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Review

Liver Resection and Transplantation for Hepatoblastoma

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Abstract

Hepatoblastoma (HB) is the most common primary malignant liver tumor in children, predominantly affecting those under five years of age. Advances in neonatal care and chemotherapy have improved survival; however, approximately 20% of cases remain unresectable, necessitating liver transplantation (LT). This review outlines current indications, surgical strategies, and outcomes of LT for HB. Transplantation is indicated when complete resection (R0) is unachievable due to multifocal disease, PRETEXT IV involvement, major vascular invasion, or inadequate future liver remnant. Living donor liver transplantation (LDLT), particularly in Japan and other Asian countries, has become a cornerstone of curative therapy, offering timely intervention without waitlist delay. Technical refinements—such as early inflow control, portocaval shunting, and fluorescence-guided surgery—have enhanced operative safety and reduced recurrence risk. Multicenter studies, including the Japanese Liver Transplantation Society and JPLT3 trial, demonstrate 5-year overall survival rates exceeding 80–90% in appropriately selected patients, comparable to resection outcomes in intermediate-risk disease. Prognostic factors influencing recurrence include vascular invasion, high AFP levels, and poor chemotherapy response. Long-term survivors typically achieve normal growth, school attendance, and psychosocial development. The Japanese experience underscores the importance of early multidisciplinary evaluation, central surgical review, and integration of LT into frontline hepatoblastoma management. With continuous advances in surgical technique, molecular profiling, and immunomodulation, liver transplantation represents a definitive and life-saving treatment for children with advanced, unresectable hepatoblastoma.

Keywords: Hepatoblastoma, hepatectomy, liver transplantation, ICG, AFP

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Hepatoblastoma (HB), the most common primary malignant liver tumor in children, represents approximately 1% of all pediatric cancers but accounts for the majority of pediatric liver malignancies, especially in children under five years of age. In recent years, an upward trend in incidence has been observed worldwide, with a current estimated rate of 0.5 to 1.5 cases per million population.[1] This increase has been attributed in part to advances in neonatal care, which have resulted in the increased survival of preterm and very-low-birth-weight infants—a population at significantly elevated risk for developing HB.[2]

HB typically presents in infancy or early childhood, with a median age of diagnosis between 12 and 18 months and shows a male predominance. While the exact etiology remains uncertain in most cases, a number of risk factors have been identified. These include genetic syndromes such as Beckwith-Wiedemann syndrome, familial adenomatous polyposis, trisomy 18, and Li-Fraumeni syndrome, as well as environmental and perinatal factors such as prematurity

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and low birth weight. The increased risk among these populations is thought to result from a combination of epigenetic dysregulation, impaired hepatic differentiation, and DNA repair deficiencies.[3]

Molecularly, HB arises from fetal hepatoblasts and is characterized by frequent activation of the Wnt/β-catenin signaling pathway, particularly through mutations in the CTNNB1 gene. Additional genetic alterations, including TERT promoter mutations and IGF2 overexpression, are found in subsets of tumors and may influence tumor biology and treatment response.[4,5]

The clinical presentation is often nonspecific, with a painless right upper quadrant abdominal mass being the most common initial sign. Other symptoms may include anorexia, vomiting, abdominal distension, and occasionally precocious puberty in males due to ectopic β-hCG production. Laboratory investigation typically reveals markedly elevated serum alpha-fetoprotein (AFP) levels, which are present in over 90% of cases and serve as a useful biomarker for both diagnosis and monitoring of treatment response.[1]

Diagnosis is confirmed through imaging and histological evaluation. Contrast-enhanced CT and MRI are essential for delineating tumor extent, vascular invasion, and the presence of metastatic disease, most commonly to the lungs. Histological subtypes range from well-differentiated fetal types to more aggressive embryonal or small cell undifferentiated variants. The latter subtypes are associated with poorer prognosis and reduced chemosensitivity.

To standardize treatment planning, the International Childhood Liver Tumor Strategy Group (SIOPEL) developed the PRETEXT (Pretreatment Extent of Disease) staging system. This radiologic system divides the liver into four sectors and classifies tumors based on the number of sectors involved and additional annotation factors such as vascular invasion, extrahepatic spread, multifocality, and metastases. The PRETEXT and POSTTEXT (post-chemotherapy) assessments help predict resectability and guide decisions regarding surgical versus transplant approaches.[6] According to PRETEXT staging system, a tumor occupying 1, 2, 3 or 4 adjacent liver sector is defined as PRETEXT I, II, III or IV, respectively. Historically, survival for HB was poor, particularly in unresectable cases. The introduction of cisplatin-based chemotherapy regimens dramatically improved outcomes by increasing the rate of complete surgical resection. In modern protocols, neoadjuvant chemotherapy enables resection in more than 60% of cases. However, approximately 20% of tumors remain anatomically unresectable after chemotherapy, necessitating consideration for liver transplantation.[7]

Indication of Liver Transplantation

Higher survival rates have been achieved through combined improvements in imaging, surgical resection and systemic chemotherapy. Although cisplatin chemotherapy regimens have dramatically improved disease-free survival rates, liver transplantation remains an alternative curative treatment for patients whose liver tumor is unresectable following systemic chemotherapy or radical hepatectomy.[8,9] Initial studies of liver transplantation in children with unresectable hepatoblastoma report a 50% survival rate.[10]

The indication for liver transplantation centers on the inability to achieve complete resection (R0 resection) due to tumor burden, vascular invasion, multifocality, or insufficient future liver remnant. Patients with PRETEXT IV tumors, which involve all four liver sectors, or with tumor thrombus extending into the main portal vein or the confluence of all three hepatic veins, are typically considered for transplantation. In such cases, extended hepatectomy may carry unacceptable risk or lead to incomplete tumor removal (Fig. 1 A, B).[11]

