Liver, Pancreas and Biliary Tract

Transjugular aspiration liver biopsy performed by hepatologists trained in HVPG measurements is safe and provides important diagnostic information

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ABSTRACT

Background: Transjugular liver biopsy (TJLB) represents an alternative to percutaneous liver biopsy especially in patients with impaired coagulation and ascites.

Aims: To describe safety and diagnostic yield of aspiration TJLB performed by hepatologists experienced in hepatic venous pressure gradient (HVPG) measurements.

Methods: 445 TJLB of 399 patients between 01/2007–12/2016 were retrospectively assessed.

Results: Histological diagnosis was obtained in 423 (95.1%) biopsies — including 11 (100%) patients with acute liver failure and 34 (97.1%) patients after liver transplantation. A median number of 5 portal tracts (interquartile range:2–9) was obtained. HVPG negatively correlated with sample length (Spearman $\rho = -0.310$; $p < 0.001$) and number of portal tracts ($\rho = -0.212$; $p < 0.001$).

Among n = 151 patients with unknown etiology of liver disease, etiology was successfully identified on liver histology in 126 patients (83.4%).

Complications occurred in 28 biopsies (6.3%) including 25 (5.6%) minor and 3 (0.7%) major complications. No deaths due to TJLB were observed.

Neither the presence of ascites (6.6% complications) nor of coagulopathy (platelets<50G/L and/or prothrombin time<50%; 4.8% complications) increased the risk for complications.

Conclusions: TJLB performed by hepatologists experienced in HVPG measurements is safe - even in patients with ascites or coagulopathy. TJLB has good diagnostic value for histological evaluation of liver disease and acute liver failure.

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1. Introduction

Different types of primary or secondary insults to the liver lead to distinct histological patterns with differences seen in location and severity of inflammation, necrosis, apoptosis, fibrosis and immune cell infiltration, which can be histologically assessed [1–5]. Therefore, liver biopsy can provide important diagnostic and prognostic information in patients with acute and chronic liver injury [6]. While non-invasive methods have been developed to estimate hepatic fibrosis and steatosis showing good correlation [7–9], liver biopsy still remains essential for assessing the type and severity of liver disease [10]. However, the gold standard of liver biopsy has been questioned due to sample error and intra [11]- and inter-observer variability [12,13]. Moreover, percutaneous liver biopsy (PLB) may be associated with complications such as bleedings and thus, may cause morbidity and mortality [14,15].

Transjugular liver biopsy (TJLB) has been developed as an alternative to percutaneous liver biopsy [16,17]. In experienced hands, TJLB is safe and associated with a lower risk of haemorrhagic complications than PLB. Specific indications for TJLB have been described, including patients with coagulopathy or ascites [6] as well as for acute liver failure (ALF) [18,19] and after liver transplantation (OLT) [16,20,21]. Moreover, the transjugular approach to the hepatic veins can also be used for measurement of the hepatic venous pressure gradient (HVPG) [22,23] and for creation of an intrahepatic portosystemic shunt [24,25]. TJLB is increasingly used to obtain liver samples in clinical practice. The technique is usually performed by interventional radiologists using either a Menghini aspiration needle or a core (Tru-cut) biopsy needle. In terms of diagnostic adequacy — considering the number of complete portal tracts, length, diameter and fragmentation of the obtained specimens, TJLB is often considered to be of inferior diagnostic accuracy as compared to percutaneously acquired liver specimens. However, with novel equipment, increasing expertise, and the use of multiple passages, TJLB produces a good diagnostic yield associated with excellent safety profile even in patients with advanced liver disease, who often show contraindications against PLB [17,21,26]. A systematic review concluded that TJLB is safe and yields liver specimens of comparable quality as compared to PLB [16]. It was suggested that using smaller Tru-cut needles (≥18G) and multiple (>3) needle passes further increases diagnostic quality [16]. Here we describe our experience with transjugular liver biopsy performed by hepatologists trained in HVPG measurements.

2. Methods

2.1. Study design

All adult patients with liver disease undergoing TJLB between 01/2007–12/2016 were retrospectively included in this study. Data were extracted from the procedure reports and medical histories of the patients. The study was approved by the Ethics Committee of the Medical University of Vienna (EK 1697/2017) and performed in accordance with the ethical guidelines of the 1975 Declaration of Helsinki. As this study is a retrospective analysis and according to the Ethic's vote no written informed consent was required.

