Reliability of an ultrasonographical scoring system for diagnosis of sinusoidal obstruction syndrome / veno-occlusive disease in patients with hematopoietic stem cell transplantation

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Abstract

Purpose: Sinusoidal obstruction syndrome (SOS) / hepatic veno-occlusive disease (VOD) is a fatal complication after hematopoietic stem cell transplantation. We previously reported the usefulness of an ultrasonographical (US) scoring system, the Hokkaido US-based scoring system consisting of 10 parameters (HokUS-10): 1) hepatomegaly in the left lobe and 2) right lobe, 3) dilatation of the main portal vein (PV), 4) hepatofugal flow in the main PV, 5) decreased velocity of the PV, 6) dilatation of the para-umbilical vein (PUV), 7) appearance of blood flow signal in the PUV, 8) gallbladder (GB) wall thickening, 9) ascites, and 10) increased resistive index of the hepatic artery, for the diagnosis of SOS/VOD. However, the reliability of this system among operators remains elusive. Therefore, we prospectively evaluated the reliability of HokUS-10.

Methods: Twenty-four healthy volunteers and 40 patients with liver dysfunction were enrolled. Inter- and intra-operator reliabilities were analyzed using three sonographers.

Results: The median concordance rate of HokUS-10 among three sonographers and intra-operator in 24 volunteers was 92% (95% CI: 73-98%) and 98% (95% CI: 92-100%), respectively. In all 64 cases, in terms of the reliability between two sonographers for three representative US parameters (amount of ascites, GB wall thickening, and appearance of PUV blood flow signal), the median concordance rate was more than 98% (95% CI: 86-106%).

Conclusion: The inter- and intra-reliabilities of HokUS-10 were excellent. Thus, US might be a reliable tool for SOS/VOD diagnosis.

Keywords

sinusoidal obstruction syndrome, hepatic veno-occlusive disease, hematopoietic stem cell transplantation, operator reliability, ultrasonography

Introduction

Sinusoidal obstruction syndrome (SOS) / hepatic veno-occlusive disease (VOD) is a fatal complication mainly arising after hematopoietic stem cell transplantation (HSCT) [1]. Chemotherapy and/or radiotherapy for cancer treatment or a conditioning regimen of HSCT can cause hepatic sinusoidal cell damage leading to sinusoidal obstruction, which increases the downstream pressure and may lead to portal hypertension. Severe SOS/VOD has a high mortality rate >80% due to multiple organ failure [2].

Clinically, the Baltimore and modified Seattle criteria have been used for the diagnosis of SOS/VOD, which consist of high bilirubin level (≥2 mg/dl), ascites, right upper quadrant pain, and increasing body weight appearing within 21 days after HSCT. However, SOS/VOD is often difficult to diagnose because weight gain and hyperbilirubinemia can occur for reasons other than SOS/VOD.

Ultrasonography (US) was reported as a useful tool to diagnose SOS/VOD, but only in two prospective studies [3, 4] and some case reports, most of which were published more than 20 years ago [3-11] . Recently, US has been incorporated in the European Blood and Marrow Transplant (EBMT) diagnostic criteria of SOS/VOD [12, 13]. Concurrently, we previously reported the usefulness of the Hokkaido US-based scoring system (HokUS-10) consisting of 10 parameters for SOS/VOD diagnosis in a prospective manner [14] (Table 1). Since then, HokUS-10 has been cited in several articles [15-19]; however, it has not been validated [19].

In this study, we prospectively analyzed the operator reliability as an intra-facility validation for HokUS-10.

Materials and Methods

Study population

In this study, healthy volunteers with no liver dysfunction were enrolled between March 2017 and March 2019 based on their most recent medical examination. Patients diagnosed with liver dysfunction at the Hokkaido University Hospital were also enrolled. Fasting over 4 h was required for healthy volunteers and patients.

Transabdominal ultrasonography

US was performed using a PVT-375 BT (center frequency, 3.75 MHz), PVT-674 BT (center frequency, 6 MHz), and PVT-704 BT (center frequency, 7.5 MHz) attached to the Aplio™ XG (Canon Medical Systems Corp., Otawara, Japan).