Biologic factors, including high AFP levels at diagnosis (>500,000 ng/mL) and at the time of surgery (>4,000 ng/mL), and poor chemotherapy response, also predict recurrence and are considered relative indications for liver transplantation. Patients whose tumors exhibit minimal radiologic or serologic response to neoadjuvant therapy may benefit from early transplant evaluation to avoid tumor progression beyond transplantable limits.[12, 13]

Previously, the presence of extrahepatic disease, especially pulmonary metastases, was considered a contraindication to liver transplantation. However, more recent data have shown that long-term survival is achievable in patients with lung metastases who undergo complete remission after chemotherapy or metastasectomy prior to transplantation. Studies from the Japanese Liver Transplantation Society and the JPLT3 trial indicate that survival in such patients is comparable to those without metastatic disease, provided that all extrahepatic foci are resolved at the time of liver transplantation.[14, 15]

Salvage transplantation may be considered for patients with isolated intrahepatic recurrence after prior hepatectomy. While survival is slightly lower than in primary transplantation, outcomes are acceptable if disease is limited to the liver and responsive to chemotherapy.[16]

The integration of real-time central surgical review, as implemented in the JPLT3 study, has significantly improved appropriate and timely referral to transplant centers. This centralized approach allows for expert assessment of resectability and facilitates coordinated

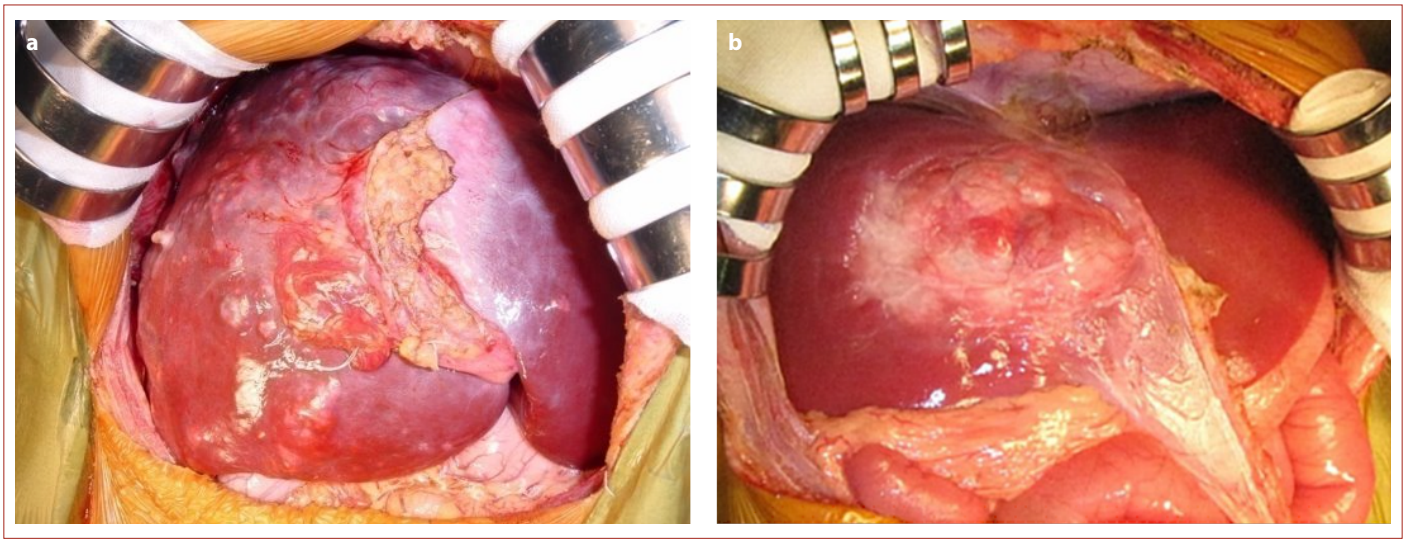

Figure 1. Lacroscopic findings of liver transplantation for hepatoblastoma. **(a)** Multifocal. **(b)** Centrally located.

planning between oncologists, hepatobiliary surgeons, and transplant teams.[15]

Timing of transplantation is crucial. Delays beyond the chemotherapy window may allow tumor progression, while early transplantation in the setting of chemotherapy-induced myelosuppression increases the risk of infectious complications. Most centers perform liver transplantation 4–6 weeks after the final chemotherapy cycle. Living donor liver transplantation (LDLT), in particular, allows optimal timing by eliminating waitlist uncertainty, which is particularly beneficial in regions with low deceased donor organ availability, such as Japan.[12, 17]

LDLT has become the dominant modality for pediatric liver transplantation in Asia and has demonstrated excellent long-term outcomes. In a multicenter Japanese study of 100 children with hepatoblastoma who underwent LDLT, the five-year overall survival exceeded 80%, and recurrence rates were low in patients without vascular invasion or extrahepatic disease. Moreover, the use of preoperative inflow exclusion techniques and portocaval shunting has been shown to minimize blood loss, improve surgical safety, and potentially reduce recurrence risk by preventing intraoperative tumor dissemination (Fig. 2).[18]

Liver transplantation has emerged as a standard and life-saving therapy for children with unresectable hepatoblastoma. Careful assessment of tumor resectability, vascular involvement, biological behavior, and treatment response is essential in determining candidacy. Early referral, multidisciplinary evaluation, and consideration of individualized surgical risk all contribute to successful outcomes. As the global experience with pediatric liver transplantation continues to expand, so too does the imperative to refine patient selection and integrate transplant strategies into frontline hepatoblastoma care.

