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Impact of small intestinal bacterial overgrowth on systemic inflammation, circulatory and renal function, and liver fibrosis in patients with cirrhosis and ascites

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Abstract

Background Small intestinal bacterial overgrowth (SIBO) occurs frequently in patients with cirrhosis, particularly in those with ascites, and promotes the translocation of gut-derived bacterial products into the portal and systemic circulation. We investigated the effects of SIBO on systemic inflammatory activity, circulatory and renal function, and the degree of liver fibrosis in patients with cirrhosis and ascites.

Methods Eighty patients with cirrhosis and ascites were prospectively enrolled. SIBO was determined by lactulose breath test. Serum levels of lipopolysaccharide-binding protein (LBP), tumor necrosis factor-α, and interleukin-6, mean arterial pressure (MAP), cardiac output (CO) by echocardiography, systemic vascular resistance (SVR) as MAP/CO ratio, plasma renin activity (PRA), plasma aldosterone, radioisotope-assessed glomerular filtration rate (GFR), and liver stiffness by shear wave elastography were evaluated.

Results SIBO was detected in 58 patients (72.5%). Compared to patients without SIBO, those diagnosed with SIBO had significantly higher LBP levels (P<0.001), significantly lower MAP (P<0.001) and SVR (P<0.001), and significantly higher CO (P=0.002) and PRA (P<0.001). Patients with SIBO had significantly lower GFR (P=0.02) and higher liver stiffness (P=0.04) compared to those without SIBO. The presence of SIBO was independently associated with LBP (P=0.007) and PRA (P=0.01). Among patients with SIBO, peak breath hydrogen concentration was significantly correlated with serum LBP (P<0.001), MAP (P<0.001), CO (P=0.008), SVR (P=0.001), PRA (P=0.005), plasma aldosterone (P<0.001), GFR (P<0.001), and liver stiffness (P=0.004).

Conclusion SIBO in patients with cirrhosis and ascites may predispose to greater systemic inflammation, circulatory and renal dysfunction, and more advanced liver fibrosis.

Keywords Small intestinal bacterial overgrowth, systemic inflammation, systemic hemodynamics, renal function, liver fibrosis

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Conflict of Interest: None

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Introduction

Cirrhosis is characterized by an increase in the passage of bacteria and their products into the portal and systemic circulation, mainly due to an increased permeability of the intestinal barrier related to portal hypertension. This process, known as bacterial translocation (BT), may have substantial clinical relevance to patients with cirrhosis [1]. Translocated gut-derived molecules, such as lipopolysaccharide (LPS)—also referred as to endotoxin—trigger a systemic inflammatory response, which is a key factor in the pathogenesis of splanchnic arterial vasodilation [2,3]. In particular, endotoxemia stimulates

monocytes and lymphocytes to release proinflammatory cytokines, including tumor necrosis factor (TNF)-α and interleukin (IL)-6. Subsequently, the inflammatory mediators can stimulate the production of potent vasodilators, mainly nitric oxide, in the splanchnic vasculature [4]. As the liver disease progresses, the BT-associated inflammatory activity and the arterial vasodilation become more intense, causing systemic hemodynamic derangement and a reduction in the effective arterial blood volume. This in turn activates potent sodium-retaining and vasoconstricting mechanisms, such as the renin-angiotensin-aldosterone system (RAAS) [5]. The activation of these systems plays a major role in the development of ascites and renal function impairment [6]. On the other hand, there is increasing evidence to suggest that gut microbiota contribute to the initiation and progression of liver fibrosis in chronic liver disease [7,8].

