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Hepatic Vein–Inferior Vena Cava Confluence Angle as a Key Anatomical Predictor of Technical Success in Transjugular Liver Biopsy

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Abstract

Background/Objectives: Transjugular liver biopsy (TJLB) occasionally fails, most commonly because of difficulty in hepatic vein (HV) catheterization. We investigated whether the HV–inferior vena cava (IVC) confluence angle measured on CT or MRI could predict the technical success of TJLB. Methods: This single-center retrospective cohort study included 100 patients who underwent TJLB. Technical success was defined as the successful catheterization of the HV and acquisition of liver tissue. The HV–IVC confluence angle was measured on CT or MRI. Factors were compared between successful and unsuccessful cases. Multivariable Firth logistic regression was performed to assess factors associated with technical failure. ROC analysis was performed to evaluate the discriminatory performance of the HV–IVC confluence angle. Results: TJLB was technically successful in 86 of 100 cases. On univariate analysis, age, sex, height, and HV–IVC confluence angle were associated with TJLB success. The confluence angle was significantly smaller in successful than in unsuccessful cases ($43.6 \pm 11.1°$ vs. $59.3 \pm 11.2°$, $p = 0.001$). In multivariable Firth logistic regression, age and the confluence angle were associated with technical failure (odds ratios, 1.08 per year and 1.16 per degree, respectively). The area under the curve was 0.85, and the exploratory cutoff was 56°. Conclusions: A larger HV–IVC confluence angle was associated with technical failure and may be a promising imaging biomarker. Given limited measurement feasibility and no external validation, the 56° cutoff should remain exploratory.

Keywords: transjugular liver biopsy; liver biopsy; technical success; inferior vena cava; hepatic vein; liver failure

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1. Introduction

Liver biopsy is the gold standard for assessing the nature and severity of liver diseases [1]. It is considered the most specific investigation for monitoring the nature and severity of liver diseases [2].

Percutaneous liver biopsy (PLB) is widely preferred because of its simplicity and the high yield of tissue samples [3]. However, PLB is sometimes contraindicated in patients with ascites, coagulation abnormalities, or other conditions that increase procedural risk [1,4]. For these cases, transjugular liver biopsy (TJLB) is a suitable alternative. TJLB is especially indicated in patients with ascites, coagulation abnormalities, peliosis hepatis, morbid obesity, liver transplantation and congenital clotting disorders [5–13]. Contraindications for TJLB include hydatid cysts, obstruction of the main biliary tract with dilatation of the intrahepatic biliary tree, cardiac anomalies, thrombosis of the hepatic vein (HV) or the internal jugular vein (IJV) [14,15]. The technical success rate for the TJLB procedure is 78.9–97% [16–18]. TJLB provides specimens that are qualitatively comparable to PLB [19–21]. The major complications and mortality rates of TJLB in adults are similar to those of PLB, despite worse baseline conditions [19]. The development of semiautomatic needles and ultrasound guidance for IJV puncture has significantly improved the safety and efficacy of TJLB [19,21–23]. However, TJLB is infrequently performed and sometimes unsuccessful.

Several anatomical, clinical, and operator-related factors may influence the technical difficulty of TJLB. Catheterization of a suitable HV may be particularly challenging in patients with altered or distorted anatomy, especially after liver transplantation [24]. In addition, a significantly lower technical success rate of TJLB has been reported in patients with cirrhosis than in those without cirrhosis, suggesting that the severity of chronic liver disease may affect procedural outcomes [25]. An increased hepatic venous pressure gradient has also been associated with smaller biopsy specimens and reduced diagnostic usefulness [26]. Furthermore, TJLB is a technically specialized procedure that requires a well-trained and experienced interventional radiologist, indicating that operator-related factors may also influence procedural outcomes [14].

Among these factors, the anatomical relationship between the HV and inferior vena cava (IVC) may be particularly relevant to HV catheterization. The right lobe is generally considered the preferred site for liver biopsy because of its larger volume and the acute angle formed between the right HV and IVC [19]. Several studies have reported technical failure of TJLB in cases with a large angle between the HV and IVC, and a systematic review identified inability to catheterize the HV as the most common cause of TJLB failure [18,19,27].

A previous study measured the angle between the HV and IVC using fluoroscopic images obtained with a multipurpose catheter positioned within the selected HV, as well as measurements from devices retrieved after the procedure. In 21.1% of patients, two attempts at HV catheterization failed because the confluence angle was excessively large, with a mean angle of 69.7° [18]. These findings suggested that the confluence angle is a key determinant of TJLB success. However, no previous studies have demonstrated that TJLB success can be predicted preprocedurally or have proposed a specific confluence angle associated with technical success.

CT or MRI is often available before TJLB as part of routine clinical evaluation. Therefore, quantitative anatomical measurements derived from existing preprocedural images are particularly attractive from a clinical perspective, as they may allow procedural difficulty to be anticipated noninvasively without additional imaging examinations, radiation exposure, or substantial costs. Such imaging biomarkers may also facilitate preprocedural planning, including selection of the venous approach, target HV, and appropriate devices or technical modifications. In the present study, we measured the HV–IVC confluence angle on CT or MRI and evaluated its association with the technical success of TJLB. We also explored an angle threshold that may help identify patients at increased risk of technical failure.

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2. Materials and Methods

2.1. Study Design and Population

This is a retrospective cohort study conducted at a single center. This study was approved by Yokohama City University Hospital (F230100017). Informed consent was waived owing to the retrospective nature of this study. We retrospectively evaluated all consecutive patients aged ≥20 years who underwent TJLB at Yokohama City University Hospital between 13 November 2014, and 15 October 2024. Patients were stratified into two groups based on procedural outcomes: unsuccessful versus successful TJLB. Technical success was defined as successful catheterization of the HV and acquisition of liver tissue. Histological adequacy, including specimen length or the number of complete portal tracts, was not evaluated.

2.2. Transjugular Liver Biopsy Technique

We used 18-G biopsy needles. The needles were TLAB® Transjugular Liver Biopsy System (Argon Medical Devices, Plano, TX, USA) or Liver Access and Biopsy Set (Cook Medical, Bloomington, IN, USA).

