

Evaluation of Early and Late Complications of Pediatric Liver Transplantation with Multi-slice Computed Tomography: A High-Volume Transplant Single-Center Study

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ABSTRACT

Background: To present abdominal multi-slice computed tomography (MSCT) results following transplantation in pediatric patients with a liver transplantation (LT), and to create awareness of early (<3 months) and late (>3 months) complications that may occur.

Methods: This retrospective study included 119 children with an LT performed in our hospital from 2014 to 2017. The descriptive statistics relating to patients' age, gender, transplantation indications, transplantation technique, and MSCT findings were calculated, and are presented as numbers and percentages. The complications were divided into 4 groups: vascular, biliary, parenchymal, and extraparenchymal.

Results: The LT procedures were performed with organs from living donors for 83 patients, and from deceased donors for 36 patients. Hepatic artery and portal vein complications were mostly seen in the early period (n = 18), and hepatic vein complications were also observed in the late period (n = 6). The most commonly encountered biliary complications were stenosis/stricture (n = 13) and bile leak/bilioma (n = 9). Stenosis/stricture frequently occurred in the late period. The most common parenchymal complications were ischemic infarct (n = 8) in the early period, and abscess (n = 4) and recurrent hepatoblastoma (n = 2) in the late period. Hematoma (n = 7), intestinal perforation (n = 3), and focal spleen infarct (n = 3) were among the most commonly observed extraparenchymal abdominal complications.

Conclusion: The complications occurring after pediatric LT varied according to the time after surgery and the transplantation technique used. Using MSCT, different abdominal complications can be assessed simultaneously, greatly contributing to diagnosis and treatment.

Keywords: Children, liver transplant, multi-slice computed tomography

INTRODUCTION

For children with severe acute and chronic liver failure, liver transplantation (LT) is an effective and life-saving treatment method.¹ In the pediatric age group, surgical planning before LT is important, and accurate identification of complications is necessary to save the post-operative graft. Child recipients of liver transplants have the potential for full and productive lives in the future. The early diagnosis and treatment of complications that may develop after transplantation are vital to ensure low mortality and morbidity rates.² Complication rates after LT are higher in children.^{3,4} Vascular and biliary complications are the most common. Parenchymal and extraparenchymal abdominal complications occur more rarely.^{5,6}

Multi-slice computed tomography (MSCT) is a practical, easily accessible, and non-invasive method to assess complications after LT. MSCT can be used to image the full abdomen with high spatial and temporal resolution within a few seconds.⁶ Different reconstruction choices, such as multiplanar reformatting (MPR), maximum intensity projection (MIP), and minimum intensity projection (MinIP), increase the diagnostic sensitivity. These enable the simultaneous assessment of the hepatic vasculature, biliary ducts, liver parenchyma, and other abdominal organs in a single examination. The crucial advantage of MSCT is that it provides excellent image quality and rapid diagnosis, even in patients with poor general status and those who are uncooperative. The most significant handicap is the exposure to ionizing radiation due to frequent

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repeat examinations, especially in pediatric patients, although the dose intake has significantly reduced due to advances in techniques over recent years.^{6,7}

Our study aimed to present abdominal MSCT findings after transplant in pediatric LT patients, to raise awareness of the early and late complications that may occur, and to assess any correlations of complications with transplant techniques.

MATERIALS AND METHODS

Study Design

This retrospective study was approved by the institutional review board. The study included 119 pediatric patients, aged 2 months to 18 years, who had LTs performed between 2014 and 2017. Dynamic abdomen MSCT imaging was performed due to different indications (fever, abdominal pain, jaundice, etc.) after LT. The patients were screened in terms of age, gender, transplantation indication, transplantation type, and MSCT, based on information from the hospital and the imaging systems. The MSCT findings were divided into 4 groups consisting of vascular, biliary, parenchymal, and extraparenchymal-abdominal. The early period was defined as <3 months after transplantation, and the late period as >3 months after transplantation. Transplantation techniques were divided into 2 categories: living donor liver transplantation (LDLT) and deceased donor liver transplantation (DDLT). In LDLT, a part of the liver is taken from a living donor and transplanted into a recipient. The transplanted liver can be functional with its renewal or growth. In DDLT, deceased donors or cadavers are the source of transplantation of organs such as the liver. After a donor is reported legally dead (brain death), the entire liver is removed and stored for transplant within 24 hours.