Small intestinal bacterial overgrowth (SIBO) is defined as an increased number and/or abnormal type of bacteria in the small bowel [9]. This condition is commonly encountered in patients with cirrhosis, as a result of impaired intestinal motility and delayed transit time [10], and its prevalence is particularly high in patients with ascites [11]. Experimental [12,13] and human observations [14] demonstrated that SIBO is a major determinant of the occurrence of BT. Nevertheless, there is only scarce evidence for the direct relationship between SIBO and systemic inflammation markers [14-16], or the effects of SIBO on systemic hemodynamics [17], in patients with cirrhosis, while such data are lacking for patients with ascites. Moreover, we have no information about the effects of SIBO on renal function or the burden of liver fibrosis in patients with cirrhosis. The aim of the present prospective study was to investigate the association of SIBO with the systemic inflammatory activity and the circulatory and renal function, along with its potential relationship with the degree of noninvasively assessed liver fibrosis in patients with cirrhosis and ascites.

Patients and methods

Patients

Consecutive patients with liver cirrhosis and a history of ascites seen in the outpatient hepatology clinics of the University Hospital of Ioannina, Greece, between May 2017 and May 2021, were prospectively evaluated. Written informed consent was obtained from every participant. The study conformed to the principles of the declaration of Helsinki and was approved by the Institutional Ethics Committee. The diagnosis of cirrhosis was based on clinical and laboratory findings, endoscopy, imaging studies, or on liver biopsy. The patients were included if they had: a) cirrhosis of any etiology; b) age between 18 and 75 years; c) diuretic-responsive grade II/III ascites; and d) stable serum creatinine <1.5 mg/dL. Exclusion criteria were: a) use of pre- and probiotics, antibiotics, prokinetics or acid suppressive therapy in the 6 weeks prior to enrolment; b) a history of hepatic encephalopathy, variceal bleeding, or spontaneous bacterial peritonitis or other bacterial infection at least 4 weeks prior to inclusion; c) portal vein thrombosis; d) hepatocellular carcinoma or other malignancy; e) serum bilirubin >5 mg/dL and/or international normalized ratio >2.5; f) recent (within 6 months) or active ethanol abuse; g) Child-Pugh score >12 points; h) transjugular intrahepatic portosystemic shunt insertion; i) a history of cardiovascular, pulmonary or renal disease; and k) uncontrolled diabetes. Beta-blockers and diuretics were not withheld during the investigations. All patients were on a sodium-restricted diet.

Study design

The day prior to investigations, a thorough clinical examination was performed and the following demographic and clinical characteristics were recorded for each patient: age, sex, etiology of cirrhosis, history of variceal bleeding, use of β-blockers, and diabetes. All patients underwent laboratory examinations, including a complete blood count, liver and renal biochemistry, and coagulation profiles. Model for end-stage liver disease (MELD) and Child-Pugh class for assessment of liver disease severity were calculated from the laboratory findings. At 8:00 a.m. on the first day of the study, blood samples were obtained, with the patient in the supine position after an overnight fast, for measurement of vasoactive factors (plasma renin activity [PRA] and plasma levels of aldosterone) and inflammatory markers (serum levels of lipopolysaccharide-binding protein [LBP], TNF-α, and IL-6). Plasma and serum samples were stored at -80°C until analysis. A hydrogen breath test (HBT) for the diagnosis of SIBO was performed after blood sampling. At 8:00 a.m. on the second day of the study, a transthoracic echocardiography assessment and evaluation of systemic hemodynamics were performed. The glomerular filtration rate (GFR), as an index of renal function, was measured subsequently to echocardiography. Liver stiffness measurement by shear wave elastography (SWE) for assessment of liver fibrosis was performed within 1 week after the HBT, after the patient had fasted for at least 4 h.

Evaluation and definition of SIBO

The lactulose HBT was used for SIBO diagnosis according to current recommendations [9]. The patients were asked to have a carbohydrate-restricted dinner on the day before the test and to fast for at least 12 h to minimize basal hydrogen excretion. Cigarette smoking and physical exercise were not permitted

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for 2 h before and during the test to prevent hyperventilation and consequent changes in breath hydrogen content. Breath hydrogen measurement was performed 4 times immediately before the lactulose loading, and the average score was used as the basal hydrogen level. A dose of 10 g of lactulose in a 20 mL solution was then administered and breath samples were taken every 15 min for 120 min. Exhaled hydrogen concentration was measured using a Micro meter H2 (Micro Medical Rochester, Kent, UK) and the results were expressed in parts per million (ppm). We considered SIBO to be present when there was an increase in breath hydrogen of at least 20 ppm above the baseline value within 90 min.