Healthy volunteers

The inclusion criteria for healthy volunteers were as follows: age above 20 years, no history of liver dysfunction, and ability to undergo two US examinations within 1 week. Ten HokUS-10 parameters, which consist of B-mode and Doppler findings, were evaluated: hepatomegaly in the (1) left lobe (≥70 mm) and (2) right lobe (≥110 mm); (3) gallbladder (GB) wall thickening (≥6 mm) [Fig. 1]; (4) dilatation of the main portal vein (PV ≥12 mm); (5) dilatation of the paraumbilical vein (PUV ≥2 mm); (6) moderate amount of ascites defined by the presence of ascites in the Douglas pouch, subhepatic space, and spleno-renal interspace (maximum thickness ≥10 mm in least two sites) [Fig. 2]; (7) decreased mean velocity of the PV (time-averaged flow velocity [TAV], <10 cm/s); (8) congestion or hepatofugal flow in the main PV; (9) appearance of a blood flow signal in the PUV (congestion or hepatofugal flow) [Fig. 3]; and (10) increased resistive index (RI) of the proper hepatic artery (PHA, ≥0.75).

The anteroposterior diameter of (1) the left liver lobe was measured in front of the abdominal aorta so that the caudate lobe was not usually included. The anteroposterior diameter of (2) the right liver lobe was measured in front of the right kidney and on the anterior clavicular line. (3) GB wall thickening was measured using the intercostal or subcostal approach in the thickest part, avoiding lesions such as adenomyomatosis and polyps. The diameters of (4) the main PV and (5) PUV were measured using the subcostal approach. The diameters of (1) the left liver lobe, (2) right lobe, (3) GB wall thickening, and (4) main PV were measured from one leading edge to another, while the diameter of (5) the PUV was measured with the endo-cavity interface.

The velocity of (7) the PV was determined with an auto-trace measurement delineated with the subcostal approach, and an insonation angle was set at less than 60 degrees, with the sample gate set at more than 2/3 of the vessel diameter. (10) Measurement of the RI in

the PHA should be able to accurately recognize the maximum flow velocity (V_{max}) and the minimum flow velocity (V_{min}). Pulse-wave Doppler measurement was performed with shallow breath holding, and sensitivities and thresholds were properly adjusted.

HokUS-10 was evaluated on the same day by three sonographers ([A] M.N. with 33 years of experience, [B] Y.K. with 7 years of experience, and [C] R.T. with 2 years of experience) in random order. All sonographers were blinded to each other's results. Repetitive US for HokUS-10 was conducted by sonographer B within 1 week. Additionally, the duration of each examination was recorded and compared among the three sonographers.

Patients

After undergoing hematopoietic stem cell transplantation, patients are mostly in a sterile room and their condition is not good. Also, US findings of SOS/VOD are similar to liver cirrhosis and portal hypertension. Thus, we enrolled patients older than 20 years with liver dysfunction instead of SOS/VOD patients. We excluded patients who were unable to undergo a second US examination, required oxygen, and/or could not move independently.

Performing US three times and measuring the same 10 items each time in the same patient is not practical as it takes a considerable amount of time and is a burden to the patient. To minimize the burden placed on the patients, we selected three critical parameters to diagnose SOS/VOD. (1) GB wall thickening, (2) amount of ascites, and (3) appearance of a blood flow signal in the PUV of HokUS-10 were evaluated in patients with liver dysfunction on the same day by two sonographers in random order (A and B). The two sonographers were blinded to each other's results.

Re-assessments

Another sonographer ([D] T.I. with 5 years of experience) subsequently remeasured or reassessed all still images of the healthy volunteers blindly obtained by the first three sonographers. Five parameters ((1) the left and (2) right lobes of the liver, (3) GB wall thickening, (4) the main PV diameter, and (5) the PUV diameter) were remeasured on the monitor of the US machine. The RI of the PHA was calculated using proportional calculation after measuring the lengths of V_{max} and V_{min} by placing a ruler on the monitor of an offline personal computer. The mean velocity of the PV (TAV) was calculated by multiplying the time-averaged maximum velocity (TAMV) by a coefficient of 0.57 [20] on still images since the TAV of PV can only be measured in real time. In addition, the amount of ascites, congestion or hepatofugal flow in the main PV, and appearance of a blood flow signal in the PUV were reassessed using stored still US images.

