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Transjugular Liver Biopsy Following Left Lobe or Lateral Segment Transplantation in Pediatric Patients

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Abstract

Purpose To evaluate the efficacy and safety of transjugular liver biopsy in pediatric patients with left lobe or lateral segment liver transplant.

Materials and Methods This was a retrospective study of data from 104 transjugular liver biopsies (57 children) using an 18- or 19-G biopsy needle. Transjugular liver biopsy was selected due to coagulopathy and/or ascites in 56 (54%) procedures. The median patient age, body weight, and interval from liver transplantation were 56 months, 16 kg, and 2 months, respectively. Technical success was defined as adequate liver specimens yield determined by the operator at the time of procedure. Complications, the longest length of obtained liver specimens according to needle type, and adequacy for histological diagnosis were analyzed.

Result Biopsy using a biopsy needle was successfully achieved in 103 procedures (99%). In one procedure, liver samples were obtained using biopsy forceps following unsuccessful attempts with a biopsy needle. Major complication occurred in one procedure following biopsies using both a biopsy needle and biopsy forceps. The patient received transfusion to manage decreased blood pressure and hemoglobin levels although post-biopsy venography did not show extravasation. The median longest length of liver specimens using 18-G ($n = 63$) and 19-G ($n = 40$) needles were 10 mm (range, 5–20) and 10 mm (range, 5–20), respectively ($p = 0.704$). Liver specimens were adequate for histological diagnosis in all procedures.

Conclusion Transjugular liver biopsy using a biopsy needle appears to be a safe and effective method to obtain liver specimens for histological diagnosis in pediatric patients with left lobe or lateral segment liver transplant.

Level of Evidence Level 4, case series.

Keywords Transjugular liver biopsy · Liver transplantation · Pediatrics

Introduction

Transjugular liver biopsy (TJLB) is an accepted alternative method of obtaining liver tissue for histological diagnosis in patients with contraindications to percutaneous transhepatic liver biopsy, including uncorrectable coagulopathy, thrombocytopenia, massive obesity, or ascites [1–5]. Even in cases where there are no classic contraindications to percutaneous transhepatic liver biopsy, TJLB is frequently used in adult liver transplantation (LT) recipients due to the reduced risk of bleeding and the possibility of evaluating hepatic vein (HV) outflow [6–11]. They have reported comparable technical success and complication rates compared with a percutaneous transhepatic liver biopsy; however, most of study population were adults, and TJLBs were frequently performed in the right HV because most of them were whole liver or living right lobe LT

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recipients [6, 7, 10, 11]. TJLB is challenging in pediatric LT recipients, particularly in patients with left lobe or lateral segment transplants, due to the small liver volume, limited number of HVs, and altered angle of the HV relative to the inferior vena cava (IVC) [12].

The aim of this study was to retrospectively evaluate the safety and efficacy of TJLB in pediatric patients who had undergone left lobe or lateral segment LT.

Materials and Methods

The protocol of this retrospective study was approved by our institutional review board, and the need for informed consent was waived in view of the retrospective observational nature of this study.

The medical record was reviewed in order to identify pediatric LT recipients (< 18 y) who had undergone TJLB between June 2009 and September 2017. The cohort was further defined by inclusion-only patients who had undergone left lobe or lateral segment LT and age < 18 years at the time of biopsy. Patient demographics, interval between LT and biopsy, underlying disease necessitating LT, and types of LT and HV anastomosis were reviewed.

One hundred and four procedures of TJLB were performed in 57 patients; 31 patients underwent a single procedure, with the remaining 26 underwent 2–6 procedures. Median patients' age and body weight at the time of TJLB were 56 months (range: 5–156 months) and 16 kg (range: 5–26 kg), respectively. TJLB was performed at a median of 2 months (range: 3 days-172 months) after LT, with 42 procedures within the first month of LT. All patients received end-to-side venous anastomosis between the donor's left HV and the recipient's IVC following unifying the ostium of the left and middle HVs or all HVs to a wide common opening. The characteristics of the patients are summarized in Table 1.