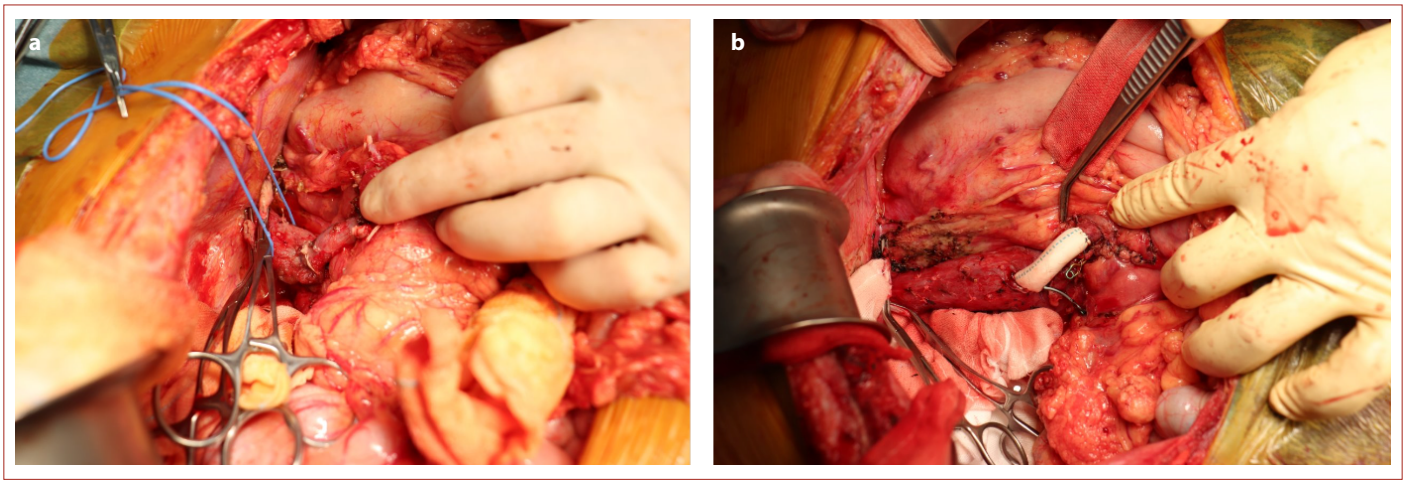

Figure 2. Portosystemic shunt. **(a)** With native portal vein. **(b)** With EPTFE graft.

Surgical Procedure

Surgical intervention remains the cornerstone of curative treatment for hepatoblastoma. Whether through partial hepatectomy or liver transplantation (LT), complete tumor removal with negative histologic margins (R0 resection) is essential to long-term survival. While cisplatin-based chemotherapy has dramatically improved tumor shrinkage and operability, about 20% of cases remain unresectable by conventional means, requiring transplant-based strategies. The surgical approach to hepatoblastoma is therefore highly nuanced, demanding meticulous planning, technical precision, and intraoperative adaptability. This section details the operative considerations, techniques, and challenges encountered in both hepatectomy and liver transplantation for hepatoblastoma.

General Principles and Preoperative Planning

Preoperative preparation begins with careful imaging review to define tumor boundaries, vascular involvement, and segmental liver anatomy. Modern protocols rely heavily on high-resolution contrast-enhanced CT or MRI to assess the post-chemotherapy tumor status (POSTTEXT classification). Multidisciplinary surgical conferences with transplant surgeons, hepatobiliary surgeons, pediatric oncologists, and radiologists are essential to determine whether a resection is feasible or a transplant is required (Fig. 3).

In patients considered for liver resection, the size, location, and degree of vascular involvement are evaluated alongside the anticipated future liver remnant by CT volumetry (FLR).[19] The widely accepted minimum remnant liver volume in living liver donors is generally around 30~35% of the donor's total liver volume to ensure donor safety and avoid postoperative liver failure.[20] This threshold is considered safe to maintain adequate liver function and regeneration capacity after donation. Pediatric patients typically tolerate resection better than adults due to a larger hepatic reserve relative to body mass. Nonetheless, extensive resections involving three or more segments may require portal vein embolization, or the associating liver partition and portal vein ligation for staged hepatectomy or FLR volumetry to ensure postoperative hepatic sufficiency.[21] In pediatric patients, an FLR as low as 18–20% is generally safe, and the standard adult thresholds are too conservative for children. The most critical factor in pediatric liver resection is not merely the FLR volume, but the precise balance between hepatic inflow and outflow. If the tumor cannot be removed with adequate margins without sacrificing critical vascular inflow or outflow, liver transplantation is considered. One of the most significant innovations is central surgical review and real-time consultation, as implemented in the JPLT3 protocol, which has improved resectability assessment and surgical outcomes. These systems enable early identification of transplant candidates, standardize surgical criteria, and reduce interinstitutional variation.[15]

