Effects of gastrointestinal endoscopy at different time points on diagnosis and treatment of upper gastrointestinal bleeding in patients with liver cirrhosis

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Abstract

Introduction: Liver cirrhosis is a common diffuse and persistent liver disease in the gastroenterology department.

Aim: To assess the effects of gastrointestinal endoscopy at different time points on the diagnosis and treatment of upper gastrointestinal bleeding (UGIB) in patients with liver cirrhosis.

Material and methods: The clinical data of 102 liver cirrhosis patients with UGIB admitted from July 2020 to May 2022 were retrospectively analysed. According to the timing of the first gastroscopy after hospitalization, the patients were divided into 4 groups: Group A (n = 25, gastroscopy performed within 12 h of the first bleeding), Group B (n = 29, gastroscopy performed within 12–48 h of the first bleeding), Group C (n = 25, elective gastroscopy performed > 48 h after the first bleeding), and Group D (n = 23, emergency gastroscopy was conducted due to active bleeding manifestations after failure of medication).

Results: The success rate of haemostasis in Group A was higher than in Groups B–D (p < 0.05). The early rebleeding rates of the 4 groups were similar (p > 0.05). After treatment, the levels of serum malondialdehyde and lipid hydrogen peroxide declined but the levels of glutathione peroxidase and superoxide dismutase rose in all groups compared to those immediately after hospitalization (p < 0.05), and these indicators were improved more significantly in Group A (p < 0.05).

Conclusions: Gastroscopy performed within 12 h of the first bleeding is more conducive to improving the haemostatic effect and thus shortening the length of hospital stay.

Key words: upper gastrointestinal bleeding, gastrointestinal endoscopy, timing, diagnosis.

Introduction

Liver cirrhosis is a common diffuse and persistent liver disease often accompanied by portal hypertension, liver failure, upper gastrointestinal bleeding (UGIB), and other complications [1]. The incidence rate of liver cirrhosis with UGIB is as high as 30–40%, which is related to the rupture bleeding of gastroesophageal varices (GOV), hepatogenic ulcer, portal hypertensive gastropathy, hepatic gastrointestinal failure, etc. [2, 3]. In the case of UGIB in patients with liver cirrhosis, acute peripheral circulatory failure may suddenly occur, resulting in decreased blood perfusion in liver tissues, often accompanied by clinical manifestations such as blood volume decline, melena, and haematemesis. This disease progresses rapidly, with a mortality rate of

above 10% if not treated promptly [4]. It is mentioned in *Expert Consensus on Emergency Diagnosis and Treatment Procedures for Acute Upper Gastrointestinal Bleeding* that gastrointestinal endoscopy is an effective means of diagnosis and treatment of UGIB upon liver cirrhosis [5]. It is well-documented that gastrointestinal endoscopy can identify the bleeding position and cause, improve the haemostatic effect, and reduce the blood transfusion volume compared with conservative treatment. However, the timing of gastrointestinal endoscopy and endoscopic treatment for UGIB remains controversial.

Saleem *et al.* found in a retrospective cohort study that there were no significant differences in the blood transfusion volume, length of hospital stay, mortality rate, and surgical rate between an early endoscopic intervention group (12–24 h) and an emergency endoscopic intervention group (< 12 h) of patients with non-variceal UGIB [6]. Also, Merola *et al.* found from 5 randomized controlled trials involving 926 patients with acute UGIB that the risk of rebleeding, length of hospital stay, and blood transfusion volume were similar between a very early endoscopy group (< 12 h) and an early endoscopy group (12–24 h) [7]. In contrast, Laursen *et al.* [8] and Jairath *et al.* [9] reported that the length of hospital stay, blood transfusion volume, and in-hospital mortality were reduced by gastrointestinal endoscopic treatment performed within 12 h of onset of UGIB.

As recommended by the European Association for the Study of the Liver in *Baveno VII – Renewing Consensus in Portal Hypertension* [10], the patients with signs of liver cirrhosis and gastrointestinal bleeding indicated by imaging should receive endoscopy as soon as possible, i.e. within 12 h, to quickly determine whether it is variceal bleeding and to determine the specific causes of bleeding, and the risk of rebleeding should be analysed according to endoscopic findings.

Aim

On the above basis, the clinical data of 102 liver cirrhosis patients with UGIB admitted to our hospital were retrospectively analysed to compare the effects of gastrointestinal endoscopy at different time points on the diagnosis and treatment, aiming to provide valuable clinical evidence.

