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PORTAL VEIN THROMBUS, PORTAL HEMODYNAMICS AND PORTAL VEIN INVASION

Relationship among gastric motility, autonomic activity, and portal hemodynamics in patients with liver cirrhosis

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Abstract

Background and Aims: We examined the effects of the autonomic nervous function and the volume of portal blood flow to clarify the mechanism of the abnormal gastric motility in patients with liver cirrhosis.

Methods: Heart rate variability, electrogastrogram (EGG), and volume of portal blood flow were measured before and after a meal in 27 patients with liver cirrhosis (LC group) and in 20 normal subjects (N group). Autonomic nervous function was evaluated by using spectral analysis of heart rate variability. We used the cine phase-contrast (PC) method, using magnetic resonance imaging (MRI) to measure the portal flow, while the peak frequency and spectral power of the EGG were measured at pre- and postprandial change.

Results: The ratio of low frequency power to high frequency power (LF/HF) was significantly higher, and the HF power was significantly lower in the LC group than in the N group both before and after a meal. In both groups, the electrogastrographic peak power ratio before and after a meal showed a positive correlation with the HF ratio, and an inverse correlation with the LF/HF ratio. In addition, portal blood flow volume was significantly decreased in the LC group than in the N group. However, the increased rate of portal blood flow after a meal correlated positively with the increased rate of electrogastrographic peak power. Moreover, gastric motility was positively correlated with esophageal varices and coma scale with the use of multivariate analysis.

Conclusions: Parasympathetic hypofunction, sympathetic hyperfunction and portal hemodynamics were closely related with gastric motility in cirrhotic patients. In addition, gastric motility was decreased, at least in part, by the ingestion of food in cirrhotic patients because of abnormalities in autonomic functions and portal blood flow following a meal.

Key words: autonomic activity, gastric motility, liver cirrhosis, portal blood flow.

INTRODUCTION

Patients with liver cirrhosis often show abnormal gastric motility associated with prolonged gastric emptying and decreased gastric wall compliance. Suyama[1] and Isobe *et al.*[2] reported the shortening of gastric emptying by half, and Mansorov and Pisanova[3] reported a decreased electrogastrographic activity in patients with liver cirrhosis. Gastric motility is controlled by gastrointestinal hormones and innervated by sympathetic and parasympathetic nerves, as well as by the mural and myenteric nerve plexus. Abnormalities in neural control and gastrointestinal hormones occur in cases of liver cirrhosis.[2,4–7] The pyloric tone is controlled by sympathetic functions.[8] Uijtdehaage *et al.* evaluated the relationship between respiratory sinus arrhythmia and electrogastrographic activity during motion sickness, and they reported that the cardiac branch of the vagus nerve nor-

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malizes the electrogastrographic rhythm, and that electrogastrographic arrhythmia is induced by a decreased vagal tone, resulting in nausea.[9] Moreover, Undeland *et al.* reported the correlation between parasympathetic hypofunction and gastric motility disturbance in diabetic patients.[10] In addition, portal hemodynamics also influences gastric motility. Non-erosive lesions are frequently observed in the gastric mucosa of patients whose cirrhosis is complicated by portal hypertension. This hypertension causes the microcirculation disorder that induces these non-erosive lesions. These studies indicate that parasympathetic nerves control antroduodenal motility by means of acetylcholine secretion.[9–10] Although these studies indicate that gastric motility is closely related to autonomic nervous function and portal blood flow, there have been a few studies about the relationship of these two factors. In the present study, by using spectral analysis of heart rate variability and a novel method of portal blood flow imaging by MRI, the relationship among abnormalities of gastric motility, autonomic functions, and portal blood flow was evaluated.

METHODS

Subjects

The subjects consisted of 20 healthy volunteers (N group (normal subjects): 13 males and seven females, mean age: 62.1 ± 8.7 years) and 27 patients with liver cirrhosis (LC group: 19 males and eight females, mean age: 65.0 ± 6.8 years). All subjects in the N group were clinically healthy, showing normal physical findings and having no history of cardiopulmonary or gastrointestinal diseases, nor showing abnormalities on standard 12-lead electrocardiogram (ECG), chest X-rays, hematological and biochemical examinations, or urinary analyses. All subjects in the LC group were diagnosed as having liver cirrhosis based on their clinical symptoms,[11] and the results of hematological and biochemical examinations, examination of coagulative function, abdominal ultrasonography, abdominal CT, and liver biopsy. According to Child's classification, patients in the LC group were classified into the following two groups: a Child A group (four males and three females, mean age: 62.9 ± 5.8 years) and a Child B and C group (15 males and five females, mean age: 65.6 ± 7.6 years). Prior to participation in the present study, all subjects gave their written informed consent and ethical approval. Table 1 shows the clinical characteristics of patients in the LC group. Regarding Child–Pugh scores, total bilirubin levels, prothrombin time, transaminase levels, the evidence of esophageal varices, and coma scales, there were significant differences between the Child A and, Child B and C groups.

Recording and analysis of electrogastrogram

By using an ambulatory electrogastrogram (EGG) recorder (NIPRO EG, A & D, Tokyo, Japan), EGGs were obtained at rest after more than a 5-h fast and continuously recorded until 2 h following a meal. The central terminal electrode for the EGG was placed at the midpoint between the xiphoideus processus and the navel, and four other electrodes were placed above, below, left, and right of the stomach (Fig. 1). This ambulatory EGG recorder weighs 300 g, and 4-channel EGGs were recorded stably because of the 10th filter sampling at 1-s cycles. Data recording was performed at 13 bits, and a frequency between 2.1 and 6.0 cycles/min (c.p.m.). Data obtained were transferred to a personal computer via an RS-232C port, and frequency analysis (fast Fourier transformation; FFT analysis) was performed with respect to 512 points by using software for EGG (NIPRO EG, A & D).