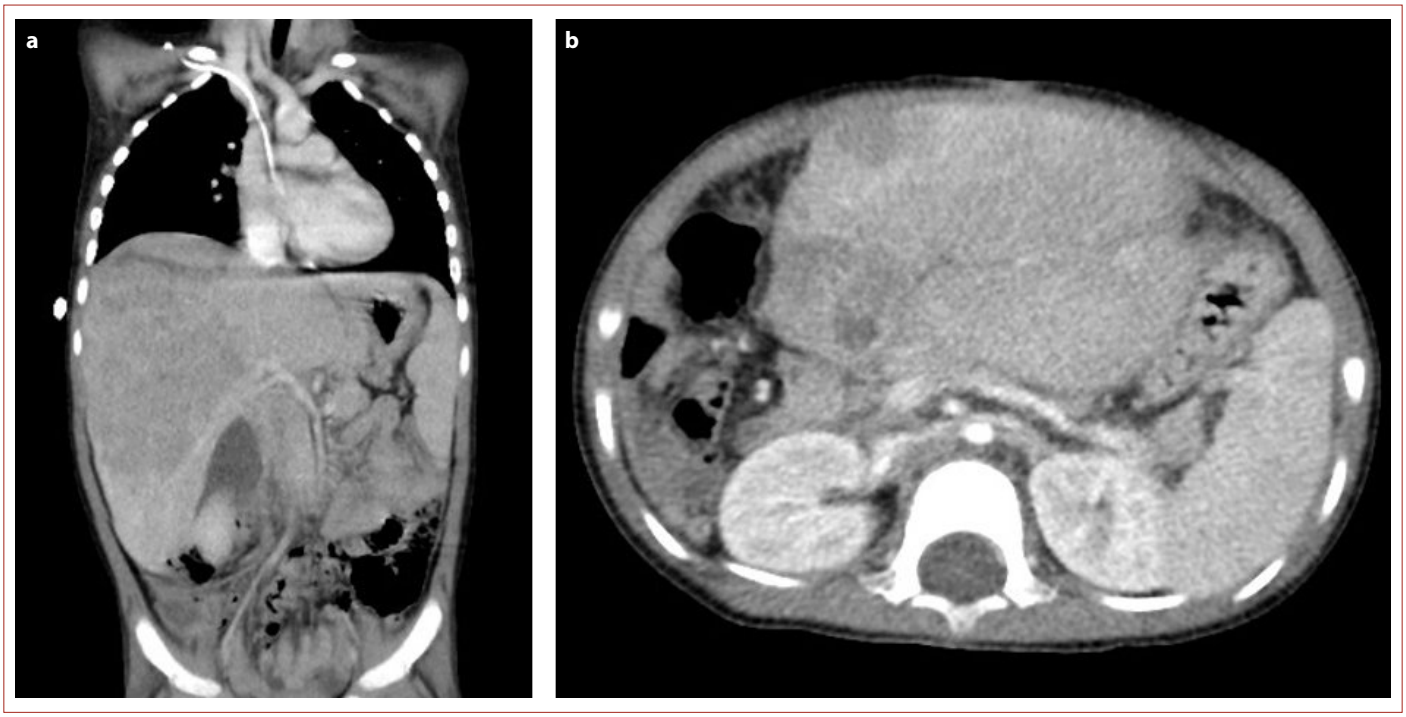

Figure 3. Preoperative imaging study. **(a)** 1y8m baby, multifocal with main PV invasion. **(b)** 2y10m baby, post right hepatectomy, multiple recurrence in the remnant left lobe.

The importance of timing cannot be overstated. For patients who will undergo liver transplantation, surgery is optimally scheduled 4 to 6 weeks after completion of neoadjuvant chemotherapy.[17] This interval allows recovery from myelosuppression while minimizing the risk of tumor progression. In LDLT, coordination between recipient and donor teams is critical to align operative schedules. In DDLT, timely listing and allocation are often complicated by organ availability and competition with other indications, particularly in regions with low donation rates.[22]

Liver Resection for Hepatoblastoma

For tumors classified as POSTTEXT II or III, resection may be possible. Depending on tumor location and liver anatomy, surgical options include left lateral segmentectomy (segments II and III), left hepatectomy (segments II–IV), right hepatectomy (segments V–VIII), or extended resections. The decision to pursue resection rather than transplantation must be guided by the ability to achieve complete tumor clearance without risking hepatic insufficiency.[23]

Intraoperatively, a subcostal or extended Chevron or reverse T incision is typically used. The liver is mobilized by dividing the triangular and coronary ligaments. Cholecystectomy is routinely performed, and the hepatic hilum is dissected to expose and control the hepatic artery, portal vein, and bile duct as a Glissonian approach.[24] Intraoperative ultrasound is critical for evaluating tumor margins, satellite nodules, and vascular anatomy, particularly after chemotherapy-induced changes. Fluorescence-guided surgery for hepatoblastoma with indocyanine green will be effective to define the tumor boundaries, and it allows for the more sensitive identification of lesions that may go undetected by conventional imaging or be invisible macroscopically (Fig. 4).[24]

Parenchymal transection is performed using a combination of techniques, including ultrasonic dissection (CUSA), bipolar sealing, and stapling devices. Bleeding control is paramount. In selected cases, low central venous pressure anesthesia and intermittent inflow occlusion (Pringle maneuver) are used to reduce blood loss. If the tumor abuts major hepatic veins or the inferior vena cava (IVC), vascular resection and reconstruction may be necessary (Fig. 5). In some institutions, advanced techniques such as extracorporeal circulation or ex vivo liver resection with autotransplantation have been attempted, although these are technically demanding and carry higher morbidity.[25, 26]

While resection offers a shorter operative time and obviates the need for lifelong immunosuppression, incomplete resection or positive margins are associated with high recurrence rates. Therefore, borderline resectable cases are increasingly managed with transplant-first strategies, particularly in centers with transplant expertise.

Liver Transplantation for Hepatoblastoma

In patients with unresectable hepatoblastoma, liver transplantation is the definitive treatment. Indications for transplantation include tumors involving all four sectors of the liver (PRETEXT IV), invasion of all three hepatic veins or main portal vein, multifocal lesions, or inadequate FLR. Living donor and deceased donor transplants are both employed depending on regional practices and organ availability.

Pre-transplant evaluation includes thorough assessment of extrahepatic disease. Pulmonary metastases must be treated and cleared before proceeding with LT. Repeat imaging and, if necessary, metastasectomy are performed prior to LT. AFP normalization or significant decline is

