Impact of spider nevus and subcutaneous collateral vessel of chest/abdominal wall on outcomes of liver cirrhosis

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Abstract

Introduction: Spider nevus and subcutaneous collateral vessel of the chest/abdominal wall are common in liver cirrhosis. This prospective study aimed to evaluate the impact of spider nevus and subcutaneous collateral vessel of the chest/abdominal wall on the outcomes of cirrhotic patients.
Material and methods: We prospectively enrolled patients with a diagnosis of liver cirrhosis consecutively admitted to our department. We recorded the number and location of spider nevi and subcutaneous collateral vessels of the chest/abdominal wall. Clinical profiles and survival were compared according to the presence of spider nevus and subcutaneous collateral vessel of the chest/abdominal wall. The study was registered (NCT02468479).
Results: Overall, 198 patients were enrolled between June 2015 and May 2016. The median follow-up duration was 350 days. The prevalence of spider nevus and subcutaneous collateral vessel of the chest/abdominal wall was 47% and 29.8%, respectively. Patients with spider nevi had a significantly higher proportion of alcohol abuse (54.84% vs. 26.67%, $p < 0.001$). Both spider nevus and subcutaneous collateral vessel of the chest/abdominal wall were significantly associated with higher Child-Pugh (8.35 ±2.19 vs. 7.47 ±1.91, $p = 0.005$; 8.57 ±2.20 vs. 7.60 ±1.98, $p = 0.002$) and MELD scores (9.91 ±6.41 vs. 7.43 ±5.40, $p = 0.008$; 10.77 ±6.76 vs. 7.68 ±5.42, $p = 0.003$). The cumulative survival was not significantly different between patients with and without spider nevi of the chest/abdominal wall ($p = 0.951$). Patients with subcutaneous collateral vessels of the chest/abdominal wall had significantly worse cumulative survival ($p = 0.018$).
Conclusions: Presence of spider nevus and subcutaneous collateral vessel of the chest/abdominal wall indicated more severe liver dysfunction. Subcutaneous collateral vessel of the chest/abdominal wall should be a simple and important predictor for the overall survival of cirrhotic patients.

Key words: physical, complication, prognosis, survival, Child-Pugh.

Introduction

Spider nevus is a common sign of liver cirrhosis [1–3]. Spider nevus is so named because of its spider-like appearance in which there is a central red arteriole and radiating thin-walled vessels resembling the body and legs of a spider, respectively. In the general population, it has been reported that the presence of spider nevus is associated with thyrotox-

icosis and excessive estrogen, such as pregnancy and oral contraceptives. In cirrhotic patients, the underlying mechanisms of spider nevus include the disturbance of sex hormones (i.e., higher ratio of estradiol to testosterone, increased level of luteinizing hormone, and decreased level of testosterone in male patients) [4–6], angiogenesis (i.e., elevated expression of vascular endothelial growth factor and fibroblast growth factor) [7], vasodilation (increased level of substance P) [8], alcohol abuse [4], hyperdynamic circulation state [9], and liver dysfunction [4, 5]. Evidence suggests that spider nevus can predict the grade of liver fibrosis in patients with chronic liver diseases [10–12], and is closely associated with the likelihood of hepatopulmonary syndrome in patients with portal hypertension [13, 14].

Subcutaneous collateral vessels of the chest/abdominal wall are also frequently observed in cirrhotic patients [15]. In the setting of portal hypertension, paraumbilical vein dilation further leads to the occurrence of subcutaneous collateral vessels of the chest/abdominal wall and even caput medusae [16, 17]. Sometimes, the subcutaneous collateral vessel of the abdominal wall acts as the drainage vessel of intra-abdominal varices, such as stomal and jejunal varices [18, 19]. However, the clinical significance of subcutaneous collateral vessels of the chest/abdominal wall in liver cirrhosis remains unclear.

We conducted a prospective observational study to analyze the impact of spider nevus and subcutaneous collateral vessel of the chest/abdominal wall on the outcomes of patients with liver cirrhosis.

Material and methods

This was a prospective observational study. The study protocol was approved by the Medical Ethical Committee of our hospital. The human study complied with the Declaration of Helsinki. The approval number was No. k(2015)06. The study was also registered in the website clinicaltrial.gov. The register number was NCT02468479. The inclusion criteria were as follows: 1) patients with a diagnosis of liver cirrhosis; and 2) agreement to perform the physical examinations. The exclusion criteria were as follows: 1) a repeated admission; and 2) a confirmed diagnosis of malignancy. The primary endpoint was survival.

Liver cirrhosis was diagnosed based on the clinical symptoms related to liver diseases and portal hypertension, biochemical laboratory tests, liver stiffness measurement, and hepatic ultrasound, computed tomography, and/or magnetic resonance images [20]. If necessary, a liver biopsy was performed. Grades of ascites and hepatic encephalopathy were based on the practice guidelines [21, 22]. Management of liver cirrhosis and portal hypertension related complications was based on the current practice guidelines [21–24].

At admission, three investigators (RW, YP, and XQ) performed the physical examinations for all eligible patients. In the case of uncertainty, they would discuss it with two primary investigators (HL and XG). According to the number of spider nevi of the chest/abdominal wall, they were divided into 0, 1–2, 3–4, and ≥ 5. According to the location of spider nevi, they were divided into chest wall alone, abdominal wall alone, and both chest and abdominal walls. According to the location of subcutaneous collateral vessels of the chest/abdominal wall, they were divided into chest wall alone, abdominal wall alone, and both chest and abdominal walls. Other baseline data were collected about the demographic profile, major clinical symptoms, etiology of liver cirrhosis, white blood cells, platelet count, hemoglobin, and hepatic, renal, and coagulation function. Child-Pugh and MELD scores were calculated according to the relevant formulae [25, 26].

Patients were followed until lost to follow-up, death, or December 31, 2016. Follow-up data were prospectively collected by two investigators (RW and XQ) from the re-admission records and by telephone contacts.

Statistical analysis

Statistical analyses were performed using SPSS statistics 17.0.0 and MedCalc 11.4.2.0 software. Continuous data were expressed as the mean ± standard deviation and median (range) and compared using the independent *t* test or non-parametric Mann-Whitney *U* test. Categorical data were expressed as frequency (percentage) and compared using the Pearson χ^2 test or Fisher's exact test. Cumulative risk was estimated by Kaplan-Meier curve analysis and compared by the log-rank test. A two-sided *p*-value of < 0.05 was considered statistically significant.