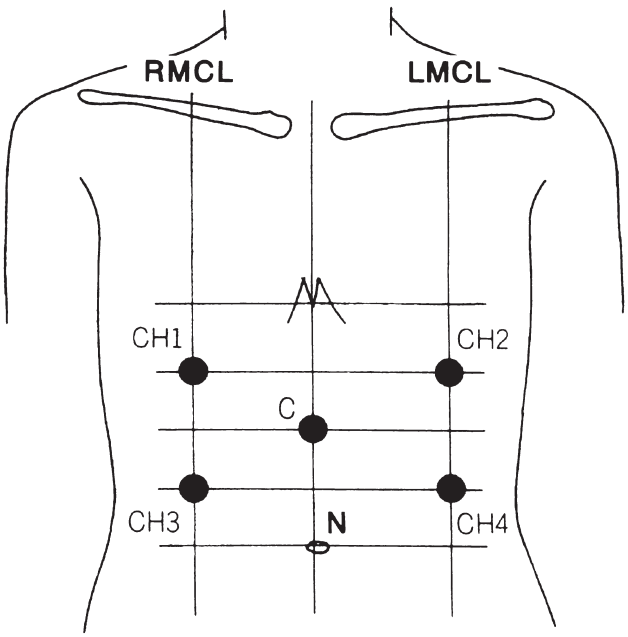

Figure 1 Electrode positions for recording electrogastrogram. RMCL, right mid-clavicular line; LMCL, left mid-clavicular line; N, navel; CH 1, channel 1; CH 2, channel 2; CH 3, channel 3; CH 4, channel 4; C, central terminal electrode.

By using FFT analysis, dominant frequencies and their amplitudes (peak powers) were obtained from 4-channel EGGs during fasting, and 30 and 60 min after a meal, and the mean values were calculated. The ratio of the dominant frequency obtained following a meal to that during fasting (frequency ratio), as well as the ratio of the peak power obtained following a meal to the peak power during fasting (power ratio) was evaluated by using previously established methods.[12–14]

Analysis of autonomic nervous functions using heart rate variability

Autonomic nervous functions were evaluated by means of spectral analysis of heart rate variability. By using a

Table 1 Clinical characteristics in the liver cirrhosis (LC) groups

	LC group		
	Child A	Child B and C	*P*
Subjects (*n*)	7	20	
Age (years)	62.9 ± 5.8	65.6 ± 7.6	NS
Gender (male/female)	4/3	15/5	NS
Child–Pugh score	5.7 ± 0.5	8.7 ± 1.4	0.001
Ascites	0 (0)	7 (35)	NS
T-Bil (mg/dL)	1.7 ± 0.6	2.3 ± 0.6	0.029
Alb (g/dL)	3.5 ± 0.5	3.1 ± 0.7	NS
PT (%)	59.6 ± 10.0	49.4 ± 7.2	0.006
AST	37.1 ± 11.0	59.8 ± 22.4	0.018
ALT	32.3 ± 7.1	51.2 ± 19.6	0.021
T-Cho	161 ± 15	154 ± 25	NS
Esophageal varices	0 (0)	14 (70)	0.002
Past history of GI bleeding	0 (0)	4 (20)	NS
Coma scale	0.3 ± 0.5	1.5 ± 0.9	0.003
Past history of hepatic encephalopathy	1 (14)	10 (50)	NS
Etiology of cirrhosis			
HBV	2 (29)	3 (15)	NS
HCV	4 (57)	17 (85)	NS
Alcohol	1 (14)	0 (0)	NS
Treatment			
Diuretic	2 (29)	10 (50)	NS
Hyperammonemia therapy	1 (14)	11 (55)	NS
EIS and/or EVL	0 (0)	13 (65)	0.007

Results in parentheses are percentages. T-Bil, total bilirubin; Alb, albumin; PT, prothrombin time; AST, aspartate aminotransferase; ALT, alanine aminotransferase; T-Cho, total cholesterol; GI bleeding, gastrointestinal bleeding; HBV, hepatitis B virus; HCV, hepatitis C virus; EIS, endoscopic injection sclerotherapy; EVL, endoscopic variceal ligation; NS, not significant.

2-channel Holter electrocardiograph (SM-50; Fukuda Denshi Corporation, Tokyo, Japan), ECG was also continuously recorded from a fasting state to 2 h after a meal. The Holter ECG was analyzed by using a work station (DWM-9000H; Fukuda Denshi Corporation, Tokyo, Japan), and transferred to a computer via an RS-232C for heart rate variability analysis. By using a time-series data-analyzing program (Fukuda Denshi Corporation), the spectral analysis of heart rate variability was performed regarding the data of 512 heart beats obtained before and after a meal.

For spectral analyses of heart rate variability, the low frequency component (LF power; 0.04–0.15 Hz), the high frequency component (HF power; 0.15–0.40 Hz), and the ratio of LF power to HF power (LF/HF) were calculated by using the FFT algorithm before and after a meal. The HF power is generally thought to reflect parasympathetic function related to respiratory activity, while LF power is a marker of sympathetic modulation or a parameter that includes both sympathetic and vagal influences. The LF/HF is an index of the sympathovagal balance or the sympathetic modulation.[15–18] The heart rate variability was analyzed using spline function and hamming window (FFT analyzing).

Magnetic resonance imaging evaluation of velocity and volume of portal blood flow

Electrogastrogram and Holter ECG were recorded simultaneously, but MR images were acquired at the same time the next day under the same dietary conditions (700 kcal, including fat 10 g, sugar 120 g, and protein 30 g). By using MRI, portal hemodynamics were evaluated by assessing velocities and volumes of portal blood flow obtained before and 1 h after a meal. Initially, cross-sectional MR images of the upper abdomen were obtained to visualize the portal vein, and MR images exhibiting the clearest view of the portal vein near the hepatic hilum were selected. By using the above cross-sectional MR images, the transverse section perpendicular to the blood vessel near the left and right bifurcations of the main portal vein was scanned to avoid the influence of the collateral vein, and the region of interest (ROI) was established along the medial wall of the cross-sectional images of the portal vein. Portal flow velocity was measured by using the pulse wave-gated cine PC method with correction for respiratory movement (TR = 33 msec, flip angle = 30 degrees, matrix size: 256 × 128, field of view = 24 cm, slice thickness = 5 mm). One cardiac cycle was divided into

32 segments, and the mean value of portal blood flow velocity in each segment was considered to be the flow velocity at the respective time points.

The blood flow boundary varies in images obtained by the cine-phase-contrast (cine-PC) method[19,20] because of the varying conditions affecting the establishment of the level and width of the windows; the respiratory and pulse wave-gated spin echo method (time of echo (TE) = 10 msec, repetition time (TR) = 1 cardiac cycle (R-R) interval, matrix size: 256 × 128, and slice thickness: 5 mm) was used to measure the vascular cross-sectional area. The cross-sectional area of the portal vein was measured at the site identical to that used for flow velocity measurement. Furthermore, the saturation pulse parallel to the measurement site was added in both the upward and downward directions, and the ROI was established along the medial wall of the portal vein in the MR images obtained.

