STORE-gastrointestinal functions and gastrointestinal hormones in patients with liver failure

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Abstract

This study aims to investigate the gastrointestinal functions of patients with liver failure (LF) based on gastrointestinal dysfunction (GD) scores and serum gastrointestinal hormone levels.

The GD in LF patients was scored using the gastrointestinal dysfunction scoring criteria. Serum gastrin (GAS), cholecystokinin (CCK), and motilin (MTL) levels were determined in LF patients. In addition, liver function and prothrombin activity were detected, and ultrasonography was performed.

The GD score was significantly higher in the LF groups than in the control group. Compared with the control group, serum GAS, CCK, and MTL levels significantly increased in the LF groups, and was positively correlated with the severity of LF. Furthermore, in the LF groups, GD was positively correlated with the severity of LF. However, the GD score and serum GAS, CCK, and MTL levels in the acute LF group were not statistically different, when compared with those in the subacute LF group, acute-on-chronic LF group and chronic LF group.

LF plays a key role in the development of GD, and may be the main cause of obvious gastrointestinal symptoms, such as abdominal distension, nausea, vomiting and anorexia, in LF patients. The severity of GD is not associated with LF type, but is positively correlated with the severity of LF, suggesting that GD in LF patients may have complicated mechanisms.

Abbreviations: ACLF = acute-on-chronic liver failure, ALF = acute LF, ALT = aspartate transaminase, AST = alanine transaminase, CCK = cholecystokinin, CLF = chronic LF, GAS = gastrin, GD = gastrointestinal dysfunction, GI = gastrointestinal, LF = liver failure, MTL = motilin, PTA = prothrombin activity, RIA = radioimmunoassay, SALF = subacute LF.

Keywords: CCK, GAS, gastrointestinal dysfunction score, liver failure, MTL.

1. Introduction

Liver failure (LF) is a frequently occurring disease in China, and poses a particular threat to human health and quality of life. Furthermore, LF is the leading cause of mortality in China, and its incidence rate is gradually increasing. LF is characterized by extreme fatigue, and can cause significant gastrointestinal dysfunction (GD) symptoms, such as anorexia, abdominal distension, nausea, and vomiting. GD not only causes pain and inconvenience to everyday life and work, but also exacerbates distension, nausea, and vomiting. GD not only causes pain and inconvenience to everyday life and work, but also exacerbates extreme fatigue, accompanying with severe GI symptoms, including anorexia, abdominal distension, nausea, and vomiting. GD (e.g., impaired esophageal motor function, decreased pressure at the lower esophageal sphincter, delayed gastric emptying, and delayed passage of food through the intestine) is present in patients with chronic liver disease, cirrhosis, or LF.[4] Gunnarsdottir et al.[5] found that abnormal intestinal motility was common in cirrhosis patients with portal hypertension. Since LF patients are clinically characterized by extreme fatigue, accompanied by severe GI symptoms, including anorexia, abdominal distension, nausea, and vomiting, studies on GI functions in LF patients are of great clinical significance. However, the etiologies of GD caused by LF have not been fully elucidated.[6]

In the present study, the GI function scores and GI hormone levels in LF patients were investigated to provide evidence for analyzing the relationship between LF and GD, the pathogenesis of LF, and the clinical interventions and therapeutic methods for this condition.

2. Material and methods

2.1. Subjects

A total of 60 individuals, who were randomly selected as the control group by internal medicine department in the First Affiliated Hospital of Henan University of Science and Technology, were no
hepatic failure. Among these 60 individuals, 35 individuals were male and 25 individuals were female, and the age of these individuals ranged within 35 to 70 years old, with an average of 45.3 ± 8.4 years old. In addition, a total of 98 LF patients, who were admitted to the Department of Gastroenterology of Sanmenxia Huanghe Hospital and the First Affiliated Hospital of Henan University of Science and Technology from October 2014 to March 2015, were enrolled in the present study. The present study was conducted in accordance with the declaration of Helsinki, and was approved by the Ethics Committee of our hospital. Among these 98 patients, 58 patients were male and 40 patients were female, and the age of these patients ranged within 35 to 68 years old, with an average of 46.7 ± 7.9 years old. These 98 LF patients were further divided into 4 groups, according to the Chinese Guidelines on the Diagnosis and Treatment of LF (2012 edition).

