Transjugular Liver Biopsy: A Retrospective Analysis of 601 Cases

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PURPOSE: To perform a retrospective analysis of all transjugular liver biopsies (TJLBs) performed during a 77-month period. The authors discuss the technical modifications adopted to achieve better procedural success and histopathologic yield apart from the safety profile of this procedure during the study period.

MATERIALS AND METHODS: Six hundred one consecutive patients underwent TJLB at the authors’ institution during the study period. TJLB was performed when percutaneous biopsy was precluded, being judged unsafe. The left internal jugular vein (IJV) was accessed only when it was not possible to cannulate the right IJV, which was the routine access for this procedure. Biopsy samples were obtained from the right lobe after right hepatic vein cannulation. Left lobe biopsy was done only in select cases. In patients with shrunken liver and unfavorable hepatic veins for cannulation and in those with hepatic veno-occlusive disease, biopsy was performed with a transcaval approach under ultrasonographic (US) guidance, improving our technical success for this procedure over the years.

RESULTS: The overall technical success rate for the procedure was 98.8% (594/601), the histopathologic positivity was 97% (576/594), and the overall complication rate was 2.5% (15/601).

CONCLUSIONS: With technical modifications such as transcaval liver biopsy and with access to US in the angiography suite, interventionalist can achieve higher technical success rates for this procedure. The authors’ institutional experience with this procedure reiterates its high histopathologic positivity and safety profile both in adult and pediatric patients.


Abbreviations: IJC = internal jugular vein, INR = international normalized ratio, IVC = inferior vena cava, MHV = middle hepatic vein, TJLB = transjugular liver biopsy, RHV = right hepatic vein

TRANSJUGULAR liver biopsy (TJLB) is an accepted alternative method of obtaining hepatic tissue for various examinations in patients with an established contraindication to percutaneous hepatic biopsy in diffuse liver disease. These are, most commonly, patients with severe coagulopathy, thrombocytopenia, and marked ascites (1). In focal liver lesions, it is necessary to use ultrasonographic (US) or computed tomographic (CT) guidance for obtaining needle biopsy specimens (2).

In our retrospective series including both adult and pediatric patients, we describe various technical modifications adopted for technically difficult TJLB procedures. These include patients with Budd-Chiari syndrome with occluded hepatic veins and small shrunken livers with unfavorable hepatic vein inferior vena cava (IVC) orientation, in whom such technical modifications achieved greater success rates. We highlight the procedure-related complications encountered and their management and also reiterate the safety and success profile of TJLB in diffuse liver disease.

MATERIALS AND METHODS

We undertook a retrospective analysis of all TJLBs performed in our institution between January 1, 2000, and May 31, 2006. Our institutional review board does not require this report to be cleared by the ethics board because this is a clinical procedure and not an experimental intervention. Our indications for TJLB are the same as those applied elsewhere. They are summarized in Table 1 with their distribution in our practice.

Our institutional guidelines for coagulopathy are as follows: international normalized ratio (INR) of more than 1.3 despite vitamin K therapy for
3 days, partial thromboplastin time of more than 6 seconds compared to control, and manual platelet count of less than 60,000/mm³. Patients with an INR of more than 2 and a partial thromboplastin time of more than 60 seconds underwent transfusion with fresh frozen plasma, whereas those with platelet counts of less than 40,000/mm³ were given platelet-rich concentrate before and during the procedure. We did not perform TJLB in patients who had undergone liver transplantation during this study period. Apart from our routine elective practice, emergency TJLB was performed in patients with fulminating and acute liver failure.

Preprocedural Work-up

Patients with a history of any allergy and/or previous reaction to contrast media received 30 mg of prednisolone (Wysolone; Wyeth Lederle, Mumbai, India) 12 hours before TJLB. This was followed by the oral administration of 30 mg of prednisolone and 25 mg of pheniramine maleate (Avil; Intervet, Pune, India) 2 hours before the procedure. Gadolinium was used in patients with renal failure during our study period. We did not use CO₂ for patients with renal failure in our series. After obtaining written consent for the procedure, patients were given intravenous sedation with 50 mg/mL pethidine hydrochloride injection (Veep Injection; Verve Health Care, Ankleshwar, India) and 25 mg/mL promethazine hydrochloride injection (Phenergan Injection; Nicholas Piramal, Mumbai, India). Blood pressure, oxygen saturation, electrocardiographic parameters, and heart rate were monitored during the procedure. Uncooperative and pediatric patients underwent TJLB while under general anesthesia.