Throughout the study period, TJLB procedures were performed primarily by two experienced hepatologists, each with more than 10 years of clinical experience. The patient was placed in the supine position with the head turned contralateral to the side of the internal jugular vein (IJV) cannulation. After administering local anesthesia with lidocaine, a short sheath was inserted into the right IJV using ultrasound imaging. The left IJV was not used. The guidewire was introduced into the right atrium, IVC, and HV under fluoroscopic guidance. We inserted the catheter into the HV and performed venography of the HV. The catheter was exchanged for a stiff guidewire and a TJLB catheter was subsequently introduced. Under ultrasonographic and fluoroscopic guidance, TJLB was performed, in principle, via the right HV. When biopsy via the right HV was technically difficult, the procedure was performed via the middle HV. We repeated biopsy passes until adequate tissue was obtained and visually confirmed.

2.3. Assessment of the Anatomical Relationship Between the IVC and HV

The HV–IVC confluence angle was measured on coronal CT images; when adequate anatomical assessment on CT was difficult, coronal MRI images were used instead. The central axes of the IVC and HV were identified, and reference lines were drawn along each vessel. The angle between these two lines was defined as the HV–IVC confluence angle. In successful cases, the angle was measured for the HV that was actually used for biopsy. In unsuccessful cases, because no HV was successfully used for biopsy, the angle was measured for the right HV, which was the primary target for TJLB (Figure 1). Representative original and annotated CT images illustrating the measurement of the HV–IVC confluence angle are shown in Figure 2. Images were analyzed by a single observer who was blinded to the procedural outcomes. The HV–IVC confluence angle was measured twice for each assessable case, and the mean of the two measurements was used for the analysis.

We also measured the distance between the IVC and HV and anteroposterior and left–right distances at a point 20 mm caudal to the confluence (Figure 1). The slice where the liver parenchyma was observed between the IVC and HV in a horizontal section was used as a reference, and the slice 5 mm cranial to it was designated as the confluence of the IVC and HV. Positive values were assigned in the anterior direction, and negative values were assigned in the posterior direction for the anterior–posterior measurements.

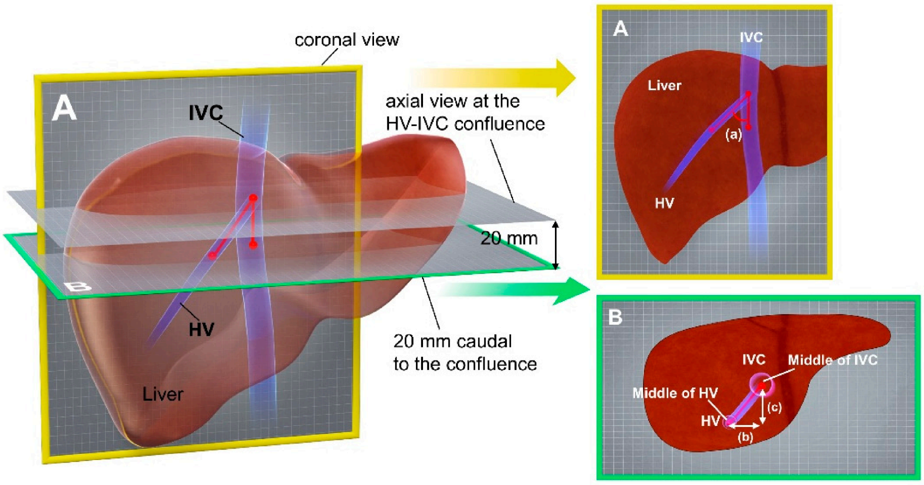

Figure 1. Method for measuring the anatomical relationship between the IVC and HV. (**A**) We measured the confluence angle between the IVC and HV, using coronal images. (**B**) We measured the distance between the IVC and HV; we measured the anterior–posterior and left–right distances at a point 20 mm caudal to the confluence. The slice where the liver parenchyma was observed between the IVC and HV in a horizontal section was used as a reference, and the slice 5 mm cranial to it was defined as the confluence of the IVC and HV. Positive values were assigned in the anterior direction and negative values in the posterior direction for anterior–posterior measurements. Abbreviation: IVC, inferior vena cava; HV, hepatic vein. (a) HV-IVC confluence angle, (b) left–right distance, (c) anterior–posterior distance.

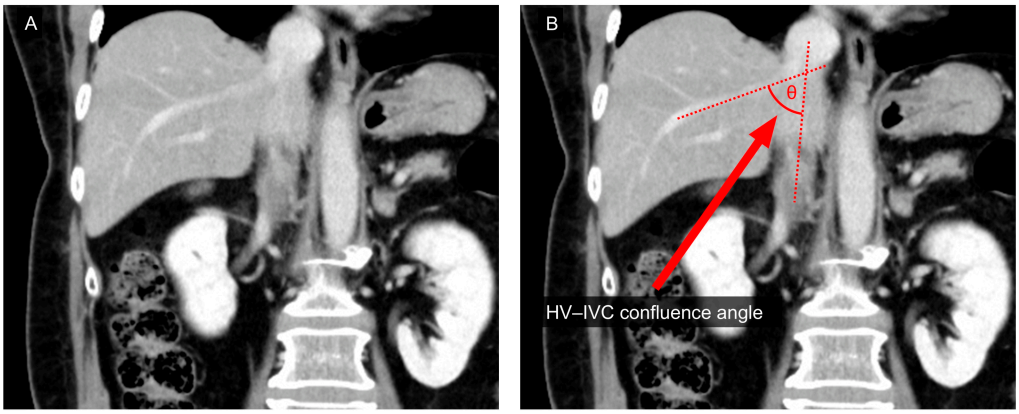

Figure 2. Representative contrast-enhanced CT images illustrating measurement of the hepatic vein–inferior vena cava confluence angle. (**A**) Original coronal CT image. (**B**) Annotated image showing the measurement of the hepatic vein–inferior vena cava confluence angle. The red reference lines indicate the longitudinal axes of the target hepatic vein and the inferior vena cava, and the angle between the two axes (θ) was defined as the confluence angle. Abbreviations: HV, hepatic vein; IVC, inferior vena cava.

Cases were excluded from anatomical measurements when the HV could not be identified on CT or MRI or when IVC catheterization was unsuccessful (e.g., due to difficulty with right IJV access).

