Major complications due to transjugular liver biopsy: Incidence, management and outcome

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Abstract
Purpose: The purpose of this study was to retrospectively evaluate the incidence of intraperitoneal bleeding and other major complications of transjugular liver biopsy (TJLB) and analyze their outcome and management.

Materials and methods: The clinical files of 341 consecutive patients who had TJLB were retrospectively analyzed. There were 237 men and 104 women (mean age: 51.38 ± 12.8 years; range: 17–89 years). All patients had TJLB because standard percutaneous transhepatic biopsy was contraindicated. Patients’ files were reviewed to search for major and minor procedure-related complications during or immediately after TJLB.

Results: TJLBs were technically successful in 331/341 patients (97.07%; 95\%CI: 94.67–98.58\%). Major complications consisted exclusively of intraperitoneal bleeding due to liver capsule perforation and were observed in 2/341 patients (0.59\%; 95\%CI: 0.07–2.10\%). They were treated using transcatheter arterial or venous embolization with a favorable outcome. The most frequent minor complications were abdominal pain (35/341; 10.26\%; 95\%CI: 7.25–13.99\%) and supraventricular arrhythmia (15/341; 4.40\%; 95\%CI: 2.48–7.15\%). No cases of inadvertent injury of the carotid artery were observed.

Conclusion: Major complications during TJLB are extremely rare and can be managed using arterial or venous embolization with a favorable outcome. Our results reinforce the general assumption that TJLB is a safe and well-tolerated technique.

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Transjugular liver biopsy (TJLB) is used for obtaining high-quality histological samples from patients with acute or chronic liver disease who have severe coagulation abnormalities or ascites for whom standard percutaneous biopsy of the liver is contraindicated [1–13]. It is well-established that in patients with severe coagulation abnormalities or ascites, standard percutaneous liver biopsy is associated with a high risk of hemoperitoneum, which can be life-threatening and even fatal [7,11]. To avoid these risks TJLB is a satisfactory alternate option [2,6,9,14–17].

Biopsy of hepatic parenchyma via the venous system reduces the risks of bleeding, because the basic concept behind TJLB is that this sampling technique is performed without penetrating the liver capsule (i.e., the capsule of Glisson), which is not perforated during the procedure [1,11,16]. However, there were some reports that described severe and potentially life-threatening complications during TJLB [1,2,6,8,18].

Although, in theory, the capsule of Glisson is not perforated during TJLB, this may happen, resulting in hemoperitoneum of varying severity in approximately 0.2% of the procedures [8,11]. In most reported studies, probably because of a limited number of patients, there were no cases of intraperitoneal hemorrhage due to TJLB [13–15,19–21]. To date, a few studies have specifically placed a special emphasis on this severe complication but the majority of them did not provide details regarding management [2,22,23]. In addition, most of reported cases were single case reports so that the actual incidence of this complication is not well known [24,25].

Accordingly, the purpose of this study was to retrospectively evaluate the incidence of intraperitoneal bleeding and those of other major complications during TJLB and analyze their management and outcome.

Materials and methods

Patients

This retrospective study was performed on the medical records of 341 consecutive patients who underwent TJLB using ultrasonographic guidance for right internal jugular vein (RIJV) puncture and an automated device (Quick-Core, Cook, Bloomington, IN) for liver biopsy in our department between April 1995 and September 2014 inclusively. The retrospective data analysis was approved by our review board and informed consent was obtained from all patients.

There were 237 men and 104 women, with a mean age of 51.38 ± 12.8 years (S.D.; range: 17–89 years). During the same period, five patients who were scheduled to undergo TJLB had thrombosis of the RIJV as evidenced by duplex and color Doppler ultrasonography and were excluded from retrospective data analysis because they did not undergo TJLB.

Percutaneous liver biopsy was contraindicated in all patients because of severe coagulopathy (221/341; 64.81%), ascites alone (20/341; 5.86%) or both (100/341; 29.33%). Severe coagulopathy was defined by a prothrombin time 6s greater than control time or by a platelet count <70×10^9/L. Marked ascites was defined as a large amount of free-fluid around the liver as evidenced by ultrasonography or computed tomography (CT) of the abdomen.