2.2. Parameters

Age, gender, body mass index (BMI), etiology (if known) of liver disease and clinical parameters were extracted from electronic medical histories. Laboratory parameters that were usually collected at the same day of the procedure were recorded. Specifically,

we recorded hemoglobin (Hb), platelet count (PLT), prothrombin time and international normalized ratio (INR). Prognostic scores such as the MELD and the Child Pugh Score were calculated and the duration of hospital stay was documented.

2.3. Procedure

The TJLB were performed by experienced hepatologists following a standard operating procedure. In almost all cases, TJLB was performed after completing a measurement of the HVPG via the same catheter introducer sheath placed in the right internal jugular vein. Briefly, after local anesthesia and ultrasound guidance the catheter introducer sheet is placed using the Seldinger technique. A guiding catheter (needle introducer sheet) is placed under fluoroscopic control in a hepatic vein, usually the middle or right hepatic vein. The TJLB in this series were performed using a Menghini aspiration needle (16G transjugular liver biopsy needle, 50.5 cm, Cook Medical) [27]. After the tip of the biopsy needle is advanced to the luminal ending of the needle introducer sheet and the needle is angled to the desired location for the biopsy tract. Under aspiration pressure applied via a 10 mL syringe prefilled with 2–5 mL of sterile saline, the transjugular needle is advanced into the liver parenchyma and then retracted under continuous aspiration force. The procedure is repeated for 3 passages. After the last passage, fluoroscopic control under forced injection of 5–10 mL of contrast media is performed in order to check for any vascular leakage. Finally, the biopsy needle guiding sheet is retracted and the percutaneous catheter introducer sheet is removed from the patient's right internal jugular vein.

2.4. Complications

Any complications occurring during or after the TJLB procedure were documented in the procedure reports. The respective treatments of the complications were recorded and evaluated. In particular, we assessed complications related to vascular access, liver bleeding and pneumothorax. Major complications were graded according to 'Society of Interventional Radiology (SIR) classification system for complications by outcome' as complications requiring therapy, minor (<48 h) or major hospitalization (>48 h), permanent adverse sequelae or death [28].

2.5. Liver specimens (Fig. 1)

Liver specimens were fixed in 4% formaldehyde and embedded in a paraffin block. Serial sections were cut and stained with haematoxylin and eosin, chromotrope aniline blue, and prussian blue.

Histological slides were read by pathologists specialized in liver histopathology. Length of biopsy and number of obtained portal tracts were assessed. Both full and partial portal tracts were counted if they could be reliably identified by the pathologist.