Results

Patients

A total of 198 patients were included in the prospective study between June 2015 and May 2016. Patient characteristics are shown in Table I. The majority of patients were male (64.6%), had a history of alcohol abuse (39.9%) and hepatitis B virus infection (32.3%), and were in Child-Pugh class B (51.3%). The in-hospital mortality was 2.02% (4/198). Two patients underwent liver transplantation during follow-up. The overall mortality was 14.14% (28/198) during a mean follow-up duration of 327.5 ±152.97 days (median: 350 days; range: 6–567).

Table I. Baseline characteristics of 198 patients

Variables	No. pts. with available data	Mean ± SD or Frequency (percentage)	Median (range)
Sex (male/female), *n* (%)	198	128 (64.65)/70 (35.35)	
Age [years]	198	56.95 ±11.41	56.38 (26.76–88.10)
Etiology of liver diseases, *n* (%):			
Hepatitis B virus infection	198	64 (32.30)	
Hepatitis C virus infection	198	18 (9.09)	
Alcohol abuse	198	79 (39.90)	
Drug-induced liver injury	198	10 (5.05)	
Autoimmune liver disease	198	9 (4.55)	
Previous gastrointestinal bleeding, *n* (%)	198	106 (53.54)	
Hepatic encephalopathy at admission, *n* (%)	198	16 (8.08)	
Gastrointestinal bleeding at admission, *n* (%)	198	106 (53.54)	
Jaundice at admission, *n* (%)	198	36 (18.18)	
Ascites at admission (no/mild/moderate-severe), *n* (%)	198	80 (40.40)/ 39 (19.70)/79 (39.90)	
Spider nevus of chest/abdominal wall, *n* (%):	198	93 (46.97)	
Number (1–2/3–4/≥ 5)	93	46 (49.46)/ 20 (21.51)/27 (29.03)	
Location (chest alone/abdomen alone/both chest and abdomen)	93	91 (97.85)/ 0 (0.00)/2 (2.15)	
Subcutaneous collateral vessel of chest/abdominal wall, *n* (%):	198	59 (29.80)	
Location (chest alone/abdomen alone/both chest and abdomen)	59	10 (16.95)/33 (55.93)/16 (27.12)	
Laboratory tests:			
Red blood cells [× 10^{12}/l]	197	3.14 ±0.83	3.04 (1.42–5.64)
Hemoglobin [g/l]	197	92.18 ±27.71	91.00 (37.00–170.00)
White blood cells [× 10^{9}/l]	197	5.14 ±3.39	4.30 (1.10–23.10)
Platelets [× 10^{9}/l]	197	91.94 ±59.00	75.00 (11.00–346.00)
Alanine aminotransferase [U/l]	195	41.62 ±60.47	25.52 (4.61–590.00)
Aspartate aminotransferase [U/l]	195	62.34 ±80.89	37.66 (6.97–719.84)
Alkaline phosphatase [U/l]	195	126.33 ±105.26	95.00 (33.00–850.45)
γ-Glutamyl transpeptidase [U/l]	195	115.38 ±176.31	46.16 (9.00–981.00)
Total bilirubin [μmol/l]	195	37.06 ±46.01	23.40 (6.40–319.90)
Prothrombin time [s]	193	16.55 ±3.31	15.70 (11.30–31.60)
International normalized ratio	191	1.38 ±0.38	1.29 (0.83–3.03)
Activated partial thromboplastin time [s]	192	40.54 ±5.99	39.65 (29.20–57.80)
Albumin [g/l]	194	30.35 ±6.84	29.70 (16.10–48.10)
Serum sodium [mmol/l]	196	138.85 ±3.91	138.40 (120.70–151.60)
Serum potassium [mmol/l]	196	3.91 ±0.46	3.87 (2.48–5.60)
Blood urea nitrogen [mmol/l]	194	7.57 ±5.88	5.72 (1.71–47.21)
Serum creatinine [μmol/l]	194	78.44 ±65.04	65.41 (32.14–533.70)
Child-Pugh score	189	7.89 ±2.09	8.00 (5.00–14.00)
Child-Pugh class A/B/C, *n* (%)	189	55 (29.10)/ 97 (51.32)/37 (19.58)	
MELD score	187	8.64 ±6.02	7.70 (–2.38–28.02)
In-hospital death, *n* (%)	198	4 (2.02)	
Overall death, *n* (%)	198	28 (14.14)	

SD – standard deviation, MELD – model for end-stage liver disease.

Table II. Comparison between patients with and without spider nevus of chest/abdominal wall

Variables	With spider nevus of chest/abdominal wall			Without spider nevus of chest/abdominal wall			*P*-value
	N	Mean ± SD or Frequency (percentage)	Median (range)	*N*	Mean ± SD or Frequency (percentage)	Median (range)	
Sex (male/female), *n* (%)	93	68 (73.12)/25 (26.88)		105	60 (57.14)/45 (42.86)		0.028
Age (years]	93	54.19 ±10.03	53.83 (27.08–82.34)	105	59.39 ±12.03	59.89 (26.76–88.10)	0.001
Etiology of liver diseases, *n* (%):							
Hepatitis B virus infection	93	25 (26.88)		105	39 (37.14)		0.104
Hepatitis C virus infection	93	5 (5.38)		105	13 (12.38)		0.099
Alcohol abuse	93	51 (54.84)		105	28 (26.67)		< 0.001
Drug-induced liver injury	93	3 (3.23)		105	7 (6.67)		0.436
Autoimmune liver disease	93	4 (4.30)		105	5 (4.76)		0.852
Previous gastrointestinal bleeding, *n* (%)	93	42 (45.16)		105	64 (60.95)		0.038
Hepatic encephalopathy at admission, *n* (%)	93	43 (46.24)		105	63 (60.00)		0.073
Gastrointestinal bleeding at admission, *n* (%)	93	20 (21.51)		105	16 (15.24)		0.339
Jaundice at admission, *n* (%)	93	2 (2.15)		105	2 (1.90)		0.701
Ascites at admission (no/mild/moderate-severe), *n* (%)	93	31 (33.33)/17 (18.28)/45 (48.39)		105	49 (46.67)/22 (20.95)/34 (32.38)		0.063
Subcutaneous collateral vessel of chest/abdominal wall, *n* (%):	93	35 (37.63)/58 (62.37)		105	24 (22.86)/81 (77.14)		0.035
Location (chest alone/abdomen alone/both chest and abdomen)	35	5 (14.29)/17 (48.57)/13 (37.14)		24	5 (20.83)/16 (66.67)/3 (12.50)		0.112
Laboratory tests:							
Red blood cells [× 10^{12}/l]	93	3.20 ±0.83	3.11 (1.69–5.06)	104	3.09 ±0.83	2.97 (1.42–5.64)	0.356
Hemoglobin [g/l]	93	97.60 ±27.95	96.00 (47.00–170.00)	104	87.33 ±26.71	83.00 (37.00–164.00)	0.012
White blood cells [× 10^{9}/l]	93	5.27 ±2.82	4.50 (1.70–16.00)	103	5.04 ±3.86	4.00 (1.10–23.10)	0.047
Platelets [× 10^{9}/l]	93	95.55 ±57.36	81.00 (19.00–282.00)	104	88.71 ±60.53	73.50 (11.00–346.00)	0.316
Alanine aminotransferase [U/l]	92	48.64 ±77.82	28.50 (6.24–590.00)	103	35.36 ±38.32	22.07 (4.61–192.51)	0.005

Table II. Cont.