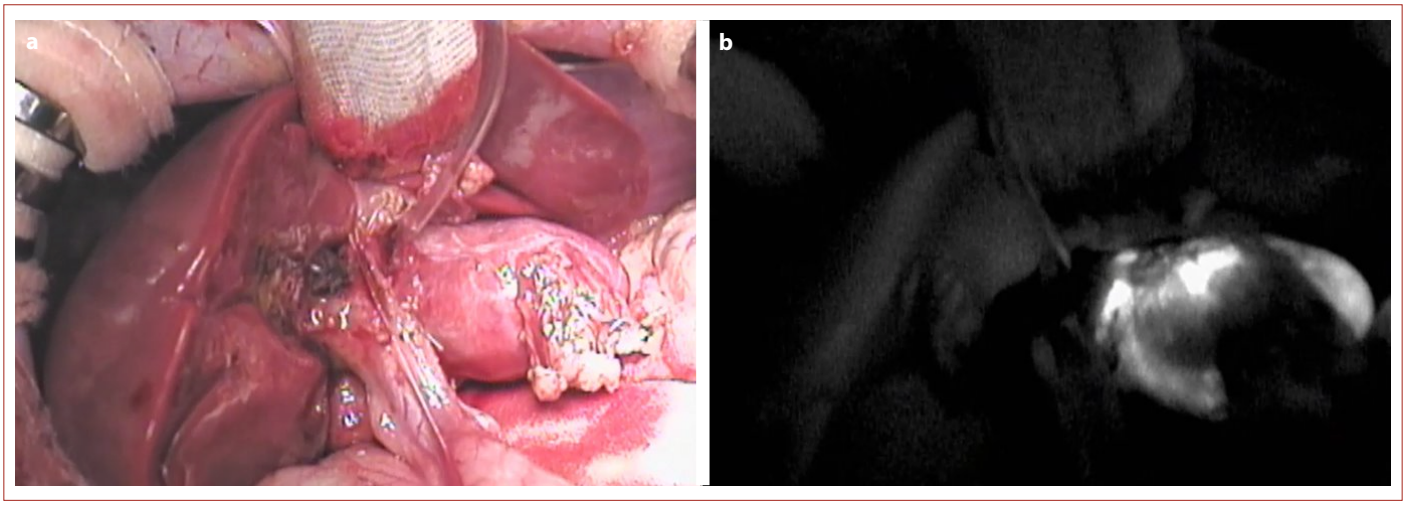

Figure 4. Fluorescence-Guided Surgery for Hepatoblastoma with Indocyanine Green. **(a)** Hepatoblastoma originated the Caudate lobe. **(b)** Fluorescence-guided surgery allows for the more sensitive identification of lesions that may go undetected by conventional imaging or be invisible macroscopically.

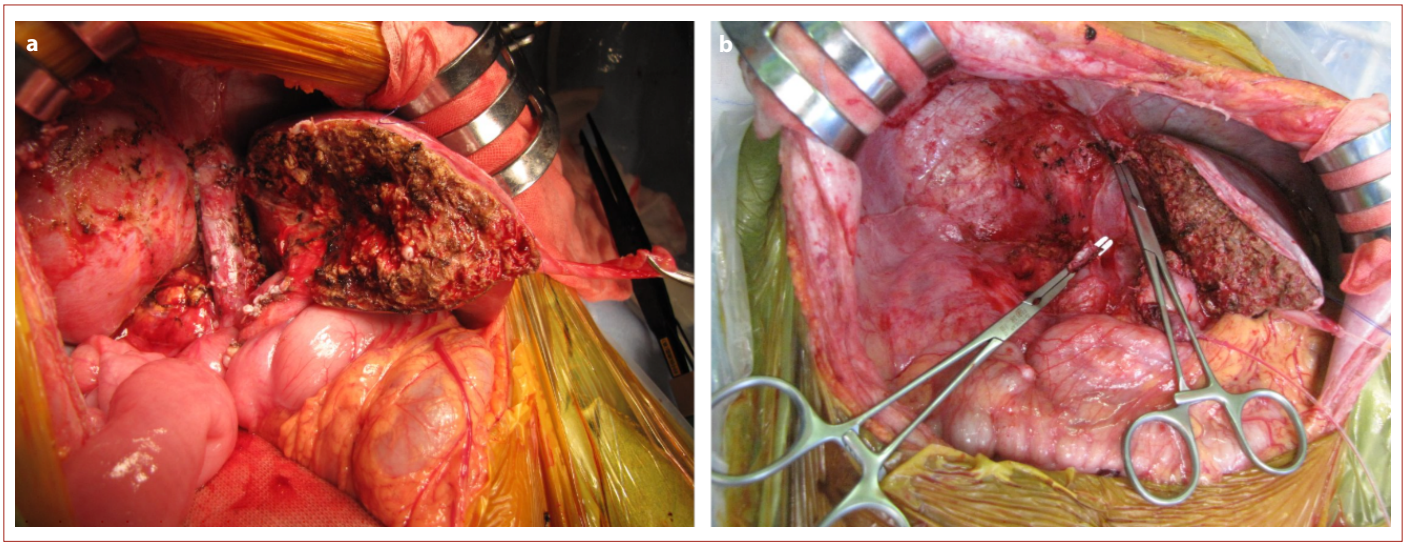

Figure 5. Extended hepatic resection in Hepatoblastoma. **(a)** 3y9m Boy, right trisectionectomy. **(b)** 10y7m boy, right trisectionectomy + IVC resection.

a favorable prognostic sign. In patients with previous hepatectomy or abdominal surgery, adhesions and altered anatomy may complicate transplant surgery.

LDLT is particularly advantageous in HB due to the ability to schedule transplantation electively and avoid waiting-list mortality. In most pediatric LDLT cases, the donor is a parent who donates the left lateral segment (segments II and III), which provides sufficient volume for infants and small children. For older children or larger recipients, a left lobe or extended left lobe graft may be required.[17]

The donor operation is performed under general anesthesia, and careful anatomical dissection of hepatic vasculature and bile ducts is performed to ensure minimal morbidity. After graft removal, the graft is flushed and preserved in HTK solution before transplantation.

The recipient operation begins with total hepatectomy. One of the significant challenges is managing large tumor burden with potential vascular invasion. To reduce the risk of intraoperative tumor dissemination, our team pioneered the strategy of early inflow control, which involves ligation of the hepatic artery and portal vein before liver mobilization.[13] This is often followed by the creation of a temporary portocaval shunt to decompress the portal system and maintain hemodynamic stability during the anhepatic phase. The native liver is then removed en bloc.