Details of the Procedure

Single-wall puncture of the right internal jugular vein (IJV) under US guidance was the preferred mode of initial venous access in the neck because it minimizes puncture-related complications in patients with abnormal bleeding parameters. The right IJV was punctured in 596 of the 601 patients (99.2%), and the left IJV was punctured in five (0.83%). The latter patients had a hypoplastic right IJV (one patient, 0.16%), a neck hematoma after attempted right IJV cannulation (two patients, 0.33%), and a thrombosed right IJV due to previous catheterization for dialysis (two patients, 0.33%).

After a 0.035-inch J guide wire was sufficiently passed into the venous system, a 9-F short vascular sheath was introduced into the jugular vein. Subsequently, the right hepatic vein (RHV) was cannulated with a 4- or 5-F multipurpose catheter (Cook, Bloomington, Ind) and a 0.035-inch guide wire in most patients. After confirming the RHV with a venogram, the metal cannula was introduced into the RHV over the guide wire. In the event of cannulating the RHV with the left IJV approach, the regular 0.035-inch J wire (Fig 1a) was exchanged for an 0.035-inch super stiff Amplatz wire (Boston Scientific, Natick, Mass) to straighten the tortuous course from the left IJV to the RHV across the mediastinum (Fig 1b), facilitating the smooth passage of the metallic cannula to the RHV (Fig 1c).

The RHV was usually identified at anteroposterior fluoroscopy as a large vein oriented toward the right side and at venography as reaching the right inferior and lateral margins of the liver (Fig 2).

Any doubt regarding the RHV or middle hepatic vein (MHV) was clarified with lateral fluoroscopy (which would show the MHV in profile and the RHV end-on) for correct identification.

For the right lobe biopsy, the RHV was cannulated and the cannula rotated counterclockwise (turned anteriorly) for biopsy, as most of the liver parenchyma is anterior to the RHV (Fig 3a).

The proximal aspect of the midthird of the hepatic vein was chosen for biopsy because the chance of capsular perforation is high if the biopsy is performed from the distal hepatic vein. If the metallic cannula is parked in the proximal third, it may slip back into the IVC if the patient performs a breathhold in inspiration for biopsy. A breathhold prevents laceration by the biopsy needle during the act of performing biopsy. Inspiration pushes the liver down and facilitates a favorable hepatic vein orientation during biopsy. The chance of large hepatic artery injury at the porta hepatis is low when the RHV is used for biopsy, as there is adequate parenchyma anterior to it.

In the event of cannulation of the MHV for biopsy, the metal cannula must be turned laterally and in a clockwise orientation that has the whole of the right lobe lateral to it. The chance of hepatic artery injury at the porta is high if the cannula is turned anteriorly and in a counterclockwise orientation (as for RHV) for biopsy, after cannulating the MHV (Fig 3b).

Hence, confirmation of the RHV and MHV by means of lateral fluoroscopy in case of doubt is important before biopsy.

The left hepatic vein was cannulated for biopsy in patients whose liver had a shrunken right lobe and hypertrophied left lobe. For biopsy of the left lobe of the liver, the cannula must be turned in a clockwise orientation after cannulation of the left hepatic vein (Fig 4). We used simultaneous real-time US in patients with a shrunken liver with volume redistribution and also before left lobe biopsies to help confirm adequate liver parenchyma ante-
rior to the biopsy needle to prevent any chance of capsular perforation after the procedure.

Right and left lobe biopsies were performed in five patients with shrunken right lobes and hypertrophied left lobes. This was done to assess the degree of fibrosis in these lobes. Because there was no substantial change in the histopathologic findings, biopsy of both lobes was not performed as a routine procedure in our practice.

Techniques for Difficult Hepatic Vein Cannulation

In patients in whom hepatic vein cannulation was difficult, such as those with less obtuse angulation of the hepatic vein to the IVC, additional techniques such as attempting cannulation in a different phase of respiration (inspiration), using a stiff guide wire, and increasing the distal curvature of the metallic cannula manually may also facilitate easier hepatic vein cannulation. A deep inspiratory effort may facilitate cannulation by making the hepatic vein and IVC orientation more obtuse by pushing the liver down during inspiration.