The inclusion criteria for the case groups were as follows: patients who met the diagnostic criteria of the Chinese Guidelines on the Diagnosis and Treatment of LF (2012 edition) issued by the Liver Failure and Artificial Liver Group, Chinese Society of Infectious Diseases, Chinese Medical Association and the Severe Liver Diseases and Artificial Liver Study Group, Chinese Society of Hepatology (11) patients without a history of use of gastric motility drugs, acid-producing drugs, H₂ receptor antagonists, or proton pump inhibitors over the past 2 weeks; patients who provided a signed informed consent. The control group consisted of subjects who received check-ups during the same period. These subjects had no underlying diseases or any obvious gastrointestinal (GI) symptoms, and not using GI motility drugs. The results of their health check-up were within the normal range.

The exclusion criteria were as follows: patients complicated with primary liver cancer, GI tumors, autoimmune diseases, diabetes, hyperthyroidism and hematological diseases; patients complicated with hepatotropic virus infection; patients with LF caused by diseases of other systems.

2.2. GI hormone determination

Serum gastrin (GAS) level was determined by radioimmunoassay (RIA). Serum cholecystokinin (CCK) and motilin (MTL) levels were determined in strict accordance with manufacturer’s instructions, which were provided in the RIA kit.

2.3. GD scoring

GD was scored according to the GD scoring criteria (based on the Revised Version of the Chinese MODS Staging and Severity Scoring Criteria, 1995 edition). GD was evaluated in strict accordance with the GD scoring criteria. The GD scores of all subjects were recorded and entered into an Excel form.

2.4. Observation of disease progression

In each case group, liver function (alanine transaminase [ALT] and aspartate transaminase AST), renal function and prothrombin activity (PTA) were detected and ultrasonography was performed to confirm the diagnosis and monitor the disease progression.

2.5. The relationship between GD and severity of LF in LF patients

The correlations of serum GAS, CCK, and MTL levels with PTA, ALT, and AST were analyzed using Pearson’s correlation coefficients.

### Table 1

GD scores in different LF groups and their differences from the control group.

| Group         | n  | Mean GD scores |
|---------------|----|----------------|
| ALF group     | 18 | 2.5±0.8*       |
| SALF group    | 22 | 2.4±0.9†       |
| ACLF group    | 28 | 2.4±0.7‡       |
| CLF group     | 30 | 2.4±0.9†       |
| Control group | 60 | 0.2±0.09       |

ACLF = acute-on-chronic LF, ALF = acute LF, CLF = chronic LF, GD = gastrointestinal dysfunction, LF = liver failure, SALF = subacute LF.

*P < 0.01, compared with control group.
†P < 0.01, compared with control group.
‡P > 0.01, compared with control group.

2.6. Statistical analysis

All data were imported into the SPSS17.0 software package for statistical analysis. Independent sample t-test, simple linear regression analysis, Pearson’s correlation analysis, univariate nonparametric test, Kruskal–Wallis test, rank sum and analysis of variance (ANOVA) of quantitative data for multiple groups were applied. The measurement data were expressed as mean ± standard deviation (X ± s). A P-value of <.05 was considered statistically significant. The manifestations and severity of GD in patients with different LF types were analyzed, and the potential risk factors of LF and GD were investigated.

3. Results

3.1. Etiologies of LF

The etiologies of LF included hepatitis B virus infection (n = 69), hepatitis C virus infection (n = 6), hepatitis E virus infection (n = 8), co-infection with 2 or more hepatitis viruses (n = 2), alcoholic hepatitis (n = 1), and idiopathic hepatitis (n = 12). LF was in the early stage in 17 cases, in the intermediate stage in 75 cases, and in the advanced stage in 6 cases.