2.6. Statistics

Statistical analyses were performed using IBM SPSS Statistics 25 (SPSS Inc., Armonk, New York, USA). Continuous variables were reported as mean ± standard deviation (SD) or median and interquartile range (IQR), and categorical variables were shown as numbers (n) and proportions (%) of patients. Spearman's rank correlation coefficient was used to investigate the correlation between severity of portal hypertension (i.e. HVPG) and number of portal tracts and length of biopsy. Kruskal–Wallis–Test was used to compare the total number of portal tracts between 10 years of investigation period. Comparison of the diagnostic
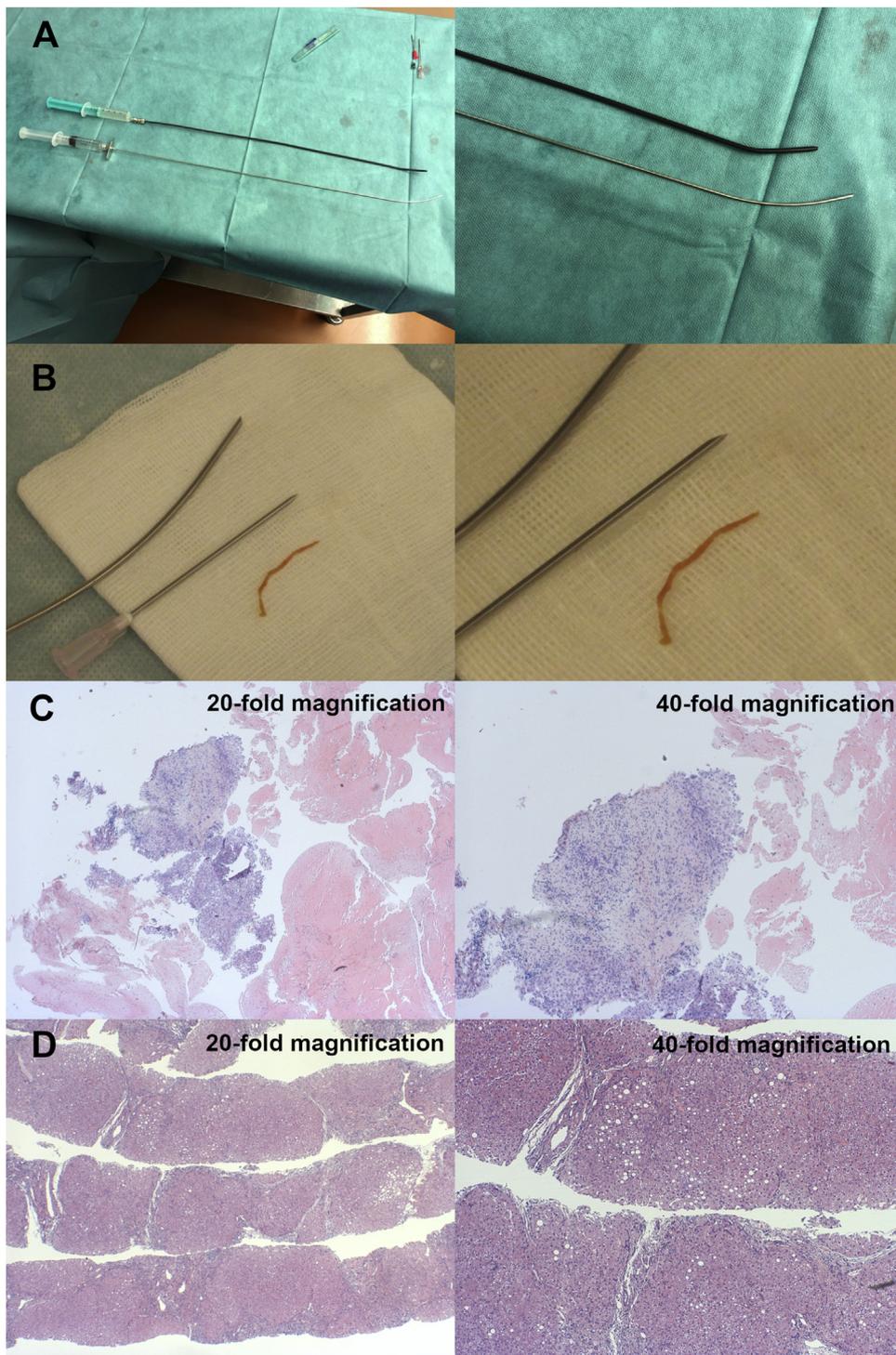
Fig. 1. **(A)** Biopsy Set, **(B)** macroscopic overview of liver specimen, **(C)** histology of a liver specimen insufficient for adequate evaluation of etiology and degree/stage of liver injury, and **(D)** histology of sufficient liver specimen.

yield among patients with different severity of portal hypertension stratified by HVPG were evaluated using one-way ANOVA with Fisher's Least Significance-Difference for post hoc comparisons and Mann–Whitney-U-Test. Chi-Square-test or Fisher's exact test were used to compare the incidence of complications during the study period and among different HVPG subgroups, as applicable. Univariate logistic regression analyses were conducted to investigate possible factors associated with occurrence of complications during TJLB. A two-sided p-value < 0.05 was considered as statistically significant.

3. Results

3.1. Patient characteristics (Table 1)

In total, 445 TJLB from 399 consecutive patients were identified and included in this retrospective analysis. 46 patients underwent a second biopsy due to changing clinical features, unclear worsening of liver disease or within a study protocol. The majority of patients were male (n = 273, 61.3%) with a mean age of 50.7 (SD ± 13.8) years. Further analyses were done regarding the total

Table 1
Patient characteristics.

Patient characteristics	
Number of patients, n	399
Total number of liver biopsies, n	445
Sex, male/female, n (%male)	273/126 (61.3%)
Age, years ± SD	50.7 ± 13.8
Previous OLT, n	36 (8.1%)
Etiology	
-AIH, n	18 (4.0%)
-ALD, n	50 (11.2%)
-Cryptogenic, n	25 (5.6%)
-DILI, n	22 (4.9%)
-Mixed ALD/Viral, n	9 (2.0%)
-NAFLD, n	32 (7.2%)
-Other, n	59 (13.3%)
-PBC/PSC, n	8 (1.8%)
-Viral, n	222 (49.9%)
Child-Pugh-Score	
-CPS-A, n	289 (64.9%)
-CPS-B, n	111 (24.9%)
-CPS-C, n	45 (10.1%)
MELD-Score	9 (8–13)
Ascites, n	151 (33.9%)
-Mild, n	94 (21.1%)
-Severe, n	57 (12.8%)
Hepatic encephalopathy, n	62 (13.9%)
-West Haven I–II, n	42 (9.4%)
-West Haven III–IV, n	20 (4.5%)
History of variceal bleeding, n	26 (5.8%)
Cirrhosis, n	263 (59.1%)
HVPG, mmHg (IQR)	9 (4–16)
CSPH, n	202 (45.4%)
NCPH, n	19 (4.3%)
Days of hospitalization after TJLB (IQR)	1 (1–3)
Hb, g/dL (IQR)	12.2 (10.6–13.6)
Platelets, G/L (IQR)	134 (80–200)
Prothrombin time index, % (IQR)	69 (52.2–88.0)
Fibrinogen, mg/dL (IQR)	273 (216–339)
INR (IQR)	1.2 (1.1–1.3)

