

Single Centre Experience of Transjugular Liver Biopsy in 152 Patients

Ankur Patel, ¹MBChB, MRCS (Ed), FRCR, Apoorva Gogna, ¹MBBS, FRCR, Farah Gillan Irani, ¹MBBS, FRCR, Terence KB Teo, ¹MBBS, FRCR, Tow Non Yeow, ¹MBBS, FRCR, Deepak Jain, ²MBBS, FRCR, Richard HG Lo, ¹MBBS, FRCR, FAMS, Kiang Hiong Tay, ¹MBBS, FRCR, FAMS, Bien Soo Tan, ¹MBBS, FRCR, FAMS, Rafay Azhar, ³MBBS, FRCPath, Jason PE Chang, ⁴MBBS, MRCP, FAMS, Manish Taneja, ¹MBBS, FRCS

Abstract

Introduction: Liver biopsy is considered the definitive investigation in the diagnosis and management of liver disease. This study describes the experience of performing transjugular liver biopsy (TJLB) over the last 9 years in a local single centre. **Materials and Methods:** A retrospective review of consecutive TJLB procedures performed at our institution was conducted. A total of 152 patients (74 males and 78 females), with a mean age of 47.4 years (range, 13 to 83 years) underwent a total of 154 TJLB procedures at our institution between March 2003 and November 2011. The principal indication for TJLB was severe coagulopathy in over 80% of patients. The technical success, number of passes, histological adequacy and complication rates were analysed. **Results:** The procedural success rate was 98.7% (152 out of 154 procedures). Adequate material for diagnosis was obtained in 149 out of 152 (98.0%) technically successful procedures. There was procedure related morbidity in 8 patients (5.2%) of which all but one were self-limiting requiring no further intervention. We also performed hepatic venous pressure gradient (HVPG) measurements in 19% of patients at the time of TJLB. **Conclusion:** TJLB performed at our institution is a safe and reliable technique in patients in whom traditional percutaneous liver biopsy may be hazardous. TJLB has a high technical success rate as well as a high diagnostic yield with a low complication rate. TJLB also has the added benefit of performing HVPG, which is of increasing importance in management and prognostication of chronic liver disease.

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Introduction

The first reported case of liver biopsy was recorded in 1883 by Ehrlich.¹ Since then, the technique of liver biopsy has been modified tremendously with major advances over the last 50 years, allowing safer and more reliable methods of performing liver biopsy.

Liver biopsy is a commonly performed procedure and is the investigation of choice in the diagnosis and investigation of liver disease. The most common method of biopsy is by the percutaneous route, either with or without image guidance. Percutaneous liver biopsy (PLB) has a small but inherent risk even in the most experienced hands, and it should therefore only be performed when the benefits of knowing the histology outweigh the risks to the patient.² PLB under image guidance, most often ultrasound, is currently considered the standard method of procuring tissue for histological assessment. This can be performed

relatively safely in patients without pre-existing deranged coagulation or ascites. PLB is a fast and technically simple procedure.³ The most common complication, which is a major limitation of PLB is post-procedure haemorrhage. Significant haemorrhage (indicated by a reduction in haemoglobin of >2g/dL) occurs in up to 0.3% to 0.5% of patients.⁴ It has been reported that subclinical haemorrhage occurs at a much higher rate, with up to 23% of patients having intrahepatic or subcapsular haematomas detectable by ultrasound 24 hours after biopsy.⁵

It has been demonstrated that taking more than one core of liver at biopsy can increase the diagnostic yield, but this may have an effect on morbidity. It has been clearly shown that making more passes increases the incidence of bleeding complications with PLB.^{4,6}

Transjugular liver biopsy (TJLB) was first reported

¹Department of Diagnostic Radiology, Singapore General Hospital, Singapore

²Department of Radiology, Institute of Liver and Biliary Sciences, Delhi, India

³Department of Pathology, Singapore General Hospital, Singapore

⁴Department of Gastroenterology and Hepatology, Singapore General Hospital, Singapore

Address for Correspondence: Dr Ankur Patel, Department of Diagnostic Radiology, Singapore General Hospital, Outram Road, Singapore 169608.