Variables	With spider nevus of chest/abdominal wall			Without spider nevus of chest/abdominal wall			*P*-value
	N	Mean ± SD or Frequency (percentage)	Median (range)	*N*	Mean ± SD or Frequency (percentage)	Median (range)	
Aspartate aminotransferase [U/l]	92	77.72 ±101.85	47.07 (13.54–719.84)	103	48.60 ±52.79	31.20 (6.97–300.70)	< 0.001
Alkaline phosphatase [U/l]	92	131.27 ±95.28	101.74 (33.00–649.21)	103	121.91 ±113.72	85.59 (35.36–850.45)	0.049
γ-Glutamyl transpeptidase [U/l]	92	153.41 ±204.87	73.60 (9.00–981.00)	103	81.41 ±138.59	34.65 (9.67–797.00)	< 0.001
Total bilirubin [μmol/l]	92	48.13 ±59.90	28.95 (6.40–319.90)	103	27.18 ±24.81	20.10 (7.10–179.20)	0.004
Prothrombin time [s]	93	16.97 ±3.54	15.90 (11.70–31.60)	100	16.15 ±3.06	15.55 (11.30–29.70)	0.080
International normalized ratio	92	1.43 ±0.40	1.31 (0.89–3.03)	99	1.34 ±0.35	1.25 (0.83–3.00)	0.065
Activated partial thromboplastin time [s]	93	41.43 ±6.08	40.30 (29.40–54.50)	99	39.71 ±5.81	38.60 (29.20–57.80)	0.040
Albumin [g/l]	92	29.84 ±6.91	29.40 (16.10–47.20)	102	30.80 ±6.78	30.20 (17.20–48.10)	0.404
Serum sodium [mmol/l]	92	136.67 ±4.18	137.50 (120.70–144.60)	104	138.89 ±3.34	139.40 (130.40–151.60)	< 0.001
Serum potassium [mmol/l]	92	3.90 ±0.45	3.85 (2.73–4.88)	104	3.92 ±0.47	3.87 (2.48–5.60)	0.987
Blood urea nitrogen [mmol/l]	93	7.43 ±6.59	5.50 (1.90–47.21)	101	7.69 ±5.16	6.03 (1.71–30.40)	0.134
Serum creatinine [μmol/l]	93	81.90 ±72.93	65.69 (32.14–533.70)	101	75.25 ±57.00	65.30 (34.90–440.06)	0.651
Child-Pugh score	91	8.35 ±2.19	8.00 (5.00–14.00)	98	7.47 ±1.91	7.00 (5.00–13.00)	0.005
Child-Pugh class A/B/C, *n* (%)	91	17 (18.68)/50 (54.95)/24 (26.37)		98	38 (38.78)/47 (47.96)/13 (13.26)		0.004
MELD score	91	9.91 ±6.41	8.86 (–1.42 – 28.02)	96	7.43 ±5.40	5.66 (–2.38 – 22.05)	0.008
In-hospital death, *n* (%)	93	2 (2.15)		105	2 (1.90)		0.701
Overall death, *n* (%)	93	13 (13.98)		105	15 (14.29)		0.887

SD – standard deviation, MELD – model for end-stage liver disease.

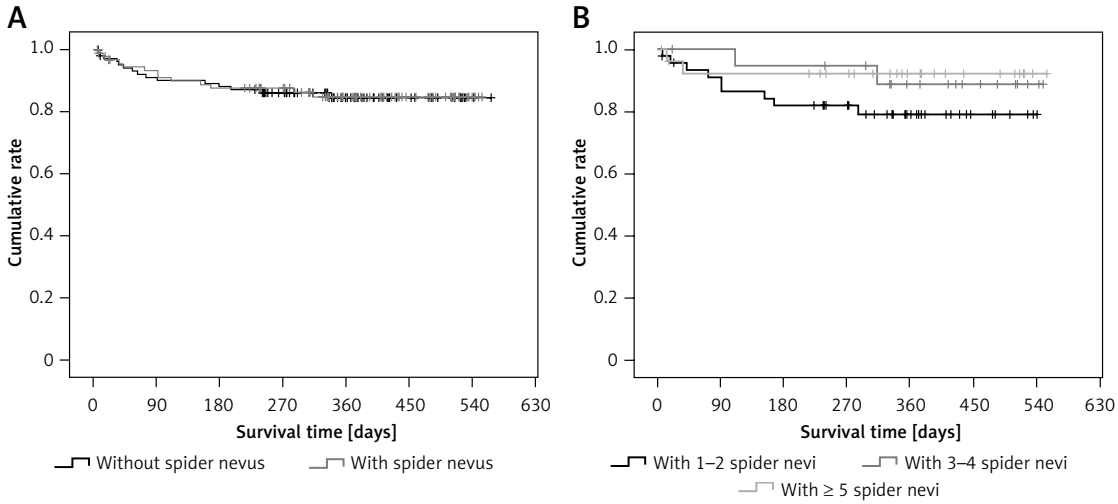

Figure 1. Kaplan-Meir curve regarding the impact of spider nevus on cumulative survival of cirrhotic patients. **A** – Patients with vs. without spider nevus. **B** – Patients with 1–2 vs. 3–4 vs. ≥ 5 spider nevi of chest/abdominal wall

Spider nevus of chest/abdominal wall

The prevalence of spider nevus of the chest/abdominal wall was 47% (93/198). Of the 93 patients with spider nevi, 49.46% (46/93), 21.51% (20/93), and 29.03% (27/93) had 1–2, 3–4, and ≥ 5 spider nevi, respectively. The location of the spider nevus was the chest wall alone in nearly all patients (97.85%, 91/93).