Vascular reconstruction includes anastomosis of the portal vein, hepatic artery, and hepatic veins (often via a venoplasty to the IVC). Biliary reconstruction is typically performed using a Roux-en-Y hepaticojejunostomy in small children. In LDLT, the smaller graft size facilitates easier placement in the abdominal cavity but may increase the risk of small-for-size syndrome. Graft-to-recipient weight ratio (GRWR) >1.0% is generally targeted.[27]

DDLT is more common in North America and Europe. It eliminates donor risk and may provide full-size or reduced-size grafts, depending on recipient needs. However, access is limited by donor availability, and patients with HB are often lower priority compared to those with end-stage liver disease due to MELD/PELD-based allocation.

DDLT for HB follows the same technical principles as LDLT. The use of reduced-size or split liver grafts is increasing, particularly in pediatric recipients. Cold ischemia times must be minimized to prevent primary graft dysfunction. In some series, DDLT has shown similar survival to LDLT when performed in experienced centers.[28]

Postoperative care includes intensive monitoring, immunosuppression initiation (often with tacrolimus monotherapy or combined with low-dose steroids), and early resumption of adjuvant chemotherapy when indicated. It has been reported that hepatoblastoma recipients trended to have fewer rejections than other recipients which may allow less immunosuppression due to the preoperative chemotherapy.[29,30]

Postoperative Management and Complications

Following surgery, patients are monitored in the pediatric intensive care unit for hemodynamic stability, graft function, and early detection of complications. Common issues include biliary leakage, vascular thrombosis (especially of the hepatic artery), and infection. In transplant recipients, immunosuppression is carefully balanced against infection and tumor recurrence risk.

Adjuvant chemotherapy (cisplatin or CPT-11) is resumed postoperatively in high-risk patients, typically within 3 to 5 weeks of transplantation, once hepatic and hematologic parameters permit.[14] The timing and regimen are based

on pretransplant protocols and pathology findings. In a large Japanese cohort, early postoperative chemotherapy was associated with improved recurrence-free survival. Rejection, both acute and chronic, is managed with immunosuppression adjustments. In the context of pediatric transplantation for malignancy, tacrolimus-based regimens with or without steroids are standard. ABO-incompatible transplants are increasingly successful due to chemotherapy-induced immunologic modulation.

Outcomes

The outcomes of liver transplantation for hepatoblastoma have improved dramatically over the past two decades, establishing LT as a curative treatment modality for patients with unresectable disease. Long-term survival now exceeds 80% in properly selected pediatric patients, a figure that rivals, and in many cases surpasses, outcomes following conventional resection for high-risk tumors. This success is a result of advances in surgical technique, improved perioperative management, timely referral, and integration of chemotherapy and surgical strategies in a multidisciplinary context.[12]

Numerous retrospective and prospective studies have demonstrated high overall survival (OS) and event-free survival (EFS) following liver transplantation for hepatoblastoma. In the Japanese national survey of 100 children who underwent LDLT for hepatoblastoma, the 5-year OS was reported as 87.5%, with a recurrence-free survival (RFS) of 84.2%.[14] These outcomes were comparable to, or even better than, those achieved with primary liver resection in intermediate-risk patients. A separate report from the National Center for Child Health and Development (NCCHD) demonstrated a 10-year overall survival of 85.7% and recurrence-free survival of 81.0% among 35 consecutive patients who underwent LDLT for advanced HB.[17]

International data from centers in Europe and North America similarly support these excellent outcomes. In a multi-institutional analysis of patients treated within the SIOPEL and COG (Children's Oncology Group) frameworks, transplant candidates had 5-year survival rates approaching 80–90% when disease was confined to the liver and metastases, if present, had resolved prior to LT. These results reinforce the utility of transplant in the treatment paradigm of high-risk and PRETEXT IV hepatoblastoma.[31,32]

While recurrence after LT for hepatoblastoma is relatively uncommon, when it occurs, it is typically within the first two years post-transplant and often portends a poor prognosis. In the Japanese LDLT cohort, recurrence was noted in 13.5% of patients. Sites of recurrence included the lungs, brain, adrenal gland, and peritoneum. Lung metastasis remains the most common form of relapse, consistent with the natural history of HB.[17]

Prognostic factors associated with recurrence include high pretransplant AFP levels, poor chemotherapy response, presence of vascular invasion, and positive surgical margins in explant pathology. In particular, persistent elevation of AFP at the time of transplant, or failure to achieve radiologic remission of pulmonary metastases, has been shown to significantly increase the likelihood of relapse.

Tumor recurrence after LT poses a difficult therapeutic dilemma. While re-resection or metastasectomy may be feasible in isolated pulmonary relapse, systemic chemotherapy is often the only option for disseminated disease. The role of immunosuppression reduction or conversion to mTOR inhibitors in the context of recurrence remains under investigation.

Factors Influencing Survival

Survival outcomes are strongly influenced by tumor biology, disease extent at diagnosis, and response to chemotherapy. In multivariate analyses, several factors have emerged as independent predictors of poor outcome:[14, 33,34]

- Vascular Invasion: Tumor thrombus in the portal vein or hepatic veins significantly increases recurrence risk. Even when removed en bloc during transplantation, vascular invasion may reflect aggressive biology.
- High AFP Levels: AFP levels >500,000 ng/mL at diagnosis and >4,000 ng/mL at transplant have both been associated with worse survival.
- Extrahepatic Disease: Although controlled pulmonary metastases do not preclude good outcomes, persistent or recurrent metastases before or after transplant are linked to poor survival.
- Histological Subtypes: Small cell undifferentiated HB and tumors with mesenchymal elements tend to behave more aggressively and respond poorly to chemotherapy.
- Explanted Liver Pathology: Microscopic residual tumor at margins, lymphovascular invasion, and multifocality are associated with recurrence.