All findings and complications were assessed in terms of the time of occurrence and the transplantation technique.

MAIN POINTS

- Post-LT complication rates are higher in children, and the early diagnosis and treatment of complications that may develop after transplantation are important in terms of securing low mortality and morbidity rates.
- In our study, MSCT has been shown to be an effective radiological method in the simultaneous evaluation of abdominal complications after pediatric LT.
- Knowing the MSCT findings of potential complications of pediatric LT cases will help in early diagnosis and correct treatment.

All the images were of optimal quality, and no cases were excluded from the study.

Imaging

Imaging was conducted using 64-slice multi-detector CT (Aquilion 64, TSX-101A, Toshiba Medical Corporation, Tochigi, Japan) devices. All patient images were obtained using a CT protocol (80-100 kVp and 60-140 mAs) in accordance with the "as low as reasonably achievable" principle. Contrast and dynamic (arterial and delayed portal venous phase) CT images were obtained. Images were transferred to a workstation for post-processing. MPR, MIP, and minimum intensity projection (MinIP) reformat images were created. The assessment was with the consensus of 2 radiologists with 4 and 8 years of relevant pediatric abdominal radiology experience, respectively. A final diagnosis accepted as a reference was created based on the patient's clinical/laboratory, histopathologic, other imaging modalities, and surgical findings.

Statistical Analysis

All statistical analyses were performed with the Statistical Packages for the Social Sciences (SPSS) version 24 (IBM Corp.; Armonk, NY, USA). Descriptive statistics regarding age, gender, type of complication, and diagnostic and therapeutic modalities were calculated and are presented as numbers and percentages.

RESULTS

Of the patients, 63 were boys (53%), and 56 were girls (47%), with a mean age of 7.27 ± 5.63 years (range, 2 months to 18 years). LT indications, in order of frequency, were fulminant hepatitis ($n = 45$, 37%), cryptogenic cirrhosis ($n = 22$, 18%), metabolic diseases (Wilson disease, tyrosinemia, glycogen storage disease, and maple syrup urinary disease) ($n = 14$, 12%), biliary atresia ($n = 8$, 7%), neonatal cholestasis ($n = 8$, 7%), Caroli syndrome ($n = 7$, 6%), hepatoblastoma ($n = 6$, 5%), Budd-Chiari syndrome ($n = 5$, 4%), and hepatocellular carcinoma ($n = 4$, 3%). Of the LTs performed, 70% were LDLT ($n = 83$) and 30% were DDLT ($n = 36$).

Of all the cases, 22% were identified as having vascular complications ($n = 27$). The most common complications related to the hepatic artery (HA) were thrombus ($n = 5$), stenosis ($n = 2$), and pseudoaneurysm ($n = 1$). In terms of portal vein (PV) complications, generally, thrombus ($n = 6$) and stenosis ($n = 5$) were seen (Figure 1). In terms of hepatic vein (HV) complications, mostly stenosis ($n = 6$) and thrombus ($n = 2$) were identified. HA and



Figure 1. A thrombus (white arrow) preventing flow in the main portal vein on 10th day after LT (DDLT) in a 16-year-old male patient.

PV complications were frequently seen in the early period ($n = 18$, 94%), whereas HV complications were seen in the later period ($n = 6$, 75%) (Figure 2) (Table 1). Vascular complications occurred more frequently in cases in which LDLT was performed ($n = 21$, 77%) (Table 2).