Abbreviations: OLT–orthotropic liver transplantation; AIH–autoimmune hepatitis; ALD–alcoholic liver disease; DILI–drug-induced liver injury; NAFLD–non-alcoholic fatty liver disease; PBC–primary biliary cholangitis; PSC–primary sclerosing cholangitis; CPS–Child-Pugh Score; HVPG–hepatic venous pressure gradient; CSPH–clinically significant portal hypertension; NCPH–non-cirrhotic portal hypertension; Hb–haemoglobin; INR–international normalized ratio

number of liver biopsies to better assess overall diagnostic performance and safety. In 36 cases (8.1%), liver biopsy samples were taken from transplanted livers. The major underlying cause of liver disease was chronic viral hepatitis B or C with a total amount of 222 samples (49.9%), followed by alcoholic liver disease (n = 50, 11.2%), non-alcoholic fatty liver disease (n = 32, 7.2%), drug-induced liver disease (n = 22, 4.9%) and autoimmune hepatitis (n = 18, 4.0%). Nine patients suffered from both alcoholic and viral liver disease (2.0%) and in 8 subjects from either primary biliary cirrhosis or primary sclerosing cholangitis (1.8%). In 25 patients (5.6%) no definite diagnosis could be established by TJLB. At the time of biopsy, 289 patients (64.9%) had Child-Pugh-Score A, 111 (24.9%) B and 45 (10.1%) C, respectively with a median MELD-Score of 9 (IQR: 8-13). Ascites was present in 151 of patients (33.9%) - rated as mild-moderate (grade 2) in 94 patients (24.9%) and severe-refractory (grade 3) in 45 patients (10.1%). 62 patients (13.9%) suffered from hepatic encephalopathy, which was severe (West-Haven III–IV) in 20 patients (4.5%). Additionally, 26 patients had a history of variceal bleeding (5.8%).

Overall prevalence of cirrhosis was 59.1% (n = 263) and 45.4% (n = 202) suffered from clinically significant portal hypertension (CSPH, HVPG ≥ 10 mmHg) with a median HVPG of 9 (IQR: 4–16) mmHg. Of note, 44 patients had clinical signs/complications of portal hypertension (i.e. presence of ascites and/or hepatic encephalopathy and/or history of variceal bleeding) in the absence of CSPH, and 19 patients (4.3%) had non-cirrhotic portal hypertension (NCPH). After a median of one day after TJLB (IQR: 1–3 days), patients were discharged from hospital, considering that one overnight hospitalization represents our local standard for TJLB post-procedure surveillance.

3.2. Diagnostic performance of TJLB (Table 2)

The median length of liver biopsy specimens was 6.0 mm (IQR: 5.0–10.3 mm) and a median number of 5 (IQR: 2–9) portal tracts was obtained. Median number of portal tracts in patients without cirrhosis was 6 (IQR: 3–9). Definite histological diagnosis was possible in 423 cases (95.1%) while 22 biopsy specimens (4.9%) were insufficient for diagnosis. 151 patients (33.9%) underwent TJLB because of unknown etiology of their liver disease prior to TJLB. In these patients, the etiology of liver disease could be determined by TJLB in 126 patients (83.4%) while in 25 cases, etiology of the underlying liver disease remained cryptogenic on histology of the specimen obtained by TJLB (16.6%).

In 24 patients, the exact number of portal tracts could not be counted due to advanced cirrhosis and in 2 patients due to hepatocellular carcinoma in the whole biopsy sample. Failure rate to obtain a liver sample was 0.4% due to two renal biopsies without liver tissue in the biopsy sample.

Furthermore, we found a significant correlation between length of biopsy and number of portal tracts (Spearman's $\rho = 0.481$, p < 0.001). When investigating the median number of portal tracts over time, there was a significant difference over the 10 years of investigation (p = 0.001) although showing no tendency towards increasing or decreasing number of portal tracts (Supplementary Fig.-1).