Indications for TJLB were as follows: 155/341 patients (45.46%) had a known viral hepatitis and liver biopsy was performed to determine if a specific treatment was needed; 144/341 patients (42.23%) were known alcohol abusers and liver biopsy was needed to evaluate the severity of the disease (n=88) or to determine if associated acute alcoholic hepatitis was present (n=56); 19/341 patients (5.57%) had suspected nonalcoholic steatohepatitis (NASH syndrome), 10/341 patients (2.93%) had suspected toxic hepatitis, 4/341 patients (1.17%) had suspected autoimmune hepatitis, 3/341 patients (0.88%) had suspected hepatic lymphoma, 3/341 patients (0.88%) had Wilson disease, 1/341 patient (0.29%) had suspected azathioprine-related nodular regenerative hyperplasia, 1/341 patient (0.29%) had suspected hepatic tuberculosis, and 1/341 patient (0.29%) had suspected hepatic candidiasis. No patients had TJLB because intrahepatic bile duct dilatation contraindicated standard percutaneous biopsy.

Technique

All procedures were performed by an experienced operator under mild analgesia. After local anesthesia with 1% lidocaine, the RIJV was punctured with an 18-G needle-catheter under ultrasound guidance using a 7.5-MHz dedicated probe. A 9-Fr, 49 cm long introducer (Radifocus, Terumo, Tokyo, Japan) was placed in the RIJV using a Seldinger technique using a 0.035-inch J-tipped guide wire (Angiodyn, Braun, Melsungen, Germany). Catheterization of the right hepatic vein was performed with a hydrophilic 0.035-inch angled guide wire (Radifocus, Terumo) and a 5-Fr end-hole catheter. To confirm optimal placement in the right hepatic vein, a quick-check angiogram was obtained with 10mL of iodinated contrast material injected by hand. A 0.035-inch, 180-cm long super-stiff Amplatz guide wire (Boston Scientific, Miami, FL, USA) was used to further introduce a curved rigid 7-Fr catheter that was placed into the right hepatic vein. Finally, the 18-G, 60-cm long Quick-Core automated biopsy device was introduced coaxially and liver biopsy was performed.

TJLB was performed using intermittent fluoroscopy control and electrocardiographic monitoring. The tip of the biopsy device was placed not too close to the liver capsule because the biopsy system advanced the needle tip 24 mm into the liver parenchyma when fired. The right hepatic vein was used as the biopsy site in all patients to better control the distance between the needle tip and the liver capsule. In patients with ascites, the location of the capsule was estimated on ultrasonography and/or CT images before TJLB. After biopsy, tissue samples were visually examined by the operator who decided if another specimen and further biopsy was needed. Mild sedation was obtained two hours before TJLB. During the procedure, vital signs (i.e., cardiac status and arterial blood pressure), were continuously monitored. After TJLB, the patients rested in bed for 24 hours and the skin puncture site and the abdomen were clinically examined every four hours. Abdominal ultrasonography and hemoglobin levels were performed only when a complication was suspected on clinical symptoms.
Table 1  Complications in 341 patients who underwent transjugular liver biopsy.

<table>
<thead>
<tr>
<th>Category</th>
<th>Proportions</th>
<th>%</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Minor complications</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervical hematoma</td>
<td>5/341</td>
<td>1.47</td>
<td>0.48–3.39</td>
</tr>
<tr>
<td>Carotid puncture</td>
<td>0/341</td>
<td>0.00</td>
<td>0.00–1.08</td>
</tr>
<tr>
<td>Supraventricular arrhythmia</td>
<td>15/341</td>
<td>4.40</td>
<td>2.48–7.15</td>
</tr>
<tr>
<td>Hypotension</td>
<td>2/341</td>
<td>0.59</td>
<td>0.07–2.10</td>
</tr>
<tr>
<td>Intrahepatic hematoma</td>
<td>12/341</td>
<td>3.52</td>
<td>1.83–6.07</td>
</tr>
<tr>
<td>Arteriovenous fistula</td>
<td>1/341</td>
<td>0.29</td>
<td>0.01–1.62</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>70/341</td>
<td>20.53</td>
<td>16.37–25.21</td>
</tr>
<tr>
<td><strong>Major complications</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large intrahepatic hematoma</td>
<td>0/341</td>
<td>0.00</td>
<td>0.00–1.08</td>
</tr>
<tr>
<td>Intrapitoneal bleeding</td>
<td>2/341</td>
<td>0.59</td>
<td>0.07–2.10</td>
</tr>
<tr>
<td>IVC perforation</td>
<td>0/341</td>
<td>0.00</td>
<td>0.00–1.08</td>
</tr>
<tr>
<td>Atrial perforation</td>
<td>0/341</td>
<td>0.00</td>
<td>0.00–1.08</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>0/341</td>
<td>0.00</td>
<td>0.00–1.08</td>
</tr>
<tr>
<td>Ventricular arrhythmia</td>
<td>0/341</td>
<td>0.00</td>
<td>0.00–1.08</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>2/341</td>
<td>0.59</td>
<td>0.07–2.10</td>
</tr>
</tbody>
</table>