The most common biliary complications (BCs) were stenosis/stricture ($n = 13$, 59%) and bile leak/bilioma

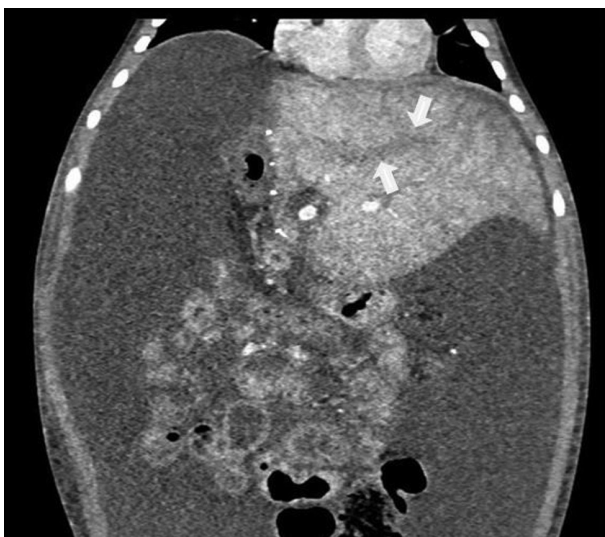


Figure 2. A thrombus (white arrows) preventing flow in the hepatic vein in the fifth month after LT (LDLT), and widespread free fluid in the abdomen in a 4-year-old female patient.

($n = 9$, 41%). In cases in which stenosis/stricture was identified, 5 had cholangitic abscesses that occurred in the late period. Of the 26 cases with biliary tract dilatation (>3 mm), 9 (35%) occurred in the early period, and 17 (65%) in the late period. In the early period (especially in the first month), 35 patients had biliary tract prominence (≤ 3), although in most cases, this was lost by the late period; 3 cases developed stenosis/stricture. The occurrence times of biliary complications and correlations with the transplant type are summarized in Tables 1 and 2.

The most common parenchymal complication seen in the transplanted liver was ischemia/infarction ($n = 8$). Most cases were observed in the early period, and in 6 cases, it was accompanied by vascular complications. A total of 3 out of 4 abscesses were identified in the early period. A rare complication of recurrent hepatoblastoma developing in the transplanted liver occurred in the late period in 2 cases (Figure 3). All 26 cases with periportal edema that developed in the early period resolved by the late period. All findings and complications related to parenchyma are summarized in Tables 1 and 2.

All extraparenchymal abdominal complications were identified in the early period, with most comprising perihepatic hematoma ($n = 7$) and intestinal wall thickening ($n = 4$). Additionally, intestinal perforation ($n = 3$), focal infarcts in the spleen ($n = 3$), cystitis ($n = 1$), invagination ($n = 1$), and diaphragmatic hernia ($n = 1$) were identified (Figure 4). Data on the time of occurrence and transplantation technique in cases of extraparenchymal abdominal complications are summarized in Tables 1 and 2.

DISCUSSION

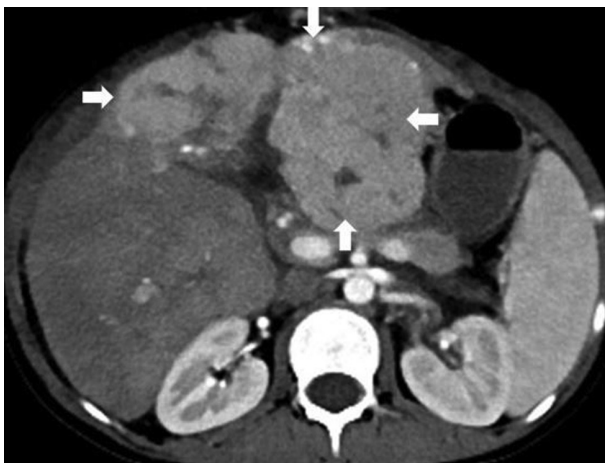
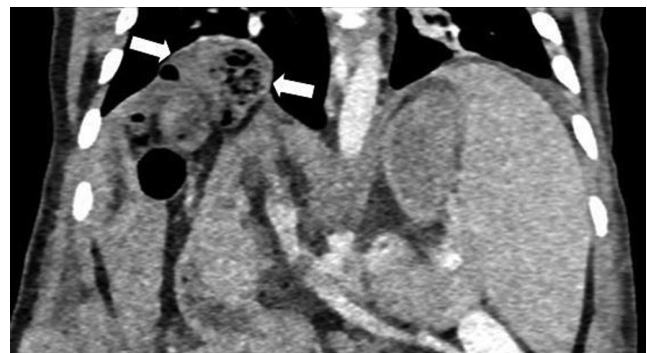
Liver transplantation is the most current treatment choice for children with end-stage liver failure. However, complications remain one of the most significant problems, despite recent advances.^{5,8,9} The surgical complications of liver transplantations may be classified as venous, arterial, and biliary.¹⁰ The most common complications are due to bile, whereas vascular complications have critical importance for graft viability. Due to the broad clinical symptoms and nonspecific findings, imaging results are a vital tool used to diagnose these complications.¹¹ This study showed that valuable data are available for use by radiologists and clinicians to assess vascular, biliary, parenchymal, and extraparenchymal abdominal complications occurring in pediatric patients after LT with simultaneous MSCT findings in relation to the time of occurrence and the transplant technique.