3.3. Safety of TJLB (Table 3, Fig. 2)

In total, we observed 28 complications during or after the procedure (6.3%), including 25 minor complications (5.6%) and 3 major complications (0.7%). Subclinical capsule perforation (n = 12, 2.7%) was the most frequent complication observed in our cohort, followed by any bleeding complications regarding the puncture site (n = 4, 0.9%) and other minor complications such as abdominal pain (n = 2, 0.4%), hypotension (n = 2, 0.4%) or tachycardia (n = 2, 0.4%) during the procedure. Two accidental renal biopsies (0.4%) were reported as well as one mediastinal hematoma (0.2%). As far as major complications are concerned, two pneumothoraxes (0.4%) occurred as well as one episode of ventricular fibrillation (0.3%). These major complications required either treatment or resulted in prolonged hospitalization. Moreover, no deaths due to complications of TJLB were noted.

While 12 patients received packed red blood cells and 10 patients received other blood products such as fresh-frozen plasma or platelet transfusion prior and after TJLB, none of those were given due to any complications of TJLB. Moreover, median delta Hb prior and after biopsy was +0.2 g/dL (IQR: −0.2 to +0.6 g/dL), a Hb decrease >2.0 g/dL was observed in only 3 patients, who did not suffer from any obvious complications of TJLB.

Although the total number of complications decreased over time (11 vs. 8 vs. 5 vs. 4), relative incidence was comparable in 10 years of investigation (7.8% vs. 6.3% vs. 7.5% vs. 3.6%, Chi-Square p = 0.431). However, major complications only occurred in the first quartile in 10 years of investigation period (Supplementary Table-1). When investigating factors associated with the occurrence of complications during TJLB, only male gender attained statistical significance in univariate logistic regression analysis while age, BMI, ALF, CSPH, PLT count, albumin, number of portal tracts or length

Table 2

Diagnostic yield of transjugular liver biopsy.

	Overall (n = 445)			
Sample length, mm (median, IQR)	6 (5–10)			
Number of portal tracts (median, IQR)	5 (2–9)			
Number of portal tracts in patients without cirrhosis (median, IQR)	6 (3–9)			
Histological diagnosis possible, n	423 (95.1%)			
Failure rate, n	2 (0.4%)			
Unclear etiology prior TJLB, n	151 (33.9%)			
-Etiology successfully determined by TJLB, n	126 (83.4%)			
	Patients with ascites (n = 151, 33.9%)	Patients with coagulopathy[a] (n = 82, 18.4%)	Patients with ALF (n = 11, 2.4%)	Patients after OLT (n = 36, 8.1%)
Number of portal tracts (median, IQR)	5 (2–8)	4 (2–7)	7 (6–15)	7 (4–10)
Diagnosis possible, n	141 (93.4%)	79 (96.3%)	11 (100%)	35 (97.2%)

Abbreviations: IQR–interquartile range; TJLB–transjugular liver biopsy; ALF–acute liver failure; OLT-orthotopic liver transplantation.

[a] Platelets<50G/L and/or prothrombin time index <50%.

Table 3

Safety and complications of transjugular liver biopsy.

	Overall (n = 445)	Patients with ascites (n = 151, 33.9%)	Patients with coagulopathy[a] (n = 82, 18.4%)	Patients with ALF (n = 11, 2.5%)	Patients after OLT (n = 36, 8.1%)
Overall complications, n	28 (6.3%)	10 (6.6%)	4 (4.9%)	2 (18.2%)	3 (8.3%)
Major complications, n	3 (0.7%)	–	–	–	1 (2.8%)
Minor complications, n	25 (5.6%)	10 (6.6%)	4 (4.9%)	2 (18.2%)	2 (5.6%)
Deaths due to TJLB, n	–	–	–	–	–

Abbreviations: IQR–interquartile range; ALF–acute liver failure; OLT-orthotopic liver transplantation; TJLB–transjugular liver biopsy.