Statistical analysis

Data are expressed as mean ± SD. Values were compared between the two groups by using the paired or unpaired Student's *t*-test, chi-squared test, and a multiple logistic regression analysis. The results of the logistic analysis were presented as estimated odds ratios. A level of $P < 0.05$ was regarded as statistically significant. Data processing and analysis were performed with a STATVIEW statistical package (StatView 5.0; SAS Institute, Cary, NC, USA).

RESULTS

Electrogastrograms in the normal and liver cirrhosis groups

Figure 2a shows the EGGs and FFT analysis in a healthy subject obtained during fasting and 60 min after a meal. Amplitudes of 4-channel EGGs were increased after a meal, and FFT analysis demonstrated that the mean values of peak power and dominant frequency from 4-channel EGGs obtained in a fasting state were 238 μVpp and 3.16 c.p.m., respectively. These values were increased after the meal (327 μVpp and 3.38 c.p.m.). The frequency ratio and power ratio in this subject between fasting and 60 min following a meal were 1.07 and 1.37, respectively. Figure 2b shows EGGs and FFT analysis in a patient with cirrhosis. Compared to healthy subjects, the amplitudes of 4-channel EGGs did not increase after a meal. Fasting peak power and dominant frequency obtained from 4-channel EGGs were 126 μVpp and 2.82 c.p.m., respectively, and those of 60 min after a meal were 97 μVpp and 2.94 c.p.m., respectively. The frequency ratio and power ratio in this patient between fasting and 60 min after a meal were 1.04 and 0.77, respectively.

Table 2 shows dominant frequencies and frequency ratio in the N and LC groups obtained at fasting, and at 30 and 60 min following a meal. Dominant frequency in the N and Child A groups was significantly increased 60 min following a meal. However, dominant frequency in the Child B and C group was not increased either 30 or 60 min following a meal. There was no significant difference in the frequency ratio between the two groups. Moreover, the frequency ratios obtained 60 min after a meal were not significantly different between the two groups, although the frequency ratio obtained 60 min following a meal was significantly higher than that of 30 min after a meal in the N group ($P < 0.01$).

Table 3 shows peak power amplitude and power ratio in the N and LC groups obtained at fasting, and at 30 and 60 min following a meal. Peak power obtained 30 and 60 min following a meal was significantly increased in the N and Child A groups. In the Child B and C group, however, the increase was not significant after a meal. There were no significant differences in power ratios obtained 30 min folowing a meal between the N and LC groups. However, the power ratios obtained 60 min following a meal were significantly higher in the N and Child A groups than in the Child B and C group.

Table 2 Dominant frequency and frequency ratio in normal (N) and liver cirrhosis (LC) groups

Group	Fasting	30 min after meal	60 min after meal
N			
Dominant frequency (c.p.m.)	3.06 ± 0.11	3.13 ± 0.21	3.27 ± 0.24†
Frequency ratio	—	1.02 ± 0.06	1.07 ± 0.06‡
LC			
Child A			
Dominant frequency (c.p.m.)	2.99 ± 0.13	3.12 ± 0.20⋆	3.19 ± 0.15†
Frequency ratio	—	1.05 ± 0.05	1.07 ± 0.03
Child B and C			
Dominant frequency (c.p.m.)	2.98 ± 0.21	3.08 ± 0.26	3.06 ± 0.25§
Frequency ratio	—	1.04 ± 0.10	1.03 ± 0.09

⋆$P < 0.05$ versus fasting; †$P < 0.01$ versus fasting; ‡$P < 0.01$ versus 30 min after meal; §$P < 0.01$ versus N group; Data are expressed as mean ± SD.