2.4. Liver Volume Measurement

We measured the liver volume using the SYNAPSE VINCENT® software package (Version 5.5, FUJIFILM Holdings Corporation, Minato-ku, Tokyo, Japan).

2.5. Statistical Analyses

Statistical analyses were performed using JMP Pro 17 (SAS Institute Inc., Cary, NC, USA), except for Firth's penalized likelihood logistic regression and calculation of the 95% confidence interval for the area under the receiver operating characteristic curve, which were performed using R version 4.6.1 (R Foundation for Statistical Computing, Vienna, Austria) with the logistf and pROC packages, respectively. Continuous variables were compared using the Mann–Whitney U test, and categorical variables were compared using Fisher's exact test. The association between the HV–IVC confluence angle and the left–right distance was assessed using Pearson's correlation coefficient. Because of the limited number of technical failure events, multivariable analysis was performed using Firth's penalized likelihood logistic regression, with technical failure as the dependent variable. The model was restricted to age and the HV–IVC confluence angle; the confluence angle was included as the primary variable of interest, and age was included as a clinically relevant adjustment variable. Multicollinearity between age and the HV–IVC confluence angle was assessed using variance inflation factors. Odds ratios and 95% confidence intervals were estimated using profile penalized likelihood. Overall model significance was assessed using the penalized likelihood ratio test. Receiver operating characteristic curve analysis was performed to assess the discriminatory ability of the HV–IVC confluence angle, and an exploratory cutoff value was determined by maximizing the Youden index. The 95% confidence interval for the area under the curve was calculated using DeLong's method. Sensitivity, specificity, positive predictive value, and negative predictive value at the selected cutoff were calculated with exact binomial 95% confidence intervals. All tests were two-sided, and p-values < 0.05 were considered statistically significant.

3. Results

Patient Characteristics

TJLB was performed 100 times for 100 patients. Baseline demographic and clinical characteristics and disease etiologies are summarized in Table 1. This study comprised 57 female and 43 male cases, with a mean age of 55.4 ± 15.0 years. The mean height, weight, and BMI were 161.4 ± 8.4 cm, 60.6 ± 15.3 kg, and 23.1 ± 4.5 kg/m^2, respectively. The most common etiologies were autoimmune hepatitis excluding overlap syndromes and MASLD, each accounting for 20 cases, followed by idiopathic portal hypertension and alcohol-associated liver disease.

Table 1. Patient characteristics, etiologies, and indications for transjugular liver biopsy.

Patient Characteristics	Values
Number of cases, *n*	100
Number of female cases, *n*	57
Number of male cases, *n*	43
Age, years ± SD	55.4 ± 15.0
Height, cm ± SD	161.4 ± 8.4
Weight, kg ± SD	60.6 ± 15.3
BMI, kg/m^2 ± SD	23.1 ± 4.5
Etiologies	Number of cases, *n*
Autoimmune hepatitis (excluding overlap syndromes)	20
MASLD	20
Idiopathic portal hypertension	8
ALD	8
Acute hepatitis	6
Hematological tumors	5

Table 1. *Cont.*

Patient Characteristics	Values
Drug-induced liver injury	5
Viral hepatitis	3
Autoimmune Hepatitis and Primary Biliary Cholangitis	3
Congested liver	3
Hemochromatosis	3
VOD/SOS	2
Others	14
Reasons for choosing TJLB	Number of cases, *n*
Ascites	50
PT-INR > 1.5	33
Plt < 50×10^9/L	13
Hematological disease or suspected	22
Hepatic venous pressure gradient measurement	17
Severe obesity	1

Abbreviations: ALD, alcoholic liver disease; MASLD, metabolic dysfunction-associated steatotic liver disease; Plt, platelet; PT-INR, prothrombin time—international normalized ratio; VOD/SOS, veno-occlusive disease/sinusoidal obstruction syndrome; BMI, body mass index.

Reasons for choosing TJLB

TJLB was primarily selected because of ascites and coagulation abnormalities (Table 1).

Outcomes of TJLB: Success and failure

TJLB was successful for 86 of 100 cases. The reasons for the failure of TJLB were as follows: difficulty in HV catheterization (11 cases), thrombosis in the IJV (1 case), perforation of the hepatic capsule by the guidewire (1 case), and unknown cause (1 case) (Table 2).

Table 2. Reasons for transjugular liver biopsy failure.

Reasons for Failure	Number of Cases, *n*
Difficulty in HV catheterization	11
Internal jugular vein thrombosis	1
Extrahepatic guidewire perforation	1
Unknown	1

Abbreviation: HV, hepatic vein.

Adverse events associated with TJLB

Adverse events occurred in 6 cases, including intraperitoneal bleeding in 2 patients. One patient required blood transfusion, and no procedure-related mortality was observed.

Risk factors behind TJLB failure

On univariate analysis, younger age, greater height, male sex, a smaller HV–IVC confluence angle, and a shorter left–right distance between the HV and IVC were associated with TJLB success, whereas other clinical, laboratory, and hemodynamic variables were not (Tables 3 and 4).

For the successful group (*n* = 86), TJLB was performed in the right HV for 75 cases (87.2%) and middle HV for 7 cases (8.1%). In the remaining four procedures (4.7%), the HV used for biopsy was not documented in the medical records. Using the coronal section method, we measured the confluence angle for 53 of the 86 cases in the successful group and 10 of the 14 cases in the unsuccessful group (Figure 3). Among the 63 procedures included in the confluence-angle analysis, the angle was measured using CT images in 58 procedures and MRI images in 5 procedures. Patients with non-measurable HV–IVC confluence angles were slightly taller than those with measurable angles, whereas age, sex, BMI and technical success rates did not differ significantly between groups

(Supplementary Table S1). Among the 36 patients in whom the HV–IVC confluence angle was not measurable, 35 had undergone CT imaging but the angle could not be reliably assessed, and one patient had no available cross-sectional imaging (neither CT nor MRI). The confluence angle was significantly smaller in the successful group (43.6 ± 11.1 vs. 59.3 ± 11.2°; p = 0.001) (Table 4). Among the 36 procedures with a non-measurable angle, TJLB was technically successful in 33 procedures (91.7%) and unsuccessful in 3 procedures (8.3%). The technical success rate in these non-measurable cases was broadly comparable to that in the overall cohort. The reasons for non-measurability included the three-dimensional or oblique course of the HV, which prevented simultaneous visualization of the HV and IVC on a single coronal image; the unavailability of source image data required for coronal reconstruction in some patients whose imaging examinations had been performed at other institutions; and insufficient delineation of the HV and IVC in patients for whom only non-contrast CT images were available.