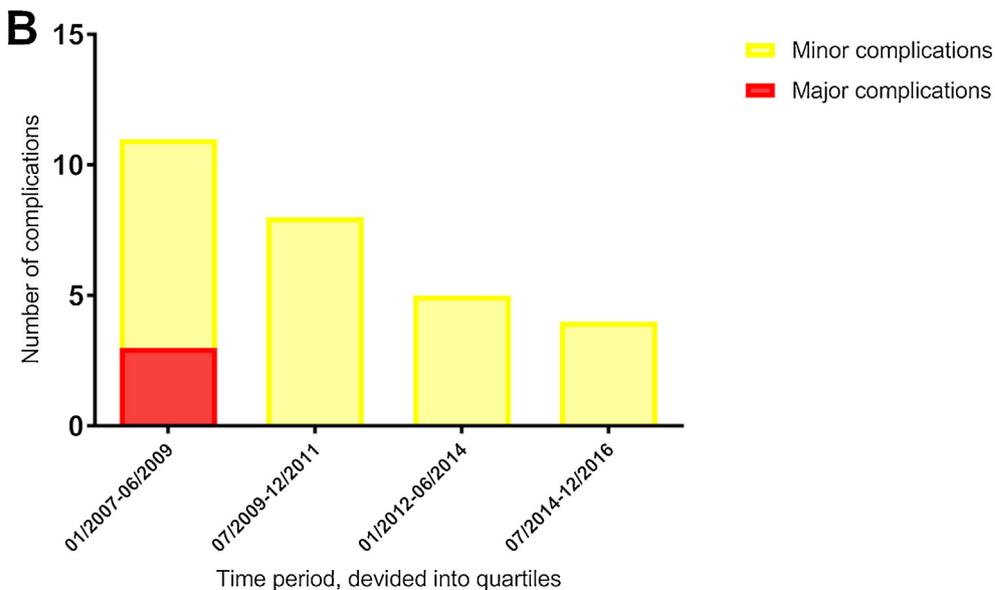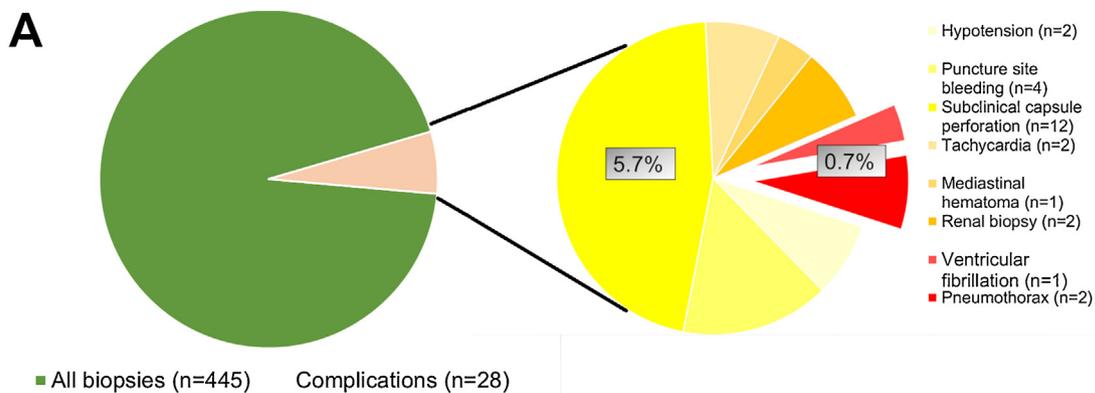[a] Platelets <50G/L and/or prothrombin time index <50%.

Fig. 2. (A) Overall complications, **(B)** incidence of complications over time.

Table 4
Safety and diagnostic performance of TJLB in patients with different severity of portal hypertension stratified by HVPG.

| | HVPG <10 mmHg (n = 236 53.0%)1 | HVPG 10–20 mmHg, (n = 134, 30.1%)2 | HVPG >20 mmHg (n = 68, 15.3%)3 | *p* Value | | | | |
				Over-all	*1 vs 2*	*1 vs 3*	*2 vs 3*	*1 vs 2 + 3*
Sample length, mm (median, IQR)	7 (5–18)	5 (4–7)	6 (5–8)	**<0.001**	**<0.001**	**<0.001**	0.928	**<0.001**
Number of portal tracts (median, IQR)	7 (3–10)	4 (2–8)	3 (1–8)	**<0.001**	**<0.001**	**0.001**	0.665	**<0.001**
Etiology successfully determined by TJLB[a] in prior unclear cases, n	41 (91.1%)	48 (78.7%)	34 (81.0%)	*0.219*	*0.085*	*0.170*	*0.779*	*0.083*
Overall complications, n	16 (6.8%)	9 (6.7%)	2 (2.9%)	*0.485*	*0.981*	*0.381*	*0.340*	*0.563*

Abbreviations: HVPG–hepatic venous pressure gradient; IQR–interquartile range; TJLB–transjugular liver biopsy.

[a] Overall cohort: n = 148, HVPG <10 mmHg: n = 45, HVPG 10–20 mmHg: n = 61, HVPG >20 mmHg: n = 42.

of liver specimen did not impact on the incidence of complications (Supplementary Table-2).

3.4. Performance of TJLB in special cohorts of patients (Table 2, Table 3)

Finally, we specifically investigated the performance of TJLB in patients with strong indication for transjugular approach of a liver biopsy such as patients with pre-existing ascites, patients with coagulopathy (platelets <50G/L and/or prothrombin time index <50%), patients with ALF and patients after OLT. In total, 220 patients (49.4%) met these criteria.