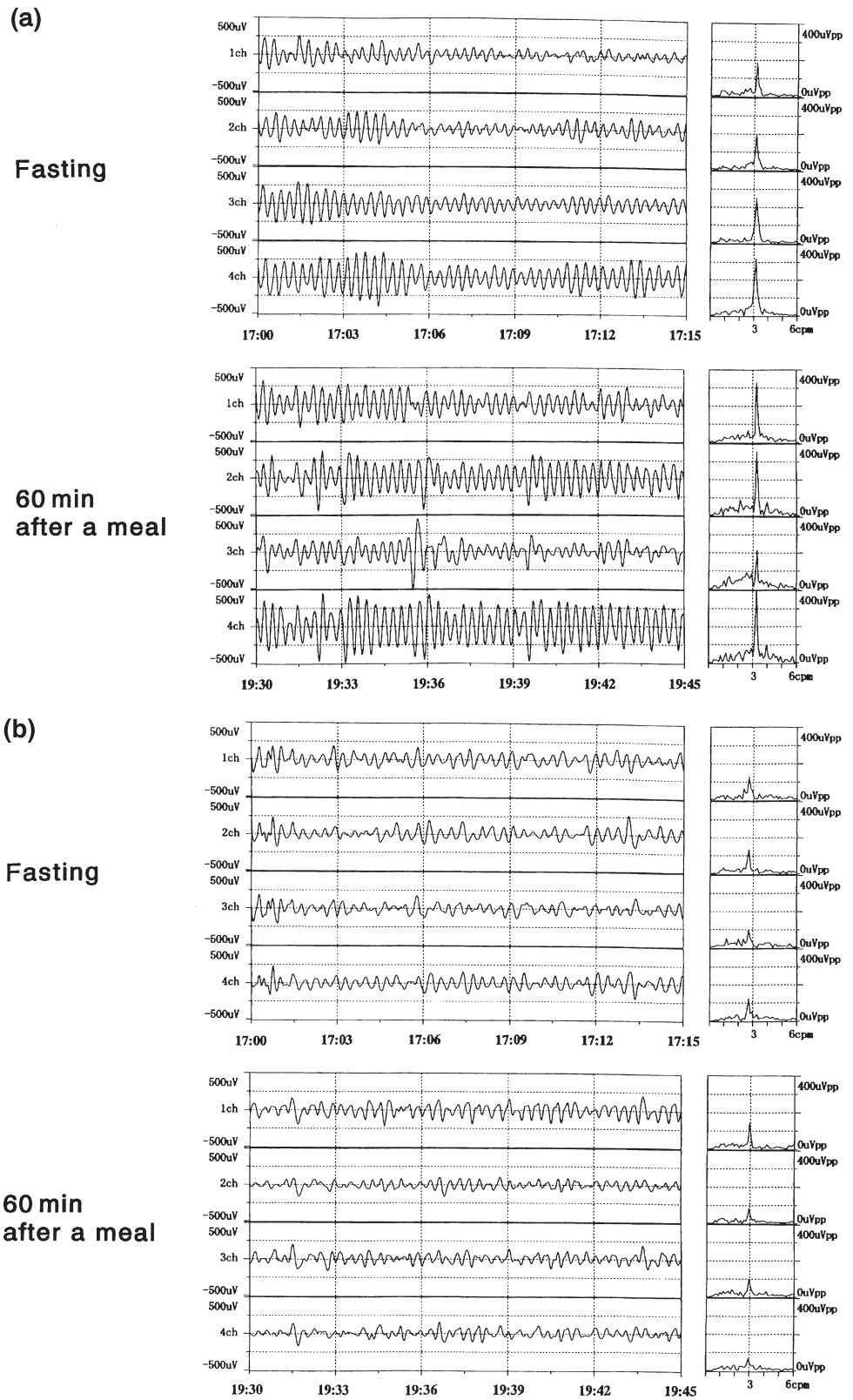

Figure 2 Electrogastrogram and fast Fourier transformation analysis during fasting and 60 min after a meal. (a) Healthy subject (62-year-old, male), (b) cirrhotic patient (67-year-old, male).

Table 3 Peak power amplitude and power ratio in normal (N) and liver cirrhosis (LC) groups

Group	Fasting	30 min after meal	60 min after meal
N			
Peak power amplitude (μVpp)	98.3 ± 38.3	151.7 ± 63.8★	210.7 ± 102.0★
Power ratio	—	1.62 ± 0.61	2.22 ± 0.86‡
LC			
Child A			
Peak power amplitude (μVpp)	98.7 ± 30.2	136.2 ± 39.9★	174.9 ± 42.6★
Power ratio	—	1.40 ± 0.23	1.87 ± 0.55†
Child B and C			
Peak power amplitude (μVpp)	97.6 ± 43.2	120.6 ± 49.0	119.2 ± 37.9§¶
Power ratio	—	1.38 ± 0.70	1.31 ± 0.31§¶

★$P < 0.01$ versus fasting; †$P < 0.05$ versus 30 min after meal; ‡$P < 0.01$ versus 30 min after meal; §$P < 0.01$ versus N group; ¶$P < 0.01$ versus Child A; Data are expressed as mean ± SD.

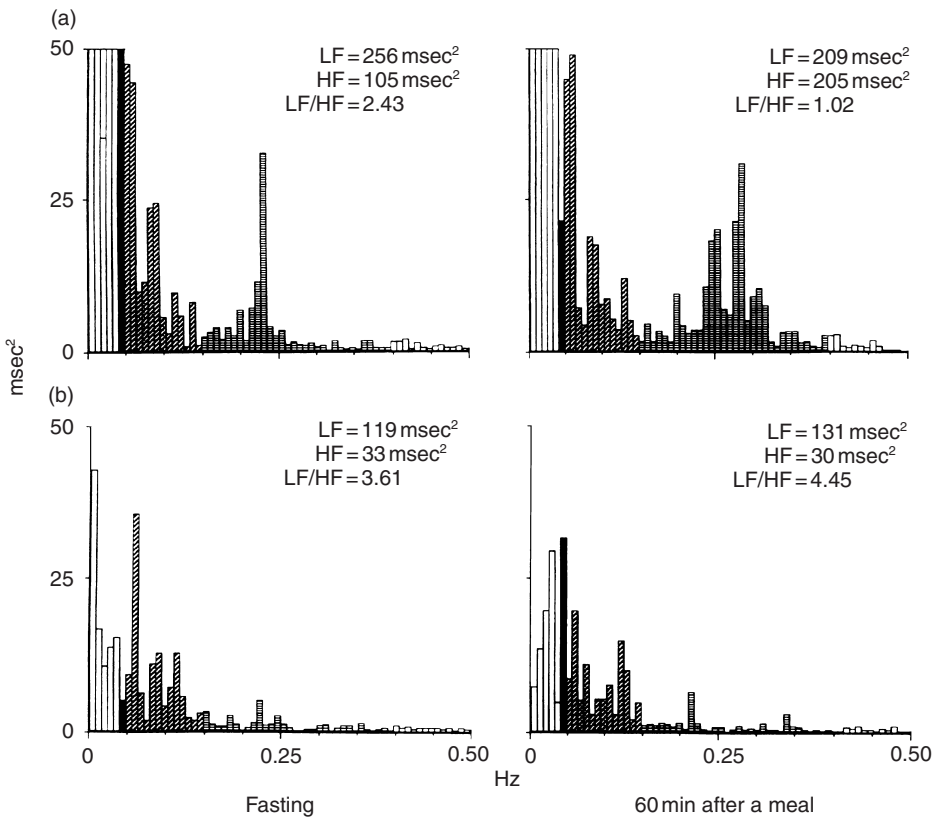

Figure 3 Spectral analysis of heart rate variability in a (a) healthy subject and a (b) cirrhotic patient (b) during fasting and 60 min after a meal. (▨) LF, low frequence component; (▤) HF, high frequency component.

Autonomic activity in the normal and liver cirrhosis groups

Figure 3 shows the results of spectral analysis of heart rate variability performed both in a healthy subject and a cirrhotic patient during fasting and 60 min following a meal. The HF power was increased in healthy subjects following a meal. However, both HF and LF powers were lower in cirrhotic patients than in healthy subjects.

Table 4 shows the serial changes in LF power, HF power, and LF/HF in the N and LC groups obtained before and after a meal. The LF power in the N and LC groups did not significantly vary 60 min after a meal. The HF power was increased in the N group 60 min after a meal, and was significantly decreased in the Child B and C group. However, the LF/HF was significantly increased in the Child B and C group 60 min after a meal. There were significant differences in LF/HF obtained 60 min following a meal between the N and Child B and C groups.

Portal hemodynamics in the normal and liver cirrhosis groups

Figure 4 shows the portal blood flow measurement in a healthy subject using an MRI. A transverse section perpendicular to the blood vessel near the left and right bifurcations of the main portal vein was set (Fig. 4a). The ROI was established along the medial wall of the cross-sectional image of the portal vein (Fig. 4b). The mean value of portal blood flow velocity before a meal and 60 min after a meal was 9.7 and 16.2 cm/s, respectively (Fig. 4c). The mean value of portal blood flow volume was increased in this subject after a meal (Fig. 4d; 537 mL/min before a meal *vs* 1251 mL/min after a meal).