Impact of Graft Type and Center Experience on Liver Transplantation Outcomes

Both living donor and deceased donor liver transplantation have demonstrated excellent outcomes in experienced hands. In Japan and other parts of Asia, where LDLT predominates due to donor scarcity, survival has been outstanding owing to meticulous donor selection, surgical technique, and perioperative care. Notably, LDLT offers the

benefit of timely, scheduled surgery without the delays associated with deceased donor allocation.[14]

Center experience plays a critical role. High-volume pediatric transplant centers with integrated oncology and surgical teams have consistently reported superior outcomes. Central surgical review and adherence to standardized protocols, such as those implemented in the JPLT3 trial, have been associated with reduced recurrence and improved survival.[36]

Long-Term Complications and Quality of Life

Survivors of pediatric LT for HB generally report good quality of life. However, they remain at risk for long-term complications, including:

- Chronic Rejection: Rare, especially in the era of tacrolimus-based regimens.
- Biliary Complications: Bile leaks and strictures are more common in LDLT but can usually be managed with endoscopic or surgical revision.
- Infection: Immunosuppression predisposes recipients to opportunistic infections, though rates have declined with modern prophylaxis.
- Growth and Development: Most children exhibit normal growth and neurocognitive development post-transplant, although those with comorbid syndromes or prematurity may be at higher risk of delays.
- Renal Dysfunction and Hypertension: Nephrotoxicity from calcineurin inhibitors remains a concern and requires careful long-term monitoring.

Recent studies have reported that survivors have excellent school attendance, social integration, and psychological well-being, particularly when they have minimal postoperative complications and no disease recurrence.[35, 36]

Institutional Experiences and Recommendations

In Japan, the standardized evaluation of FLR using three-dimensional imaging and intraoperative strategies has been adopted in centers of excellence such as NCCHD. The JPLT3 protocol includes volumetric thresholds and central review mechanisms to guide surgical planning and ensure safe margin acquisition without compromising hepatic function. Uchida et al. have emphasized that early identification of inadequate FLR—and referral to transplantation—contributes significantly to the high survival seen in Japanese LDLT series.[13] These results support the growing consensus that FLR assessment in HB should not merely be based on volumetry but must integrate patient age, chemotherapy effects, functional studies, and institutional surgical expertise.

Choosing between radical hepatectomy and liver transplantation (LT) remains the pivotal surgical decision in the management of hepatoblastoma, one that determines not only short-term perioperative risk but also long-term survival, quality of life, and exposure to lifelong immunosuppression. Although complete resection with negative margins is universally recognised as the most powerful predictor of cure, the path to achieving this goal differs profoundly between partial hepatectomy and total hepatectomy with graft replacement. Over the past two decades, accumulated experience—particularly from large Japanese series in which living-donor liver transplantation (LDLT) is commonplace—has clarified the indications, advantages, and limitations of each strategy and has highlighted the importance of tailoring the operative plan to individual tumour biology, hepatic anatomy, chemotherapy response, and institutional capability.[14]

Historically, hepatectomy was considered first-line treatment for virtually all patients, largely because early transplantation programmes reported modest survival and substantial perioperative mortality. The advent of cisplatin-based neoadjuvant chemotherapy in the 1980s and 1990s transformed resectability; tumours once deemed inoperable shrank sufficiently to permit margin-negative excision, and five-year survival for children with PRETEXT II–III disease who underwent successful resection rose into the 70–80 % range.[6,10,37] Nevertheless, approximately one fifth of tumours remained unresectable after chemotherapy, and outcomes for these children were dismal until transplantation emerged as a viable alternative. Kasahara and colleagues were among the first to demonstrate that LDLT could be performed safely in this setting, reporting five-year survival of 65 % in their initial series and >90 % in patients without macroscopic vascular invasion or extrahepatic disease.[12] These results, corroborated by multicentre surveys, shifted the paradigm: the question was no longer whether transplantation could cure hepatoblastoma but rather which patients should receive it and when.

The decision framework that has since evolved is anchored on two overarching considerations: technical resectability and oncological soundness. Technical resectability encompasses the ability to remove all gross tumour while preserving an adequate FRL with intact inflow, outflow, and biliary drainage. Oncological soundness refers to the probability that complete resection will eradicate microscopic disease and deliver durable remission. A child with a solitary tumour confined to the left lateral sector, for example, meets both criteria and is offered an anatomic

left lateral segmentectomy. Conversely, a child whose tumour involves all four Couinaud sections (PRETEXT IV) fails the technical criterion—any resection would leave an insufficient FLR—and is therefore routed to transplantation. Between these extremes lie tumours with borderline characteristics—partial vascular encasement, multifocal satellitosis, poor chemotherapy response, or histologic subtypes associated with high relapse risk—which require nuanced appraisal.

Vascular involvement remains the dominant anatomical barrier to safe resection. Magnetic resonance angiography and contrast-enhanced CT permit high-resolution mapping of the hepatic veins, inferior vena cava (IVC), and portal structures. Invasion of all three hepatic veins or the retro-hepatic IVC, circumferential encasement of the main portal bifurcation, or tumour thrombus extending into central vessels dramatically increases operative complexity and the likelihood of residual disease. Uchida and co-workers showed that such involvement predicts recurrence after hepatectomy even when margins appear negative, whereas transplantation that removes the entire hepatic venous outflow tract can yield excellent disease-free survival.[13] Similarly, the Japanese nationwide survey identified macroscopic venous invasion and extrahepatic spread as the principal determinants of post-transplant relapse, underscoring the need for meticulous vascular assessment before choosing resection over LT.[14]

Chemotherapy response provides a complementary biological lens. Alpha-fetoprotein (AFP) kinetics and radiologic shrinkage after two to three cycles are powerful surrogates of chemosensitivity. Children whose AFP falls precipitously and whose tumours shrink to half or less of pretreatment volume frequently achieve long-term remission after partial hepatectomy. In contrast, tumours that remain bulky or in which AFP remains above 4,000 ng mL^{-1} despite adequate dosing behave aggressively; these children experience high relapse rates if treated with extended resection, prompting many centres to recommend primary transplantation. Such biologically driven decision-making avoids the morbidity of futile hepatectomy and the subsequent need for salvage LT, which, although feasible, is associated with increased operative difficulty, adhesions, and slightly lower survival.