Email: ankur.patel@sgh.com.sg

experimentally in 1964 by Dotter.⁷ It was subsequently utilised as a clinical tool in 1974.⁸ Since its introduction, TJLB has been most commonly performed in patients in whom the risks of conventional PLB were deemed unacceptable. TJLB is considered safer in these patients as the needle exits the hepatic vein into the liver parenchyma and then cuts the tissue. Any bleeding complication from TJLB is usually into the hepatic vein, theoretically making the procedure safer in these patients compared to PLB, which breaches the liver capsule. Bleeding from TJLB has been shown not to change significantly with increasing passes.⁹ The most common indications for using the transjugular route are coagulopathy (congenital or acquired), ascites, liver transplant recipients and acute liver failure.³

In this study, we reported our single centre experience of TJLB in 152 patients encompassing a total of 154 procedures over the last 9 years.

Materials and Methods

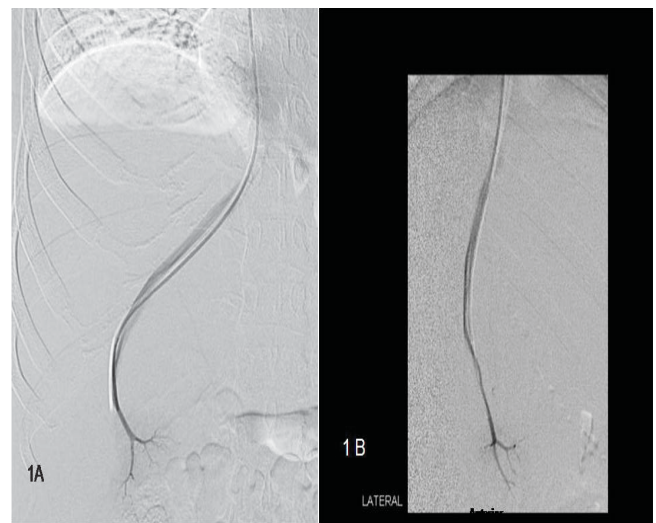
A retrospective review of consecutive TJLB procedures performed between March 2003 and November 2011 at our institution was conducted. Institutional Review Board approval was obtained. The patients were identified using our hospital Radiology Information System. Thereafter, the procedural and histological reports were reviewed as well as the clinical indications and laboratory results.

Technique

Prior to the procedure, the most recent cross-sectional imaging of the liver was reviewed to assist in pre-procedural planning, particularly with respect to hepatic venous anatomy. Informed and written consent was obtained for all patients undergoing TJLB.

All TJLB procedures were performed in the angiography suite in our Interventional Radiology Centre under conscious sedation. Continuous monitoring of heart rate, oxygen saturation and electrocardiographic readings was performed.

The right internal jugular vein (IJV) was the principal access point for the vast majority of patients. The left IJV was used in one patient due to occlusion of the right IJV. The IJV was accessed under ultrasound guidance after infiltration of local anaesthetic. Using a Seldinger technique, a guide wire was introduced and under fluoroscopic guidance was manipulated into the inferior vena cava. A 9 Fr vascular sheath was inserted. An angiographic catheter, most commonly a MPA-1 catheter (Cordis, New Jersey, USA), and a hydrophilic guide wire (Terumo, Tokyo, Japan) were manipulated into the hepatic vein, usually the right, and hepatic venography was performed (Figs. 1A and 1B). Hepatic venous pressure gradient (HVPG) measurements were performed at this stage if clinically indicated.



Figs. 1(A) and 1(B). Right hepatic vein venogram—Anteroposterior (AP) and lateral projection.

After cannulation of the target vein, exchange for a superstiff guide wire (Amplatz, Cook Medical Inc, Bloomington, USA) was performed, and the 7 Fr long and metal cannula of the TJLB set (Liver Access Biopsy Set – LABS 100, Cook) were slowly introduced. Through the sheath, the 60 cm long 18G (2 cm throw) biopsy needle was inserted co-axially through the 7 Fr sheath and under fluoroscopic guidance positioned in the proximal segment of the hepatic vein. The cannula was then rotated, usually anteriorly and the hepatic vein wall was then traversed and the tip of the needle advanced into the liver parenchyma (Fig. 2A). Biopsies were then performed (Fig. 2B). The number



Fig. 2(A). Biopsy needle within the right hepatic vein prior to biopsy.