Statistical analysis

Each HokUS-10 parameter was evaluated by the concordance rate and/or the kappa coefficient. The concordance rate is the value where the score of each item matches in the inter- and intra-operator assessment. HokUS-10's inter-operator reliability was evaluated with the concordance rate and Krippendorff's alpha coefficient (ordinal), and its intra-operator reliability was evaluated with the concordance rate and weighted kappa coefficient. The kappa coefficient and Krippendorff's alpha values were interpreted as follows: 0.00-0.20, slight agreement; 0.21-0.40, fair agreement; 0.41-0.60, moderate agreement; 0.61-0.80, substantial agreement; and 0.81-1.00, almost perfect agreement [21]. All statistical analyses were performed using standard statistical software (SPSS Statistics Version 23.0 [IBM, Armonk, NY, USA], BellCurve for Excel Version 2.11 [Social Survey Research Information Co., Ltd., Tokyo, Japan], and R [version 3.5.2. http://www.Rproject.org/]).

Results

One volunteer was excluded because she could not undergo a second US examination within 1 week. Thus, 24 healthy volunteers and 40 patients were enrolled. The characteristics of the study population are shown in Table 2.

Inter-operator reliability of HokUS-10

The inter-operator reliability in healthy volunteers is shown in Table 3. The concordance rate was higher than 80% for hepatic diameter in the left lobe, diameter of the main PV, blood flow direction in the main PV, dilatation of the PUV, appearance of a blood flow signal in the PUV, GB wall thickening, and existence/amount of ascites. The concordance rate for hepatic diameter in the right lobe, PV mean velocity, and RI of the PHA were 71%, 63%, and 58%, respectively. Agreement could be evaluated by Fleiss' kappa coefficient for five items. RI of the PHA showed low agreement (0.16); however, the other four US items showed moderate to almost perfect agreement. The concordance rate (with a cutoff value of 5 or more) and Krippendorff's alpha coefficient of HokUS-10 were 100% and 0.63, respectively.

The examination times of sonographers A and B were significantly faster than that of sonographer C. The median examination times of sonographers A, B, and C were 9.8 min (range, 5.5-15.9 min), 8.2 min (range, 5.8-15.4 min), and 12.6 min (range, 5.9-23.2 min), respectively.

Intra-operator reliability of HokUS-10

The intra-operator reliability in healthy volunteers is shown in Table 4. The intra-operator reliability was very good, with a higher than 88% concordance rate for all 10 items, and there were no items with a significantly lower kappa coefficient. The HokUS-10 concordance rate and weighted kappa coefficient showed almost perfect agreement, 100% and 0.87, respectively.

The examination times did not differ between the first and second US examinations. The median examination times of the first and second examinations were 8.2 min (range, 5.8-15.4 min) and 9.4 min (range, 5.3-14.0 min), respectively.

Inter-operator reliability of three US criteria

The inter-operator reliability in all study participants is shown in Table 5. The inter-operator reliability was very good, with a higher than 91% concordance rate. There was high agreement for all three US criteria. The kappa coefficient of the amount of ascites and appearance of a PUV blood flow signal showed almost perfect agreement, while GB wall thickening showed substantial agreement.

Re-assessments

Remeasurements in healthy volunteers are shown in Table 6. No parameters showed significant differences in the measured values between all three sonographers and sonographer D. There was no significant difference between these measurements. The concordance rate (with a cutoff value of 5 or more) and Krippendorff's alpha coefficient of HokUS-10 were 100% and 0.64, respectively.

Discussion

The inter-operator reliability among three sonographers with varying years of experience was primarily good. A low tendency of differences in the measurements of the right lobe, PV velocity, and RI of the PHA could have resulted from differences in selecting the measurement position, setting the Doppler angle, and the degree of breath-holding in the subjects. In the measurement of RI of the PHA, the differences could have occurred due to the adjustment of the threshold degree in auto-tracing. In some cases, due to the deeper location of the PHA and interference of intestinal gas, the Doppler wave form became obscure, and auto-tracing could not accurately detect the peak and end-diastolic velocity.

To improve accuracy, it is recommended to measure RI using the intercostal approach instead of the subcostal one. Measurement of PV mean velocity is highly influenced by several factors. First, Doppler US for measuring velocity requires the insonation angle to be within 60 degrees; otherwise, overestimation can occur. For instance, the overestimation error becomes 50% at 80 degrees, and 15% at 60 degrees [24]. The PV

main trunk naturally runs vertical to the Doppler insonation angle. Operators try to set the angle at less than 60 degrees by tilting the probe and/or applying pressure. The degree of tilting and pressure may sometimes slightly differ among operators, which may result in different velocity values. Second, the PV main trunk is located at a deeper area and intestinal gas can easily interfere, as is the case for the PHA. The above may interfere with accurate measurements but could be expected to improve with use of the intercostal approach [22, 23].