Evaluation of systemic hemodynamics

Two-dimensional echocardiography with tissue Doppler imaging (Philips EPIQ 7C, Philips Healthcare, Andover, MA, USA) was performed by an experienced cardiologist (LL), who had no knowledge of the clinical and laboratory data. Cardiac output (CO) was obtained using M-mode. Systolic and diastolic blood pressure, mean arterial pressure (MAP) and heart rate were measured by an automated oscillometric device before the echocardiographic assessment. The ratio MAP to CO was used as an index of systemic vascular resistance (SVR).

Evaluation of renal function

GFR was evaluated as previously reported [18]. In brief, an activity of approximately 148 MBq (5 mCi) of 99mTc-diethylene-triamine-pentaacetic acid (99mTc-DTPA; PENTACIS, CIS bio international, Saclay, France), was injected as an intravenous bolus, and GFR was measured by calculating the plasma disappearance rate for the radiopharmaceutical, through antecubital blood sampling at 120 and 240 min. The radioactivity within each blood sample was measured in a well-type gamma counter (Atomlab 950 Medical Spectrometer, Biodex Medical Systems, USA).

Liver stiffness measurement

SWE was performed using an Aixplorer US system (Supersonic Imagine S.A, Aix-en-Provence, France) equipped with elastographic software and a convex array transducer. All SWE measurements were made by an experienced sonographer with more than 7 years of experience in real-time elastography studies. The shear wave was generated by a continuously repeated ultrasound beam focused on the target tissue along the direction of propagation of the longitudinal wave. The velocity of the generated shear wave was measured by performing an ultra-fast ultrasound scan at a very high frame rate (more than 4000 frames/sec), and the stiffness of the corresponding liver tissue was calculated by measuring the shear-wave velocity generated. After grayscale ultrasound, SWE was performed using the same probe. The curved transducer was placed intercostally at the level of the right lobe of the liver, with the target area located in the right anterior hepatic segment at a depth of more than 2 cm from the hepatic capsule to avoid major vessels. Liver stiffness was measured within a 5 s breath hold. The measurement was performed 10 times for each patient, and the results were expressed in kilopascals (kPa). The median value was considered representative of the liver stiffness.

Assays

Inflammatory markers

The LEGENDplex™ Human TNF-α Capture Bead B3, 13X (Cat. No. 740053, Biolegend, USA) and the LEGENDplex™ Human IL-6 Capture Bead A7, 13X (Cat. No. 740044, Biolegend, USA) were used for the measurement of TNF-α and IL-6 serum levels, respectively, according to the manufacturer's instructions. The samples were analyzed in duplicate by Cytometric Bead Array flow cytometry in a BD FACSCalibur Flow Cytometer using CellQuest V3 Software (BD Biosciences, San Jose, CA, USA), and the data were analyzed using LEGENDplex™ Data Analysis Software V8.0 (BioLegend, USA). The assay sensitivities were 1.97 pg/mL for TNF-α and 2.01 pg/mL for IL-6. A commercially available enzyme-linked immunosorbent assay kit (ALX-850-304-KI01, Enzo Life sciences, Farmingdale, NY, USA) was used to measure serum LBP concentrations in accordance with the manufacturer's instructions. The assay sensitivity was 5 ng/mL.

Vasoactive factors

PRA and the plasma concentrations of aldosterone were measured by specific radioimmunoassays (RIAZEN Renin plasma activity, ZenTech, Belgium; and RIA Aldosterone, IMMUNOTECH, Czech Republic, respectively). The radioactivity from the radioimmunoassay samples was counted in a gamma scintillation counter (Wizard 2, Perkin Elmer, USA).