3.2. GD scores in different LF groups and differences from the control group

The GD scores of the 4 LF groups were significantly higher than that of the control group ([t = 23.5, P = .000], [t = 18.4, P = .000], [t = 23.5, P = .000], and [t = 18.5, P = .000], respectively; Table 1).

3.3. GI hormone levels in the different LF groups and their relationships with the severity of LF

The mean GI hormone levels were significantly higher in the 4 LF groups than in the control group (Table 2).

3.4. The relationship between GI hormone levels and severity of LF

The mean ALT and AST levels were significantly higher in all LF groups than in the control group (P < .05). The GI hormone levels in all LF groups were positively correlated with the severity and progression of LF. The more severe the LF was, the higher the GI hormone levels were. Based on clinical stage, PTA and liver function test results, LF in all LF groups were divided into 3 stages: early stage (n = 17), intermediate stage (n = 75), and advanced stage (n = 6).
It was found that serum GAS, CCK, and MTL levels in LF patients were negatively correlated with PTA at the 0.01 level. Serum GAS, CCK, and MTL levels increased with the decrease in PTA. In LF patients, the linear equation for serum GAS levels and PTA was \( y = -2.4372x + 251.58, R^2 = 0.7226 \) (\( P = 0.000 \)). The linear equation for serum CCK level and PTA was \( y = -0.1789x + 11.425, R^2 = 0.5897 \) (\( P = 0.000 \)). The linear equation for serum MTL levels and PTA was \( y = -11.023x + 800.9, R^2 = 0.5999 \) (\( P = 0.000 \)).

It was found that serum GAS, CCK, and MTL levels in LF patients were positively correlated with ALT at the 0.01 level. That is, serum GAS, CCK, and MTL levels increased with the increase in ALT. In LF patients, the linear equation for serum GAS levels and ALT was \( y = 0.1258x + 140.74, R^2 = 0.6282 \) (\( P = 0.000 \)). The linear equation for serum CCK level and ALT was \( y = 0.0111x + 2.6386, R^2 = 0.7421 \) (\( P = 0.000 \)). The linear equation for serum MTL levels and ALT was \( y = 0.7287x + 244.26, R^2 = 0.835 \) (\( P = 0.000 \)).

It was found that serum GAS, CCK, and MTL levels in LF patients were positively correlated with AST at the 0.01 level. That is, serum GAS, CCK, and MTL levels increased with the increase of AST. In LF patients, the linear equation for serum GAS level and AST was \( y = 0.0737x + 138.19, R^2 = 0.7298 \) (\( F = 259.3, P < 0.05 \)). The linear equation for serum CCK level and AST was \( y = 0.0056x + 2.9879, R^2 = 0.6363 \) (\( F = 167.9, P < 0.05 \)). The linear equation for serum MTL level and AST was \( y = 0.3721x + 263.89, R^2 = 0.7298 \) (\( F = 294.4, P < 0.05 \)).

3.5. The relationship between GD and severity of LF in LF patients

In the LF groups, GD was positively correlated with the severity of LF (\( P < 0.05 \)). That is, the GD score increased with the severity of LF. The GD score revealed a significantly positive correlation with ALT and AST at the 0.05 level, with regression equations being \( y = 0.0051x + 0.6559, R^2 = 0.3253; r = 0.52, P = 0.00 \) and \( y = 0.0028x + 0.6587, R^2 = 0.3361; r = 0.50, P = 0.00 \), respectively. The GD score was negatively correlated with PTA, but exhibited a significantly positive correlation at the 0.01 level, with the regression equation being \( y = -0.0934x + 5.0024, R^2 = 0.333, r = -0.55, P = 0.00 \) (both, \( P < 0.05 \)).