Figure 5 shows the portal blood flow measurement in a cirrhotic patient using an MRI. A transverse section perpendicular to the blood vessel near the left and right bifurcations of the main portal vein was set (Fig. 5a). The ROI was established along the medial wall of the cross-sectional image of the portal vein (Fig. 5b). The mean value of portal blood flow velocity before a meal and 60 min after a meal was 8.8 and 9.7 cm/s, respectively (Fig. 5c). The mean portal blood flow volume was only slightly increased in this patient following a meal (Fig. 5d; 518 mL/min before a meal *vs* 682 mL/min after a meal).

Table 5 shows the vertical sectional area of the portal vein, and the portal blood flow velocity and volume between the N and LC groups before and after a meal. Although the vertical sectional area of the portal vein in the Child B and C group did not vary significantly 60 min after a meal, it was significantly increased in the N and Child B and C groups. The portal blood flow velocity and volume in the N and LC groups was significantly increased 60 min after a meal. Moreover, portal blood flow velocity before a meal and 60 min after a meal were significantly higher in the N and Child A groups than in the Child B and C group. Portal blood flow volume 60 min following a meal was significantly higher in the N and Child A groups than in the LC group.

Table 4 Low frequency component (LF) power, high frequency component (HF) power and LF/HF in normal (N) and liver cirrhosis (LC) groups

Group	Fasting	60 min after meal
N		
LF power ($msec^2$)	215.5 ± 60.9	206.2 ± 68.0
HF power ($msec^2$)	151.8 ± 82.5	177.5 ± 94.0†
LF/HF	1.42 ± 1.00	1.20 ± 1.01★
LC		
Child A		
LF power ($msec^2$)	200.2 ± 16.7	178.4 ± 30.9
HF power ($msec^2$)	139.7 ± 40.0	148.6 ± 22.3
LF/HF	1.56 ± 0.71	1.25 ± 0.20
Child B and C		
LF power ($msec^2$)	173.4 ± 55.8‡	188.3 ± 83.3
HF power ($msec^2$)	138.8 ± 75.9	77.2 ± 57.3†§★★
LF/HF	2.08 ± 1.62	3.56 ± 2.31†§¶

★$P < 0.05$ versus fasting; †$P < 0.01$ versus fasting; ‡$P < 0.05$ versus N group; §$P < 0.01$ versus N group; ¶$P < 0.05$ versus Child A; ★★$P < 0.01$ versus Child A; Data are expressed as mean ± SD.

Gastric motility, autonomic activity, and portal hemodynamics in the liver cirrhosis group

Figure 6 shows the correlation between the changes in LF power, HF power, and LF/HF, and the EGG power ratio in the N and LC groups obtained during fasting and 60 min after a meal. In both groups, the changes in

Table 5 Portal blood flow velocity and volume in normal (N) and liver cirrhosis (LC) groups

Group	Fasting	60 min after meal
N		
Area of portal vein (cm^2)	1.29 ± 0.30	1.65 ± 0.44†
Portal blood flow velocity (cm/s)	9.7 ± 3.0	16.2 ± 2.7†
Portal blood flow volume (mL/min)	630 ± 84	1225 ± 362†
LC		
Child A		
Area of portal vein (cm^2)	1.20 ± 0.29	1.48 ± 0.26†
Portal blood flow velocity (cm/s)	9.2 ± 2.3	11.8 ± 4.5★
Portal blood flow volume (mL/min)	631 ± 69	1034 ± 100†
Child B and C		
Area of portal vein (cm^2)	0.98 ± 0.29	1.12 ± 0.35‡¶
Portal blood flow velocity (cm/s)	6.8 ± 2.2§¶	8.5 ± 1.5★§¶
Portal blood flow volume (mL/min)	596 ± 225	825 ± 231★§¶

★$P < 0.05$ versus fasting; †$P < 0.01$ versus fasting; ‡$P < 0.05$ versus N group; §$P < 0.01$ versus N group; ¶$P < 0.05$ versus Child A; Data are expressed as mean ± SD.