Patients with spider nevi of the chest/abdominal wall had significantly higher proportions of male sex, alcohol abuse, subcutaneous collateral vessel of the chest/abdominal wall, and Child-Pugh classes B and C, significantly higher hemoglobin, white blood cells, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, gamma-glutamyl transpeptidase, total bilirubin, activated partial thromboplastin time, Child-Pugh score, and MELD score, and significantly lower sodium, and were significantly younger than those without spider nevi of the chest/abdominal wall (Table II). The cumulative survival was not significantly different between patients with and without spider nevi of the chest/abdominal wall (p = 0.951) (Figure 1 A).

Proportions of male sex and alcohol abuse were significantly different among patients with different numbers of spider nevi of the chest/abdominal wall (Table III). The cumulative survival was not significantly different among them (p = 0.151) (Figure 1 B).

Subcutaneous collateral vessel of chest/abdominal wall

The prevalence of subcutaneous collateral vessel of the chest/abdominal wall was 29.8% (59/198). The location of the subcutaneous collateral vessel was the chest wall alone, the abdominal wall alone, and both chest and abdominal walls in 16.9% (10/59), 55.9% (33/59), and 27.1% (16/59), respectively.

Patients with subcutaneous collateral vessels of the chest/abdominal wall had significantly higher proportions of moderate to severe ascites at admission, spider nevus, and Child-Pugh class C, significantly higher alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, γ-glutamyl transpeptidase, total bilirubin, Child-Pugh score, and MELD score, significantly lower proportions of previous history of gastrointestinal bleeding and gastrointestinal bleeding at admission, and significantly lower sodium than those without subcutaneous collateral vessel of chest/abdominal wall (Table IV). The cumulative survival was significantly worse in patients with a subcutaneous collateral vessel of the chest/abdominal wall than in those without a subcutaneous collateral vessel of the chest/abdominal wall (p = 0.018) (Figure 2 A).

Age, proportion of alcohol abuse, white blood cells, platelets, and gamma-glutamyl transpeptidase were significantly different among patients with different locations of the subcutaneous collateral vessel (Table V). The cumulative survival was not significantly different among them (p = 0.532) (Figure 2 B).

Discussion

The patients enrolled in our study had several major features. First, our patients formed a group of the northeastern Chinese population with liver cirrhosis. In northeastern China, the most common etiologies of liver cirrhosis are alcohol abuse and hepatitis B virus infection [27]. Indeed, one third of our patients had a history of alcohol abuse

Table III. Comparison among patients with different number of spider nevi

Variables	With 1–2 spider nevi of chest/abdominal wall			With 3–4 spider nevi of chest/abdominal wall			With ≥ 5 spider nevi of chest/abdominal wall			*P*-value
	N	Mean ± SD or Frequency (percentage)	Median (range)	*N*	Mean ± SD or Frequency (percentage)	Median (range)	*N*	Mean ± SD or Frequency (percentage)	Median (range)	
Sex (male/female), *n* (%)	46	28 (60.87)/ 18 (39.13)		20	15 (75.00)/ 5 (25.00)		27	25 (92.59)/ 2 (7.41)		0.013
Age [years]	46	56.43 ±11.52	56.62 (27.08–82.34)	20	52.48 ±7.91	53.28 (32.45–66.89)	27	51.63 ±7.93	35.71 (35.74–69.03)	0.098
Etiology of liver diseases, *n* (%):							27			
Hepatitis B virus infection	46	13 (28.26)		20	7 (35.00)		27	5 (18.52)		0.125
Hepatitis C virus infection	46	4 (8.70)		20	1 (5.00)		27	0 (0.00)		0.371
Alcohol abuse	46	19 (41.30)		20	10 (50.00)		27	22 (81.48)		0.004
Drug-induced liver injury	46	2 (4.35)		20	0 (0.00)		27	1 (3.70)		0.647
Autoimmune liver disease	46	2 (4.35)		20	2 (10.00)		27	0 (0.00)		0.248
Previous gastrointestinal bleeding, *n* (%)	46	22 (47.83)		20	8 (40.00)		27	12 (44.44)		0.838
Hepatic encephalopathy at admission, *n* (%)	46	5 (10.87)		20	2 (10.00)		27	4 (14.81)		0.846
Gastrointestinal bleeding at admission, *n* (%)	46	24 (52.17)		20	9 (45.00)		27	10 (37.04)		0.453
Jaundice at admission, *n* (%)	46	10 (21.74)		20	3 (15.00)		27	7 (25.93)		0.665
Ascites at admission (no/mild/moderate-severe), *n* (%)	46	15 (32.61)/ 7 (15.22)/ 24 (52.17)		20	6 (30.00)/ 4 (20.00)/ 10 (50.00)		27	10 (37.03)/ 6 (22.22)/ 11 (40.74)		0.885
Subcutaneous collateral vessel of chest/abdominal wall, *n* (%):	46	13 (28.26)/ 33 (71.74)		20	10 (50.00)/ 10 (50.00)		27	12 (44.44)/ 15 (55.56)		0.169
Location (chest alone/abdomen alone/both chest and abdomen)	13	0 (0.00)/ 7 (53.85)/ 6 (46.15)		10	2 (20.00)/ 4 (40.00)/ 4 (40.00)		12	3 (25.00)/ 6 (50.00)/ 3 (25.00)		0.398
Laboratory tests:										
Red blood cells [× 10^{12}/l]	46	3.18 ±0.86	3.05 (1.69–5.06)	20	3.32 ±0.81	3.18 (2.09–4.81)	27	3.15 ±0.80	3.13 (1.74–5.02)	0.755
Hemoglobin [g/l]	46	91.91 ±26.75	83.50 (54.00–149.00)	20	102.80 ±32.74	100.00 (47.00–151.00)	27	103.44 ±25.08	101.00 (52.00–170.00)	0.152

Table III. Cont.