Table 3. Comparison of the successful and unsuccessful groups: Univariate analysis.

	Successful Group *n* = 86	Unsuccessful Group *n* = 14	*p*-Value
Age, years	54.0 (15.1)	63.7 (11.0)	0.0124
Height, cm	162.1 (8.2)	157.2 (9.0)	0.0294
Weight, kg	60.8 (14.8)	59.7 (18.7)	0.520
BMI, kg/m^2	23.0 (4.3)	23.8 (4.3)	0.682
Female	45	12	0.0214
Male	41	2	0.0214
Ascites(+)	44	6	0.774
Acute liver failure	19	2	0.728
Chronic liver disease	43	7	0.999
Blood test			
AST, U/L	303 (842)	160 (240)	0.515
ALT, U/L	410 (1305)	145 (250)	0.340
T.Bil, mg/dL	5.5 (6.4)	4.0 (5.5)	0.223
Alb, g/dL	3.1 (0.7)	3.0 (0.8)	0.968
Cre, mg/dL	1.1 (1.5)	0.9 (0.4)	0.769
Hb, g/dL	11.3 (2.5)	10.6 (2.8)	0.274
Plt, $\times 10^9$/L	140 (112)	129 (99)	0.706
PT-INR	1.46 (0.50)	1.43 (0.9)	0.059

Values are presented as mean (SD). Abbreviations: Alb, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Cre, creatinine; Hb, hemoglobin; Plt, platelet; PT-INR, Prothrombin time–international normalized ratio; T.Bil, total bilirubin.

Table 4. Univariate analysis of anatomical features between the successful and unsuccessful TJLB groups.

	Successful Group	Unsuccessful Group	*p*-Value
HV–IVC confluence angle	43.6 ± 11.1° (*n* = 53)	59.3 ± 11.2° (*n* = 10)	0.001
Left–right distance between the HV and IVC †	39.8 ± 12.4 mm (*n* = 72)	51.4 ± 14.0 mm (*n* = 9)	0.023
Anteroposterior distance between the HV and IVC †	−2.4 ± 10.8 mm (*n* = 72)	−5.0 ± 15.1 mm (*n* = 9)	0.532
Volume of the liver	1387 ± 655 mL (*n* = 80)	1127 ± 401 mL (*n* = 11)	0.212

† 20 mm caudal to the junction of the HV and inferior vena cava. Values are presented as mean ± SD (*n*). Abbreviation: HV, hepatic vein; IVC, inferior vena cava.

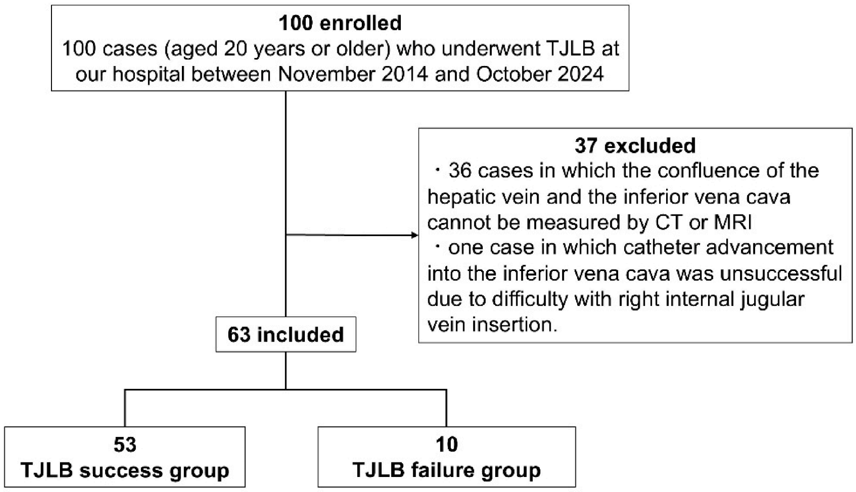

Figure 3. Flowchart of patient selection and group allocation. A total of 100 patients aged ≥20 years who underwent TJLB at our hospital between 13 November 2014, and 15 October 2024 were initially enrolled. Among them, 37 patients were excluded from the angle-based analysis: the confluence angle between the HV and IVC could not be measured by CT or MRI for 36 cases, and the IVC catheterization was unsuccessful for one case because of difficulty with right internal jugular vein access. Consequently, 63 patients were included in the angle-based analysis: 53 in the successful group and 10 in the unsuccessful group. Abbreviation: CT, computed tomography; MRI, magnetic resonance imaging; TJLB, transjugular liver biopsy.

Using the horizontal sectioning method, we measured the left–right and anteroposterior distances between the IVC and HV for 72 of the 86 cases in the successful group and 9 of the 14 cases in the unsuccessful group. The mean left–right distance was significantly shorter for the successful than for the unsuccessful group (39.8 ± 12.4 vs. 51.4 ± 14.0 mm; $p = 0.023$) (Table 4). In contrast, no significant difference was found in the anteroposterior distance between the HV and IVC (−2.4 ± 10.8 vs. −5.0 ± 15.1 mm; $p = 0.532$). Among the 62 procedures in which both anatomical parameters were measurable, the HV–IVC confluence angle was positively correlated with the left–right distance between the HV and IVC (Pearson's r = 0.465, 95% CI: 0.243–0.640, $p < 0.001$; Figure 4). Liver volume did not differ significantly between the two groups (1387 ± 655 vs. 1127 ± 401 mL; $p = 0.212$).