Statistical analysis

The baseline characteristics were expressed as absolute and relative frequencies for categorical variables and as mean ± standard error for continuous variables. Pearson's chi-square test and Student's unpaired *t*-test were used to compare categorical and continuous variables, respectively. Variables with $P<0.05$ in univariate analysis were entered into a forward stepwise multivariate logistic regression analysis to determine independent predictive factors associated with the presence of SIBO. The relationship between peak breath hydrogen concentration and other variables was assessed by the Spearman rank correlation coefficient. A P-value of <0.05 was considered statistically significant for all analyses. All statistical analyses were performed using the SPSS 26.0 statistical package (IBM Corp., Armonk, N.Y., USA).

Results

Prevalence of SIBO and clinical characteristics of patients

The final cohort included 80 patients who satisfied the inclusion and exclusion criteria. SIBO was diagnosed in 58 (72.5%) patients (Table 1). As expected, mean peak breath hydrogen concentration was significantly higher in patients with SIBO than in those without (44.2±2.4 vs. 11.7±1 ppm; P<0.001). There were no significant differences among patient subgroups with regard to the evaluated clinical characteristics, including MELD score and Child-Pugh classification. The proportion of patients with GFR less than 60 mL/min was similar between patients with and without SIBO: n=5/58 (8.6%) vs. n=1/21 (4.7%); P=0.5.

Relationship between SIBO and systemic inflammation markers

As shown in Table 1, serum LBP levels were significantly higher in patients with SIBO than in those without (7.28±0.1 vs. 6.32±0.15 ng/mL; P<0.001). Patients with SIBO had higher serum TNF-α and IL-6 levels as compared to those without SIBO, though the difference did not attain statistical significance.

Impact of SIBO on systemic hemodynamics, vasoactive factors, and renal function

Patients with SIBO had significantly lower MAP (84.6±1.2 vs. 92.9±1 mmHg; P<0.001) and SVR (1172±43 vs. 1579±67 dynes/sec/cm^{-5}; P<0.001), and significantly higher CO (7.72±0.29 vs. 6.11±0.28 L/min; P=0.002) and PRA (8.79±0.5 vs. 5.17±0.56 ng/mL/h; P<0.001) compared to patients without SIBO (Table 1). GFR was significantly lower in patients who were diagnosed with SIBO than in those who were not (73.5±1.1 vs. 79.4±2.5 mL/min; P=0.02).

Impact of SIBO on the degree of liver fibrosis

Patients with SIBO showed significantly higher liver stiffness compared to patients without SIBO (26.7±7.5 vs. 22.2±6.8; P=0.04) (Table 1).

Factors independently associated with the presence of SIBO

Serum LBP (odds ratio [OR] 2.447, 95% confidence interval [CI] 1.088-5.557; P=0.007) and PRA (OR 1.412, 95%CI 1.100-1.812; P=0.01) were independently associated with the presence of SIBO (Table 2).

Table 1 Baseline data of included patients

	SIBO (n=58)	No SIBO (n=22)	P-value
Clinical characteristics			
Age (years)	54.7±2.3	55.1±2.1	0.4
Male sex (%)	41 (70.6%)	17 (77.2%)	0.5
Etiology of cirrhosis (alcohol/viral/other)	44/8/6	17/3/2	0.9
History of variceal bleeding (n, %)	13 (22.4%)	4 (18.1%)	0.6
Child–Pugh A/B/C	16/32/10	8/12/2	0.5
MELD score	13.5±1.2	13.2±1.1	0.2
Beta-blockers (n, %)	38 (65.5%)	14 (62.6%)	0.8
Diabetes (n, %)	15 (25.8%)	3 (13.6%)	0.2
Inflammatory markers			
Lipopolysaccharide-binding protein (ng/mL)	7.28±0.1	6.32±0.15	<0.001
Tumor necrosis factor-α (pg/mL)	22.5±3.1	14.3±3	0.07
Interleukin-6 (pg/mL)	36.6±7.8	20.6±5.4	0.09
Systemic hemodynamics			
Mean arterial pressure (mmHg)	84.6±1.2	92.9±1	<0.001
Heart rate (beats/min)	76±3	74±2	0.4
Cardiac output (L/min)	7.72±0.29	6.11±0.28	0.002
Systemic vascular resistance (dynes/sec/cm^{-5})	1172±43	1579±67	<0.001
Neurohumoral factors			
Plasma renin activity (ng/mL/h)	8.79±0.5	5.17±0.56	<0.001
Aldosterone (ng/mL)	576±36.8	443±58.4	0.08
Renal function			
Glomerular filtration rate (mL/min)	73.5±1.1	79.4±2.5	0.02
Liver fibrosis assessment			
Liver stiffness (kPa)	26.7±1.4	22.2±0.9	0.04