Variables	With 1–2 spider nevi of chest/abdominal wall			With 3–4 spider nevi of chest/abdominal wall			With ≥ 5 spider nevi of chest/abdominal wall			*P*-value
	N	Mean ± SD or Frequency (percentage)	Median (range)	*N*	Mean ± SD or Frequency (percentage)	Median (range)	*N*	Mean ± SD or Frequency (percentage)	Median (range)	
White blood cells [× 10^9/l]	46	5.54 ±3.15	4.45 (1.70–14.50)	20	4.78 ±1.28	4.70 (2.30–6.70)	27	5.18 ±3.06	4.30 (1.80–16.00)	0.588
Platelets [× 10^9/l]	46	93.67 ±56.56	74.00 (29.00–282.00)	20	112.40 ±67.45	95.50 (36.00–282.00)	27	86.26 ±49.67	84.00 (19.00–192.00)	0.290
Alanine aminotransferase [U/l]	45	46.16 ±70.77	25.85 (13.42–466.75)	20	61.61 ±125.73	29.87 (6.24–590.00)	27	43.15 ±31.60	41.89 (12.54–170.79)	0.697
Aspartate aminotransferase [U/l]	45	72.22 ±108.88	39.85 (18.16–719.84)	20	82.24 ±136.02	47.47 (13.54–645.00)	27	83.53 ±51.22	72.00 (15.35–166.49)	0.881
Alkaline phosphatase [U/l]	45	121.17 ±107.03	94.64 (39.17–649.21)	20	145.25 ±98.69	116.00 (47.00–444.88)	27	137.75 ±69.28	118.46 (33.00–386.00)	0.593
Gamma-glutamyl transpeptidase [U/l]	45	117.82 ±191.67	60.66 (9.00–929.28)	20	191.77 ±266.82	67.74 (10.00–981.00)	27	184.33 ±168.48	94.00 (12.18–552.26)	0.265
Total bilirubin [µmol/l]	45	47.24 ±59.91	26.00 (7.70–316.90)	20	35.63 ±30.14	27.55 (8.80–138.00)	27	58.86 ±74.70	37.50 (6.40–319.90)	0.422
Prothrombin time [s]	46	17.07 ±3.82	15.85 (11.70–31.60)	20	16.40 ±3.52	15.80 (12.30–28.90)	27	17.23 ±3.10	15.90 (13.00–25.20)	0.703
International normalized ratio	45	1.44 ±0.43	1.30 (0.89–3.03)	20	1.37 ±0.41	1.28 (0.93–2.89)	27	1.45 ±0.35	1.31 (0.97–2.36)	0.720
Activated partial thromboplastin time [s]	46	40.90 ±6.33	40.30 (29.40–54.50)	20	40.16 ±5.15	38.50 (32.70–52.80)	27	43.29 ±6.07	43.10 (34.30–54.50)	0.154
Albumin [g/l]	46	29.72 ±7.03	29.15 (17.80–47.20)	19	31.22 ±5.86	30.10 (19.80–42.40)	27	29.10 ±7.48	29.30 (16.10–43.40)	0.587
Serum sodium [mmol/l]	46	137.05 ±3.57	137.20 (129.80–144.60)	19	137.54 ±3.86	138.40 (128.00–143.40)	27	135.43 ±5.13	137.50 (120.70–141.20)	0.168
Serum potassium [mmol/l]	46	3.90 ±0.41	3.88 (3.01–4.85)	19	3.89 ±0.48	3.81 (2.73–4.66)	27	3.91 ±0.50	3.94 (2.96–4.88)	0.990
Blood urea nitrogen [mmol/l]	46	7.85 ±5.67	6.13 (2.45–32.70)	20	6.37 ±4.75	5.24 (2.24–25.59)	27	7.50 ±8.96	4.86 (1.90–47.21)	0.710

Table III. Cont.

Variables	With 1–2 spider nevi of chest/abdominal wall			With 3–4 spider nevi of chest/abdominal wall			With ≥ 5 spider nevi of chest/abdominal wall			*P*-value
	N	Mean ± SD or Frequency (percentage)	Median (range)	*N*	Mean ± SD or Frequency (percentage)	Median (range)	*N*	Mean ± SD or Frequency (percentage)	Median (range)	
Serum creatinine [μmol/l]	45	75.74 ±48.06	64.55 (32.14–317.30)	20	89.17 ±89.74	70.19 (44.00–463.47)	27	87.01 ±93.83	64.20 (41.76–533.70)	0.723
Child-Pugh score	45	8.40 ±2.26	8.00 (5.00–14.00)	19	8.05 ±1.47	8.00 (5.00–10.00)	27	8.48 ±2.53	8.00 (5.00–13.00)	0.794
Child-Pugh class A/B/C, *n* (%)	45	8 (17.78)/ 26 (57.78)/ 11 (24.44)		19	2 (10.53)/ 14 (73.68)/ 3 (15.79)		27	7 (25.92)/ 10 (37.04)/ 10 (37.04)		0.175
MELD score	44	9.52 ±6.44	8.89 (–1.42–22.78)	20	9.41 ±6.41	8.15 (0.41–28.02)	27	10.92 ±6.47	9.16 (–1.15 – 23.47)	0.624
In-hospital death, *n* (%)	46	1 (2.17)		20	0 (0.00)		27	1 (3.70)		0.688
Overall death, *n* (%)	46	9 (19.57)		20	2 (10.00)		27	2 (7.41)		0.297

SD – standard deviation, MELD – model for end-stage liver disease.

and another one third of them had hepatitis B virus infection. Second, a majority of our patients were at the decompensation status, because approximately half of them had developed gastrointestinal bleeding and about two thirds of them had ascites at their admission. Third, most of our patients had relatively severe liver dysfunction, because about two thirds of them were in Child-Pugh class B or C at their admission.

The characteristics of spider nevi and subcutaneous collateral vessels should be interpreted as follows. First, about half of cirrhotic patients had spider nevi of the chest/abdominal wall. Notably, nearly all spider nevi occurred at the chest wall; by comparison, spider nevus was hardly observed at the abdominal wall. Therefore, no comparison was performed according to the location of the spider nevus. Second, about one third of cirrhotic patients had subcutaneous collateral vessels of the chest/abdominal wall. Notably, a majority of them occurred at the abdominal walls.

In line with previous findings by Li *et al.* [4], our study also confirmed that alcohol abuse was significantly associated with the presence of spider nevus. More importantly, the proportion of subjects with a history of alcohol abuse increased with the number of spider nevi. Considering that alcohol abuse is more common in male patients, we can further explain the association of sex with spider nevus of the chest/abdominal wall. By contrast, the potential etiology of chronic liver diseases did not influence the development of a subcutaneous collateral vessel of the chest/abdominal wall.