TJLB was selected due to coagulopathy and/or ascites in 56 (54%) of the 104 procedures; coagulopathy was defined as international normalized ratio > 1.5, partial thromboplastin time > 50 s, or platelet count < 50 × 10^3/μL, and ascites was defined as continuous Jackson–Pratt drainage > 100 mL/day or gross perihepatic ascites on ultrasonography or computed tomography. Of these 56 procedures, 35 required TJLB along with other interventional procedures, including evaluation of HV/IVC outflow, measurement of wedged HV pressure, central venous line placement, effusion drainage, and biliary drainage catheter exchange. In the remaining 48 procedures without coagulopathy or ascites, 26 procedures were performed as concurrent other interventional procedures. The remaining 22 procedures were performed arbitrary to minimize a risk of post-biopsy bleeding.

Table 1 Patient demographics (n = 104 procedures)

Age at the time of LT, median, month (range)	26 (3–156)
Age at the time of TJLB, median, month (range)	56 (5–185)
Sex, male/female	66/38
Body weight, median, kg (range)	16 (5–56)
Transplant type, LDLT/DDLT	83/21
Engrafted lobe, left lobe/lateral segment	28/76
Coagulopathy (%)[a]	25 (24%)
Ascites (%)[a]	50 (48%)
Underlying disease	
Toxic or fulminant hepatitis	40
Biliary atresia	35
Progressive familial intrahepatic cholestasis	12
Hepatoblastoma	10
Wilson's disease	4
Others[b]	3

LT liver transplantation, *TJLB* transjugular liver biopsy, *LDLT* living donor liver transplantation, *DDLT* deceased donor liver transplantation

[a]Coagulopathy was defined as international normalized ratio > 1.5, partial thromboplastin time > 50 s or platelet count < 50 × 10^3/μL, and ascites was defined as continuous Jackson–Pratt drainage > 100 mL/day or gross perihepatic ascites on ultrasonography or computed tomography

[b]Congenital hepatic fibrosis, primary sclerosing cholangitis, and ornithine transcarboxylase deficiency-associated liver cirrhosis

TJLB Technique

Written informed consent was obtained from each patient or the patient's legal guardian before the procedure. The transplanted liver volume, patency of vascular structures (including the HV and the IVC), and anatomic relationship between the IVC and the HV were reviewed on computed tomography or Doppler ultrasound images. Prophylactic antibiotics were not routinely used.

TJLB was performed by three interventional radiologists (GYK, KBS, and DIG) with minimum experience of 10 years. The procedure was performed in the same way as the previous reports [12, 13]. Venous access into the right (n = 99) or left (n = 5) internal jugular vein was obtained under general anesthesia (n = 86) or conscious intravenous sedation (n = 18). After venography and/or manometry in the left HV to evaluate the patency of HV/IVC flow, a 7-F stiffening cannula (Cook; William Cook Europe, Bjaeverskov, Denmark) with a 5-F multipurpose catheter was advanced into the HV over a 0.035″ guide wire (Terumo; Tokyo, Japan) or a 0.035″ Amplazter guide wire (Cook). Biopsy was performed in the proximal or middle third of the HV to minimize the risk of liver capsule penetration during the needle passage using an 18- or 19-G biopsy

needle (Cook) with 2-cm biopsy notch. The biopsy sets used in this study was the same as those used in adults. The number of needle passes was related to the integrity of the specimen obtained with each pass and requested liver specimen types. Two passes were usually performed in the case of unfragmented liver specimens for formalin-fixed section; additional needle passes were performed if the specimens were severely fragmented or additional specimens were required for frozen sections and/or electron microscopy. Procedure was terminated when the presumptive total length of specimen for formalin-fixed section was approximately 30 mm, or $\geq$ 10 mm for frozen or electron microscopic section.

In patients with failed TJLB using a biopsy needle, biopsy was performed using 5.5-F forceps (Taewoong, Gyeonggido, Korea) through a 7-F braided long sheath (Cook).