3.6. Comparison of GD scores among the LF groups

The test for the homogeneity of variances yielded a \( P \)-value of .77. Thus, the variances were considered to be homogeneous.

| GD score | \( I, g \) | \( J, g \) | Mean deviation \((I-J)\) | Standard deviation | \( P \) value | 95% Confidence interval |
|----------|-----------|-----------|-------------------|-------------------|-------------|-----------------------|
| ALF      | SALF      | .114      | 277               | .682              | .44         | .66                   |
|          | AOLF      | .071      | 263               | .787              | .45         | .59                   |
|          | CLF       | .083      | 260               | .749              | .43         | .60                   |
| SALF     | ALF       | .114      | 277               | .682              | .44         | .44                   |
|          | AOLF      | .042      | 248               | .865              | .54         | .45                   |
|          | CLF       | .030      | 245               | .902              | .52         | .46                   |
| ACLF     | ALF       | .071      | 263               | .787              | .59         | .45                   |
|          | SALF      | .042      | 248               | .865              | .45         | .54                   |
|          | CLF       | .012      | 229               | .959              | .44         | .47                   |
| CLF      | ALF       | .083      | 260               | .749              | .60         | .43                   |
|          | SALF      | .030      | 245               | .902              | .46         | .52                   |
|          | AOLF      | .012      | 229               | .959              | .47         | .44                   |

ALF = acute-on-chronic LF, ALF = acute LF, CLF = chronic LF, GD = gastrointestinal dysfunction, LF = liver failure, SALF = subacute LF.
Therefore, ANOVA was applied for comparing quantitative data among multiple groups. As shown in the ANOVA (F = 0.059, P = .981), Levene’s test (F = 0.368, P = .776), and multiple comparisons of means, the GD scores were not significantly different among the different LF groups. In addition, the GD score of ALF was not significantly different from that in the other 3 groups (all, P > .05). The results of the multiple comparisons are presented in Table 3.

### 3.7. Comparison of GI hormone levels among LF groups

The comparisons of the 3 GI hormone levels among the 4 groups of ALF, SALF, ACLF, and CLF using the univariate nonparametric test and Kruskal–Willis test are presented in Table 4.

### 3.8. Comparison of serum GAS levels among the 4 LF groups

The test for homogeneity of variances for serum GAS levels among the 4 LF groups yielded a P-value of .025. Thus, these variances were not homogeneous. Therefore, rank sum test was applied to compare the quantitative data among multiple groups. Kruskal–Willis test revealed X² = 3.231 and P = .357. The difference in serum GAS level among the 4 LF groups was not significant. Intergroup multiple comparisons revealed that the differences in serum GAS levels among the 4 LF groups were not statistically significant (P > .05, Table 5).

### 3.9. Comparison of serum CCK levels among the 4 LF groups

The test for homogeneity of variances for serum CCK levels among the 4 LF groups yielded a P-value of .043. Thus, the variances were not homogeneous. Therefore, rank sum test was applied to compare the quantitative data among multiple groups. Kruskal–Willis test revealed X² = 4.297 and P = .231. Serum CCK levels among the 4 LF groups were not significantly different. Inter-group multiple comparisons revealed that the differences in serum CCK levels among the 4 LF groups were not statistically significant (P > .05). The results of these multiple comparisons are presented in Table 6.

### 3.10. Comparison of serum MTL levels among the 4 LF groups

The test for homogeneity of variances for serum MTL levels among the 4 LF groups yielded a P-value of .000. Thus, these variances were not homogeneous. Therefore, rank sum test was applied to compare the quantitative data among multiple groups. Kruskal–Willis test revealed X² = 9.1 and P = .46. Serum MTL levels were not significantly different among the 4 LF groups.