Dilatation and the appearance of PUV blood flow signal are important findings, and they showed good agreement. Consequently, the intra-operator reliability was excellent (85%) or had a higher agreement rate for all items.

There was no difference among the three sonographers' measurements and re-measurements by sonographer D; most of the re-measurements and assessments matched well. This result suggests that measurements and assessment of US images can be performed afterward, when the US images are correctly captured. Overall, the scoring of the HokUS-10 was generally consistent between both inter- and intra-operators.

There were a few limitations. First, this study was mainly conducted with healthy volunteers. Since a few items showed positive scores, we could not perform statistical analyses for other items, which were ascites, direction of PV flow, and appearance of PUV blood flow signals. Second, this study was conducted at a single institution. In the future, larger multicenter population-based studies are warranted to confirm the validity of the HokUS-10 scoring system.

Conclusion

The inter- and intra-reliabilities of HokUS-10 might be acceptable for the assessment of SOS/VOD under a suitable unified assessment.

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Authorship

T. I. and M. N. participated in the research design, the writing of the paper, the performance of the research, and data analysis.
Y. K. and R. T. participated in the performance of the research.
I. Y. and R. T. performed statistical analysis.
H. S. participated in the review of the paper.
J. S. and S. T. participated in the research design, the data analysis, and the review of the paper.
T. T. participated in the research design, data analysis, and the writing and review of the paper.

Compliance with ethical standards

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical statement

This study was approved by the institutional review board (016-0075), and written informed consent was obtained from all study participants in accordance with the World Medical Association Declaration of Helsinki: Ethical principles for medical research involving human subjects, 2013.

Role of the funding source

There is none.

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Figure captions

Fig. 1 Gallbladder thickening. B-mode ultrasonography shows stratified thickening (≥6 mm).

Fig. 2 Moderate-to-severe ascites in the Douglas pouch (a), subhepatic space (b), and spleno-renal interspace (c).
*Catheter and balloon in the urinary bladder, † Liver, ‡ Spleen

Fig. 3 Dilatation of the paraumbilical vein (≥2 mm) and the appearance of hepatofugal flow can be seen.

Table 1. HokUS-10

Parameters	Description	Points
Hepatic left lobe vertical diameter	≥70mm	1
Hepatic right lobe vertical diameter	≥110mm	1
Gallbladder wall thickening	≥6mm	1
PV diameter	≥12mm	1
PUV diameter	≥2mm	2
Amount of ascites	Mild	1
	Moderate to severe	2
PV mean velocity	<10cm/s	1
Direction of PV flow	Congestion or hepatofugal flow	1
Appearance of PUV blood flow signal	Yes (Congestion or hepatofugal flow)	2
Proper hepatic artery RI	≥0.75	1

RI was calculated by the formula of Vmax - Vmin / Vmax.

PV, portal vein; PUV, paraumbilical vein; PV mean velocity, time-averaged flow velocity (TAV); RI, resistive index

Table 2. Characteristics of the study population

	Healthy volunteers (n=24)	**Patients (n=40)**	**Total (n=64)**
Gender (male/female)	16/8	21/19	37/27
Age, years	39 (24 - 65)	58 (21 - 85)	52 (21 - 85)
Weight, kg	66 (40 - 89)	60 (37 - 114)	64 (37 - 114)
Height, cm	167 (153 - 181)	163 (136 - 183)	165 (136 - 183)
BMI, kg/m^2	22.8 (16.0 - 28.2)	23.2 (15.8 - 40.0)	22.8 (15.8 - 40.0)
2^{nd} time US (day from 1^{st} study)	2 (1 - 6)	-	-
Clinical backgrounds			
HBV positivity	-	16 (40.0%)	-
HCV positivity	-	7 (17.5%)	-
HEV positivity	-	1 (2.5%)	-
NAFLD	-	4 (10.0%)	-
ALD	-	2 (5.0%)	-
AIH	-	2 (5.0%)	-
Others	-	8 (20.0%)	-