Transcaval biopsies were performed in cases in which hepatic venous cannulation by the metallic cannula was not possible due to occluded hepatic veins (Budd-Chiari syndrome) or a much shrunken liver with unfavorable morphology of hepatic vein to IVC (right angle orientation of hepatic vein with IVC). Transcaval biopsies were performed with real-time US and fluoroscopic guidance. After correctly identifying the intrahepatic IVC on the venogram, the metal cannula was positioned in the intrahepatic vena cava and the tip of the cannula pointed anteriorly and to the right side, wedging it into the liver parenchyma. Liver biopsy was then performed only after real-time transabdominal US to confirm adequate liver parenchyma anterior to the cannula tip.

The biopsy samples were obtained with an 18-gauge, 65-cm-long Quick core biopsy needle (LABS-100 set; Cook). Multiple passes were made until adequate samples were obtained for various investigations (eg, histopathology, dry weight estimation of copper or iron, cultures in patients with fever of unknown origin). The documented number of passes ranged from two to seven, which was done in only 110 of 594 patients in this series. The adequacy of the biopsy specimen for

Figure 1. (a) Fluoroscopic images showing tortuous course of the J wire from the left IJV to the RHV across the mediastinum. (b) Super stiff Amplatz wire straightening the course from the left IJV to the RHV to facilitate easy cannulation of the metallic cannula. (c) Metal cannula in the RHV from left IJV access.

Figure 2. Right hepatic venogram shows its extent from the right lateral and inferior margin of the liver.
various investigations was assessed by the performing interventionalist. This was based on our recording of specimen length in 110 procedures in this series by correlating specimen length and a positive histopathologic report. In our remaining patients, we tried to obtain at least two biopsy specimens more than half the cutting length of the biopsy needle (which is 2 cm) for histopathologic evaluation.

Free hepatic vein, wedge hepatic, IVC, and right atrial pressures can also be recorded during this procedure. In our practice, this was done only on request from the clinician. The procedure was done under real time fluoroscopy, and hepatic venography was performed for confirmation and documentation.

After the procedure, patients were seated in a wheelchair before removing the venous cannula to reduce the chance of neck hematoma. Patients were monitored for pulse rate, respiratory rate, blood pressure, neck hematoma, and abdominal girth every 2 hours for the next 6 hours. They were started on a graded oral feeds beginning with a liquid diet and graduating later to solid food over a 6-hour period. Those who were admitted only for the procedure were discharged after an overnight stay in the hospital. Procedural and postprocedural complications were documented according to the SIR guidelines (3), as shown in Table 2.

The adequacy of the specimen for histopathologic examination was determined by the reporting histopathologist as per the guidelines established by the Consensus Conference of the Sociedade Brasileira de Patologia e Hepatologia, as more than 1.0 cm in length or more than 10 portal triads per specimen (4).

RESULTS

Of the 601 patients who underwent TJLB during this study period at our
Table 2
SIR Classification System for Complications according to Outcome

<table>
<thead>
<tr>
<th>Minor Complications</th>
<th>Major Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. No therapy, no consequences.</td>
<td>C. Require therapy, minor hospitalization (&lt;48 h).</td>
</tr>
<tr>
<td>B. Nominal therapy, no consequences, includes overnight admission for observation only.</td>
<td>D. Require major therapy, unexplained increase in the level of care, prolonged hospitalization (&gt;48 h).</td>
</tr>
<tr>
<td>E. Permanent adverse sequela.</td>
<td>F. Death.</td>
</tr>
</tbody>
</table>

Note.—From reference 3.

institutions, the male:female ratio was 371:230. Patients ranged in age from 2 to 75 years (median age, 50 years; mean age, 40 years). The highest INR recorded was 4.6, and the lowest platelet count was 3,000/mm³.

The size of the biopsy specimen was documented in only 110 patients. In these 110 patients, the size of the biopsy specimen ranged from fragments 4 mm to 2 cm; the median size of the documented samples was 1.2 cm.

The biopsy specimen was obtained from the right lobe in 583 of the 594 patients in whom the procedure was technically successful (98.1%) and from the left lobe in 11 (1.8%).

Fluoroscopy time and radiation doses were measured for all patients. The fluoroscopic time ranged from 2.5 to 6.5 minutes (average, 4 minutes). Radiation dose ranged from 0.5 to 1 mSv (average, 0.66 mSv).