### Table 4

Comparison of 3 GI hormone levels among LF groups.

| Group | n | GI hormones | Mean | Standard deviations | Minimum | Maximum |
|-------|---|-------------|------|---------------------|---------|---------|
| ALF   | 18| GAS         | 193.8| 12.1                | 180.7   | 232.7   |
|       |   | CCK         | 6.9  | 1.1                 | 3.6     | 7.9     |
|       |   | MTL         | 528.2| 52.9                | 325.7   | 557.7   |
| SALF  | 22| GAS         | 197.3| 21.1                | 180.5   | 242.7   |
|       |   | CCK         | 6.2  | 1.3                 | 3.4     | 8.1     |
|       |   | MTL         | 521.7| 33.4                | 376.1   | 547.4   |
| ACLF  | 28| GAS         | 195.5| 16.1                | 170.3   | 242.7   |
|       |   | CCK         | 6.7  | 0.8                 | 5.2     | 7.9     |
|       |   | MTL         | 520.9| 44.3                | 336.9   | 581.9   |
| CLF   | 30| GAS         | 188.1| 13.4                | 169.5   | 216.5   |
|       |   | CCK         | 6.2  | 1.5                 | 2.8     | 8.5     |
|       |   | MTL         | 477.1| 101.1               | 319.2   | 564.8   |

ACLF = acute-on-chronic LF, ALF = acute LF, CLF = chronic LF, GI = gastrointestinal, LF = liver failure, SALF = subacute LF.

### Table 5

Multiple comparisons of serum GAS levels among 4 LF groups.

| Serum GAS Bonferroni | I, g | J, g | Mean deviation (I–J) | Standard deviation | P value | 95% Confidence interval |
|----------------------|------|------|----------------------|-------------------|---------|------------------------|
| ALF                  | SALF | 3.5227 | 5.0872 | 1.000 | 17.234 | 10.188 |
| ACLF                 | 1.6857 | 4.8357 | 1.000 | 14.679 | 11.348 |
| SALF                 | 5.7033 | 4.7722 | 1.000 | 7.069 | 18.656 |
| ALF                  | SALF | 3.5227 | 5.0872 | 1.000 | 10.188 | 17.234 |
| ACLF                 | 1.6857 | 4.8357 | 1.000 | 10.188 | 17.234 |
| SALF                 | 5.7033 | 4.7722 | 1.000 | 7.069 | 18.656 |
| ACLF                 | 9.3161 | 4.4929 | 2.25 | 14.128 | 14.128 |
| CLF                  | 7.4790 | 4.2060 | .472 | 3.857 | 18.815 |

ACLF = acute-on-chronic LF, ALF = acute LF, CLF = chronic LF, GAS = gastrin, LF = liver failure, SALF = subacute LF.
Intergroup multiple comparisons revealed that the differences in serum MTL levels among the 4 LF groups were not statistically significant ($P > .05$). The results of the multiple comparisons are presented in Table 7.

### Table 6

| CCK Bonferroni | i, g  | j, g  | Mean deviation (i–j) | Standard deviation | $P$ value | 95% Confidence interval | Lower limit | Upper limit |
|----------------|-------|-------|----------------------|--------------------|-----------|-------------------------|-------------|-------------|
| ALF            | SALF  | ALF   | .6773                | .3899              | .514      | $-374$ to $1728$        |             |             |
|                | ACFL  | ALF   | .2321                | .3707              | 1.000     | $-767$ to $1231$        |             |             |
|                | CLF   | ALF   | .6133                | .3658              | .581      | $-373$ to $1599$        |             |             |
| SALF           | ALF   | .6773  | .3899                | .514              | $-1728$  | $-374$ to $1728$        |             |             |
|                | ACFL  | .4451  | .3495                | 1.000             | $-1387$  | $.497$                  |             |             |
|                | CLF   | .0639  | .3444                | 1.000             | $.902     | $.3495                  |             |             |
| ACLF           | ALF   | .2321  | .3707                | 1.000             | $.902     | $.3495                  |             |             |
|                | SALF  | .4451  | .3495                | 1.000             | $.902     | $.3495                  |             |             |
|                | CLF   | .3812  | .3224                | 1.000             | $.902     | $.3495                  |             |             |
| CLF            | ALF   | .6133  | .3658                | .581              | $-1599$  | $.373$                  |             |             |
|                | SALF  | .0639  | .3444                | 1.000             | $.902     | $.3495                  |             |             |
|                | ACLF  | .3812  | .3224                | 1.000             | $.902     | $.3495                  |             |             |

ACLF = acute-on-chronic LF, ALF = acute LF, CCK = cholecystokinin, CLF = chronic LF, LF = liver failure; SALF = subacute LF.