Variceal bleeding is the most common type of gastrointestinal bleeding in liver cirrhosis [28–30]. Variceal bleeding is primarily associated with the degree of portosystemic pressure gradient [31], rather than coagulation abnormalities or other abnormal factors [32]. Gastrointestinal endoscopy [31], but not other alternative diagnostic methods [33–35], is the diagnostic gold standard. Our study found that the presence of subcutaneous collateral vessel of the chest/abdominal wall was negatively associated with the probability of previous gastrointestinal bleeding or gastrointestinal bleeding upon admission. Such a significant association might be explained by the fact that subcutaneous collateral vessel of the chest/abdominal wall, a type of spontaneous portosytemic shunt, might produce a lower portosystemic pressure gradient, thereby decreasing the risk of variceal bleeding. However, we must acknowledge that only a proportion of our patients underwent endoscopic examinations for the diagnosis of gastroesophageal varices. Thus, in future, well-designed studies should be performed to explore the association between subcutaneous collateral vessel of

Table IV. Comparison between patients with and without subcutaneous collateral vessel of chest/abdominal wall

Variables	With subcutaneous collateral vessel of chest/abdominal wall			Without subcutaneous collateral vessel of chest/abdominal wall			*P*-value
	N	Mean ± SD or Frequency (percentage)	Median (range)	*N*	Mean ± SD or Frequency (percentage)	Median (range)	
Sex (male/female), *n* (%)	59	37 (62.71)/22 (37.29)		139	91 (65.47)/48 (34.53)		0.835
Age [years]	59	57.19 ±11.75	57.01 (31.96–88.10)	139	56.84 ±11.30	56.31 (26.76–82.34)	0.713
Etiology of liver diseases, *n* (%):							
Hepatitis B virus infection	59	18 (30.51)		139	46 (33.09)		0.850
Hepatitis C virus infection	59	3 (5.08)		139	15 (10.79)		0.314
Alcohol abuse	59	28 (47.46)		139	51 (36.69)		0.209
Drug-induced liver injury	59	1 (1.69)		139	9 (6.47)		0.294
Autoimmune liver disease	59	2 (3.39)		139	7 (5.04)		0.892
Previous gastrointestinal bleeding, *n* (%)	59	24 (40.68)		139	82 (58.99)		0.027
Hepatic encephalopathy at admission, *n* (%)	59	4 (6.78)		139	12 (8.63)		0.879
Gastrointestinal bleeding at admission, *n* (%)	59	19 (32.20)		139	87 (62.59)		< 0.001
Jaundice at admission, *n* (%)	59	16 (27.12)		139	20 (14.39)		0.055
Ascites at admission (no/mild/moderate-severe), *n* (%)	59	15 (25.42)/9 (15.25)/35 (59.32)		139	65 (46.76)/30 (21.58)/44 (31.65)		0.001
Spider nevus of chest/abdominal wall, *n* (%):	59	35 (59.32)		139	58 (41.73)		0.035
Number (1–2/3–4/≥ 5)	35	13 (37.14)/10 (28.57)/12 (34.29)		58	33 (56.90)/10 (17.24)/15 (25.86)		0.169
Location (chest alone/abdomen alone/ both chest and abdomen)	35	34 (97.14)/0 (0)/1 (2.86)		58	57 (98.28)/0 (0.00)/1 (1.02)		0.071
Laboratory tests:							
Red blood cells [× 10^{12}/l]	59	3.14 ±0.78	3.06 (1.42–5.02)	138	3.15 ±0.85	3.04 (1.43–5.64)	0.839
Hemoglobin [g/l]	59	93.92 ±26.08	95.00 (38.00–170.00)	138	91.44 ±28.45	84.00 (37.00–164.00)	0.455
White blood cells [× 10^{9}/l]	59	5.16 ±3.26	4.40 (1.40–16.00)	138	5.13 ±3.46	4.30 (1.10–23.10)	0.810
Platelets [× 10^{9}/l]	59	97.02 ±61.34	83.00 (11.00–282.00)	138	89.77 ±58.07	74.00 (17.00–346.00)	0.439
Alanine aminotransferase [U/l]	59	42.98 ±37.79	30.22 (6.24–192.51)	136	41.04 ±68.12	24.41 (4.61–590.00)	0.046

Table IV. Cont.

Variables	With subcutaneous collateral vessel of chest/abdominal wall			Without subcutaneous collateral vessel of chest/abdominal wall			*P*-value
	N	Mean ± SD or Frequency (percentage)	Median (range)	*N*	Mean ± SD or Frequency (percentage)	Median (range)	
Aspartate aminotransferase [U/l]	59	70.23 ±56.98	52.42 (13.54–300.70)	136	58.91 ±89.27	33.27 (6.97–719.84)	0.003
Alkaline phosphatase [U/l]	59	161.57 ±131.87	124.79 (33.00–850.45)	136	111.04 ±87.59	86.82 (35.36–649.21)	0.003
γ-Glutamyl transpeptidase [U/l]	59	137.47 ±175.01	74.58 (10.00–929.28)	136	105.80 ±176.65	41.26 (9.00–981.00)	0.009
Total bilirubin [µmol/l]	59	53.34 ±64.62	29.20 (7.90–319.90)	136	30.00 ±32.89	22.20 (6.40–316.90)	0.009
Prothrombin time [s]	59	17.06 ±3.61	15.70 (12.50–29.70)	135	16.33 ±3.17	15.70 (11.30–31.60)	0.318
International normalized ratio	58	1.44 ±0.41	1.29 (0.95–3.00)	133	1.36 ±0.36	1.28 (0.83–3.03)	0.258
Activated partial thromboplastin time [s]	58	42.47 ±6.12	41.15 (29.50–56.10)	134	39.71 ±5.76	38.50 (29.20–57.80)	0.004
Albumin [g/l]	59	29.89 ±6.29	29.20 (17.20–47.80)	135	30.55 ±7.08	30.10 (16.10–481.00)	0.557
Serum sodium [mmol/l]	58	136.36 ±4.71	137.50 (120.70–143.00)	138	138.48 ±3.35	138.50 (128.00–151.60)	0.019
Serum potassium [mmol/l]	58	3.89 ±0.48	3.88 (2.73–4.88)	138	3.92 ±0.45	3.87 (2.48–5.60)	0.808
Blood urea nitrogen [mmol/l]	59	7.90 ±6.61	5.62 (2.24–32.70)	135	7.42 ±5.54	5.82 (1.71–47.21)	0.858
Serum creatinine [µmol/l]	59	87.89 ±77.69	65.81 (32.14–463.47)	135	74.31 ±58.52	64.42 (34.90–533.70)	0.192
Child-Pugh score	58	8.57 ±2.20	8.00 (5.00–14.00)	131	7.60 ±1.98	7.00 (5.00–14.00)	0.002
Child-Pugh class A/B/C, *n* (%)	58	11 (18.97)/29 (50)/18 (31.03)		131	44 (33.59)/68 (51.91)/19 (14.50)		0.014
MELD score	58	10.77 ±6.76	9.16 (–1.42–28.02)	129	7.68 ±5.42	6.16 (–2.38 – 23.47)	0.003
In-hospital death, *n* (%)	59	1 (1.69)		139	3 (2.16)		0.734
Overall death, *n* (%)	59	13 (22.03)		139	13 (9.35)		0.022

SD – standard deviation, MELD – model for end-stage liver disease.