Following completion of TJLB, hepatic venography was repeated by hand injection to evaluate the presence of extravasation or other potential complications. In patients with suspected HV/IVC stenosis, venous pressure measurement followed by balloon angioplasty and/or stent placement was performed before or after TJLB.

Prophylactic transfusion of fresh-frozen plasma or platelet concentrate were used in patients with platelets $< 50 \times 10^3/\mu L$.

Assessment and Definitions

The primary outcome measurements were the safety and efficacy of TJLB, defined as the technical success and procedural complication rates. Technical success was defined as adequate liver specimens yield determined by the operator at the time of the procedure. Complications were categorized according to the CIRSE classification system [14]. Secondary outcome measurements included the number of needle passes, number of fragments and the longest length of obtained liver specimens according to needle type, adequacy for histological diagnosis, additional interventional procedures during TJLB, fluoroscopy time, and radiation dose (air kerma) recorded by the fluoroscopy equipment. The adequacy for histological diagnosis was determined by pathological evaluation. HV/IVC stenosis was defined as a stenosis $>$ 50% of the normal HV/IVC diameter or a pressure gradient across an anastomosis $>$ 5 mm Hg.

Statistical Analysis

Two-sample *t* test was used to analyze differences in the number of needle passes, longest length of liver specimens, and number of fragments between 18- and 19-G needles. The analysis was performed using SPSS statistical software (version 21.0; SPSS, Chicago, IL); a *p* value of < 0.05 was considered to indicate statistical significance.

Results

TJLBs using biopsy needles were successfully achieved in all procedures except one (Fig. 1). In a 5-month-old baby, liver samples were eventfully obtained using biopsy forceps where liver samples could not be obtained sufficiently even three passes of a biopsy needle. TJLB was performed following transfusion in 15 procedures (11 patients).

Grade 3 complication occurred in one patient who underwent TJLB using biopsy forceps following unsuccessful attempts with a biopsy needle; there was no evidence of extravasation on the post-biopsy HV venography; however, the patient received 25 ml of red blood cells 14 h later to manage decreased hemoglobin levels (2.5 g/dl drop) and tachycardia. The patient's vital signs were stabilized following transfusion without the need for further intervention. Grade 1 complication occurred in one patient. In this patient, a dilated intrahepatic bile duct was visualized on post-biopsy venography in 3 of 4 procedures. However, there were no subsequent events.

The number of needle passes was recorded in 88 of 103 procedures; these data plus the number of fragments and the longest length of liver specimen according to needle type are shown in Table 2. According to histological examination of liver samples obtained from 103 procedures with biopsy needles, the median longest length of liver specimens using 18-G (n = 63) and 19-G (n = 40) needles was 10 mm (range, 5–20) and 10 mm (range, 5–20), respectively (p = 0.704). The liver specimens were adequate for histological diagnosis in all procedures.

Pressure measurement in the wedge HV, free HV, and IVC was performed in 59 procedures; balloon angioplasty of HV (n = 12) and/or IVC (n = 2) and stent placement of HV (n = 1) was performed in 14 procedures (9 of 38 patients). In 4 of the 14 procedures, stenosis of HV/IVC was diagnosed for the first time during TJLB. Central venous line insertion (n = 3), effusion drainage (n = 2), and change of percutaneous transhepatic biliary drainage catheters (n = 2) were performed uneventfully after TJLB. Fluoroscopy time and cumulative radiation dose (air kerma) were recorded in 63 procedures with the median being 6 min (range, 2–28) and 54 mGy (range, 9–548), respectively, at 7.5 pulses/sec frame rate of fluoroscopy.