In addition, the serum levels of some GI hormones significantly differed among the LF groups and control group. Furthermore, serum GAS, CCK, and MTL levels were significantly higher in the 4 LF groups, when compared to the control group, suggesting that LF can elevate serum GAS, CCK, and MTL levels. GAS, CCK and MTL are important GI hormones. GAS, which is secreted by G-cells in the antrum and duodenum, mainly stimulates parietal cells to secrete hydrochloric acid. It can also stimulate the secretion of pancreatic juice and bile, and mildly stimulate gastric chief cells to secrete pepsinogen. GAS is metabolized mainly in the liver and kidney. CCK mainly plays a role as a hormone and neurotransmitter. It can stimulate the duodenum and liver to secrete bile, and has a strong effect in contracting the gallbladder, leading to the contraction of gastric and pyloric sphincter muscles under rest. It also has an inhibitory effect on the contraction of the lower esophageal sphincter and Oddi’s sphincter. Furthermore, the half-life of CCK is prolonged, and its serum concentration is markedly increased in patients with cirrhosis. MTL is secreted by Mo cells, and is distributed in the small intestine. By acting on MTL neurons in the enteric nervous system, MTL can trigger the occurrence of phase II migrating motor complex (MMC). MTL is inactivated mainly via the liver. The normal levels of these 3 hormones are the basis for maintaining the normal activities of the GI. Therefore, serum GI hormone levels markedly increase in LF patients, which is

### Table 7

| MTL Bonferroni | i, g  | j, g  | Mean deviation (i–j) | Standard deviation | $P$ value | 95% Confidence interval | Lower limit | Upper limit |
|----------------|-------|-------|----------------------|--------------------|-----------|-------------------------|-------------|-------------|
| ALF            | SALF  | ALF   | 6.4985               | 15.3049            | 1.000     | $-34.752$ to $47.749$   |             |             |
|                | ACFL  | ALF   | 7.3131               | 14.5483            | 1.000     | $-31.808$ to $46.524$   |             |             |
|                | CLF   | ALF   | 21.1433              | 14.3573            | .865      | $-17.553$ to $59.840$   |             |             |
| SALF           | ALF   | 6.4985  | 15.3049               | 1.000             | $-47.749$ | $34.752$                |             |             |
|                | ACFL  | ALF   | .8146                | 13.7196            | 1.000     | $-36.163$ to $37.792$   |             |             |
|                | CLF   | ALF   | 14.6448              | 13.5169            | 1.000     | $-21.786$ to $51.076$   |             |             |
| ACLF           | ALF   | 7.3131  | 14.5483               | $.865             | $-46.524$ | $31.898$                |             |             |
|                | SALF  | 8.146   | 13.7196              | 1.000             | $-37.702$ | $36.163$                |             |             |
|                | CLF   | 13.8302 | 12.6538              | 1.000             | $.902     | $.3495                  |             |             |
| CLF            | ALF   | 21.1433 | 14.3573              | $.865             | $-59.840$ | $17.553$                |             |             |
|                | SALF  | 14.6448 | 13.5169              | 1.000             | $.902     | $.3495                  |             |             |
|                | ACLF  | 13.8302 | 12.6538              | 1.000             | $.902     | $.3495                  |             |             |

ACLF = acute-on-chronic LF, ALF = acute LF, CCK = cholecystokinin, CLF = chronic LF, LF = liver failure; MTL = motilin; SALF = subacute LF.
consistent with the description of Feldman.\textsuperscript{14} The possible reasons may include the decreased GI hormone inactivation by the liver following LF, the direct release of hormones into the blood due to portal hypertension, increased hormone production, and decreased hormone excretion.\textsuperscript{15}