Fig. 2(B). Core biopsy needle advanced into the liver parenchyma prior to biopsy.



Fig. 3. Right hepatic venogram completed.

of passes required was determined by the radiologists' macroscopic assessment of the specimens obtained. A post-biopsy venogram was performed to exclude any haemorrhagic complications (Fig. 3). The vascular sheath was then removed and manual compression applied to the access site on the neck until haemostasis was achieved. Following the procedure, all patients were closely monitored in the ward for 6 hours, and then discharged only after 24 hours.

Technical failure of TJLB was classified as the failure to obtain a liver sample for any reason. The specimen was considered adequate if it allowed a histological diagnosis to be made in the given clinical context. Minor and major

complications were classified according to the Society of Interventional Radiology criteria.¹⁰

Results

The study group comprised 74 males and 78 females with a mean age of 47.4 years (range, 13 to 83 years). The most common indication for TJLB was coagulopathy (82.4%) followed by ascites and post-liver transplantation (Table 1). In 4 patients, HVPG measurements were required as well procurement of liver tissue, hence TJLB biopsy was performed concurrently, obviating the need for PLB. All patients with an abnormal coagulation profile received pre- and intra-procedural transfusions of fresh frozen plasma and/or pooled platelets as per our departmental protocol (Table 2). A total of 154 TJLB procedures were performed over the review period on 152 patients. Two postoperative liver transplant recipients underwent TJLB twice to assess for rejection.

The overall technical success rate was 98.7% (152/154 procedures). In one patient, it was not possible to perform the biopsy due to the failure to achieve a stable sheath/cannula

Table 1. Indications for Performing TJLB

Indication for TJLB	No. of Patients	%
Coagulopathy	127	82.4
[Platelets]	55	
[APTT and/or PT]	34	
[Platelets and APTT/PT]	38	
Ascites	13	8.4
Ascites and coagulopathy	1	<1
Post-liver transplant	4	2.6
HVPG (principal)	4	2.6
Unknown	5	3.2

TJLB: Transjugular liver biopsy; APTT: Activated partial thromboplastin time; PT: Promthrombin time; HVPG: Hepatic venous pressure gradient

Table 2. Departmental Parameters for Abnormal Coagulation

	Normal range	Indication for TJLB
Activated partial thromboplastin time (APTT)	27.0 – 36.1 seconds	>40.1 seconds
Prothrombin time (PT)	9.2 – 11.2 seconds	>3.2 seconds
Platelets	140 – 440 x 10 ⁹ /L	<100 x 10 ⁹ /L

position. The technical failure was attributed to a very shrunken cirrhotic liver resulting in unfavourable hepatic venous anatomy. A specimen was subsequently obtained at a later date via the percutaneous route after infusion of clotting factors to partially reverse the coagulopathy. In another patient with known cryptogenic liver cirrhosis, who required a repeat biopsy and HVPG measurements, the biopsy needle could not penetrate the liver. This was felt to be due a very hard liver as a result of the underlying severe cirrhosis.

The right hepatic vein was the most commonly cannulated vein, being used in 140/153 procedures (91.5%) with the middle hepatic (12/152) and accessory right hepatic vein (1/152) being used for the remainder of cases.

The number of passes varied amongst patients from 1 to 7. The average number of passes was 3.5. Only 12 patients had 5 or more passes.

Of the specimens obtained in 152 patients, histological assessment in 149 patients was deemed adequate for histological diagnosis. The specimens in 3 patients were assessed to be either too small or too fragmented.

The average specimen length could not be determined as this was not routinely reported. However, the range of specimen lengths obtained was stated in all 149 (adequate quality) biopsy reports. The mean range of specimen length was 5.7 mm to 10.6 mm (range, 1 to 18 mm). The number of complete portal tracts (CPTs) was only reported numerically in only 36 patients, with the vast majority being reported from 2009 onwards. The average number of CPTs in this group was 6.9 (range, 1 to 18).

Repeat biopsy was subsequently performed in 2 of the patients via the percutaneous approach (with attempted correction of coagulation with clotting factors). One of these patients developed a small subcapsular haematoma after PLB, which was managed conservatively. In a few cases, more than one aetiological feature was described in the histological report (e.g. cholestasis with features compatible with primary biliary cirrhosis). In such cases, the primary aetiological pathology (i.e. primary biliary cirrhosis) was given as the diagnosis. The principal histological diagnoses are detailed in Table 3.