151 patients underwent biopsy in presence of ascites. By obtaining a median of 5 (IQR: 2–8) portal tracts, diagnosis could be made in 93.8% (n = 141) while only ten minor complications occurred (6.6%).

82 patients had laboratory evidence of coagulopathy as defined by either PLT <50G/L or prothrombin time <50%. In these patients, definite diagnosis was possible in 96.3% (n = 79) leaving a median of 4 (IQR: 2–7) portal tracts and 4 minor complications (4.8%).

11 patients presented with (fulminant) ALF. In this special subgroup of patients, etiology of ALF was successfully determined by TJLB in all cases (11/11, 100%) with drug-induced liver injury in 5 patients, acute autoimmune hepatitis in 4 patients, alcoholic steatohepatitis in one patient and congestive liver disease in another patient. 7 (IQR: 6–15) portal tracts were obtained in these patients.

Finally, 36 patients underwent TJLB after OLT. 97.2% (n = 35) were successfully diagnosed by histology with a median of 7 (IQR: 4–10) portal tracts. One major complication (pneumothorax, 2.8%) and two minor complications (5.6%) occurred.

3.5. Performance of TJLB among patients with different HVPG levels (Table 4)

To investigate the influence of HVPG on the diagnostic accuracy and safety of TJLB, patients with no/mild portal hypertension (HVPG<10 mmHg), CSPH (HVPG 10–20 mmHg) and high-risk portal hypertension (HVPG>20 mmHg) were compared regarding sample length, number of portal tracts, successful determination of underlying etiology and overall complications. These analyses revealed a significant difference in the median sample length (p < 0.001) and number of portal tracts (p < 0.001) among these three subgroups, especially between HVPG < 10 mmHg and HVPG 10–20 mmHg and between HVPG <10 mmHg and HVPG ≥ 10 mmHg (in both cases median sample length: 7 vs 5 mm, median number of portal tracts: 7 vs 4; all p < 0.001). Importantly, we found an indirect correlation of HVPG and sample length (ρ = −0.335, p < 0.001) as well as HVPG and number of portal tracts (ρ = −0.212, p < 0.001) in patients with liver disease etiologies causing sinusoidal portal hypertension. However, there was also a correlation of HVPG with sample length Spearman's (ρ = −0.310, p < 0.001) and portal tracts (ρ = −0.212, p < 0.001) when considering all etiologies of liver disease.

Additionally, the etiology of liver disease could be more often determined in patients with HVPG <10 mmHg (91.1%) than in patients with HVPG ≥ 10 mmHg (79.6%, p = 0.083). Importantly, no difference regarding overall complications was observed between patients with vs. without CSPH.

4. Discussion

Liver biopsy provides essential diagnostic information in patients with both acute and chronic liver disease. Especially in patients with indications for TJLB such as the presence of severe ascites or coagulopathy [6,16,20] as well as acute liver failure [18,19] or patients after liver transplantation [21], TJLB plays a central role in the management of these particular patients. In our study we could demonstrate that TJLB is not only safe but yields good diagnostic results and enables accurate diagnosis when performed by experienced hepatologists trained in HVPG measurements.

While a number of 6–8 portal tracts is claimed to be necessary for adequately assessing the stage of chronic liver disease [6], we could obtain a median number of 6 portal tracts in our cohort in patients without cirrhosis, which goes in line with published literature, reporting a median number of 6.5 and a mean number of 6.8 [16]. On the one hand, the number of portal tracts ranged between 0 and 25 in our cohort, which indicates some kind of sample variability, but on the other hand it must be taken into account that the majority of patients included in this study already had cirrhosis (58.9%), a stage of liver disease where portal tracts cannot be counted and identified as accurately as in patients with a more healthy liver [16]. We counted only a median number of 5 portal tracts in patients with cirrhosis comprising the majority of our cohort, indicating that some specimens were of borderline diagnostic quality. However, this retrospective analysis focused on aspiration technique using a 16G Menghini needle. Nevertheless, core biopsy needles (Tru-cut) are increasingly used in clinical routine, especially if sufficient material cannot be obtained after 3 passages using the Menghini aspiration needle. Since some studies report a better performance of Tru-cut needles than of aspiration needles [16], the diagnostic value may further improve if only Tru-cut needles are used.