Data are reported as mean ± standard error or absolute (percentage)
Predictors at a level of P<0.05 were considered for multivariate analysis
SIBO, small intestinal bacterial overgrowth; MELD, model for end-stage liver disease

Table 2 Variables independently associated with the presence of small intestinal bacterial overgrowth in patients with cirrhosis and ascites

Variables	Odds ratio	95%CI	P-value
Lipopolysaccharide-binding protein	2.447	1.088-5.557	0.007
Plasma renin activity	1.412	1.100-1.812	0.01

CI, confidence interval

Correlation between peak breath hydrogen concentration and other variables

Among patients with SIBO, peak breath hydrogen concentration was correlated significantly with serum LBP (r=0.678; P<0.001) (Fig. 1) Positive but non-significant correlations were noted between peak breath hydrogen concentration and the levels of TNF-α and IL6 (r=0.205; P=0.09 and r=0.198; P=0.1, respectively). Significant correlations between peak breath hydrogen concentration and MAP (r=-0.549; P<0.001), CO (r=0.343; P=0.008), SVR (r=-0.492; P=0.001), PRA (r=0.366; P=0.005), plasma aldosterone (r=0.465; P<0.001) and GFR (r=0.467; P<0.001) were observed in patients with SIBO (Fig. 2). Finally, peak breath hydrogen concentration was correlated significantly with liver stiffness (r=0.370; P=0.004) in the latter patient subgroup (Fig. 3). No significant correlations were found between peak breath hydrogen concentration and other variables in patients without SIBO (data not shown).

Correlation between inflammatory markers and other variables in patients with SIBO

Among the inflammatory markers, only serum LBP was correlated significantly with MAP (r=-0.435; P=0.001), SVR (r=-0.371; P=0.004), PRA (r=0.548; P<0.001), GFR (r=0.462; P<0.001), and liver stiffness (r=0.315; P=0.01) in patients with SIBO.

Discussion

The present study demonstrated a high prevalence of SIBO in a cohort of patients with cirrhosis and ascites, which is in agreement with the results of previous studies [14,19]. Hydrogen breath testing was used for the diagnosis of SIBO in our study. This method is based on the fact that bacterial metabolism of carbohydrates is the sole source of hydrogen in humans. As the absorbed hydrogen is exhaled, its production can be measured with a breath analyzer. Accordingly, breath hydrogen concentration is measured before and after the oral administration of non-absorbed carbohydrates. Glucose and lactulose are the most commonly used substrates for the diagnosis of SIBO. Lactulose HBT has been assumed to be more accurate than glucose HBT for detecting SIBO in patients with cirrhosis [11].