Discussion

Several studies have demonstrated the efficacy and safety of TJLB in LT recipients [4, 6–11, 15–19]. However, studies of TJLB using a biopsy needle in pediatric LT recipients are scarce and involve only a limited number of cases [7, 12, 18]. The main limitations of TJLB in pediatric

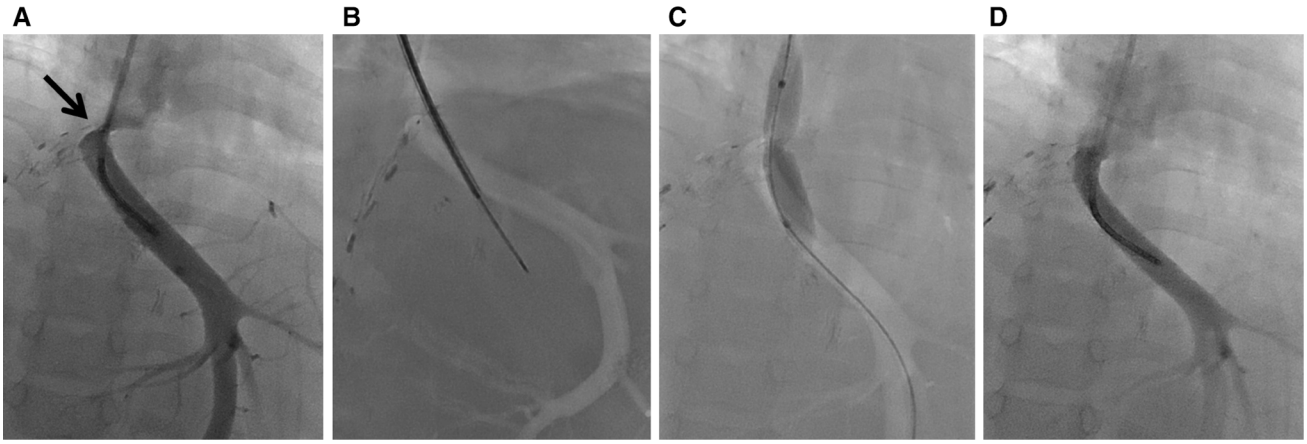

Fig. 1 Twenty-one-month-old girl (body weight, 9.7 kg) who had undergone second cadaveric donor split lateral segment liver transplantation owing to familial intrahepatic cholestasis. **A** Left hepatic venogram obtained 82 days after liver transplantation showed a tight stenosis (arrow) at the hepatic vein anastomosis. The pressure gradient across the anastomosis was 17 mmHg. **B** Biopsy with four needle passes was performed in the left hepatic vein using a 19-G needle. **C** Balloon angioplasty using a 9-mm-diameter balloon was performed after the biopsy. **D** Venogram following the biopsy and balloon angioplasty showed improved stenosis with no extravasation. The pressure gradient across the anastomosis decreased to 4 mm Hg

Table 2 Outcomes of transjugular liver biopsy by biopsy needle type (n = 88 procedures)

	18-G	19-G	P value
Number of procedures	48	40	
Number of needle passes, median (range)	4 (1–9)	3 (2–6)	0.786
Number of fragments, median (range)	5 (1–11)	5 (2–13)	0.153
Longest length, median, mm (range)	10 (5–20)	10 (5–20)	0.580

LT recipients are primarily related to the small volume of engrafted liver as well as an alteration of the angle between the HV and IVC. Unlike whole liver transplant recipients, the number of HVs is limited in pediatric LT recipients with left lobe or lateral segment, which represents another limitation of TJLB. However, Miraglia et al. [12] reported a series of 8 TJLBs in 6 pediatric LT recipients with split LS (median age, 44 months; median body weight, 13 kg). In their study, the technical success rate was 100% with no complications despite severe coagulopathy in all recipients.

Our data were comparable to the findings of Miraglia et al. The introduction of a stiffening cannula to HVs was successfully achieved in all procedures in the present study, even in patients with HV anastomotic stenosis. Liver specimens also could be obtained in all but one procedure, and all the specimens were adequate for histological diagnosis.