No deaths were reported. CI indicates confidence interval. Classification was performed according to the Society of Interventional Radiology criteria [26].

Data collection

For all patients qualitative and quantitative variables were tabulated using a standardized data collection form. Original interventional radiology reports were reviewed in consensus by two radiologists with extensive experience in TJLB. Details of each procedure were recorded after reviewing the interventional radiology and monitoring data sheets, including details regarding the number of needle passes and the results of pathology reports.

TJLB was initially analyzed in terms of technical success and technical failure depending on a successful or a failed catheterization of hepatic vein and satisfactory or unsatisfactory liver tissue sample.

Associated morbidity and mortality ≤30 days were also documented by reviewing clinical and imaging files and discharge summaries.

For all patients, interventional radiology reports, clinical files and discharge summaries were reviewed to detect any complications related to the procedure. Complications were categorized as major or minor complications according to the Society of Interventional Radiology criteria (Table 1) [26].

Statistical analysis

Quantitative data (continuous) were expressed as means, standard deviation (S.D.) and ranges. Qualitative data were expressed as raw numbers, proportions and percentages along with their 95% confident intervals (CIs).

Results

TJLB was technically successful in 331/341 patients (97.07%; 95%CI: 94.67–98.58%) and gross liver tissue specimens (mean length: 11.1 ± 5.4 [S.D.]; range: 5.0–20.0 mm) were obtained in the 331 patients. TJLB failure was reported in 10/341 patients (2.93%; 95%CI: 1.42–5.33%). In nine patients, technical failure was due to an acute angle (i.e., <90°) between the right hepatic vein and the inferior vena cava. In these patients, catheterization of the right hepatic vein was achieved with the 5-French catheter and the superstiff guide wire. However, marked angulation did not allow securing the curved rigid 7-Fr catheter into the right hepatic vein, thus precluding safe introduction of the biopsy needle. These nine patients had atrophy of the liver and severe ascites as evidenced on CT scan. In the remaining patients, histopathological analysis revealed that tissue sampling was obtained from the right kidney.

The number of passes needed to obtain adequate hepatic tissue samples ranged from 1 to 4 needle passes (mean: 1.43 ± 0.49 [S.D.]). A single pass was done in 230/331 patients (69.49%), two passes were needed in 68/331 patients (20.54%), three passes in 25/331 patients (7.55%) and four passes in 8/331 patients (2.42%).