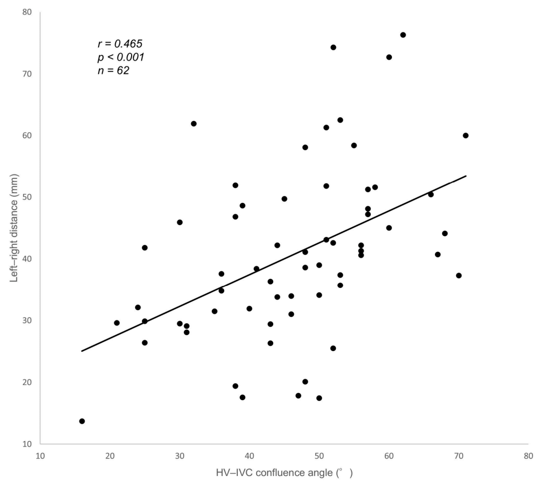

Figure 4. Relationship between the HV–IVC confluence angle and the left–right distance between the hepatic vein and the inferior vena cava. Each point represents one procedure in which both anatomical parameters were measurable ($n = 62$). The solid line represents the fitted linear regression line.

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Firth's penalized likelihood logistic regression analysis was performed using age and the HV–IVC confluence angle as covariates, with technical failure as the outcome. In this model, both age and the confluence angle were significantly associated with technical failure (Table 5). An increase in age was associated with a higher likelihood of technical failure (odds ratio per 1-year increase, 1.08; 95% confidence interval, 1.01–1.20; $p = 0.022$). Similarly, an increase in the confluence angle was associated with a higher likelihood of technical failure (odds ratio per 1° increase, 1.16; 95% confidence interval, 1.07–1.31; $p < 0.001$). No evidence of multicollinearity was observed between age and the HV–IVC confluence angle; the variance inflation factor was 1.00 for both variables. The overall model was statistically significant according to the penalized likelihood ratio test ($p < 0.001$).

Table 5. Firth penalized logistic regression analysis of factors associated with technical failure of TJLB.

	Odds Ratio (Failure)	95% Confidence Interval	*p*-Value
Age (per 1-year increase)	1.08	1.01–1.20	0.022
HV–IVC confluence angle (per 1° increase)	1.16	1.07–1.31	<0.001

Firth's penalized likelihood logistic regression was performed with technical failure as the outcome. The model included 63 patients, of whom 10 experienced technical failure. Odds ratios greater than 1 indicate a higher likelihood of technical failure. Confidence intervals were estimated using profile penalized likelihood.

For the confluence angle, a receiver operating characteristic curve was generated, and an optimal cutoff value of 56° was determined using the Youden index (Supplementary Figure S1). The area under the receiver operating characteristic curve was 0.85 (95% confidence interval, 0.68–1.00). At this exploratory cutoff, 8 of 10 procedures with technical failure and 7 of 53 procedures with technical success had an HV–IVC confluence angle of ≥56° (Supplementary Table S2). The sensitivity, specificity, positive predictive value, and negative predictive value for technical failure were 80.0% (95% confidence interval, 44.4–97.5%), 86.8% (74.7–94.5%), 53.3% (26.6–78.7%), and 95.8% (85.7–99.5%), respectively (Supplementary Table S3).

In a sensitivity analysis using the exploratory cutoff value of 56°, Firth's penalized likelihood logistic regression was performed with technical failure as the outcome and age and the dichotomized HV–IVC confluence angle as covariates. Both age and an HV–IVC confluence angle ≥ 56° were significantly associated with technical failure. The odds ratio for technical failure was 1.08 per 1-year increase in age (95% confidence interval, 1.02–1.19; $p = 0.009$) and 33.64 for an HV–IVC confluence angle ≥ 56° compared with <56° (95% confidence interval, 6.18–294.42; $p < 0.001$) (Table 6).

Table 6. Sensitivity analysis using Firth penalized logistic regression with the dichotomized HV–IVC confluence angle.

	Odds Ratio (Failure)	95% Confidence Interval	*p*-Value
Age (per 1-year increase)	1.08	1.02–1.19	0.009
HV–IVC confluence angle ≥ 56° (vs. <56°)	33.6	6.2–294.4	<0.001

Firth's penalized likelihood logistic regression was performed with technical failure as the outcome. The analysis included 63 patients, of whom 10 experienced technical failure. The 56° cutoff was an exploratory, data-derived threshold determined by maximizing the

Youden index in the ROC analysis. The 95% confidence interval was estimated using profile penalized likelihood.

4. Discussion

4.1. Indications for TJLB

In a previously published systematic review analyzing 7649 cases, the reasons for selecting TJLB were as follows: coagulopathy in 35% of cases, ascites in 13%, coagulopathy and/or ascites in 46%, and coagulopathy and ascites in 3.2% [19]. Similarly, the most common indications for TJLB were ascites and coagulopathy in our cohort, which was consistent with previous findings. This is likely because TJLB was preferentially selected for cases in which PLB was contraindicated, such as in the presence of ascites or coagulation abnormalities.

4.2. Success Rate and Reasons for TJLB Failure

In the present study, the technical success rate was 86%, which was comparable to rates reported in previous studies [16–18]. Difficulty in catheterizing the HV was the most common cause of TJLB failure, consistent with prior reports [19,24].

4.3. Confluence Angle Between the IVC and HV

A larger HV–IVC confluence angle was identified as a significant risk factor for TJLB failure. In previous reports, the HV–IVC confluence angle in the TJLB unsuccessful group was reported to be 69.7°, whereas it was 59.3° in our cohort [18]. This discrepancy may be largely attributable to differences in the methods used to measure the HV–IVC confluence angle. In the previous report, the angle was evaluated using fluoroscopic images obtained during TJLB, and catheter manipulation during the procedure may have altered venous morphology, resulting in an overestimation of the HV–IVC confluence angle. In contrast, in the present study, the HV–IVC confluence angle was measured noninvasively using CT and MRI images, which may more accurately reflect the physiological venous course.

Given the limited number of technical failure events, the multivariable analysis was performed using Firth's penalized likelihood logistic regression and was restricted to two covariates: age and the HV–IVC confluence angle. The confluence angle was included as the primary variable of interest because it represented the central hypothesis of this study. Age was selected as the single adjustment variable based on its clinical relevance and its association with technical outcome in the univariate analysis. In addition, age was considered more appropriate than sex or height as an adjustment variable because sex and height may partly reflect overlapping information related to body size. Both age and the confluence angle were significantly associated with technical failure, indicating that the association between a larger confluence angle and technical failure persisted after adjustment for age.