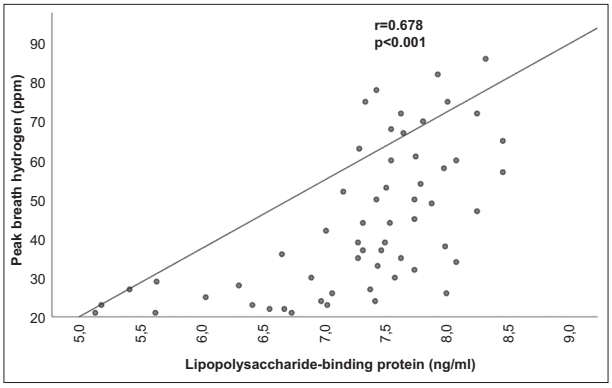

Figure 1 Correlation between peak breath hydrogen concentration and serum levels of lipopolysaccharide-binding protein in patients with cirrhosis, ascites, and small intestinal bacterial overgrowth

Our findings showed that, among patients with cirrhosis, ascites, and similar liver disease severity, the presence of SIBO is associated with a more pronounced systemic inflammatory activity. In particular, serum LBP was identified as an independent factor for the presence of SIBO. Moreover, a strong correlation between peak breath hydrogen concentration and LBP levels was demonstrated among patients with SIBO. In the present study, LBP was utilized as a surrogate marker of LPS, the major molecular component of the outer membrane of gram-negative bacteria, since the latter has a half-life of only 2-4 min as compared to 12-24 h for LBP [20]. Evidence from a limited number of studies also pointed to a link between SIBO and systemic inflammation state in patients with cirrhosis, but patients with ascites were not analyzed separately. In the study by Jun *et al* [14], serum bacterial DNA was detected in 10 of 32 (31.3%) patients with SIBO, as opposed to only 1 of 21 (4.8%) patients without SIBO. Moreover, SIBO was independently associated with the presence of bacterial DNA in the peripheral blood. Other studies found significantly higher circulating levels of endotoxin [15,16], TNF-α, and IL-6 [15] in patients with cirrhosis and SIBO than in those without SIBO. A trend toward higher serum TNF-α and IL-6 levels in patients with SIBO was also observed in our study.

The presence of SIBO in this study identified a subset of patients with cirrhosis and ascites whose hemodynamic status was more deranged. Lower SVR in these patients, compared to those without SIBO, was the consequence of lower MAP and higher CO. As a result, patients with SIBO exhibited an enhanced homeostatic activation of the RAAS. Furthermore, the occurrence of SIBO was independently associated with PRA. It was notable that peak breath hydrogen concentration was correlated significantly with the systemic hemodynamic measurements and the activity of vasoactive factors among patients with SIBO. Our findings corroborate that of a previous study showing a relationship between SIBO and more intense features of hyperdynamic circulation in patients with cirrhosis (56% with ascites) [17]. Our study also indicated a potential involvement of inflammatory burden in systemic hemodynamic impairment in patients with SIBO. In keeping with our observations, a previous study by Albillos *et al* [21]

