>0.104</td>
</tr>
<tr>
<td>Follow-up in Months</td>
<td>64.0 [42.0;91.5]</td>
<td>170 [52.5;224]</td>
<td>0.127</td>
</tr>
<tr>
<td>Follow-up in years</td>
<td>5.00 [3.00;7.00]</td>
<td>14.0 [4.25;18.5]</td>
<td>0.093</td>
</tr>
<tr>
<td>Neoadjuvant Chemotherapy</td>
<td>27 (96.4%)</td>
<td>9 (90%)</td>
<td>0.43</td>
</tr>
<tr>
<td>Adjuvant Chemotherapy</td>
<td>27 (96.4%)</td>
<td>1 (12.5%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AFP</td>
<td></td>
<td></td>
<td>0.178</td>
</tr>
<tr>
<td>&lt; 999</td>
<td>0 (0.00%)</td>
<td>1 (12.5%)</td>
<td></td>
</tr>
<tr>
<td>1,000–9,999</td>
<td>5 (20.8%)</td>
<td>0 (0.00%)</td>
<td></td>
</tr>
<tr>
<td>10,000–99,999</td>
<td>6 (25.0%)</td>
<td>4 (50.0%)</td>
<td></td>
</tr>
<tr>
<td>100,000-999,999</td>
<td>11 (45.8%)</td>
<td>3 (37.5%)</td>
<td></td>
</tr>
<tr>
<td>&gt; 1,000,000</td>
<td>2 (8.33%)</td>
<td>0 (0.00%)</td>
<td></td>
</tr>
</tbody>
</table>
Table 2
Complications after Liver Transplantation and Liver Resection

<table>
<thead>
<tr>
<th></th>
<th>Liver Resection</th>
<th>Liver Transplantation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 28</td>
<td>N = 10</td>
</tr>
<tr>
<td><strong>Early Complications</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biliary</td>
<td>5 (17.86%)</td>
<td>3 (30%)</td>
</tr>
<tr>
<td>Vascular</td>
<td>0 (0%)</td>
<td>2 (20%)</td>
</tr>
<tr>
<td>Bleeding</td>
<td>3 (10.71%)</td>
<td>2 (20%)</td>
</tr>
<tr>
<td>Infection</td>
<td>0 (0%)</td>
<td>1 (10%)</td>
</tr>
<tr>
<td>Acute rejection</td>
<td>0 (0%)</td>
<td>1 (10%)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (7.14%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td><strong>Late Complications</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ototoxicity</td>
<td>3 (10.71%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Adhesions</td>
<td>0 (0%)</td>
<td>1 (10%)</td>
</tr>
<tr>
<td>Immunosuppression side-effects</td>
<td>0 (0%)</td>
<td>1 (10%)</td>
</tr>
<tr>
<td>Bile strictures</td>
<td>2 (7.14%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Recurrence</td>
<td>3 (10.71%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

One patient after LT had impaired renal function postoperatively without the necessity of dialysis. One patient rejected once resolved by corticosteroid pulse treatment. Another patient suffered from two phases of acute rejection both successfully treated with steroids. One patient suffered from one instance of short-term leukopenia under tacrolimus therapy.

**LongTerm Complications and Survival**

Two patients after LR suffered from chronic bile strictures and required frequent endoscopic therapy. Three patients in the LR group had tumor recurrence, one month, 6 months and 8 months after resection, by the means of metachronous pulmonary metastases and in one case additional intrahepatic metastases.

The 1-,5-,10-year recurrence-free rates were 89%, 89%, 89% for LR and 100%,100%, 100% for LT (p = 0.94). Overall survival 1-,5-,10-year survival was 90%,90,90% for LT and 96%,96%,96% for LR (p = 0.44) (Fig. 1). One patient died after emergency adhesiolysis surgery as a result of his abdominal sepsis three months after LT. The second patient died due to septic shock caused to pneumococcal infection 23 years after LT.
One patient in the LR group, who had already undergone surgery in an M1 setting (pulmonary, osseous metastases), died 3 months after LR due to extensive intrahepatic recurrence after initial R0 resection with all other patients being alive at the date of the last follow up.

Discussion

Hepatoblastoma is a rare, but the most frequent intrahepatic malignancy of the childhood. In general, hepatoblastomas are diagnosed at a late stage with often large size and frequent vascular infiltration. Neoadjuvant CTx is the gold standard before surgical resection. Excellent results can be achieved with a monotherapy of cisplatin in standard risk tumors, cisplatin alternating with carboplatin-doxorubicin in high risk tumors and dose-intensive weekly cisplatin/doxorubicin induction therapy for very high risk tumors by the means of shrinkage of the primary tumor and control of distant metastasis. A combination of chemotherapy and resection reaches survival rates of 81.5% and 81.0% at 5/10 years. However, despite advances in CTx, in certain cases, resection is not always feasible for anatomical or functional reasons, leaving LT as the only curative option. We herein analyzed our own data comparing outcomes in children with hepatoblastoma after resection with LT.

Demographic data showed an equal distribution in both groups. As expected, in the LT cohort, disease severity according to PRETEXT was significantly higher. Similarly, Kulkarni et al. demonstrated that patients with bilobar involvement were more likely to receive LT based on an analysis of the National Cancer Database for surgical therapy of pediatric hepatoblastoma. However, patients in the LT group had a longer overall time from diagnosis to surgery associated with waiting list time in addition to neoadjuvant chemotherapy. With respect to early and late complications, long-term course and metastases, the results of our analysis show an equal distribution in both groups. Interestingly, none of the patients developed hepatic local recurrence or intrahepatic metastasis after LT and only three patients after LR.