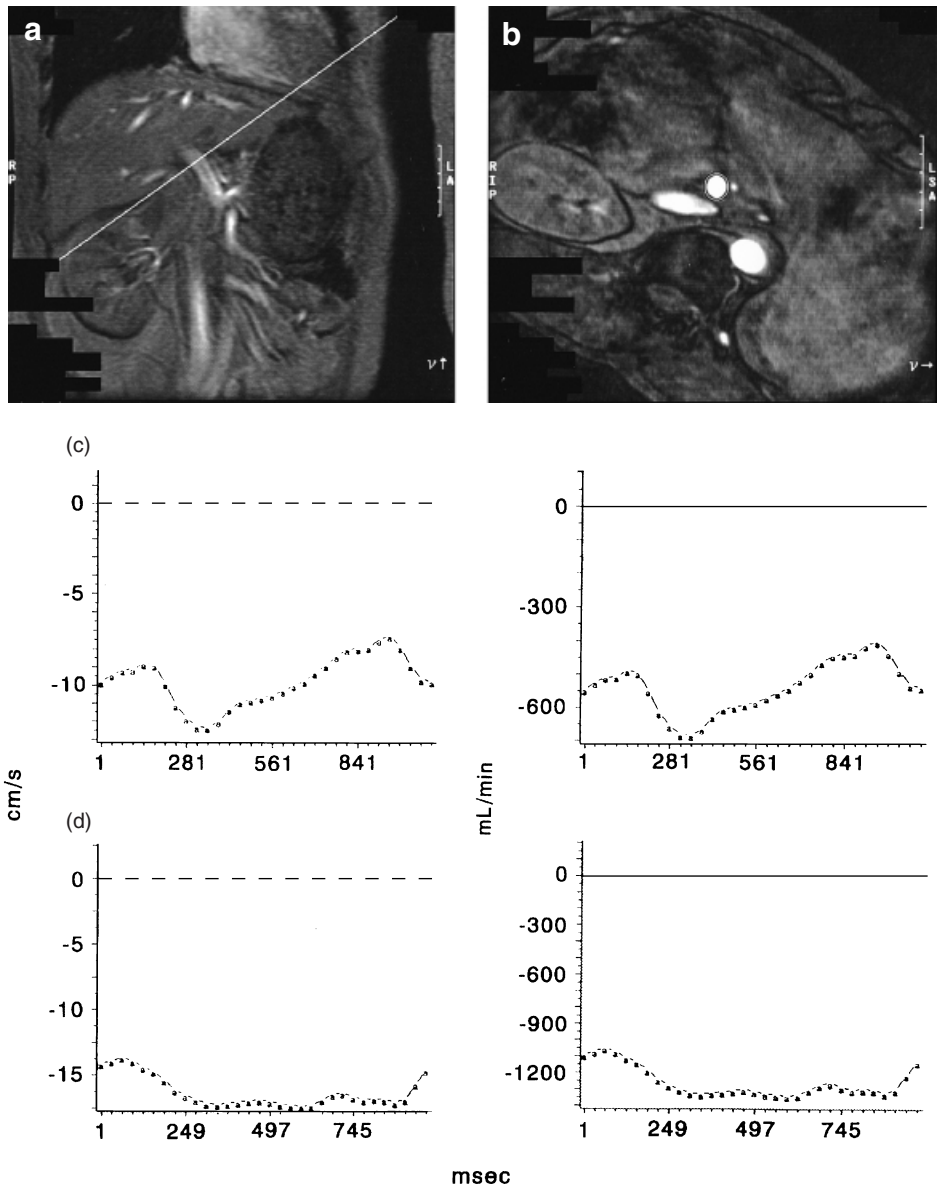

Figure 4 Portal blood flow measurement using MRI in a healthy subject. (a) Coronal gradient-echo image at the level of the portal vein, (b) oblique spin echo image. Portal vertical sectional area measurement was performed by manually traced region of interest, (c) mean value of portal blood flow velocity and volume (fasting), (d) mean value of portal blood flow velocity and volume (60 min after a meal). (---) Portal blood flow verlocity, (–) portal blood flow volume. a, average values of portal blood flow velocity and volume.

LF power and LF/HF were inversely correlated with the EGG power ratio. In addition, the ratio of changes in HF power positively correlated with the EGG power ratio in both groups.

Figure 7 shows the correlation between the changes in portal blood flow and the EGG power ratio in the N and LC groups obtained 60 min after a meal. A positive correlation between the changes in portal blood flow and the EGG power ratio was seen in both groups obtained after a meal.

Figure 8 shows the correlations among the changes in portal blood flow and changes in LF power, HF power, and LF/HF in the N and LC groups obtained during fasting and 60 min after a meal. Although a positive correlation was observed between changes in the HF power and increases in portal blood flow in the N group, there was no significant correlation between the two in the LC group.

Multivariate analysis of factors associated with gastric motility

The results of multivariate analysis of factors associated with gastric motility are shown in Table 6. Gastric motility was positively correlated with esophageal varices, coma scale, LF ratio, HF ratio, LF/HF ratio, and changes in portal blood flow.

DISCUSSION

The present study aimed to demonstrate that sympathetic and parasympathetic activities and portal hemodynamics are closely related to gastric motility in patients with liver cirrhosis. The results showed that in patients with liver cirrhosis, gastric motility was

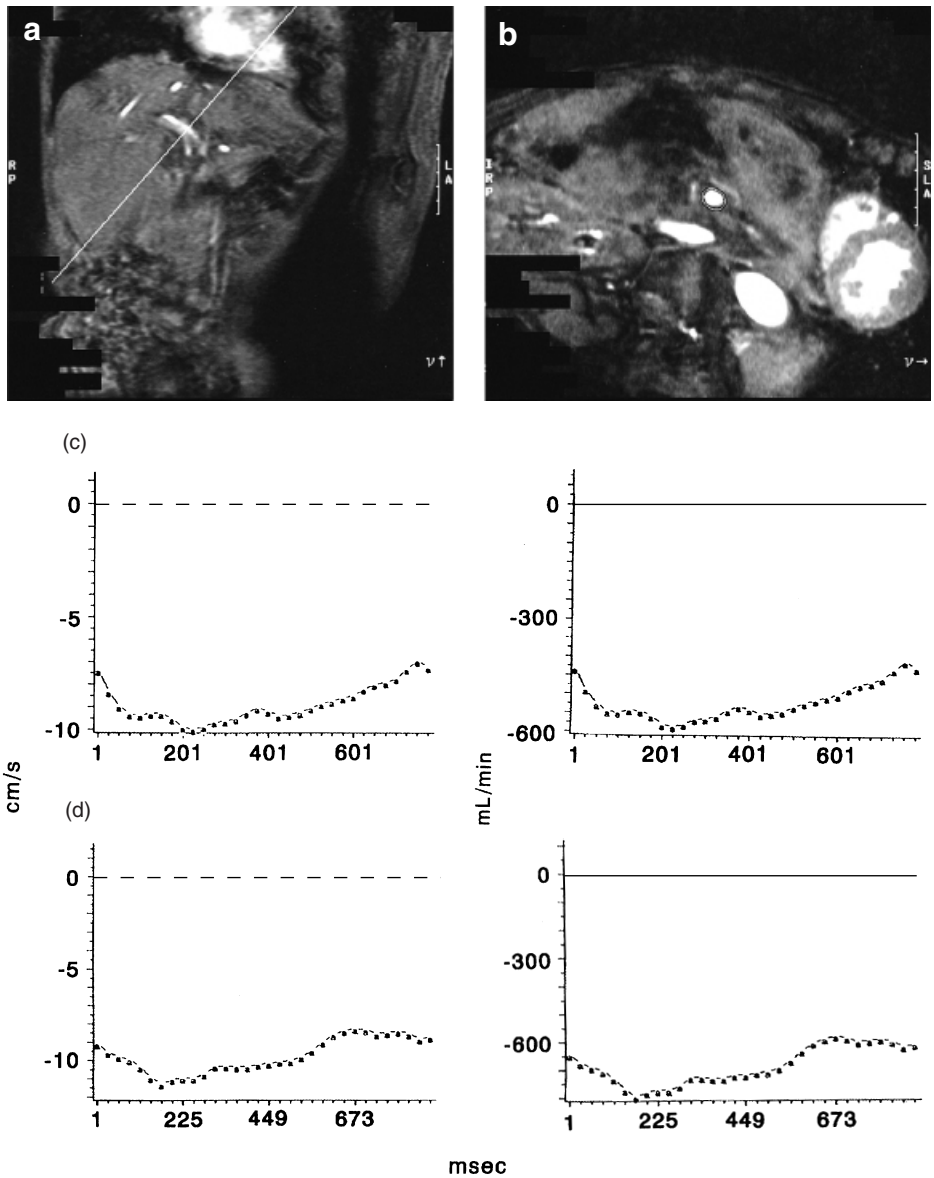

Figure 5 Portal blood flow measurement using MRI in a cirrhotic patient. (a) Coronal gradient-echo image at the level of the portal vein, (b) oblique spin echo image. Portal vertical sectional area measurement was performed by manually traced region of interest, (c) mean value of portal blood flow velocity and volume (fasting), (d) mean value of portal blood flow velocity and volume (60 min after a meal). (---) Portal blood flow velocity, (–) portal blood flow volume. a, average values of portal blood flow velocity and volume.

decreased because of increases in the sympathetic tone, decreases in parasympathetic tone, portal flow, and the ingestion of food.