From an anatomical perspective, this association may be explained by the difficulty of advancing the relatively stiff access kit required to deliver the biopsy needle into the HV. Failure to access the HV is the most common cause of TJLB failure, and our findings suggest that the HV–IVC confluence angle is a key anatomical determinant.

ROC analysis identified 56° as the optimal cutoff value for discriminating technical failure in the present cohort, with an area under the receiver operating characteristic curve of 0.85. At this exploratory cutoff, the sensitivity and specificity for technical failure were 80.0% and 86.8%, respectively. The negative predictive value was relatively high at 95.8%, suggesting that an angle below 56° may help identify procedures with a relatively low likelihood of technical failure. In contrast, the positive predictive value was modest at 53.3%, indicating that an angle of 56° or greater should not be interpreted as a definitive predictor of failure. Rather, in patients in whom the angle can be measured reliably, this threshold may serve as an adjunctive marker for greater procedural preparedness, including consideration of alternative venous access, catheter selection, or other technical modifications. However, because the cutoff was derived retrospectively from a small, single-center cohort and was not externally validated, it should not be regarded as an established clinical decision threshold. Further validation in larger independent cohorts is required to determine whether this exploratory cutoff is reproducible and clinically useful.

Because measurement of the confluence angle was not feasible in a substantial proportion of procedures, we also explored an axial image-based distance parameter as a secondary anatomical surrogate. The left–right distance between the HV and IVC was evaluated as a secondary, axial image-based surrogate for the HV–IVC confluence angle. This parameter could be assessed in a greater number of procedures than the confluence angle and was intended to provide a more objective anatomical measure when simultaneous visualization of the HV and IVC on a single coronal image was difficult.

Among the 62 procedures in which both anatomical parameters were measurable, the HV–IVC confluence angle was moderately and positively correlated with the left–right distance between the HV and the IVC (Pearson's r = 0.465, 95% confidence interval, 0.243–0.640; $p < 0.001$). This finding supports the anatomical relationship between the two measurements, although the moderate correlation indicates that they are not interchangeable. Because the left–right distance was designed as a surrogate for the confluence angle and the two variables represented conceptually overlapping anatomical features, they were not included simultaneously in the same multivariable model.

Although the left–right distance was explored as a more objective axial image-based parameter, the HV–IVC confluence angle was retained as the primary anatomical variable because it directly represented the central hypothesis of this study and was more readily interpretable from an anatomical and procedural perspective. The left–right distance was considered a secondary surrogate parameter. Because the two measurements reflect overlapping aspects of HV–IVC geometry and the number of technical failures was limited, they were not included simultaneously in the multivariable model to avoid redundancy and model overfitting. The moderate positive correlation between the two parameters supports their anatomical relationship but also indicates that they are not interchangeable. Accordingly, these findings support the anatomical plausibility of the HV–IVC confluence angle as an investigational predictor, while its measurement feasibility and reproducibility require further validation.

Progressive hepatic remodeling associated with cirrhosis and portal hypertension may alter liver morphology and the spatial relationship between the HV and IVC [25,26]. However, liver stiffness measurements were unavailable in a substantial proportion of the cohort, precluding direct evaluation of the relationship between fibrosis-related remodeling and HV–IVC geometry. Portal pressure-related variables were not significantly associated with technical success, and liver volume did not differ significantly between the successful and unsuccessful groups. Nevertheless, given the limited sample size and small number of technical failures, these nonsignificant findings do not exclude potentially relevant effects of portal hypertension or changes in liver volume.

Taken together, these findings support the anatomical plausibility of the HV–IVC confluence angle as an investigational marker; however, important limitations related to measurement feasibility, reproducibility, and validation must be considered.

4.4. Limitations

A major limitation of the present study was the limited feasibility of measuring the HV–IVC confluence angle using a single coronal image. The angle was measurable in only

64 of the 100 procedures, and 63 procedures were ultimately included in the angle-based analyses after excluding one technical failure caused by unsuccessful internal jugular vein puncture before HV catheterization. Among the 36 procedures in which the angle was not measurable, TJLB was technically successful in 33 procedures (91.7%) and unsuccessful in 3 procedures (8.3%). Although this success rate was broadly comparable to that in the overall cohort, similar procedural outcomes do not necessarily indicate similar HV anatomy, and selection bias cannot be excluded.

Non-measurability resulted from both anatomical and imaging-related factors. In some procedures, the HV could not be visualized simultaneously with the IVC on a single coronal image, potentially reflecting an anteroposterior or oblique course of the HV relative to the IVC. In the axial image-based analysis, however, the anteroposterior distance between the HV and IVC did not differ significantly between the technically successful and unsuccessful groups. This finding suggests that anteroposterior displacement alone may not be a major anatomical determinant of technical failure. However, this analysis did not directly compare procedures with measurable and non-measurable confluence angles, and a distance measured on a fixed axial image may not fully capture the three-dimensional or oblique course of the HV. Therefore, this finding does not establish comparable HV anatomy between the measurable and non-measurable groups and does not exclude selection bias associated with the exclusion of non-measurable procedures.

Other causes of non-measurability included the unavailability of source image data suitable for coronal reconstruction, particularly when imaging had been performed at another institution, and insufficient delineation of the HV and IVC when only non-contrast CT images were available. Accordingly, the 63 procedures included in the final angle-based analysis may not fully represent the entire population undergoing TJLB, particularly patients with complex HV anatomy or limited-quality preprocedural imaging. This restriction may have affected the estimated association between the HV–IVC confluence angle and technical failure and limits the external validity and generalizability of the present findings.

Because the current single-coronal-image method was applicable to only approximately two-thirds of the study population, the HV–IVC confluence angle should not yet be considered a routinely applicable clinical parameter. Rather, it should be regarded as a promising investigational marker requiring further methodological development. Future studies should evaluate whether multiplanar reconstruction, patient-specific oblique reconstruction, or three-dimensional image analysis can improve measurement feasibility and reproducibility, particularly in patients with complex HV anatomy.