Material and methods

General data

The clinical data of 102 liver cirrhosis patients with UGIB admitted to our hospital from July 2020 to May 2022 were collected for retrospective analysis. There were 60 males and 42 females aged 23–72 years, with an average of 52.16 ±11.85 years. Bleeding occurred 1–8 times, with an average of 2.21 ±0.99 times, and the duration of liver cirrhosis was 2–8 years, with an average of 5.33 ±1.59 years. The model for end-stage liver disease (MELD) score was 11.18 ±2.25 points, and the Rockall score was 4.41 ±1.085 points. Causes for liver cirrhosis: 65 cases of viral cirrhosis, 11 cases of alcoholic cirrhosis, 3 cases of primary biliary cirrhosis, 19 cases of cryptogenic cirrhosis, and 4 cases due to other reasons. Child-Pugh classification: 23 cases of grade A, 46 cases of grade B, and 33 cases of grade C.

According to the timing of the first gastroscopy after hospitalization, the patients were divided into 4 groups: Group A ($n = 25$, gastroscopy performed within 12 h of the first bleeding), Group B ($n = 29$, gastroscopy performed within 12–48 h of the first bleeding), Group C ($n = 25$, elective gastroscopy performed > 48 h after the first bleeding), and Group D ($n = 23$, emergency gastroscopy was conducted due to active bleeding manifestations after failure of medication). There were no statistically significant differences in gender, age, bleeding frequency, duration of liver cirrhosis, MELD score, Rockall score, cause for liver cirrhosis, or Child-Pugh grade among the 4 groups ($p > 0.05$) (Table I).

Inclusion and exclusion criteria

The inclusion criteria were as follows: a) patients meeting the diagnostic criteria for UGIB in liver cirrhosis [11], b) those with typical symptoms such as peripheral circulatory failure, melena, and haematemesis, c) those with a history of hepatitis B, d) those with bleeding for the first time, and e) those with complete clinical data.

The exclusion criteria included: a) patients with liver cirrhosis induced by drugs or alcohol, b) those with gastrointestinal bleeding caused by malignancies, severe gastric ulcer or oesophageal ulcer, c) those accompanied by autoimmune liver diseases such as primary sclerosing cholangitis and autoimmune hepatitis, d) those with a history of hepato-

Table I. General data (n, mean ± SD)

Group	N	M/F	Age [years]	Bleeding frequency (times)	Duration of liver cirrhosis [years]	MELD score	Rockall score	Cause Viral/alcoholic/ primary biliary/ cryptogenic/others	Child-Pugh grade
A	25	14/11	51.69 ±11.57	2.41 ±1.09	5.12 ±1.74	11.65 ±2.58	4.36 ±1.28	17/3/1/4/0	5/13/7
B	29	17/12	52.81 ±12.58	2.18 ±0.98	5.32 ±1.58	11.08 ±2.68	4.68 ±1.19	17/4/0/6/2	7/12/10
C	25	15/10	51.02 ±11.67	2.32 ±1.12	5.28 ±1.65	10.99 ±2.15	4.71 ±1.05	16/2/1/5/1	6/11/8
D	23	14/9	52.84 ±12.25	2.25 ±0.94	5.38 ±1.51	11.58 ±2.64	4.22 ±1.21	15/2/1/4/1	5/10/8
χ^2/F		0.137	0.426	0.411	1.625	0.562	1.152	3.796	0.738
P-value		0.987	0.536	0.621	0.102	0.497	0.215	0.987	0.994

biliary surgery, e) those complicated with bleeding in other tissues or organs, f) pregnant or lactating women, g) those with haematopoietic or immune disorders, or h) those complicated with hyperthyroidism or other diseases that could affect the stress state.

Main apparatus and reagents

A GIF-XQ-260 electronic gastroscope and matching NM-1K injection needle were purchased from Olympus (Japan). An MBL-6-F ligator was bought from Wilson-Cook (USA). The mucosal injection needle was obtained from Boston (USA). Lauromacrogol injection was used as the sclerosing agent (NMPA H20080445, strength: 10 ml: 100 mg, Shaanxi Tianyu Pharmaceutical Co. Ltd., China). Human tissue adhesive (GXZZ 20173653182, LT type 0.25 ml/vial) was provided by Beijing Compont Medical Devices Co. Ltd. (China).

Preoperative preparation of gastroscopy

The preoperative preparation of gastroscopy was as follows: (1) The patient was asked about the medical history and underwent routine preoperative examinations, including tests for biochemistry, blood glucose, liver function, coagulation function and renal function, routine blood and urine tests, blood pressure inspection, and electrocardiography. (2) Somatostatin and proton pump inhibitor (PPI) were infused intravenously before operation. (3) The topical anaesthetic 0.1% Dyclonine Hydrochloride (NMPA H20041523, strength: 10 ml: 0.1 g, Yangtze River Pharmaceutical Group Co. Ltd., China) was taken orally for pharyngeal anaesthesia before the operation. (4) The patient or his/her family members

signed an informed consent form before the operation.