Major complications consisted exclusively of intrapitoneal bleeding due to liver capsule perforation and were observed in 2/341 patients (0.59%; 95%CI: 0.07–2.10%) with hepatic cirrhosis due to alcohol abuse and suspected superimposed acute alcoholic hepatitis. These two patients (one 63-year-old woman and one 40-year-old man) experienced marked abdominal pain during TJLB in association with a drop (15 and 20 mmHg) in arterial pressure and a rise (20 and 20 BPM) in cardiac frequency. Of note, for both patients TJLB was technically successful and two needle passes were performed. In both patients, a venous angiogram was immediately performed using the 5-Fr catheter placed in the right hepatic vein and showed intraparenchymal extravasation of iodinated contrast material (Figs. 1 and 2). Transcatheter embolization of the intraparenchymal venous track was thus
performed using torpedoes of gelatin sponge (Gelitaspon®), Gelita Medical BV, Amsterdam, The Netherlands) measuring $1 \times 1 \times 20 \text{mm}^3$. The female patient was successfully treated using 3 torpedoes of gelatin sponge and control venogram did not show further extravasation (Fig. 1). Control CT examination of the abdomen was performed and showed no active bleeding but intraperitoneal accumulation of iodinated contrast material that was injected during TJLB, thus confirming liver capsule disruption (Fig. 1). No transfusions were required and she recovered well. In the male patient, venous embolization was performed using 5 torpedoes and control venogram did not show further extravasation. However, the patient experienced worsening in hemodynamic status and received two packs of red blood cells. CT examination was thus performed and confirmed persisting bleeding (Fig. 2). The patient was immediately treated with transcatheter arterial embolization using 5 torpedoes of gelatin sponge (Gelitaspon®) and one metallic coil placed in the right branch of the hepatic artery. He received two additional packs of red blood cells and recovered well. In both patients TJLV allowed diagnostic tissue sampling and histopathological analysis confirmed acute alcoholic hepatitis.

The most frequent minor complication was abdominal pain at the liver biopsy site irradiating to the right shoulder during the procedure that resolved spontaneously within
less than three hours (Table 1). Abdominal pain was observed in 35/341 patients (10.26%; 95%CI: 7.25—13.99%). Among these 35 patients, ultrasonographic examination of the abdomen immediately after TJLB showed self-limited hypechogenic area in the right liver corresponding to the biopsy site in 12 of them; this finding in the setting of a recent TJLB was considered as a limited intrahepatic hematoma. In one of them, because of a transient worsening in hemodynamic status, abdominal CT examination was performed and disclosed arteriovenous fistula at the biopsy site that did not require further treatment (Fig. 3).

Supraventricular arrhythmia was reported in 15/341 patients (4.40%; 95%CI: 2.48—7.15%). Limited cervical hematoma at the RIJV puncture site was reported in 5/341 patients (1.47%; 95%CI: 0.48—3.39%). Cervical hematomas were further confirmed by ultrasonographic examination and measured less than 3 cm in diameter. All resolved after manual compression of 15 to 25 minutes. Other minor complications are listed in Table 1. No cases of inadvertent injury of the carotid artery were observed.

Discussion

In our retrospective analysis of 341 TJLBs, we observed two major complications in two patients that required further treatment, yielding a major complication incidence rate of 0.59%. In both patients, subsequent percutaneous endovascular treatment allowed controlling the bleeding and was followed by a favorable outcome. Of interest, no deaths due to this severe complication were observed in our study population, whereas a fatal outcome has been reported by other researchers [2].

Shin et al. have reported an incidence of 1.4% for intraperitoneal bleeding after TJLB [22]. In their series, 1/65 patient experienced intraperitoneal bleeding that required readmission and red blood cell transfusion [22]. No further treatment and no embolization were needed [22]. In another study, Gamble et al. have reported 4 occurrences of intraperitoneal bleeding in four patients following capsular perforation in a series of 461 TJLBs, yielding an incidence of 0.87% [6].

Steadman et al. have reported four severe complications in a series of 67 patients who underwent TJLB [21]. Of these, one patient experienced myocardial ischemia, two patients had severe but transient chest pain and in the latter patient, the introducer placed in the RIJV migrated to the inferior vena cava and was retrieved percutaneously through the common femoral vein. In their series, no cases of intraperitoneal bleeding were observed [21].

In our study, the two cases of intraperitoneal bleeding occurred immediately after TJLB so that continuous monitoring of the hemodynamic status during the procedure helped detect this major and potentially life-threatening complication. This short delay between tissue sampling and clinical worsening is consistent with previous reports that indicate a delay of less than 3 hours following TJLB [2,24]. However, the bleeding may be delayed when it is due to hepatic artery pseudoaneurysm rupture [24].