An additional important limitation was the lack of a formal reproducibility assessment for the imaging measurements. Although the HV–IVC confluence angle was measured twice for each assessable procedure and the mean value was used for the analysis, all measurements were performed by a single observer. Therefore, interobserver reproducibility was not assessed, and uncertainty remains regarding the reliability and future applicability of this anatomical marker.

Imaging acquisition represents another limitation. The HV–IVC confluence angle was measured primarily on CT images, whereas MRI was used in five procedures when adequate anatomical assessment on CT was difficult. Because MRI was used in only a small number of procedures and was selected specifically when evaluation on CT was difficult, systematic differences in angle measurement or predictive performance between CT and MRI could not be reliably assessed. In addition, the respiratory phase was not standardized across imaging examinations. Changes in diaphragmatic position during respiration may alter the spatial relationship between the HV and IVC and may therefore have influenced angle measurements. Because of the retrospective design and the small number of MRI procedures, the effects of imaging modality and respiratory phase could not be separately quantified.

Operator- and procedure-related factors represent another potential limitation. Although TJLB procedures were performed primarily by two experienced hepatologists throughout the study period, TJLB is an operator-dependent procedure, and procedural techniques and technical proficiency may have evolved over the approximately 10-year study period. An operator-specific analysis was not performed. Therefore, residual confounding related to differences or temporal changes in operator experience and procedural technique cannot be excluded.

The measured target HV differed between successful and unsuccessful procedures. In successful procedures, the angle was measured for the HV actually used for biopsy, whereas in unsuccessful procedures, it was measured for the right HV because this was the primary target for TJLB. This methodological difference may have introduced measurement bias. In addition, the type of biopsy needle was not standardized, and device-related differences may have influenced procedural outcomes.

Finally, this was a relatively small, single-center, retrospective observational study, and the statistical power to detect relevant associations may have been limited. Although Firth's penalized likelihood logistic regression was used because of the limited number of technical failure events, internal validation procedures, such as bootstrap resampling or cross-validation, were not performed. Therefore, the stability and generalizability of the multivariable model remain uncertain, and validation in larger independent cohorts is required.

Future prospective multicenter studies involving larger patient populations are required to validate these findings. Such studies should use standardized imaging and respiratory-phase protocols, include formal intraobserver and interobserver reproducibility assessments, and evaluate whether multiplanar or three-dimensional image analysis can improve measurement feasibility. External validation will also be essential to determine whether the exploratory 56° cutoff is reproducible and clinically useful across different institutions and clinical settings.

5. Conclusions

A larger HV–IVC confluence angle was associated with technical failure of TJLB and may represent a promising imaging biomarker with potential clinical utility. In patients in whom the angle can be measured reliably, an angle of approximately 56° or greater may serve as an exploratory marker of increased technical difficulty. However, given the substantial proportion of non-measurable procedures and the lack of external validation, this cutoff should not yet be used as a definitive clinical decision threshold. Further methodological refinement, standardized imaging protocols, formal reproducibility assessments, and validation in larger prospective multicenter cohorts are required to confirm these findings and determine the applicability of this imaging marker across different institutions and clinical settings.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/livers6040079/s1, Supplementary Table S1: Comparison between patients with measurable and non-measurable HV–IVC confluence angles; Supplementary Table S2: Two-by-two contingency table for the 56° HV–IVC confluence angle cutoff and technical outcome; Supplementary Table S3: Diagnostic performance of the 56° HV–IVC confluence angle cutoff for predicting technical failure; and Supplementary Figure S1: Receiver operating characteristic curve of the hepatic vein–inferior vena cava confluence angle.

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Abbreviations

The following abbreviations are used in this manuscript:

IJV	internal jugular vein
IVC	inferior vena cava
HV	hepatic vein
PLB	percutaneous liver biopsy
TJLB	transjugular liver biopsy

References

1. Bravo, A.A.; Sheth, S.G.; Chopra, S. Liver biopsy. *N. Engl. J. Med.* **2001**, *344*, 495–500. [CrossRef] [PubMed]
2. Rockey, D.C.; Caldwell, S.H.; Goodman, Z.D.; Nelson, R.C.; Smith, A.D. Liver biopsy. *Hepatology* **2009**, *49*, 1017–1044. [CrossRef] [PubMed]
3. Singhal, S.; Pradeep, M.D.; Inuganti, S.; Botcha, S.; Deepashree, D.T.; Uthappa, M.C. Percutaneous ultrasound-guided plugged liver biopsy: A single-centre experience. *Pol. J. Radiol.* **2021**, *86*, 239–245. [CrossRef] [PubMed]
4. Neuberger, J.; Patel, J.; Caldwell, H.; Davies, S.; Hebditch, V.; Hollywood, C.; Hubscher, S.; Karkhanis, S.; Lester, W.; Roslund, N.; et al. Guidelines on the use of liver biopsy in clinical practice from the British Society of Gastroenterology, the Royal College of Radiologists and the Royal College of Pathology. *Gut* **2020**, *69*, 1382–1403. [CrossRef] [PubMed]
5. Ble, M.; Procopet, B.; Miquel, R.; Hernandez-Gea, V.; García-Pagán, J.C. Transjugular liver biopsy. *Clin. Liver Dis.* **2014**, *18*, 767–778. [CrossRef] [PubMed]
6. Abujudeh, H.; Huggins, R.; Patel, A. Emergency transjugular liver biopsies in post-liver-transplant patients: Technical success and utility. *Emerg. Radiol.* **2004**, *10*, 268–269. [CrossRef] [PubMed]
7. Romero, M.; Bañares, R.; Salcedo, M.; Alvarez, E.; Peligros, I.; Clemente, G.; Cos, E. Diagnostic value of transjugular liver biopsy in liver transplant recipients. *Gastroenterol. Hepatol.* **1999**, *22*, 493–496. [PubMed]
8. Azoulay, D.; Raccuia, J.S.; Roche, B.; Reynes, M.; Bismuth, H. The value of early transjugular liver biopsy after liver transplantation. *Transplantation* **1996**, *61*, 406–409. [CrossRef] [PubMed]
9. Dawson, M.A.; McCarthy, P.H.; Walsh, M.E.; McLean, C.A.; Thomson, K.; Roberts, S.; Street, A.M. Transjugular liver biopsy is a safe and effective intervention to guide management for patients with a congenital bleeding disorder infected with hepatitis C. *Intern. Med. J.* **2005**, *35*, 556–559. [CrossRef]