Correlation between autonomic nervous functions and gastric motility

Both increased sympathetic tone and decreased parasympathetic tone are frequently observed in patients with liver cirrhosis, especially those in a hyperdynamic state, presumably because of increased nitric oxide (NO) production[21–28] and increased activity of the renin–angiotensin system.[29–31] In the present study, LF/HF (an index of sympathetic activity or balance between sympathetic and parasympathetic activities) was significantly higher and HF values (an index of parasympathetic functions) were significantly lower in the Child B and C group than in the N and Child A groups 60 min after a meal. The LF/HF were significantly more increased in the Child B and C group than in the N and Child A groups after the meal. Moreover, electrogastrographic peak power showed a positive correlation with the HF power and an inverse correlation with LF/HF in the LC group. These results indicate that both decreased HF power and increased LF/HF were closely related to abnormal gastric motility.

The present study was the first to clarify that this abnormal autonomic activity is closely related to decreased gastric motility. In agreement with our study, Stoddard *et al.* reported that increased sympathetic activity is an important factor in the development of

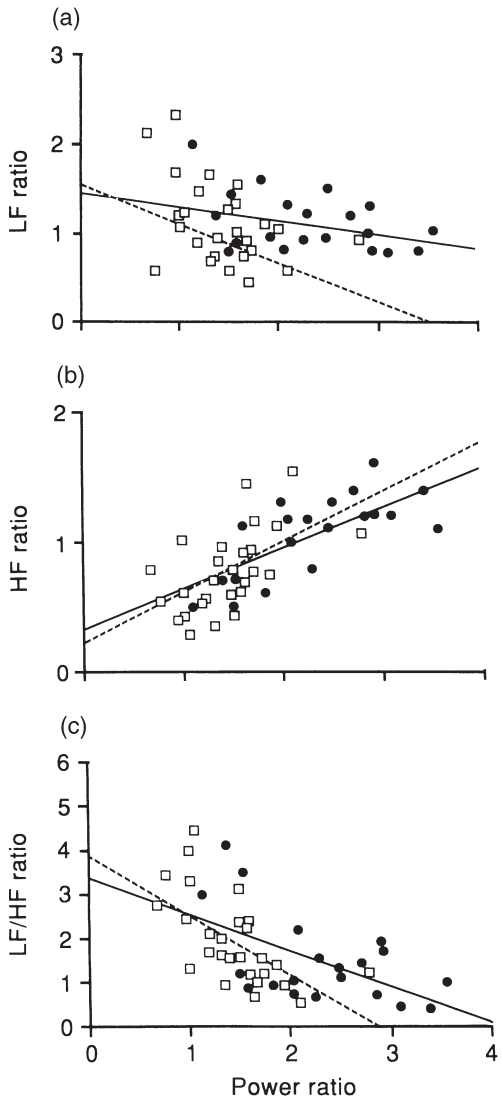

Figure 6 Correlation between the rate of changes in low frequency component (LF) power, high frequency component (HF) power, and LF/HF and the electrogastrogram power ratio in the (●, –) normal (N) and (□, ---) liver cirrhosis (LC) groups obtained during fasting and 1 h after a meal. (a) N group, $r=-0.45$, $P<0.05$; LC group, $r=-0.42$, $P<0.05$, (b) N group, $r=0.73$, $P<0.01$; LC group, $r=0.57$, $P<0.01$, (c) N group, $r=-0.56$, $P<0.05$; LC group, $r=-0.62$, $P<0.01$. LF 60 min after a meal, LF power at 60 min after a meal; HF 60 min after a meal, HF power at 60 min after a meal; LF/HF 60 min after a meal, LF/HF at 60 min after a meal; LF ratio = LF 60 min after a meal/LF fasting; HF ratio = HF 60 min after a meal/HF fasting; LF/HF ratio = (LF/HF 60 min after a meal)/(LF/HF fasting).

arrhythmia in patients who have undergone vagotomy.[32] Liang and Chen also reported that increased sympathetic tones inhibit the action potentials of the gastric smooth muscle and induce unsynchronous pacemaking in the stomach, resulting in the occurrence of electrogastrographic arrhythmia.[33]

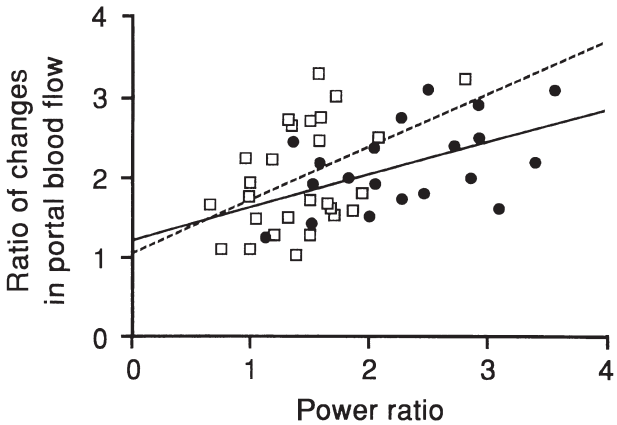

Figure 7 Correlation between portal blood flow and the electrogastrogram power ratio in the (●, –) normal (N; $r=0.49$, $P<0.05$) and (□, ---) liver cirrhosis (LC; $r=0.45$, $P<0.05$) groups obtained 60 min after a meal.

Table 6 Multivariate analysis of factors associated with gastric motility

Variable	Odds ratio (95% CI)	*P* value
Age	1.0 (0.9~1.1)	NS
Gender	0.4 (0.1~1.9)	NS
Ascites	0.4 (0.1~2.1)	NS
T-Bil	0.5 (0.2~1.1)	NS
Alb	1.5 (0.7~3.2)	NS
PT	1.0 (1.0~1.1)	NS
AST	1.0 (0.9~1.0)	NS
ALT	1.0 (0.9~1.0)	NS
T-Cho	1.0 (1.0~1.0)	NS
Esophageal varices	0.2 (0.0~0.7)	0.017
Past history of GI bleeding	0.3 (0.0~2.4)	NS
Coma scale	0.4 (0.2~0.8)	0.016
Past history of hepatic encephalopathy	0.4 (0.1~1.4)	NS
LF ratio	0.1 (0.0~0.6)	0.0109
HF ratio	872 (11~66 900)	0.002
LF/HF ratio	0.3 (0.1~0.6)	0.002
Changes in portal blood flow	5.0 (1.2~20.1)	0.024

T-Bil, total bilirubin; Alb, albumin; PT, prothrombin time; AST, aspartate aminotransferase; ALT, alanine aminotransferase; T-Cho, total cholesterol; LF, low frequency component; HF, high frequency component. CI, confidence interval; LF ratio = LF 60 min after a meal/LF fasting; HF ratio, HF, 60 min after a meal/HF fasting; LF/HF ratio, (LF/HF 60 min after a meal)/(LF/HF fasting); LF 60 min after a meal, LF power at 60 min after a meal; HF 60 min after a meal, HF power at 60 min after a meal; LF/HF 60 min after a meal, LF/HF at 60 min after a meal.