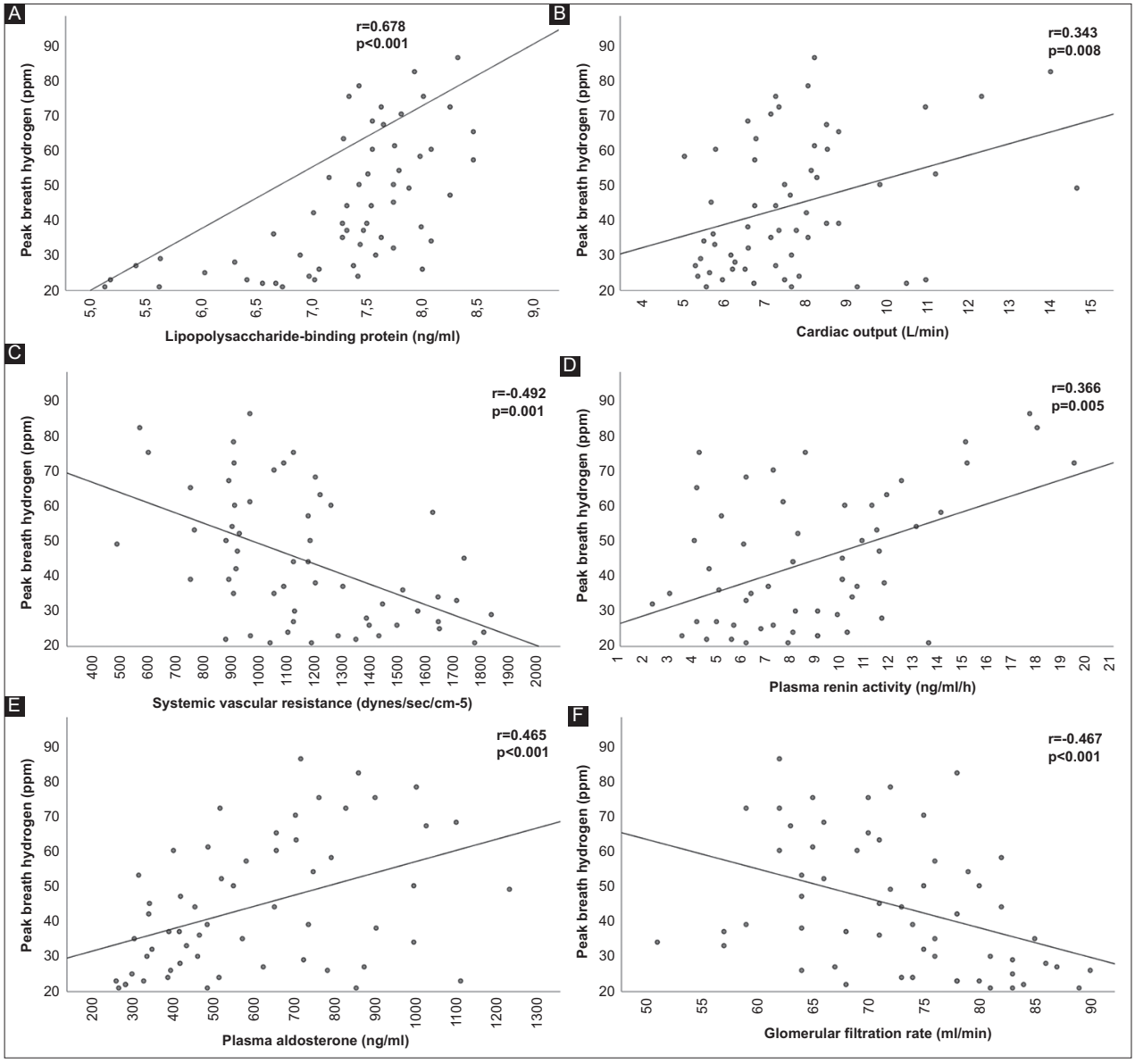

Figure 2 Correlation between peak breath hydrogen concentration and mean arterial pressure (panel A), cardiac output (panel B), systemic vascular resistance (panel C), plasma renin activity (panel D), plasma aldosterone levels (panel E), and glomerular filtration rate (panel F) in patients with cirrhosis, ascites, and small intestinal bacterial overgrowth

provided indirect but compelling evidence regarding the association of gut microflora with systemic inflammation and circulatory abnormalities in patients with cirrhosis and ascites. Moreover, selective intestinal decontamination in these patients, using oral norfloxacin [21,22] or rifaximin [23], significantly reduced the circulating levels of endotoxin, LBP and proinflammatory cytokines, and improved systemic hemodynamics in association with a marked reduction in the activity of endogenous vasoactive systems.