All values are expressed as median (range), unless otherwise noted as n (%) for number (frequency)
BMI, body mass index; HBV, hepatitis B virus; HCV, hepatitis C virus; HEV, hepatitis E virus; NAFLD, non-alcoholic fatty liver disease; ALD, alcoholic liver disease; AIH, autoimmune hepatitis; Others included primary biliary cholangitis, Idiopathic portal hypertension, drug induced liver disease, and thrombocytopenia, anasarca, fever, reticulin fibrosis and organomegaly syndrome, and idiopathic cirrhosis

Table 3. Inter-operator reliability of HokUS-10 in healthy volunteers (n=24)

Parameters	Concordance rate	Agreement	Sonographers (US experiences)		
			A (33-years)	B (7-years)	C (2-years)
Hepatic left lobe vertical diameter (mm)	96%	0.92	48.6 (25.9 - 82.0)	49.1 (30.4 - 80.1)	53.0 (31.2 - 83.0)
Hepatic right lobe vertical diameter (mm)	71%	0.57	104.6 (85.9 - 133.4)	101.3 (87.3 - 122.9)	104.9 (84.0 - 132.4)
Gallbladder wall thickening (mm)	100%	NA*	1.2 (0.8 - 2.9)	1.3 (0.8 - 2.7)	1.4 (0.8 - 2.5)
PV diameter (mm)	88%	NA	9.7 (6.0 - 12.3)	10.2 (7.8 - 12.4)	9.4 (6.3 - 11.7)
PUV diameter (mm)	100%	NA*	0.8 (0.4 - 1.2)	0.9 (0.7 - 1.1)	0.9 (0.5 - 1.5)
Amount of ascites (points)	83%	0.63	0 (0 - 1)	0 (0 - 1)	0 (0 - 1)
PV mean velocity (cm/s)	63%	NA	14.2 (9.7 - 23.2)	11.6 (7.7 - 34.2)	14.3 (8.4 - 42.0)
Direction of PV flow (points)	100%	NA*	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)
Appearance of PUV blood flow signal (points)	100%	NA*	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)
Proper hepatic artery RI	58%	0.16	0.69 (0.50 - 0.85)	0.73 (0.63 - 0.85)	0.69 (0.46 - 0.81)
HokUS-10 [cut off value 5]	100%	0.63	1 (0 - 4)	1 (0 - 4)	1 (0 - 3)
Examination time (minutes)	-	-	9.8 (5.5 - 15.9)	8.2 (5.8 - 15.4)	12.6 (5.9 - 23.2)

Values are expressed as median (range). Agreement, each item of HokUS-10 was evaluated by the Fleiss' Kappa coefficient, and whether the cutoff value was 5 or more was evaluated with the Krippendorff's alpha coefficient. RI was calculated by the formula of V_{max} - V_{min} / V_{max}.

NA, not available (NA*, Kappa coefficient was inestimable because the degree of match was too high); PV, portal vein; PUV, paraumbilical vein; PV mean velocity, time-averaged flow velocity (TAV); RI, resistive index.

Table 4. Intra-operator reliability of HokUS-10 in healthy volunteers (n=24)

Parameters	Concordance rate	Kappa	Sonographer B (7-years)	
			First scan	Second scan
Hepatic left lobe vertical diameter (mm)	96%	0.86	49.1 (30.4 - 80.1)	48.2 (28.6 - 78.1)
Hepatic right lobe vertical diameter (mm)	100%	1.00	101.3 (87.3 - 122.9)	98.7 (88.6 - 126.2)
Gallbladder wall thickening (mm)	100%	NA*	1.3 (0.8 - 2.7)	1.3 (0.8 - 2.7)
PV diameter (mm)	92%	0.46	10.2 (7.8 - 12.4)	10.0 (8.4 - 12.1)
PUV diameter (mm)	100%	NA*	0.9 (0.7 - 1.1)	0.8 (0.5 - 1.4)
Amount of ascites (points)	96%	0.88	0 (0 - 1)	0 (0 - 1)
PV mean velocity (cm/s)	88%	0.73	11.6 (7.7 - 34.2)	11.7 (7.1 - 22.0)
Direction of PV flow (points)	100%	NA*	0 (0 - 0)	0 (0 - 0)
Appearance of PUV blood flow signal (points)	100%	NA*	0 (0 - 0)	0 (0 - 0)
Proper hepatic artery RI	88%	0.75	0.73 (0.63 - 0.85)	0.72 (0.64 - 0.83)
HokUS-10 [cut off value 5]	100%	0.87	1 (0 - 4)	1 (0 - 4)
Examination time (minutes)	-	-	8.2 (5.8 - 15.4)	9.4 (5.3 - 14.0)

Values are expressed as median (range). The RI was calculated by the formula of V_{max} - V_{min} / V_{max}.