FLR evaluation also shapes strategy. In adults a threshold of 25–30 % of standard liver volume is generally accepted, whereas paediatric livers regenerate faster, and an FLR as low as 20 % of total volume can sometimes suffice.[23] However, chemotherapy-induced sinusoidal injury, small body size, and potential hepatic steatosis in syndromic children argue for caution. When projected FLR falls near institutional cut-offs—often 30–40 % after intensive chemotherapy—transplantation offers a safer oncological and physiological solution, avoiding postoperative hepatic failure.

LDLT adds an additional dimension. Because a parental left-lateral-segment graft can be procured electively, LDLT abolishes the uncertainty of deceased-donor waiting times and permits synchronous planning with chemotherapy completion. Early inflow exclusion and temporary portocaval shunting, pioneered in NCCHD, have further reduced blood loss and preserved renal function during LDLT, translating into low perioperative mortality and facilitating prompt resumption of adjuvant chemotherapy. These technical refinements, together with proactive central surgical review in the JPLT3 trial, have driven Japanese five-year survival beyond 85 %, a benchmark now influencing Western practice.[14]

Notwithstanding these advances, partial hepatectomy retains important advantages. It avoids lifelong immunosuppression, eliminates donor morbidity, and preserves future transplant options should late recurrence occur. For tumours clearly amenable to R0 resection—typically PRETEXT I–II or favourable POSTTEXT III lesions—hepatectomy remains the preferred route. Moreover, innovations such as intraoperative indocyanine-green fluorescence imaging have enhanced the surgeon's ability to detect occult nodules and secure wider margins, further improving oncologic safety.

Ultimately, the decision between hepatectomy and transplantation hinges on an integrated appraisal of anatomical feasibility, biological aggressiveness, chemotherapy response, and institutional expertise. Centres with robust transplant programmes lean toward earlier LT for borderline cases, whereas those with limited access to grafts may push the envelope of resection. What is universally accepted, however, is that delayed referral to transplant units after failed or marginal resections compromises survival. Multidisciplinary evaluation early in the treatment algorithm, preferably after the second chemotherapy cycle, ensures that each child receives the operation most likely to achieve durable cure with acceptable risk.

As the field advances, molecular profiling and real-time predictive analytics may refine selection further, identifying tumours whose intrinsic biology favours transplantation despite anatomical resectability, and vice versa. For now, the art of choosing between hepatectomy and liver transplantation lies in marrying objective radiological criteria with nuanced clinical judgement, always in service of the child's long-term well-being.

Conclusion

Liver transplantation has emerged as a definitive, life-saving intervention for children with advanced hepatoblastoma who candidates for safe or curative hepatic resection are not. What was once considered a last resort for patients with inoperable tumors has, over the past two decades, evolved into a proactive first-line strategy for carefully selected children. This evolution has been driven by key clinical insights: the inadequacy of aggressive resection in cases of major vascular invasion or insufficient liver remnant; the consistently high cure rates achieved with transplantation; and the cumulative experience of expert centers, particularly in Japan, where living donor liver transplantation (LDLT) has been refined to an exceptional degree of safety and efficacy.

At the heart of successful hepatoblastoma management is the principle of complete tumor clearance—achievable either through surgical resection or through total hepatectomy with liver replacement. The decision between these options is nuanced, requiring detailed assessment of tumor burden, anatomical complexity, vascular involvement, chemotherapy response, and the future liver remnant. While partial hepatectomy remains appropriate and effective for low- to intermediate-risk disease, transplantation offers the best oncologic outcome for patients with PRETEXT IV tumors, multifocal lesions, central vascular invasion, or those with poor response to chemotherapy. In these cases, LT avoids the risks of residual microscopic disease, inadequate liver regeneration, and postoperative hepatic failure.

The survival rates now routinely reported after LT for hepatoblastoma—ranging from 80% to 90%—are a testament to multidisciplinary coordination. This includes careful patient selection, precise surgical planning, intraoperative strategies to minimize blood loss and preserve hemodynamics, and meticulous postoperative care including timely chemotherapy when needed. The Japanese experience, especially from institutions like the National Center for Child Health and Development, has illustrated the advantages of coordinated LDLT, central surgical review, and national consensus protocols such as JPLT3. These elements have collectively helped establish a new standard of care.

Importantly, the decision to pursue transplantation must not be delayed. Patients who undergo futile or marginal resections, only to relapse and require salvage transplantation, have worse outcomes than those who undergo LT as their primary surgical treatment. Early referral to transplant centers, ideally after the second or third cycle of chemotherapy when the tumor biology is clearer, allows for appropriate evaluation and scheduling. With the increasing availability of living donors and the growing use of split or reduced-size deceased donor grafts, timely transplantation is feasible in a majority of healthcare settings.

Despite these successes, challenges remain. The risk of tumor recurrence, particularly in patients with vascular invasion or persistent metastases, underscores the need for continued refinement of selection criteria and adjuvant treatment protocols. Furthermore, the lifelong need for immunosuppression raises concerns about infection, metabolic complications, and long-term graft survival. In the coming years, greater integration of molecular diagnostics may allow for better risk stratification and treatment personalization. Novel strategies such as immunotherapy, targeted molecular agents, and refinements in preoperative imaging may further reduce relapse rates and expand transplant indications.

In conclusion, liver transplantation has solidified its role as a curative modality for hepatoblastoma in children with otherwise unresectable disease. When applied judiciously and within an integrated treatment framework, LT offers excellent survival, minimal recurrence, and a pathway to normal growth and development. Continued progress in surgical technique, transplant immunology, and cancer biology will further enhance outcomes for this uniquely curable childhood liver cancer.

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