We observed a reduction in technical failures and improved histopathologic results in the later years of our study period, as described in Table 3. Technical failures recorded early in our series in 2001 and 2002 were due to unfavorable hepatic vein IVC anatomy in four patients with a shrunken liver and to Budd-Chiari syndrome in two patients.

Transcaval liver biopsy, which was performed in four patients (two patients with unfavorable hepatic venous anatomy due to shrunken liver and two with Budd-Chiari syndrome) improved our technical success in 2003 and 2004 to 100%. One technical failure recorded in 2005–2006 was due to poor patient compliance because the patient had hepatic encephalopathy due to fulminant hepatic failure during the procedure and was unfit for the procedure under general anesthesia.

The procedure was considered a technical success when the procedure was performed and liver specimens were obtained; this was so in 594 of 601 patients (98.8%). Histopathologic positivity is claimed when adequate specimens are obtained for histopathologic evaluation, which occurred in 576 of the 594 patients (97%). Fragmented specimens that permitted histologic evaluation except for quantification of hepatic fibrosis were considered histopathologically positive; this was noted in 77 patients. Fragmented specimens inadequate for histopathologic evaluation were documented in 18 patients. Of these 18 patients, repeat biopsy was performed in two. The remaining 16 patients with inadequate biopsy samples did not undergo a repeat procedure due to various reasons (eg, poor patient compliance, shrunken liver with features of cirrhosis at US, positive etiology from serology and other blood tests, and anticipation of fragmented samples from a repeat procedure due to advanced cirrhosis). None of the patients underwent more than one repeat biopsy.

Complications

Complications after TJLB were observed in 15 of the 601 patients (2.49%). These complications occurred during the procedure or within 2 days after the procedure. Minor complications were treated conservatively, and major complications were managed with active intervention. One patient succumbed to complications despite active intervention. The minor and major complications in our series, with descriptions, are listed in Tables 4 and 5, respectively.

Pediatric Patients

In our series, 48 patients 15 years of age or younger (median age, 5 years) underwent TJLB. Only cooperative patients underwent biopsy under intravenous sedation and local anesthesia. General anesthesia was used only in uncooperative patients. Biopsy was performed with the same adult TJLB set. TJLB was considered to be technically successful in 47 of the 48 pediatric patients (98%). The sole technical failure occurred early in our series (in 2001) in a patient with a small shrunken liver with acute hepatic vein IVC confluence. The specimen was documented as being inadequate for histopathologic examination in five of the 48 patients (10.4%). The only complication was postprocedural fever ranging from 102°–104°F in three patients (6.3%). These patients had negative blood culture and were treated symptomatically with antipyretics, with resolution of the fever within 48 hours of hospital admission. As the number of patients who developed fever was few, we were unable to arrive at any firm conclusion regarding the occurrence of fever in these patients.

DISCUSSION

Transjugular biopsy of the liver has been performed in patients with contraindications to standard percutaneous biopsy since 1973 (5). The biopsy procedure evolved from an endhole needle aspiration technique described in earlier series (6–8) to a trucut biopsy technique (9,10), as the latter provided higher histopathologic yield.

A previous report of TJLB from our center comparing aspiration biopsy with trucut biopsy (11) also concluded that histologic positivity was superior with the latter method. Since then we have been using only trucut biopsy for TJLB at our institution.

The most common cause of technical failure reported in the literature is failure to cannulate the hepatic vein (12). In our series, this was observed in two groups, one with unfavorable orientation of the hepatic vein and IVC, hampering adequate cannulation of the hepatic vein with the metallic cannula, and the second in patients with hepatic venous occlusion (Budd-Chiari syndrome). In both of these situations, the transcaval biopsy technique proved to be a safe and viable option for obtaining adequate liver samples. To the best of our knowledge, this technical modification has not yet been mentioned in the English medical literature.

We graduated from blindly access-
ing the IJV to marking of the same with US in the later 1990s and, subsequently, to real-time US-guided single-wall puncture for IJV cannulation from early 2004 and succeeded in minimizing puncture-related complications, the second most common cause of technical failure for the procedure in the literature (12). Access to US in the interventional suite has improved our technical success to near 100% and minimized our procedure-related complications in the later years. Our overall technical success, histologic yield, and complication rates are in agreement with those of other larger series by Gamble et al (13) and Smith et al (1).