Kappa, weighted Kappa coefficient; NA, not available (NA*, Kappa coefficient was inestimable because the degree of match was too high); PV, portal vein; PUV, paraumbilical vein; PV mean velocity, time-averaged flow velocity (TAV); RI, resistive index.

Table 5. Inter-operator reliability of three items in the entire study population (n=64)

Parameters	Concordance rate	Kappa	Sonographers (US experiences)	
			A (33-years)	B (7-years)
Gallbladder wall thickening (mm)	98%	0.79	1.1 (0.6 - 10.1)	1.3 (0.8 - 12.8)
Amount of ascites (points)	91%	0.85	0 (0 - 2)	0 (0 - 2)
Appearance of PUV blood flow signal (points)	98%	0.92	0 (0 - 2)	0 (0 - 2)

Values are expressed as median (range)

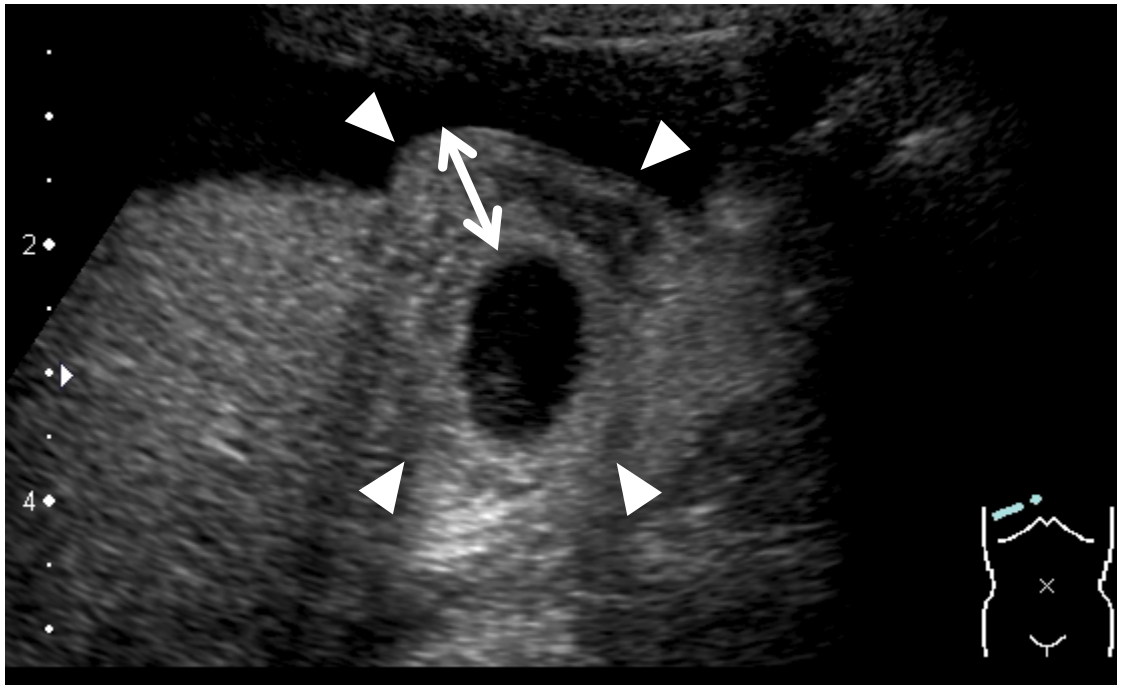
Kappa, weighted Kappa coefficient; PUV, paraumbilical vein

Table 6. Re-assessments in healthy volunteers (n=24)