10. Shin, J.L.; Teitel, J.; Swain, M.G.; Bain, V.G.; Adams, P.C.; Croitoru, K.; Peltekian, K.; Schweiger, F.; Simons, M.E.; Heathcote, E.J. A Canadian multicenter retrospective study evaluating transjugular liver biopsy in patients with congenital bleeding disorders and hepatitis C: Is it safe and useful? *Am. J. Hematol.* **2005**, *78*, 85–93. [CrossRef]
11. Saab, S.; Cho, D.; Quon, D.V.K.; Ibrahim, A.B.; Dong, P.; Marder, V.; Logan, L. Same-day outpatient transjugular liver biopsies in haemophilia. *Haemophilia* **2004**, *10*, 727–731. [CrossRef]
12. Stieltjes, N.; Ounnoughene, N.; Sava, E.; Paugy, P.; Roussel-Robert, V.; Rosenberg, A.R.; Terris, B.; Salmon-Céron, D.; Sogni, P. Interest of transjugular liver biopsy in adult patients with haemophilia or other congenital bleeding disorders infected with hepatitis C virus. *Br. J. Haematol.* **2004**, *125*, 769–776. [CrossRef] [PubMed]
13. DiMichele, D.M.; Mirani, G.; Canchis, P.W.; Trost, D.W.; Talal, A.H. Transjugular liver biopsy is safe and diagnostic for patients with congenital bleeding disorders and hepatitis C infection. *Haemophilia* **2003**, *9*, 613–618. [CrossRef] [PubMed]
14. Dohan, A.; Guerrache, Y.; Boudiaf, M.; Gavini, J.-P.; Kaci, R.; Soyer, P. Transjugular liver biopsy: Indications, technique and results. *Diagn. Interv. Imaging* **2014**, *95*, 11–15. [CrossRef]
15. García-Compean, D.; Cortés, C. Transjugular liver biopsy: An update. *Ann. Hepatol.* **2004**, *3*, 100–103. [CrossRef]
16. Lebrec, D.; Goldfarb, G.; Degott, C.; Rueff, B.; Benhamou, J.P. Transvenous liver biopsy: An experience based on 1000 hepatic tissue samplings with this procedure. *Gastroenterology* **1982**, *83*, 338–340. [PubMed]
17. Gamble, P.; Colapinto, R.F.; Stronell, R.D.; Colman, J.C.; Blendis, L. Transjugular liver biopsy: A review of 461 biopsies. *Radiology* **1985**, *157*, 589–593. [CrossRef] [PubMed]
18. Chevallier, P.; Dausse, F.; Berthier, F.; Saint-Paul, M.C.; Denys, A.; Schnyder, P.; Bruneton, J.N. Transjugular liver biopsy: Prospective evaluation of the angle formed between the hepatic veins and the vena cava main axis and modification of a semiautomated biopsy device in cases of an unfavorable angle. *Eur. Radiol.* **2007**, *17*, 169–173. [CrossRef] [PubMed]
19. Kalambokis, G.; Manousou, P.; Vibhakorn, S.; Marelli, L.; Cholongitas, E.; Senzolo, M.; Patch, D.; Burroughs, A.K. Transjugular liver biopsy: Indications, adequacy, quality of specimens, and complications. A systematic review. *J. Hepatol.* **2007**, *47*, 284–294. [CrossRef] [PubMed]
20. Bruzzi, J.F.; O'Connell, M.J.; Thakore, H.; O'Keane, C.; Crowe, J.; Murray, J.G. Transjugular liver biopsy: Assessment of safety and efficacy of the Quick-Core biopsy needle. *Abdom. Imaging* **2002**, *27*, 711–715. [CrossRef] [PubMed]
21. Ishikawa, T.; Kamimura, H.; Tsuchiya, A.; Togashi, T.; Watanabe, K.; Seki, K.-I.; Ohta, H.; Yoshida, T.; Ishihara, N.; Kamimura, T. Comparison of a new aspiration needle device and the Quick-Core biopsy needle for transjugular liver biopsy. *World J. Gastroenterol.* **2006**, *12*, 6339–6342. [CrossRef] [PubMed]
22. Choo, S.W.; Do, Y.S.; Park, K.B.; Kim, S.H.; Han, Y.H.; Choo, I.-W. Transjugular liver biopsy: Modified Ross transseptal needle versus Quick-Core biopsy needle. *Abdom. Imaging* **2000**, *25*, 483–485. [CrossRef] [PubMed]
23. Mammen, T.; Keshava, S.N.; Eapen, C.; Raghuram, L.; Moses, V.; Gopi, K.; Babu, N.S.; Ramachandran, J.; Kurien, G. Transjugular liver biopsy: A retrospective analysis of 601 cases. *J. Vasc. Interv. Radiol.* **2008**, *19*, 351–358. [CrossRef] [PubMed]
24. Behrens, G.; Ferral, H. Transjugular liver biopsy. *Semin. Interv. Radiol.* **2012**, *29*, 111–117. [CrossRef] [PubMed]
25. Eichholz, J.C.; Kirstein, M.M.; Book, T.; Wedemeyer, H.; Voigtländer, T. Transjugular liver biopsy and hepatic venous pressure gradient measurement in patients with and without liver cirrhosis. *Eur. J. Gastroenterol. Hepatol.* **2021**, *33*, 1582–1587. [CrossRef] [PubMed]
26. Brenard, R.; Horsmans, Y.; Rahier, J.; Druez, P.; Descamps, C.; Geubel, A. Transjugular liver biopsy: An experience based on 500 procedures. *Acta Gastroenterol. Belg.* **1997**, *60*, 138–141. [PubMed]
27. Soyer, P.; Fargeaudou, Y.; Boudiaf, M.; Rymer, R. Transjugular liver biopsy using ultrasonographic guidance for jugular vein puncture and an automated device for hepatic tissue sampling: A retrospective analysis of 200 consecutive cases. *Abdom. Imaging* **2008**, *33*, 627–632. [CrossRef] [PubMed]