Table 1. List of Findings and Complications in the Early and Late Periods

Time	Complication Type			
	Parenchymal	Biliary	Vascular	Extraparenchymal-Abdominal
Early (<3 months)	Periportal edema (n = 26) Perfusion defect (n = 6) Abscess (n = 3)	Biliary tract prominence (n = 32) Biliary tract dilatation (n = 9) Bilioma (n = 8) Stenosis/stricture (n = 3)	HA thrombus (n = 5) HA stenosis (n = 2) HA pseudoaneurysm (n = 1) PV thrombus (n = 6) PV anastomosis stenosis (n = 4) HV anastomosis stenosis (n = 1) HV thrombus (n = 1)	Hematoma (n = 7) Focal infarcts in spleen (n = 3) Intestinal perforation (n = 3) Diaphragmatic hernia (n = 1) Cystitis (n = 1) Invagination (n = 1) Intestinal wall thickening (4)
Late (>3 months)	Recurrent hepatoblastoma (n = 2) Perfusion defect (n = 2) Chronic rejection (n = 2) Abscess (n = 1)	Biliary tract dilatation (n = 17) Stenosis/stricture (n = 10) Cholangitic abscess (n = 5) Biliary tract prominence (n = 3) Bilioma (n = 1)	PV anastomotic stenosis (n = 1) HV anastomotic stenosis (n = 5) HV thrombus (n = 1)	

Table 2. List of Findings and Complications According to the Transplant Technique Used

Transplant Technique	Complication Type			
	Parenchymal	Biliary	Vascular	Extraparenchymal Abdominal
LDLT	Periportal edema (n = 18) Perfusion defect (n = 3) Abscess (n = 3)	Biliary tract prominence (n = 27) Biliary tract dilatation (n = 9) Stenosis/stricture (n = 5) Bilioma (n = 7) Cholangitic abscess (n = 3)	HA thrombus (n = 4) HA stenosis (n = 2) PV thrombus (n = 5) PV anastomotic stenosis (n = 2) HV thrombus (n = 2) HV anastomotic stenosis (n = 6)	Hematoma (n = 5) Focal infarct in spleen (n = 3) Intestinal perforation (n = 2) Diaphragm hernia (n = 1) Cystitis (n = 1) Ileo-ileal invagination (n = 1) Intestinal wall thickening (n = 3)
DDLT	Periportal edema (n = 8) Recurrent hepatoblastoma (n = 2) Perfusion defect (n = 5) Abscess (n = 1)	Biliary tract dilatation (n = 17) Stenosis/stricture (n = 8) Biliary tract prominence (n = 13) Cholangitic abscess (n = 2) Bilioma (n = 2)	HA thrombus (n = 1) HA pseudoaneurysm (n = 1) PV thrombus (n = 1) PV anastomotic stenosis (n = 3)	Hematoma (n = 2) Intestinal perforation (n = 1) Intestinal wall thickening (n = 1)

**Figure 3.** Mass histopathologically identified as a recurrent hepatoblastoma (white arrows) in the ninth month after LT (DDLT) in a 9-year-old male patient.**Figure 4.** Identification of intestinal loops with hernia appearance in the thorax posterior to the diaphragm on the right (white arrows) on the 40th day after LT (LDLT) in a 10-month-old male patient.