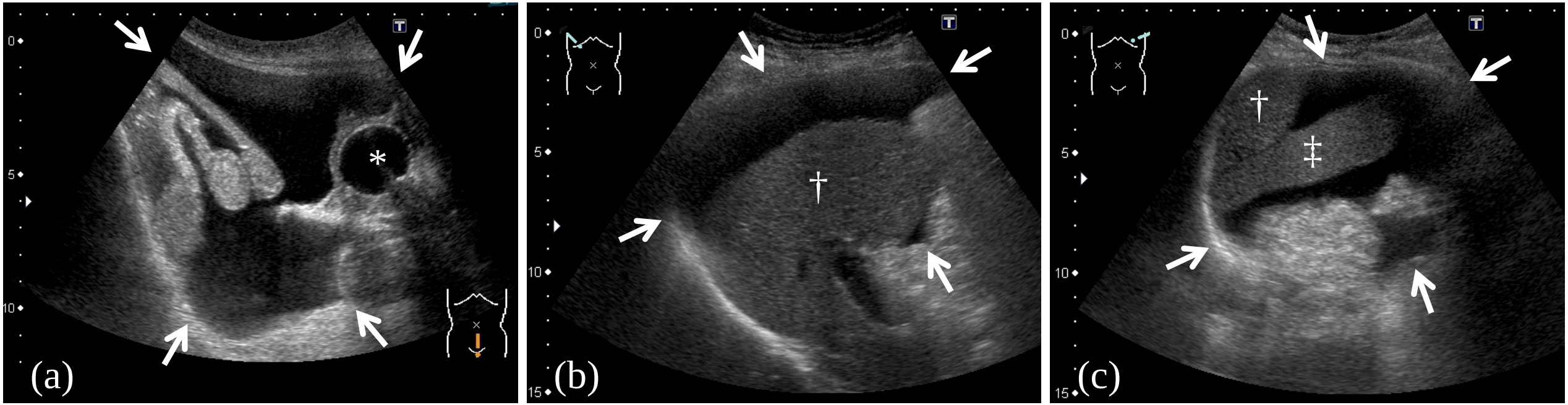
	Images captured by Sonographer A		Images captured by Sonographer B		Images captured by Sonographer C	
	measurement		measurement		measurement	
Parameters	**Sonographer A**	**Sonographer D**	**Sonographer B**	**Sonographer D**	**Sonographer C**	**Sonographer D**
Hepatic left lobe vertical diameter (mm)	48.6 (25.9 - 82.0)	48.5 (26.7 - 82.1)	49.1 (30.4 - 80.1)	50.8 (29.4 - 81.8)	53.0 (31.2 - 83.0)	53.1 (30.4 - 83.4)
Hepatic right lobe vertical diameter (mm)	104.6 (85.9 - 133.4)	106.4 (83.2 - 132.6)	101.3 (87.3 - 122.9)	101.3 (88.8 - 126.3)	104.9 (84.0 - 132.4)	106.5 (84.8 - 133.8)
Gallbladder wall thickening (mm)	1.2 (0.8 - 2.9)	1.3 (0.8 - 2.5)	1.3 (0.8 - 2.7)	1.4 (0.8 - 2.4)	1.4 (0.8 - 2.5)	1.4 (0.8 - 2.4)
PV diameter (mm)	9.7 (6.0 - 12.3)	10.5 (7.1 - 13.0)	10.2 (7.8 - 12.4)	10.0 (8.0 - 12.3)	9.4 (6.3 - 11.7)	9.7 (7.0 - 12.8)
PUV diameter (mm)	0.8 (0.4 - 1.2)	0.7 (0.4 - 1.1)	0.9 (0.7 - 1.1)	0.8 (0.5 - 1.4)	0.9 (0.5 - 1.5)	0.8 (0.5 - 1.2)
Amount of ascites (points)	0 (0 - 1)	0 (0 - 1)	0 (0 - 1)	0 (0 - 1)	0 (0 - 1)	0 (0 - 1)
PV mean velocity (cm/s)	14.2 (9.7 - 23.2)	15.8 (10.9 - 29.2)	11.6 (7.7 - 34.2)	12.9 (7.9 - 42.1)	14.3 (8.4 - 42.0)	15.0 (10.5 - 52.2)
Direction of PV flow (points)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)
Appearance of PUV blood flow signal	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)
Proper hepatic artery RI	0.69 (0.50 - 0.85)	0.71 (0.56 - 0.87)	0.73 (0.63 - 0.85)	0.72 (0.63 - 0.83)	0.69 (0.46 - 0.81)	0.69 (0.50 - 0.81)
HokUS-10 [cut off value 5]	1 (0 - 4)	1 (0 - 4)	1 (0 - 4)	1 (0 - 4)	1 (0 - 3)	1 (0 - 3)