The major complications we encountered secondary to TJLB were heomobilia and hemoperitoneum, which were managed by aggressively supplementing blood, blood products, and fresh-frozen plasma (10–15 mL/kg) and, in unresponsive cases, with diagnostic hepatic angiography and venography followed by coil embolization in identifying culprit lesions.

Usual puncture site complications in the neck are hematoma and caroticojugular fistula. Neck hematoma responds well to manual compression in most patients. Caroticojugular fistula can be managed in symptomatic patients by means of surgical excision of the fistula or endovascularly with placement of a stent-graft in the carotid artery, obliterating the fistula (14,15).

We encountered a rare complication of cutaneous pseudoaneurysm at the puncture site in the neck in a patient with an INR of 2.7. Because repeated manual compression to occlude the pseudoaneurysm failed, thrombin injection (16) and surgical repair were our other options. Our patient was a poor surgical candidate because of grossly abnormal parameters. Because thrombin was not available in our institution, we planned to use histacryl injection to deal with the same. A hematologic opinion sought for this problem advised oral and topical tranexamic acid (antifibrinolytic) and compression bandage because the patient’s grossly abnormal parameters were thought to be due to aggravated fibrinolytic process secondary to the underlying liver disease. There was complete resolution of the cutaneous pseudoaneurysm within 48 hours. The use of an antifibrinolytic in the management of cutaneous pseudoaneurysm in patients with hepatic failure is also not mentioned in the English medical literature.

Because this is a retrospective study, it does have limitations. Documentation of the dimension of the biopsy specimen and number of passes was done in only 110 patients in our series. Adequacy of the specimen sample obtained was assessed subjectively by the practicing interventionalist in the remaining patients. Separate documentation of the abnormal INR and

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of Procedures</th>
<th>No. of Technically Successful Procedures</th>
<th>Histopathologic Positivity</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>48</td>
<td>48 (100)</td>
<td>46 (96)</td>
<td>0</td>
</tr>
<tr>
<td>2001</td>
<td>96</td>
<td>93 (97)</td>
<td>88 (94)</td>
<td>3 (0.005)</td>
</tr>
<tr>
<td>2002</td>
<td>84</td>
<td>81 (96)</td>
<td>81 (100)</td>
<td>2 (0.0033)</td>
</tr>
<tr>
<td>2003</td>
<td>111</td>
<td>111 (100)</td>
<td>109 (98)</td>
<td>2 (0.0033)</td>
</tr>
<tr>
<td>2004</td>
<td>110</td>
<td>110 (100)</td>
<td>108 (98)</td>
<td>3 (0.005)</td>
</tr>
<tr>
<td>2005–2006 May 31st</td>
<td>152</td>
<td>151 (99)</td>
<td>146 (97)</td>
<td>5 (0.00831)</td>
</tr>
</tbody>
</table>

Note.—Numbers in parentheses are percentages.

<table>
<thead>
<tr>
<th>Complication</th>
<th>SIR Grade</th>
<th>No. of Patients</th>
<th>Cause</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transient supraventricular tachycardia</td>
<td>A</td>
<td>1</td>
<td>Irritation of the endocardium during guide wire manipulation in the right atrium</td>
<td>Guide wire removal and carotid massage</td>
<td>Resolved completely</td>
</tr>
<tr>
<td>Neck hematoma</td>
<td>B</td>
<td>4</td>
<td>Puncture site hematoma due to grossly abnormal parameters</td>
<td>Manual compression and compression bandage</td>
<td>Near total resolution within 4–6 d</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>B</td>
<td>1</td>
<td>Presumed to be due to low puncture of right IJV in the neck</td>
<td>Because it was less than 20% of the chest volume and asymptomatic, it was followed up with serial chest radiography</td>
<td>Resolved radiographically by 24 h</td>
</tr>
</tbody>
</table>
partial thromboplastin time was not done but was documented together, as patients with coagulopathy.

With technical modifications, in particular with the transcaval liver biopsy technique, the interventionalist can, with no additional risk, obtain adequate liver tissue samples in otherwise technically challenging situations. Access to US during the procedure can increase the safety profile and success rate in technically demanding situations. We also describe the option of antifibrinolytic medication in the management of cutaneous pseudoaneurysm complicating puncture site hematoma in patients with hepatic failure.

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References