In an early series of TJLB using Menghini needle in patients with severe fibrosis or cirrhosis, diagnosis could be achieved in 71% [29] whereas recent studies report success-rates up to 99% in cohorts including both patients with cirrhosis and without [21,30,31]. We could achieve a diagnosis in 95.1% of all TJLB and notably, etiology could be determined according to TJLB in 83.4% of former unclear cases of liver disease. Technical failure rate in our study was comparable to those reported in literature (0.4% vs. 0.5–3.2%) [16,26,30].

According to the largest systemic review on this topic [16], diagnosis was possible in 87.8% of liver transplant recipients and in 92.3% of patients with ALF. We observed an excellent diagnostic performance of TJLB in these special groups as we were able to diagnose 97.2% of patients after OLT and 100% of patients pre-

senting with ALF. Thus, we consider TJLB as the standard route to obtain liver samples in the setting of ALF and OLT, since it provides important input for the clinical management of these patients with excellent safety.

Overall complication rates in literature range from 0.5% to 29% when pain is included, with major complications in 0.5% to 0.9% of patients [16,19,26,31,32]. We observed an overall complication rate of 6.3% while major complications -defined by the Society of Interventional Radiology (SIR) classification system [16,28] -occurred in only 0.7% Unfortunately, most studies do not report details of their classification system of complications which makes it difficult to directly compare complications rates among published studies.

In our series, the median duration of hospitalization after TJLB was 1 (IQR: 1–3) day. However, one overnight hospitalization represents our local standard of care for TJLB due to reimbursement policies and not primarily due to the risk of 'late' complications after TJLB. Notably, complications were either evident immediately (paravasate) or evident within the first 4 h at latest in our series of patients.

Compared to mortality rates of 0.01–0.09% equal to 1 in 1.111–1 in 10.000 patients as documented in literature [6,16], we observed no deaths due to liver biopsy, yet the number of liver biopsies was not high enough to fully compare our results in this issue.

While cirrhosis is reported to be a risk factor for bleeding after percutaneous liver biopsy [6], we did not observe any clinical significant liver related bleeding indicating that TJLB is a safe tool especially in patients with advanced chronic liver disease.

Interestingly, diagnostic accuracy of TJLB in terms of sample length, number of portal tracts and ability to determine the etiology of liver disease was superior in patients without CSPH as compared to those with HVPG ≥ 10 mmHg. This might be mainly attributed to the structural changes of liver parenchyma in severe cirrhosis accompanying CSPH resulting in large fibrous bands, more pronounced distortion of hepatic architecture and therefore greater difficulty in obtaining sufficiently intact liver specimen by aspiration biopsy. However, using a Tru-cut system might improve quality of liver specimen in these patients [16].

Overall, we would highly encourage the use of TJLB during HVPG measurements, which are currently used by hepatologists to guide primary [23,33] and secondary prophylaxis [34]. Even in patients without strong indication for TJLB (i.e. without ascites or coagulopathy) and Child-Pugh A cirrhosis, liver biopsy can be safely done after HVPG-measurement using the transjugular approach and yields comparable results to PLB [16,21]. Since beta-blockers represent an essential pharmacological component in the prevention of variceal bleeding and rebleeding [35,36] and have additional beneficial effects on bacterial translocation [37], HVPG-guided betablocker therapy improves the outcome of cirrhotic patients [38]. We have successfully used repetitive TJLB in previous studies prior and after antiviral therapy in patients with chronic viral hepatitis [39,40] and in patients with hepatocellular carcinoma prior and after sorafenib therapy [41]. Thus, if etiology of liver disease remains unclear or if additional hepatic comorbidities are suspected, TJLB should be performed in addition to HVPG in clinical routine.

In addition to measurement of portal pressure, pulmonary and systemic hemodynamics can be assessed in detail by performing right-heart catheterization via the same venous access and without putting the patient at additional risk [39]. This is recommended in candidates for liver transplantation and TIPS, or in patients with suspected (porto-)pulmonary hypertension [42].

Some limitations of this study need to be acknowledged: First, the retrospective design of this study might have introduced some bias related to non-uniform documentation in clinical routine. While minor and major complications were documented carefully, the use of any blood products as a treatment of complications might be underreported. Second, some liver biopsy samples had to be re-assessed due to unclear pathology reports, which was not performed during past clinical routine. Although technical failure rate was documented very carefully, the number of failure to gain vascular access as for HVPG-measurement could not be addressed due to the retrospective study design.

In summary, our findings demonstrate an excellent safety of TJLB when performed by hepatologists experienced in HVPG measurements even in patients with ascites and coagulopathy. We recorded a good diagnostic accuracy using a transjugular Menghini aspiration needle, including the setting of ALF or after OLT.

Acknowledgement

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.dld.2019.01.020.

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