Values are expressed as median (range). RI was calculated by the formula of V_{max} - V_{min} / V_{max}. PV mean velocity by Sonographer A, B, C was time-averaged flow velocity (TAV). The PV mean velocity in Sonographer D was calculated by multiplying the time-averaged maximum velocity (TAMV) by 0.57. PV, portal vein; PUV, paraumbilical vein; RI, resistive index

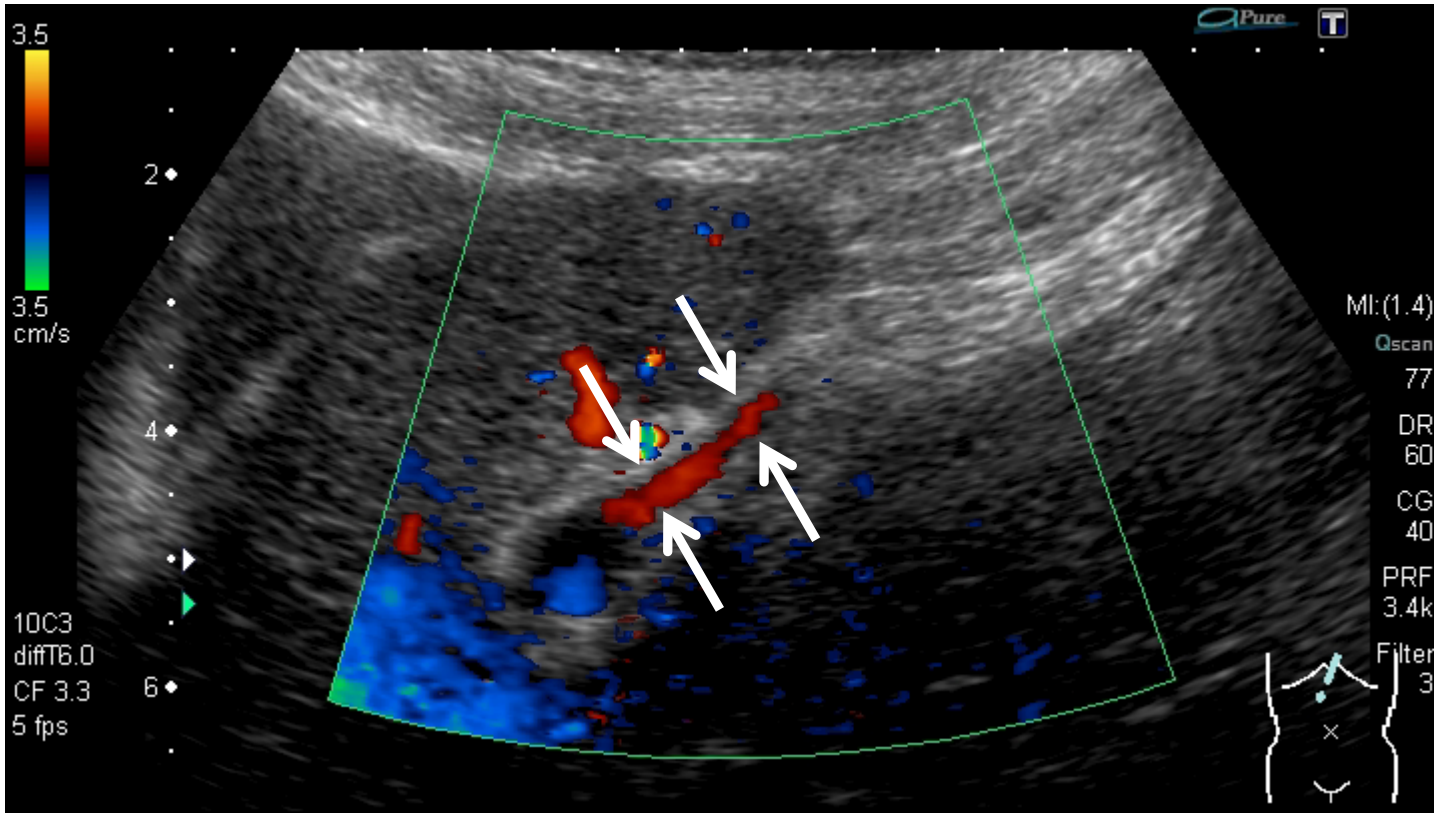
Figue.1



Figue.2



Figue.3


3.5
3.5
cm/s
2
4
6
10C3
diffT6.0
CF 3.3
5 fps
MI:(1.4)
Qscan
77
DR
60
CG
40
PRF
3.4k
Filter
3