Vascular complications are important causes of significant morbidity and mortality in pediatric LT. Vascular complications occurring in the postoperative period following LT are probably caused by surgical factors and the interactions of thrombotic causes linked to transplantation. The increasing tendency toward VC in smaller and younger recipients with a smaller graft area is probably due to technical difficulties occurring due to the recipients and the smaller vascular pedicles in partial grafts.¹ The first choice of the radiologic method to assess possible complications following transplant in children is ultrasonography (US). Hepatic parenchyma, biliary tracts, and basic vascular structures can be assessed at high resolution using linear probes. The most crucial disadvantage is that it is linked to the operator, and investigations may be limited due to dressings being present in the postoperative period.¹⁰ Dynamic contrast MSCT is used as a problem-solving method when the US is abnormal or not diagnostic. The imaging protocol can include non-enhanced, angiographic, PV, and delayed phases, depending on the clinical question and the abnormality shown on the US.¹ Vascular complications are more commonly observed in the early period after LT and with LDLT. Additionally, they occur more in pediatric patients compared to adults.¹² The clinical findings range broadly from mild elevation of hepatic function tests to acute fulminant failure. If not rapidly diagnosed and treated, graft loss, or even death may occur.¹³ Using MSCT angiography and MIP, vascular complications can be assessed with up to 100% sensitivity and specificity.^{8,14} In the study by Kayahan et al., HA complication was demonstrated by MSCT in 38 of 110 patients.¹⁵ In terms of vascular complications, the most common is HA thrombosis (3-26%). PV thrombosis (2-16%) and HV stenosis (1-11%) are the other common vascular complications.^{8,12} In our study, HA thrombosis (4%), PV thrombosis (5%), and HV stenosis (5%) were observed. It is notable that hepatic vein stenosis after LT occurred in the late period for 83% (5 of 6 hepatic vein anastomotic stenoses were observed in the late period), whereas other vascular complications were observed in the early period. Consistent with other studies, we found that vascular complications were more pronounced after LDLT (77%).

BCs are observed very frequently after LT (6-34%).⁹ They are encountered more in pediatric patients, due to the different surgical and transplantation techniques, compared to adult patients.¹ Among these complications are stricture of the biliary tract, stenosis of the anastomosis level, bile leak, and bilioma.¹⁶ Stenosis not linked to anastomosis mostly occurs secondary to ischemia; as a result,

HA should be carefully assessed in the presence of intrahepatic dilatation. Though US is the basic imaging modality, it is insufficient for diagnosis. Using MRCP, especially the MinIP technique, MSCT can show BCs.⁴ However, all 3 imaging techniques remain insufficient to diagnose leaks and bilioma. When these complications are suspected clinically and radiologically, endoscopic retrograde cholangiopancreatography, percutaneous transhepatic cholangiography, or sampling, accompanied by imaging, should be performed.^{4,17,18} In our study, 22 patients (18%) had BCs. In the early period, leak/bilioma was more frequent, while in the later period, stenosis/stricture was more frequently observed. In patients where stenosis/stricture was observed ($n = 13$), 5 were identified as having cholangitic abscesses in the late period. It is reported that BCs are generally more commonly observed in the early period.¹⁹ In our study, different BCs were encountered more frequently in the early and late periods. In 94% ($n = 33$) of 35 patients with LDLT, the biliary tract was more prominent in the early period. In 74% of these patients ($n = 26$), this was not identified in the late period. From this aspect, it is shown that the biliary tract may be more prominent in patients with LDLT within the first month. We do not believe it is necessary to investigate patients with only this finding in the early period in terms of BCs. However, 89% of patients ($n = 8$) with biliary tract dilatation in the early period were identified as having BCs.