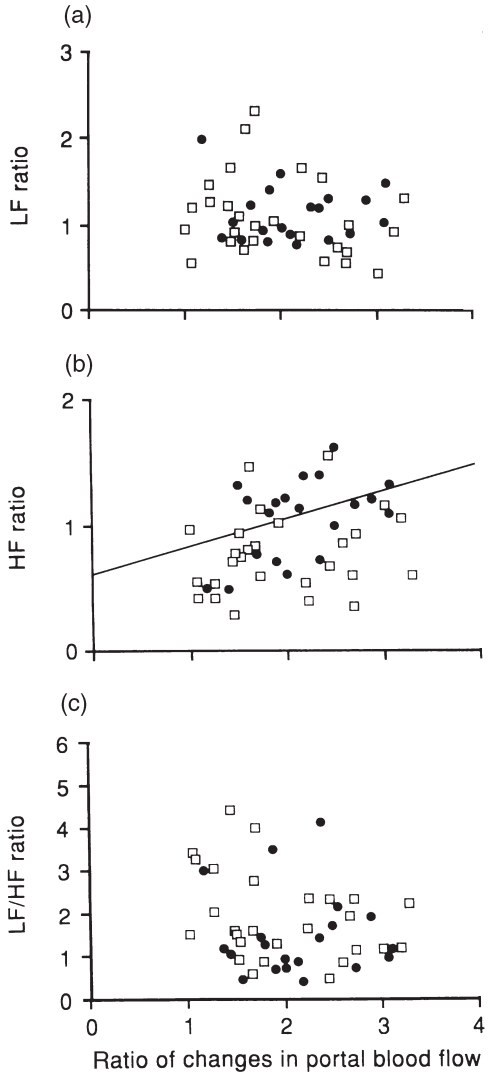

Figure 8 Correlations among the changes in portal blood flow and changes in low frequency component (LF) power, high frequency component (HF) power, and LF/HF in the (●) normal (N) and (□) liver cirrhosis (LC) groups obtained during fasting and 60 min after a meal. (a) N group, NS and LC group, NS; (b) N group, $r=0.22$, $P<0.05$ and LC group, NS; (c) N group, NS and LC group, NS. NS, not significant.

Charneau *et al.* evaluated gastric motility in cirrhotic patients, and they reported that antral motility differs widely among such patients depending on the presence or absence of gastric antral vascular ectasia (GAVE).[34] In their study, gastric motility was impaired in cirrhotic patients with GAVE. They reported the impairment of antral motility in GAVE, which might be caused by propulsive and coordinate activity because of parasympathetic denervation in the gastrointestinal tract, because parasympathetic function controls anteroduodenal motility via acetylcholine. The present evaluation suggests that the impairment of parasympathetic function, which is frequently observed in liver cirrhosis, is closely associated with decreased gastric motility.

Correlation between portal blood flow and gastric motility

Magnetic resonance imaging, as well as ultrasonography, is used clinically to evaluate portal hemodynamics in cirrhotic patients.[35–42] Miyake *et al.* reported that the cine-PC method is accurate in measuring flow velocity, and can be used for evaluating portal hemodynamics.[19] In the present evaluation, there were no significant differences in the fasting cross-sectional area of the portal vein between the N and LC groups, and this finding differed from Doppler sonographic findings reported by Gaiani *et al.*[37] However, in an MRI study, Miyake *et al.* reported that the cross-sectional area of the portal vein was smaller in cirrhotic patients than in healthy subjects, which was similar to our findings.[19] Although the ultimate reason for this discrepancy remains unclear, one of the probable reasons lies in the methodological differences between Doppler sonography and MRI. However, there have been a few reports on the correlation between portal hemodynamics and gastric motility.

We found that the cross-sectional area of the portal vein was smaller, and portal blood flow velocity was lower in cirrhotic patients of Child B and C than in healthy individuals after a meal. Furthermore, the increase of portal blood flow volume in cirrhotic patients of Child B and C was smaller than normal subjects and Child A patients after a meal, suggesting increased vascular resistance in the portal vein or the presence of an extrahepatic shunt. Blood stagnates in the gastric wall, and decreases in gastric wall compliance may decrease gastric motility in cirrhotic patients.

The frequency of portal regurgitation increases with the severity of liver cirrhosis.[34,39,41] In the present study, although portal regurgitation was not detected by MRI in the cirrhotic patients, portal blood flow velocity was decreased, suggesting increased vascular resistance in the portal vein and the presence of an extrahepatic shunt. Furthermore, the increased rate of portal blood flow was positively correlated with the increased rate of electrogastrographic peak power. These results suggest that abnormal portal hemodynamics greatly influence decreased gastric motility.

As previously reported by Usami *et al.*[4] and other authors,[43–48] it is certain that gastrointestinal hormones or peptides are closely related to gastric motility. However, the present study evaluated only the correlations among autonomic functions, portal blood flow, and gastric motility.

In conclusion, parasympathetic hypofunction, sympathetic hyperfunction and portal hemodynamics were closely related with gastric motility in cirrhotic patients. In addition, the present study indicates that gastric motility was decreased, at least in part, by the ingestion of food by cirrhotic patients because of abnormalities in autonomic functions and portal blood flow following a meal.

Limitation

In the present study, we found positive correlations among autonomic dysfunction, portal hemodynamic abnormalities, and gastric dysmotility in patients with liver cirrhosis. Furthermore, multivariate analysis revealed that both autonomic activity and portal hemodynamics were independent factors associated with gastric motility. However, it is difficult to conclude whether autonomic nervous dysfunction and portal hemodynamic abnormalities are the cause or the result of gastric dysmotility. Further studies are necessary to clarify whether gastric dysmotility in liver cirrhosis results in these two factors.

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