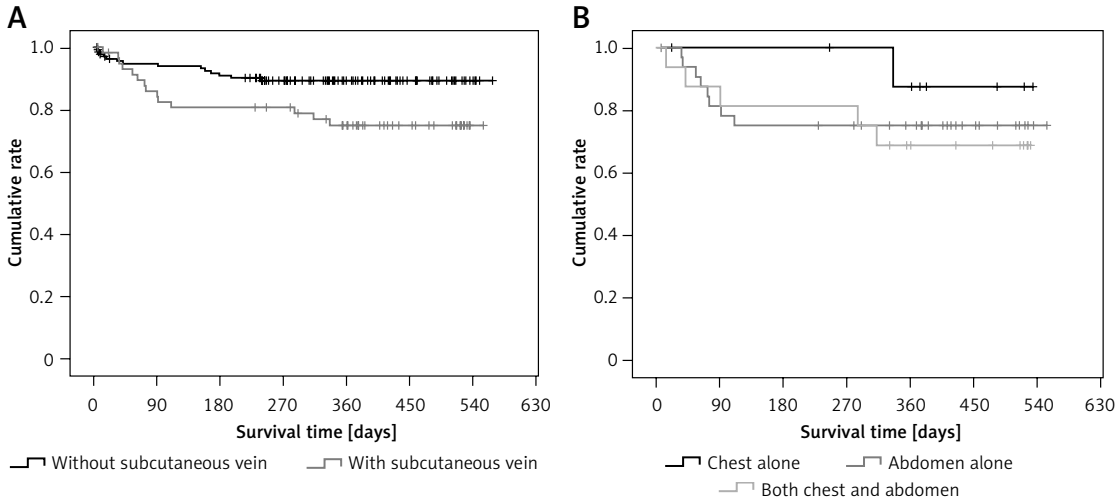

Figure 2. Kaplan-Meir curve regarding the impact of subcutaneous collateral vessel of abdominal/chest wall on cumulative survival of cirrhotic patients. **A** – Patients with versus without subcutaneous collateral vessel of abdominal/chest wall. **B** – Patients with subcutaneous collateral vessel of chest wall alone versus abdominal wall alone versus both abdominal and chest walls

the chest/abdominal wall and gastroesophageal varices or hepatic vein pressure gradient. On the other hand, in our study the association of spider nevus with the probability of gastrointestinal bleeding was obscure. A possible explanation is that spider nevus might reflect the severity of liver dysfunction and its associated disturbance of sex hormones, but not that of portal hypertension.

Both spider nevus and subcutaneous collateral vessel of the chest/abdominal wall were positively associated with the severity of liver dysfunction, such as alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, γ-glutamyl transpeptidase, total bilirubin, Child-Pugh score, and MELD score. These findings were similar to those of previous research [4, 5]. To the best of our knowledge, no study has evaluated the impact of spider nevus and subcutaneous collateral vessel of the chest/abdominal wall on the survival of patients with liver cirrhosis. We found that neither of them was associated with in-hospital mortality. However, subcutaneous collateral vessels of the chest/abdominal wall, rather than spider nevus, could significantly predict worse overall survival during the follow-up period. Considering that spider nevus and subcutaneous collateral vessel of the chest/abdominal wall are readily available at the physical examinations, they should be considered as routine markers of liver dysfunction and death in our clinical work.

Our study had limitations. First, numerous studies have shown high prevalence of spider nevus in children regardless of chronic liver diseases [36–38]. Because our patients were adults, rather than children or adolescents, we could not extrapolate from our findings to the pediatric population. Second, spider nevus is distributed all over the body. However, we only collected data regarding spider nevi and subcutaneous collateral vessels on the abdominal and chest walls, and not other body positions. Third, CT examinations might be more accurate and objective for identifying the number of subcutaneous collateral vessels of the chest/abdominal wall [15]. However, we only collected data regarding the presence of subcutaneous collateral vessel of the chest/abdominal wall on the basis of physical examinations, and not CT examinations.

In conclusion, based on the results of a prospective observational study, physical examinations regarding spider nevus and subcutaneous collateral vessel of the chest/abdominal wall should be carefully performed for early and accurate prognostic evaluation of liver cirrhosis.

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Conflict of interest

The authors declare no conflict of interest.

Table V. Comparison among patients with different location of subcutaneous collateral vessel of chest/abdominal wall

Variables	Chest wall alone			Abdominal wall alone			Both			*P*-value
	N	Mean ± SD or Frequency (percentage)	Median (range)	*N*	Mean ± SD or Frequency (percentage)	Median (range)	*N*	Mean ± SD or Frequency (percentage)	Median (range)	
Sex (male/female), *n* (%)	10	5 (50.00)/ 5 (50.00)		33	18 (54.55)/ 15 (45.45)		16	14 (87.50)/ 2 (12.50)		0.054
Age [years]	10	61.01 ±15.01	57.54 (45.17–88.10)	33	59.15 ±11.69	62.23 (31.96–78.67)	16	50.77 ±6.70	51.31 (39.61–62.71)	0.034
Etiology of liver diseases, *n* (%):										
Hepatitis B virus infection	10	3 (30.00)		33	14 (42.42)		16	1 (6.25)		0.099
Hepatitis C virus infection	10	0 (0.00)		33	1 (3.03)		16	2 (12.50)		0.266
Alcohol abuse	10	3 (30.00)		33	12 (36.36)		16	13 (81.25)		0.006
Drug-induced liver injury	10	0 (0.00)		33	1 (3.03)		16	0 (0.00)		0.670
Autoimmune liver disease	10	0 (0.00)		33	2 (6.06)		16	0 (0.00)		0.442
Previous gastrointestinal bleeding, *n* (%)	10	6 (60.00)		33	13 (39.39)		16	5 (31.25)		0.340
Hepatic encephalopathy at admission, *n* (%)	10	0 (0.00)		33	2 (6.06)		16	2 (12.50)		0.453
Gastrointestinal bleeding at admission, *n* (%)	10	4 (40.00)		33	7 (21.21)		16	8 (50.00)		0.109
Jaundice at admission, *n* (%)	10	2 (20.00)		33	8 (24.24)		16	6 (37.50)		0.531
Ascites at admission (no/mild/moderate-severe), *n* (%)	10	4 (40.00)/ 3 (30.00)/ 3 (30.00)		33	8 (24.24)/ 5 (15.15)/ 20 (60.61)		16	3 (18.75)/ 1 (6.25)/ 12 (75.00)		0.237
Spider nevus of chest/abdominal wall, *n* (%):	10	5 (50.00)		33	17 (51.52)		16	13 (81.25)		0.112
Number (1–2/3–4/≥ 5)	5	0 (0.00)/ 2 (40.00)/ 3 (60.00)		17	7 (41.18)/ 4 (23.53)/ 6 (35.29)		13	6 (46.15)/ 4 (30.77)/ 3 (23.08)		0.398
Location (chest alone/abdomen alone/both chest and abdomen)	10	5 (50.00)/ 5 (50.00)/ 0 (0.00)		33	16 (48.48)/ 16 (48.48)/ 1 (3.03)		16	3 (18.75)/ 13 (81.25)/ 0 (0.00)		0.238