Rejection and chronic hepatitis are complications that cause graft failure. As these complications have no specific parenchymal imaging findings, they are diagnosed by excluding any other complications.¹ Ischemia/infarction is frequently observed after vascular complications. It is most commonly reported for the hepatic artery, and more rarely after portal vein pathologies.^{19,20} In our study, 6 out of 8 patients with ischemia/infarction had vascular complications. Of these vascular complications, 4 were related to the HA and 2 to the PV. The cause could not be identified in the other 2 cases. Another complication observed after LT is tumor recurrence. This is commonly observed in the lungs, but the second-most observed tumor recurrence was that of lesions found in the transplanted liver. These lesions are thought to be linked to extrahepatic metastases not identified before the LT, or to the seeding of tumor cells during surgery.^{8,21} In our study, liver tumor recurrence was identified in 2 of 5 patients who had LT performed due to hepatoblastoma. Periportal edema is known as the periportal collar sign on CT. Although accepted as a strong indicator of graft rejection in the past, recent studies have not supported this correlation. It is now believed to be due to the dilatation of the

lymphatic canals as a result of lymphatic drainage problems in the early period after LT, and has been reported to resolve within several weeks after LT.^{5,9} The results of our study agreed with this finding, and 26 patients with periportal edema in the early period no longer had it during follow-up. No patient developed graft rejection.

Several extraparenchymal abdominal complications are frequently seen as findings secondary to the transplant operation. For example, localized free fluid in the peri-subhepatic area and hematoma are frequently observed in the early period (especially the first 1-2 weeks). These findings are lost during follow-up and rarely become complications.^{5,18} In our study, nearly all patients in the early period had free fluid as the only finding, which was accepted as a secondary change after the operation. Furthermore, the hematoma identified in 7 patients regressed, and was lost during follow-up. Extraparenchymal abdominal complications have been rarely reported in the literature, but we observed 1 case in a 10-month-old patient who developed diaphragmatic hernia on the 40th day post-surgery. Among the risk factors that can cause hernias are left lobe and large-sized grafts, insufficient nutrition, damage to the diaphragmatic nerve and veins, immunosuppressants, and diathermia.²² We think that our case was linked to the young age of the patient and the early period. Other rare complications are intestinal perforation and wall thickening, invagination (ileo-ileal), and cystitis. These complications highlight the need to carefully monitor not just the transplanted liver and its surroundings after the operation, but also the other abdominal organs. From this aspect, MSCT is an advantageous imaging method as it provides a simultaneous assessment of all organs.

Among the limitations of this study are the retrospective design, and the limited data sourced from a single center. Although the sample size was relatively small, to date, it represents the largest study on this topic with the greatest number of cases. The other limitations were due to the equipment used during imaging, and technical problems, operator-based limitations in interpreting the images. Since the assessment was done with the consensus of 2 radiologists, intra and interobserver variability could not be performed. In the future, more accurate and up-to-date results will be obtained from studies involving additional organizations and an increased number of patients.

The complications occurring after pediatric LT vary according to the time and transplant technique. MSCT

is very beneficial imaging technique for the simultaneous assessment of different abdominal complications. Understanding MSCT findings of potential complications of pediatric LT will aid early diagnosis and encourage timely treatment.

Ethics Committee Approval: Ethics committee approval was received for this study from the Institutional Review Board (Decision date April 4, 2017. Decision number 2017/8-14).

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

Peer review: Externally peer-reviewed.

Author Contributions: Concept – M.O.; Design – M.O.; Supervision – N.D.; Resource – N.D., M.O.; Materials – A.S.; Data Collection and/or Processing – S.Y.; Analysis and/or Interpretation – M.O., A.S.; Literature Search – N.D.; Writing – M.O., N.D.; Critical Reviews – A.S., S.Y.

Conflicts of Interest: The authors have declared that no conflicts of interest exist.

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