In one procedure of this study, liver specimens were obtained using biopsy forceps. This baby also had to receive transfusion following TJLB, although extravasation from a HV was not detected on post-procedural venography. These events were probably attributed to TJLB in the HV with thin surrounding liver parenchyma and subsequent penetration of the liver capsule by a biopsy needle. Therefore, selection of a HV with a sufficient thickness ($>$ 20 mm) of surrounding liver parenchyma, and needle passes in the proximal portion of the HV, are important for effective and safe TJLB. A technique reported by Miraglia et al. [12] involved maintaining a biopsy needle parallel to the HV with only minimal anterior rotation of the stiffening cannula; this appears to be a valuable technique to avoid penetration of the liver capsule in pediatric LT recipients with left lobe or lateral segment. Identification of the needle position under combined fluoroscopy and ultrasonography may also be useful to prevent penetration of the liver capsule [18].

The number of complete portal tracts is important for accurate histological diagnosis and is associated with the length and fragmentation of specimens [3, 4, 20]. More needle passes to obtain longer liver specimens may increase procedural complications, but several studies have reported no bleeding complications with $\geq$ 3 passes during TJLB [4, 20–22]. In a systemic review, TJLB was shown to offer the possibility of multiple passes without increasing complications, and thinner needles provided significantly longer and less fragmented specimens [3].

Therefore, $\geq$ 2 needle passes were usually performed in the current study to obtain approximately 30 mm specimens for fixed section, and since 2013, when a 19-G needle became available, this has been preferred to an 18-G needle

to reduce fragmentation. However, there were no statistically significant differences between the two needles regarding the longest length of specimens and the number of fragments in the current study. Further investigation is required to confirm the advantages of a 19-G needle over an 18-G needle.

In the current study, grade 2 or higher complications occurred in one procedure; this was comparable to the major complication rate (1.3%) related to liver puncture demonstrated in a systemic review of TJLB in pediatric patients [3]. Therefore, TJLB using a biopsy needle appears to be a safe approach for obtaining liver specimens in pediatric LT recipients with left lobe or lateral segment.

An additional benefit of TJLB in LT recipients is the ability to obtain pressure measurements and the treatment of HV/IVC stenosis [6, 12, 23, 24]. Venous outflow abnormalities are generally diagnosed by Doppler ultrasonography; however, a diagnosis can be difficult because of nonspecific symptoms of HV/IVC stenosis and discrepancies between symptoms and image findings [24]. Stenosis of HV/IVC was diagnosed for the first time during TJLB in four procedures in the present study. Therefore, TJLB can be considered in recipients with abnormal liver enzymes, as well as unexplained ascites or effusion.

There are several potential pitfalls associated with TJLB in pediatric recipients, including the risk of exposure to contrast media and radiation and need for general anesthesia. Efforts to reduce such limitations are required. Percutaneous liver biopsy with tract embolization may be a useful and safe alternative that can be performed quickly without such limitations [25, 26]. In a series of 67 pediatric patients who underwent percutaneous liver biopsy with tract embolization, no bleeding complication occurred [26]. In a study comparing TJLB and percutaneous liver biopsy with tract embolization in pediatric patients, complication rates were not statistically different between the two groups [25]. However, complications requiring transfusion occurred in 3 out of 120 percutaneous liver biopsies, but did not occur in 39 TJLBs despite lower platelet counts and higher international normalized ratio than percutaneous liver biopsy. Therefore, further investigations are needed to confirm the safety of percutaneous liver biopsy with tract embolization. In addition, the inability to diagnose or treat HV outflow abnormalities is another limitation of this technique.

The main limitation of the current study is its retrospective nature. Data regarding number of needle passes, total length of liver specimens, and fluoroscopy time were not complete. No information on the number of complete portal tracts was available as the pathologic reports only stated the number of fragments, the longest length of liver specimens, and the adequacy of samples for diagnosis.

In summary, TJLB with a biopsy needle is an effective and safe method of obtaining adequate liver specimens for histological diagnosis in pediatric LT recipients with left lobe or lateral segment.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

Informed Consent This study has obtained IRB approval from Asan Medical Center Institutional Review Board, and the need for informed consent was waived.

Consent for Publication Consent for publication was obtained for every individual person's data included in the study.

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