Complications

There were 8 (5.3%) procedure related complications, of which 7 were classified as minor in terms of severity (Table 4). The single major complication resulted in procedure related mortality. A 40-year-old woman with a history of systemic lupus erythematosus presented with fulminant acute hepatitis and acute renal failure as well as deranged coagulation. At presentation, her liver function tests were severely deranged. The patient was in established multiorgan

Table 3. Histological Diagnosis for 152 Technically Successful Procedures

Histology	No. of Patients
Acute/chronic hepatitis	53
Cirrhosis (all aetiology)	21
Cholestasis	15
Haemosiderosis	14
Steatosis	11
Malignancy	9
Drug induced hepatitis	5
Autoimmune hepatitis	3
Regenerative hyperplasia	3
Fibrosis	3
Primary biliary cirrhosis	2
Graft versus host disease	2
Rejection	2
Cystinosis	1
Myelofibrosis	1
Citrullinaemia	1
Normal	3
Non diagnostic	3
Total	152

Table 4. Minor Complications of TJLB

Type of Minor Complication	No. of Patients
Small subcapsular haematoma / self limiting capsular rupture	2
Portal vein penetration	1
Biliary tree penetration	1
Entanglement of Amplatz guide wire within right ventricle	1
Small self-limiting haematoma at IJV puncture site	1
Contrast allergy	1

TJLB: Transjugular liver biopsy; IJV: Internal jugular vein

failure, requiring ventilatory support as well as artificial extracorporeal liver support and renal replacement therapy by way of continuous veno-veno haemofiltration. At the time of TJLB, one week after initial presentation, her coagulation remained impaired with an APTT of 63.3 seconds, PT of 18.5 seconds and platelets of $48 \times 10^9/L$. The patient underwent TJLB via the right hepatic vein (5 passes) without immediate complication. No evidence of extravasation was demonstrated on the post-biopsy venogram. Approximately 6 hours after the procedure, the patient became hypotensive and dyspnoeic. Her haemoglobin level reduced from 10.8 to 3.5 g/dL. An emergency CT scan showed active contrast extravasation from the right lobe of the liver with a large

amount of haemoperitoneum. Initial hepatic angiography failed to show any active bleeding. The patient then developed disseminated intravascular coagulopathy with an APTT >180 seconds and PT >120 seconds. Due to deterioration of her condition, repeat emergent hepatic angiography was performed with successful coil embolisation of the bleeding point from a segment 5/6 artery. Despite cessation of bleeding, the patient continued to deteriorate despite maximum intensive care therapy and passed away 48 hours after TJLB.

Overall, 5 complications were liver-puncture related (3.3%) and 3 were non-liver puncture related (2.0%). All minor complications (Table 4) were self-limiting with no further subsequent intervention necessary in any of the patients.

Discussion

TJLB is usually indicated when PLB is contraindicated most commonly due to severe coagulopathy, and also in patients with ascites. Patients with chronic liver disease often have impaired synthesis of coagulation factors, which may result in prolongation of the APTT and PT. In addition, thrombocytopenia as well as platelet dysfunction is a common finding in patients with portal hypertension and cirrhosis, due to hypersplenism and splenic sequestration of platelets.

Several advantages of TJLB over PLB have been described. One such advantage is the relative safety of using the transjugular approach. In both percutaneous and transjugular approaches, the overall complication rate has been stated as 7.1% (6.6% minor and 0.5% major).¹¹ The major concern with any visceral biopsy, particularly with regards to liver biopsy is that of haemorrhage. Taking into account that patients who are referred for TJLB invariably have some degree of coagulopathy (and therefore are at high risk of bleeding), it can be inferred that TJLB is seen as a relatively safe procedure. It is well known that in PLB, the risk of haemorrhage-related complications increases with the number of passes made.⁴ With TJLB, however, it has been shown that increasing the number of passes does not have a significant effect of increasing haemorrhage-related complications.⁹ Importantly, although the complication rates of both TJLB and percutaneous liver biopsy are similar, with the more stringent demand for larger specimens it is likely that the complication rate from percutaneous biopsies may increase as more passes will be required to obtain a larger amount of tissue. Conversely, TJLB offers the feasibility of several passes without necessarily increasing the complication rate.¹¹