Table V. Cont.

Variables	Chest wall alone			Abdominal wall alone			Both			*P*-value
	N	Mean ± SD or Frequency (percentage)	Median (range)	*N*	Mean ± SD or Frequency (percentage)	Median (range)	*N*	Mean ± SD or Frequency (percentage)	Median (range)	
Laboratory tests:										
Red blood cells [10^{12}/l]	10	3.35 ±0.99	3.42 (1.42–4.89)	33	3.27 ±0.76	3.11 (2.09–5.02)	16	2.75 ±0.58	2.73 (1.69–3.91)	0.093
Hemoglobin [g/l]	10	97.10 ±29.35	100.50 (38.00–131.00)	33	97.91 ±25.75	95.00 (55.00–170.00)	16	83.69 ±23.25	84.5 (47.00–128.00)	0.185
White blood cells [× 10^9/l]	10	3.42 ±1.26	3.40 (1.40–5.30)	33	4.63 ±2.57	4.20 (1.70–14.00)	16	7.34 ±4.28	5.75 (2.90–16.00)	0.003
Platelets [× 10^9/l]	10	90.20 ±59.44	71.50 (34.00–228.00)	33	82.24 ±42.91	73.00 (11.00–171.00)	16	131.75 ±81.88	116.5 (22.00–282.00)	0.025
Alanine aminotransferase [U/l]	10	51.33 ±45.86	44.26 (11.77–164.25)	33	45.40 ±42.13	30.22 (6.24–192.51)	16	32.78 ±17.41	27.57 (13.42–73.00)	0.416
Aspartate aminotransferase [U/l]	10	76.34 ±59.34	64.72 (15.85–211.18)	33	66.99 ±61.31	48.46 (13.54–300.70)	16	73.11 ±48.67	64.78 (19.64–161.31)	0.846
Alkaline phosphatase [U/l]	10	210.63 ±164.21	142.37 (49.82–542.00)	33	156.70 ±145.44	114.00 (33.00–850.45)	16	140.94 ±61.83	136.5 (45.00–282.00)	0.410
γ-Glutamyl transpeptidase [U/l]	10	120.78 ±115.29	89.85 (19.22–399.94)	33	92.31 ±92.99	47.00 (10.00–349.83)	16	241.04 ±275.49	122 (11.00–929.28)	0.017
Total bilirubin [µmol/l]	10	34.91 ±27.13	33.85 (7.90–97.30)	33	52.94 ±64.98	24.40 (8.00–281.70)	16	65.68 ±79.42	41.6 (10.50–319.90)	0.432
Prothrombin time [s]	10	16.91 ±3.40	15.60 (13.40–25.20)	33	17.01 ±3.90	15.70 (12.50–29.70)	15	17.26 ±3.27	15.5 (12.80–22.50)	0.967
International normalized ratio	10	1.42 ±0.38	1.28 (1.04–2.36)	33	1.44 ±0.45	1.29 (0.95–3.00)	15	1.47 ±0.37	1.26 (0.98–2.07)	0.965
Activated partial thromboplastin time [s]	10	43.67 ±7.35	42.60 (34.80–54.50)	33	42.07 ±6.41	40.30 (29.50–56.10)	16	42.57 ±4.72	42.9 (34.00–51.00)	0.773
Albumin [g/l]	10	31.08 ±8.13	31.05 (17.20–41.70)	33	30.82 ±6.51	31.00 (18.90–47.80)	16	27.21 ±3.49	28.9 (19.90–31.00)	0.136
Serum sodium [mmol/l]	10	138.08 ±3.59	139.85 (131.90–141.20)	33	136.77 ±4.73	138.40 (120.70–142.10)	15	134.29 ±4.86	134.7 (123.20–143.00)	0.105
Serum potassium [mmol/l]	10	3.82 ±0.52	3.77 (2.90–4.44)	33	3.88 ±0.45	3.88 (2.73–4.66)	15	3.95 ±0.54	3.84 (3.01–4.88)	0.789
Blood urea nitrogen [mmol/l]	10	6.46 ±3.52	5.10 (4.18–15.89)	33	8.03 ±7.05	5.58 (2.35–30.40)	16	8.55 ±7.34	7.16 (2.24–32.70)	0.733
Serum creatinine [µmol/l]	10	83.97 ±47.27	69.20 (50.29–212.26)	33	91.46 ±96.47	65.30 (35.05–463.47)	16	82.96 ±45.59	72.75 (32.14–193.66)	0.926
Child-Pugh score	10	7.80±1.99	8.00 (5.00–11.00)	33	8.39 ±2.37	8.00 (5.00–13.00)	15	9.47 ±1.73	9.00 (8.00–14.00)	0.141
Child-Pugh class A/B/C, *n* (%)	10	4 (40.00)/ 4 (40.00)/ 2 (20.00)		33	7 (21.21)/ 16 (48.49)/ 10 (30.30)		15	0 (0.00)/ 9 (60.00)/ 6 (40.00)		0.161
MELD score	10	10.06 ±3.84	8.78 (5.63–18.35)	33	10.33 ±7.95	7.66 (–1.42–28.02)	15	12.22 ±5.38	12.77 (0.62–20.41)	0.633
In-hospital death, *n* (%)	10	0 (0.00)		33	0 (0.00)		16	1 (6.25)		0.255
Overall death, *n* (%)	10	1 (10.00)		33	8 (24.24)		16	5 (31.25)		0.462

SD – standard deviation, MELD – model for end-stage liver disease.

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