Timing of gastroscopy

According to the timing of the first gastroscopy after hospitalization, the patients were divided into 4 groups: Group A (n = 25, gastroscopy performed within 12 h of the first bleeding, and no active bleeding manifestations such as frequent haematochezia, haematemesis, and persistent decreases in haemoglobin (Hb) and blood pressure), Group B (n = 29, gastroscopy performed within 12–48 h of the first bleeding, and no frequent active bleeding manifestations), Group C (n = 25, elective gastroscopy performed > 48 h after the first bleeding, and no frequent active bleeding manifestations after medication), and Group D (n = 23, emergency gastroscopy was conducted due to active bleeding manifested as frequent haematemesis, blood in the stool, as well as continuous reduction in blood pressure and haemoglobin level after failure of medication).

Treatment methods

The treatment methods were as follows: (1) GOV tissue glue embolization: The tissue glue was injected by endoscopic stratified injection. Specifically, the tissue glue was aspirated into a syringe, and 2 ml of lipiodol (or lauromacrogol, or 50% glucose) into another 2 syringes. The syringe was endoscopically punctured into the target vein to rapidly inject the tissue glue, and the injection dose (1.0–2.0 ml) was dependent on the size of the varicose vein. (2) GOV ligation: Gastric varices (GV) were directly ligated using the MBL-6-F ligator, or oesophageal varices (EV) were spirally moved from the gastroesophage-

al junction to the opening for ligation. Two ligation rings were about 1.5 cm away from each other, with 6–12 rings in total. (3) GOV sclerotherapy: The sclerosing agent was per vascularly or intravascularly injected at 1–2 ml and 10–15 ml at each point, respectively, and the total dose of a single injection should be < 35 ml.

Evaluation indicators

The following indicators were evaluated.

(1) Type of varices. The degree of simple EV was evaluated with reference to the *Trial Protocol for Endoscopic Diagnosis of Esophagogastric Varices* [12]: mild – straight or slightly curved varicose veins, a negative red-colour sign, and the diameter of varicose veins ≤ 0.3 cm; moderate – a positive red-colour sign, and the diameter of varicose veins ≤ 0.3 cm, or serpentine and bulging varicose veins – a negative red-colour sign, and the diameter of varicose veins within the range 0.3–1.0 cm; and severe – the diameter of varicose veins > 1.0 cm, or nodular, beaded, or tumour-like varicose veins. Isolated GV (IGV) and GOV were evaluated with reference to the *Consensus on Prevention and Treatment for Gastroesophageal Varices and Variceal Haemorrhage in Liver Cirrhosis* [13]: IGV1 – nodular, tumour-like or beaded and tortuous varicose veins located in the fundus of the stomach. IGV2 – varicose veins located around the antrum, body, or pylorus of the stomach. GOV1 – varicose veins extending along the lesser curvature of the fundus to approximately 2–5 cm below the gastroesophageal junction. GOV2 – varicose veins extending along the greater curvature of the fundus beyond the gastroesophageal junction, and nodular bulges in the cardiac part with tortuosity. GOV3 – varicose veins extending both to the fundus and to the lesser curvature.

(2) Characteristics, position, and detection rate of bleeding. The bleeding characteristics included acute bleeding, red thrombus on the surface of varicose veins, white thrombus on the surface of varicose veins, ulcer and erosion of varicose vein mucosa, and diffuse bleeding of gastric mucosa. The bleeding position included GV rupture bleeding (cardiac region and other parts of the stomach), EV rupture bleeding (upper segment, middle segment, and lower segment), and bleeding from portal hypertensive gastropathy.

(3) Haemostasis-related indicators. Bleeding was considered uncontrolled and continued if any of the following occurred within 72 h: a) intermittent haematemesis or haematochezia, an increase in heart rate of more than 20 beats/min or a decrease in systolic blood pressure of more than 20 mm Hg, and blood transfusion required to maintain the stability of Hb; b) transfusion of 4 or more units of red blood cells within 6 h, systolic blood pressure < 70 mm Hg, an increase in heart rate of more than 20 beats/min or heart rate > 100 beats/min; or c) haematemesis still occurring after gastrointestinal endoscopy or medication, no red blood cell transfusion, and a decrease in Hb > 30 g/l. Early rebleeding was defined as the presence of active bleeding (haematochezia or haematemesis, no red blood cell transfusion, a decrease in Hb > 30 g/l, an increase in heart rate by more than 20 beats/min, or a decrease in systolic blood pressure by more than 20 mm Hg) within 72 h to 6 weeks after bleeding control. Delayed rebleeding was defined as the presence of active bleeding 6 weeks after bleeding control. All patients were followed up for 6 months, and the mortality rate and complication rate were recorded.