Nevertheless, the decision, when to opt for surgical resection, LT or CTx without surgical intervention can become a balancing act: In general, the basic recommendation for LT in PRETEXT stage IV tumors and centrally placed PRETEXT stage III tumors with infiltration of vascular structures after neoadjuvant CTx is primary resection. Additionally, according to the current surgical guidelines of the Children’s Oncology Group, children with suspected inoperable findings should be referred to a specialized center at an early stage, so that a decision between liver tumor resection and transplantation by a liver specialist can be made. Especially, as LT as an emergency therapy after primary LR with a small for size liver remnant or in case of a relapse after LR must be considered, as described for one patient in our cohort. The decision-making process for the most suitable therapy after neoadjuvant CTx is determined by specific tumor characteristics, such as particularly hepatoblastoma size, critical anatomical localization for LR (involvement of vascular/biliary structures, multicenter localization) and probable function of the future liver remnant. As Meyers et al. showed, the Children's Hepatic Tumors International Collaboration (CHIC), has created a unified global approach to risk stratification for children with hepatoblastoma.
Regardless of this, molecular biological studies on prognostic tumor markers may play a decisive role in risk stratification and optimized patient selection in the future and will have the potential to increase the number of primarily resectable patients.

Excellent tumor control was achieved in our series with the combination of CTx and LT, considering that immunosuppression would be assumed bearing a higher recurrence risk (e.g. like in hepatocellular carcinoma in adults)\textsuperscript{35}. There was no incidence of local recurrence or secondary malignant tumors in our LT group.

Due to concerns for the transplanted graft, only one patient received adjuvant chemotherapy after LT (i.e. our patient with pulmonary metastases). In contrast, 96.4\% of the patients in the LR group received adjuvant treatment. This is of special interest, as the recurrence rate was 0\% in the LT group. While there is no unique strategy or consent on adjuvant chemotherapy after LT, admittedly there are centers following this concept. Without any decisive evidence, this decision probably has to be made on an individualized level. SIOPEL-1 and the World Experience Review showed even superior survival rates of 85\% at 10 years and 82\% at 10 years after primary transplantation\textsuperscript{30,31}. Zsiros et al. showed in the SIOPEL-3 and-4 studies that transplantation was associated with a 75\% 3-year survival rate\textsuperscript{32,33}.

With respect to peri- and post-operative complications, these were comparable in our cohort between both groups. However, as expected, operative time, ICU stay and hospital stay were considerably longer in the LT group, matching the study by Kulkarni et. al.\textsuperscript{23}. In general, outcomes after LT in pediatric patients are superior to adults, independent of donor or indication for transplantation, reaching 1-year survival rates of up to 95\%\textsuperscript{34}. Adults undergoing LT for malignant tumors, have unsatisfactory outcomes, in part due to tumor recurrence. Certainly, hepatocellular carcinoma or cholangiocellular carcinoma cannot be directly compared to hepatoblastoma with respect to long term recurrence outcomes, however, hepatoblastoma patients must be considered for LT in unresectable cases, despite donor organ scarcity due to the excellent results.

Limitations of our study are the small sample size, the retrospective study design and the variance in the different therapy strategies. However, data to hepatoblastoma are not widely published and we feel indeed, that our study adds to previously published research.

In conclusion, we want to highlight the necessity of a detailed assessment by an experienced interdisciplinary team in a center for HPB, pediatric and transplant surgery for LR in hepatoblastoma, especially in advanced cases. Results after CTx plus LT in advanced cases of HB are excellent and long term outcome is comparable to resection in combination with CTx.

Abbreviations
CITA  |  cisplatin-tetrahydropyranyl-adriamycin
---|---
CTx  |  chemotherapy
HEPATOBLASTOMA  |  Hepatoblastoma
HEPATOBLASTOMA99  |  Carboplatin/VP16
HDI  |  high human development index
ICU  |  Intensive care unit
IPA  |  Ifosfamide, Cisplatin, Doxorubicin
LDLT  |  Living Donor Liver Transplantation
LT  |  Liver Transplantation
LR  |  Liver Resection
MMF  |  Mycophenolate Mofetil
PRETEXT  |  Pretreatment Extent of Disease
SIOPEL  |  International Childhood Liver Tumors Strategy Group

**Declarations**

**Ethics approval and consent to participate**

We hereby declare that our work contains an ethical approval and consent of the Ethics Committee of the Charité - Universitätsmedizin Berlin (EA2/267/20).

**Consent for publication**

Not applicable

**Availability of data and materials**

The data sets used and/or analyzed in the current study are available on reasonable request from the corresponding author and with approval of the ethics committee of Charité - Universitätsmedizin Berlin.

**Competing interests**

The authors declare that they have no competing interests.

**Funding**

Dr. Simon Moosburner and Dr. Brigitta Globke are participants in the BIH-Charité Clinician Scientist Program funded by the Charité –Universitätsmedizin Berlin and the Berlin Institute of Health.
Authors’ contributions

SM, SGK, RÖ designed and wrote the manuscript. AK and PS collected data. AK completed and approved all data. SM, SGK interpreted and statistically analyzed the data. All authors read and approved the final manuscript.

Acknowledgements

We acknowledge support from the German Research Foundation (DFG) and the Open Access Publication Fund of Charité—Universitätsmedizin Berlin for open access publication costs.

References


**Figures**
Figure 1

Patient survival after liver resection and liver transplantation. A Overall patient survival after liver resection or liver transplantation B Time to Recurrence after Surgery.