In the present study, the mean ALT and AST levels were also significantly higher in all LF groups than in the control group. Furthermore, the GI hormone levels in all LF groups were positively correlated with the severity and progression of LF. The more severe the LF was, the significantly higher the GI hormone level became. This is consistent with the findings of Karlsen et al.\textsuperscript{16} Furthermore, it was found that serum GAS, CCK, and MTL levels in LF patients were negatively correlated with PTA at the 0.01 level. That is, serum GAS, CCK, and MTL levels increased with the decrease in PTA.\textsuperscript{17} PTA is a sensitive indicator for judging the severity and prognosis of liver cell necrosis, with a normal range of 75% to 100%. Coagulation factors are synthesized mainly in hepatocytes.\textsuperscript{18} When liver function is normal, the levels and activities of coagulation factors are within the normal range. When the liver parenchyma is damaged, the levels and activities of coagulation factors can be reduced by varying degrees, which often causes bleeding, congestion, and other clinical manifestations.\textsuperscript{19} In the early stage of LF, patients already have an underlying bleeding tendency (30%<PTA<40%). In the intermediate stage, this bleeding tendency becomes more obvious (bleeding spots or ecchymosis) (20%<PTA<30%). In the advanced stage of LF, patients have a severe bleeding tendency (ecchymosis at the injection site) (PTA<20%). Thus, serum GAS, CCK, and MTL levels are closely correlated to the progression and severity of LF, which is consistent with the findings of Pan et al.\textsuperscript{201} In the present study, it was found that serum GAS (F=162.2, P<.01), CCK (F=276.2, P<.01) and MTL (F=565.9, P<.01) levels in LF patients were positively correlated with both ALT and AST at the 0.01 level. That is, serum GAS, CCK, and MTL levels increase with the increase in ALT or AST. In LF patients, serum GI hormone levels are positively correlated with transaminase before the phenomenon of enzyme-jaundice separation appears.\textsuperscript{21} Hence, it can be speculated that serum GI hormone levels markedly increase in LF patients. Since GI hormones are the basis of GI motility, increased GI hormone levels can produce a series of GI symptoms, including delayed gastric emptying, anorexia, abdominal distension and constipation, which can further lead to malabsorption and malnutrition. LF and GD can interact and easily form a vicious cycle, and thereby exacerbate the disease.

In the LF groups, GD score was positively correlated with the severity of LF, and its linear equation revealed a statistical significance (P<.01). That is, the GD score increased with the severity of LF. Thus, GI function scoring and GI hormone determination are valuable for research on LF. These not only provide evidence for evaluating the progression of LF, but also provide scientific evidence and feasible methods for clinical interventions. However, the etiology of GD caused by LF has not been fully elucidated, and further investigations are warranted.

As shown in the present study, GD scores were not significantly different among the different LF groups. The GD score in the ALF group was not significantly different when compared with the other groups. Furthermore, there was no significant difference in serum GI hormone levels among the 4 LF groups. Therefore, the severity of GD is not associated with the type of LF, but is positively correlated with the severity of LF, suggesting that the mechanism of GD is complicated in LF patients. LF plays a key role in the development of GD, and may be the main cause of obvious gastrointestinal symptoms, such as abdominal distension, nausea, vomiting and anorexia, in LF patients. The severity of GD is not associated with LF type, but is positively correlated with the severity of LF, suggesting that GD in LF patients may have complicated mechanisms.

The relatively small sample size of the study group was a limitation of the present study. Furthermore, the case number of the etiology type of LF was unevenly distributed. For example, only one case of alcoholic hepatitis-induced LF was sampled in the present study, when compared with 69 cases of hepatitis B virus infection. Moreover, the role that gender and age plays in LF progression were not investigated and mentioned in the present study. The inclusion criteria, the exclusion criteria for the case groups and the control group criteria can affect research findings without strict quality control.

**Author contributions**

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