Another advantage of the transjugular approach is the ability to perform HPVG measurements, which

has prognostic value as well as allowing assessment of pharmacological treatment response of portal hypertension.¹² In our series, we performed HPVG in 19% (29/154) of our patients who underwent TJLB. Furthermore, recent research suggests that HPVG might be a better endpoint than histology for the assessment of therapeutic benefit of antiviral treatment in patients with chronic hepatitis C infection.^{13,14} As such, it has been mooted that in this subgroup of patients TJLB together with HPVG measurements may be the standard approach and therefore negate the increased cost of performing TJLB over PLB.¹²

In our series, we performed an average of 3.5 passes per procedure, slightly more than stated in the literature (average of 2.7),¹¹ however, we did not feel that this impacted significantly on our complication rate of 5.3%. Our liver puncture related complication rate was 3.3%, the same as stated in the literature of 3.3%.¹¹ In particular, in these patients, the average number of passes was 3.8. The increase in the average number of passes in this subgroup may have possibly contributed to the development of haemorrhagic complications, but this is difficult to prove due to the small numbers involved. We routinely perform biopsies in a more proximal segment of the hepatic vein rather than peripherally. Performing proximal rather than peripheral biopsies has been shown to be safer and is associated with fewer capsular perforations/haematomas.¹¹

Traditionally, TJLB specimens have been considered comparatively smaller and more fragmented, resulting in reduced diagnostic yields. This has often been cited particularly in specimens obtained in patients with liver fibrosis or cirrhosis, with the smaller size of the needle being the cause of such.^{15,16} In our practice, both our TJLB and PLB core biopsy needles are 18G in size with a 2 cm throw. Several studies have assessed the minimum length and number of portal tracts necessary for optimal histological evaluation.³ It has been accepted that a specimen of >15 mm in length as well as containing 6 to 8 CPTs should be present for the diagnosis in chronic liver disease. A large systematic review assessing the quality of liver biopsy showed that the length of specimens obtained by the transjugular route are on average 4.2 mm shorter compared to the percutaneous method (13.5 mm vs 17.7 mm). More significantly, the number of CPTs obtained were almost similar (6.8 vs 7.5).¹⁷ In our study, it was difficult to accurately ascertain the average specimen length. Our average ranges were 5.7 to 10.6 mm. However, the number of CPTs obtained averaged 6.9. Interestingly, subgroup assessment of average specimen ranges in the 36 patients where the number of CPTs was stated was 4.8 to 9.8 mm. The recent trend has been towards staging and grading of chronic liver disease for prognostication purposes, particularly in the assessment of fibrosis in patients with chronic hepatitis C and NASH. In

these patients, specimens of 20 mm to 25 mm in length or with 11 CPTs or more have been considered to be necessary for reliable histological evaluation.¹⁸ However, more recent studies assessing the adequacy of biopsy specimens using the newer generation cutting biopsy needles, including a large systematic review of over 7000 TJLB procedures,¹¹ has shown that the quality of specimens obtained using the transjugular approach is comparable, if not better,³ to those obtained via the percutaneous approach.

A limitation of our study was the inconsistent description of specimen length, which was often described in terms of the range of sizes of specimens received. This precluded detailed assessment of specimen fragmentation. Also, our study was retrospective and spanned nearly 9 years. As the importance of assessing the number of CPTs has only come to light recently, complete analysis of this parameter could not be performed. In addition, no comparative assessment with PLB procedures performed over the same period of time was made.

Conclusion

TJLB is a safe and reliable method of liver biopsy in our patients and has a high diagnostic yield and low complication rate. Although more time consuming and technically more difficult compared to PLB, in a selected group of (higher risk) patients, the benefit of performing TJLB outweighs these technical factors. TJLB should be considered as a complimentary procedure to PLB with the added benefit of performing HVPG at the time of biopsy. In our institution, TJLB is now considered the first line approach to obtaining a histological diagnosis in those groups of patients suspected of having liver disease with impaired coagulation or ascites.

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