Intraperitoneal bleeding is a rare complication of TJLB. Early detection helps start timely and effective management. Our results suggest that opacification of the right hepatic vein using the biopsy catheter allows detection of intraperitoneal extravasation, thus confirming capsule disruption. Of note, some authors recommend opacification of the hepatic vein to detect any break in the liver capsule and leakage of contrast agent following each needle pass [5,8]. In addition, as suggested by our observations, when capsular perforation is visible plugging of the needle track using gelatin sponge through the transjugular catheter should be undertaken to obliterate the vascular track and stop the bleeding with a favorable outcome [5]. However, one must keep in mind that it is important to safely deposit the gelatin distally and into the intraparenchymal portion of the venous tract to avoid unwanted reflux. It is also possible to use metallic coils via the transjugular catheter to do so [8] but at the penalty of an increased cost. When this simple and direct venous approach fails, arterial embolization can be considered to definitively stop the bleeding as it was performed in one of our patients.

Percutaneous arterial embolization is an effective treatment for intraperitoneal bleeding secondary to percutaneous biopsy of the liver [27]. Our results show that this technique can be used also for the treatment of intraperitoneal bleeding due to TJLB, thus confirming the results obtained by others [6].

In our study, we observed only one case of arteriovenous fistula that was diagnosed with abdominal CT. This was a minor complication that did not require any specific treatment. It may be hypothesized that the true incidence of this minor complication in our study was underestimated because evaluation of the true incidence should have needed performing CT examination to all patients after TJLB. However, arteriovenous fistula may be a major complication of TJLB in rare instances [23]. In this regard, Esposito et al. have reported one case of arteriovenous and arteriobiliary fistula with severe intraperitoneal bleeding and anemia that was successfully treated using...
percutaneous arterial embolization with a favorable outcome [23].

TJLB is not free from complications. In the literature, the overall rate of complications of TJLB is estimated to 7.1%, consisting of minor complications (6.5%), major complications (0.6%) and death (0.1%) [1,2,8,10,12,18]. In this regard, there have been reported cases of life-threatening intraperitoneal bleeding after laceration of the liver capsule during TJLB [2,5,6]. Hemoperitoneum has been reported in approximately 0.2% of all procedures, and is generally due to perforation of the capsule of Glisson [6,8,28]. Causes of mortality are almost exclusively hemoperitoneum (0.06%) and ventricular arrhythmia (0.04%) [2,8]. Of note, fatal intraperitoneal bleeding secondary to capsular rupture has been described by Lebrec et al. and other researchers [2,8,29]. Of interest, one must note that this fatal complication can occur during TJLB performed by well-trained operators [2].

The correlation between the number of needle passes and the frequency with which complications occur remains debated. Lebrec et al. found that complications correlated with an increase in the number of passes necessary to obtain adequate hepatic tissue samples [2] although others found that the occurrence of major complication did not correlate with the number of samples taken [9]. In our study, only two needle passes were performed in the two patients with intraperitoneal bleeding, but this does not allow drawing particular conclusion.

The overall failure rate of TJLB is estimated around 3.2%, mostly due to the impossibility to cannulate the hepatic vein (43.3%) or the jugular vein (25.8%) and for multiple other causes [8]. An acute angle of less than 90° between the axis of the inferior vena cava and the hepatic vein was the most common cause of failed TJLB and occurs in approximately 1% of TJLBs [8]. Unwanted renal sampling has also been reported due to the biopsy device being placed in the right renal vein rather than the hepatic vein as observed in 1/341 patients of our series [2].

In our study, no cases of inadvertent puncture of the carotid artery were observed. As already suggested, this may be due to the use of ultrasonographic guidance for RIJV puncture [15,30]. The use of ultrasonography has been strongly recommended to avoid complications such as pneumothorax, carotid artery puncture and other vascular damages, which may lead to life-threatening and fatal internal hemorrhage [15,30].

**Conclusion**

In conclusion, TJLB is a simple procedure in the majority of cases. However, this technique is not free from complications. Besides minor complications that do not require specific treatment, liver capsule damage during TJLB may lead to life-threatening intraperitoneal bleeding. Our results demonstrate that life-threatening complications during TJLB are extremely rare. In addition, they can be managed using transvenous or transarterial embolization with a favorable outcome. Our results reinforce the general assumption that TJLB is a safe and well-tolerated technique.

**Disclosure of interest**

The authors declare that they have no conflicts of interest concerning this article.

**References**