Our results also demonstrated a negative impact of SIBO on renal function in nonazotemic patients with cirrhosis and ascites, which was possibly linked to worse systemic hemodynamics in the SIBO subgroup. In particular, peak breath hydrogen levels were significantly inversely correlated with renal function in patients with SIBO. In support of these observations, we have previously reported an improvement of renal function, along with amelioration of systemic hemodynamics, in patients with cirrhosis and ascites after prevention of endotoxemia with rifaximin treatment [23]. Experimental evidence has also confirmed that LPS may directly impair renal function in cirrhosis [24] via distortion of glomerular integrity [25] and renal vasoconstriction [26,27], independently of systemic hemodynamic changes [27]. On the other hand, it could be hypothesized that differences in renal function might be a potential factor contributing to SIBO in this subgroup [28]. However, such an association has been mainly reported for patients with chronic kidney disease, and particularly for those with end-stage renal disease [28,29]. By

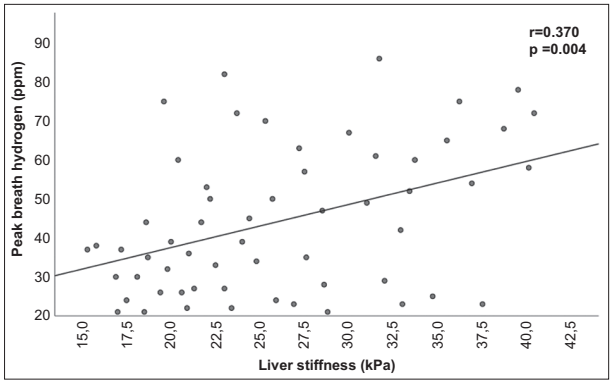

Figure 3 Correlation between peak breath hydrogen concentration and liver stiffness in patients with cirrhosis, ascites, and small intestinal bacterial overgrowth

contrast, only a minority of patients with SIBO in the present study had GFR below 60 mL/min, a threshold used to define chronic kidney disease in patients with renal impairment, including patients with cirrhosis [30].

As the liver is constantly exposed to gut-derived bacterial products through the portal vein system [31], the potential connection between gut microbiota and hepatic fibrogenesis in patients with chronic liver disease has attracted growing interest [32]. The current study is the first to present data showing that SIBO in patients with cirrhosis and ascites is associated with a higher degree of hepatic fibrosis, as assessed by SWE. Moreover, a significant correlation between peak breath hydrogen concentration and liver stiffness was found in patients with SIBO. In line with our observations, a recent study demonstrated significant correlations between markers of liver fibrogenesis and systemic inflammatory markers, including LBP, in patients with established cirrhosis [7]. Experimental findings have also shown that LPS promotes the development and progression of liver fibrosis by activating hepatic stellate cells through functional Toll-like receptors 4 [33,34]. On the other hand, inhibition of the Toll-like receptor 4 signaling pathway in mouse models of chronic liver injury attenuated liver fibrosis [35].

A limitation of our study is that we did not use jejunal aspiration and culture to diagnose SIBO, which is considered the gold standard [9]. However, this method is invasive, requiring intubation of the small bowel and a laboratory equipped with isolating anaerobes. For this reason, carbohydrate breath tests are currently recommended as the first-line investigation as they are convenient, noninvasive and cost-effective [9,10]. The relatively small number of included patients is another limitation of this study, even though clear differences were found between patients with and without SIBO for a number of variables, particularly LBP and those related to circulatory function.

In conclusion, our findings suggest that SIBO in patients with cirrhosis and ascites may contribute to enhanced systemic inflammatory activity, worse systemic hemodynamic status and renal function, and more severe liver fibrosis. On the basis our results, we consider that the clinical consequences of SIBO treatment in patients with advanced cirrhosis need to be investigated in future studies.

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Summary Box

What is already known:

- Cirrhosis is characterized by translocation of bacteria and their products into the systemic circulation, triggering a systemic inflammatory response that has been associated with circulatory and renal dysfunction
- Gut-derived bacterial molecules can stimulate fibrogenic activity in the liver
- Small intestinal bacterial overgrowth (SIBO) is a major determinant of bacterial translocation in cirrhosis and is more common in patients with ascites

What the new findings are:

- The presence of SIBO in patients with cirrhosis and ascites was strongly associated with greater systemic inflammation
- SIBO in these patients predisposed to worse circulatory and renal function
- Among patients with cirrhosis and ascites, the presence of SIBO was linked to a higher degree of liver fibrosis

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