(4) Hospitalization- and blood transfusion-related indicators. The length of hospital stay, red blood cell transfusion volume, and plasma transfusion volume were recorded.

(5) Oxidative stress response. Fasting peripheral blood (3 ml) was drawn immediately after hospitalization and after treatment and centrifuged (3000 r/min, radius: 6 cm) for 10 min. The separated serum was stored in a refrigerator at –80°C for later use. The levels of serum malondialdehyde (MDA), lipid hydrogen peroxide (LHP), glutathione peroxidase (GSH-Px), and superoxide dismutase (SOD) were measured using radioimmunoassay and kits (Shanghai X-Y Biotechnology Co. Ltd., China).

Statistical analysis

SPSS 23.0 software was used for statistical analysis. The measurement data with normal distribution were described as mean ± SD and compared by one-way analysis of variance among groups, and the LSD-t test was used for further pairwise comparison. The count data were described as percentage (%) and compared by the χ^2 test. $P < 0.05$ was considered statistically significant.

Results

Gastroscopic treatment

Among the 102 patients receiving gastroscopy, 88 (86.27%) underwent gastroscopy-assisted treatment, including 3 cases of GOV tissue glue emboliza-

tion, 60 cases of GOV ligation, and 25 cases of GOV sclerotherapy. The remaining 14 (13.73%) patients who underwent no gastroscopy-assisted treatment required interventional therapy or surgical treatment.

Types of varices

Among the 102 patients receiving gastroscopy, GOV and EV were the major types of varices. There was no statistically significant difference in the type of varices among the 4 groups ($p > 0.05$) (Table II).

Bleeding characteristics

Among the 102 patients receiving gastroscopy, 41 cases had no active bleeding, while the remaining 61 cases had active bleeding under gastroscopy. The bleeding characteristics showed no statistically significant difference among the 4 groups ($p > 0.05$) (Table III).

Position and detection rate of bleeding

Among the 61 patients with active bleeding under gastroscopy, EV and GV rupture bleeding was dominant. There were no statistically significant differences in the bleeding position, causes of bleeding, and detection rate of bleeding among the 4 groups ($p > 0.05$) (Table IV).

Success rate of haemostasis, rebleeding rate, 6-month mortality rate, and incidence rate of short-term complications

The success rate of haemostasis in Group A was higher than those of Groups B-D ($p < 0.05$). The early or delayed rebleeding rate, 6-month mortality rate, and incidence rate of short-term complications showed no statistically significant differences among the 4 groups ($p > 0.05$) (Table V).

Hospitalization- and transfusion-related indicators

Group A had shorter length of hospital stay, and lower transfusion volumes of red blood cells and plasma than those of Groups B-D ($p < 0.05$) (Table VI).

Stress response

No statistically significant differences were found in the levels of serum MDA, LHP, GSH-Px, and SOD among the 4 groups immediately after hospitaliza-

Table II. Types of varices among the 102 patients receiving gastroscopy [n (%)]

Group	N	EV	GOV			IGV
			GOV1	GOV2	GOV3	
A	25	10 (40.00)	6 (24.00)	4 (16.00)	4 (16.00)	1 (4.00)
B	29	10 (34.48)	6 (20.69)	6 (20.69)	7 (24.14)	0 (0.00)
C	25	8 (32.00)	5 (20.00)	4 (16.00)	7 (28.00)	1 (4.00)
D	23	7 (30.43)	7 (30.43)	3 (13.04)	4 (17.39)	2 (8.70)
χ^2/Z		0.572		0.562		2.576
P-value		0.903		0.385		0.462

EV – simple oesophageal varices, GOV – gastroesophageal varices, IGV – isolated gastric varices.

Table III. Bleeding characteristics among the 102 patients receiving gastroscopy [n (%)]

Group	N	Acute bleeding	Red thrombus on the surface of varicose veins	White thrombus on the surface of the varicose veins	Ulcer and erosion of varicose vein mucosa	Diffuse bleeding of gastric mucosa	No active bleeding
A	25	4 (16.00)	3 (12.00)	7 (28.00)	1 (4.00)	0 (0.00)	10 (40.00)
B	29	5 (17.24)	4 (13.79)	7 (24.14)	1 (3.45)	1 (3.45)	11 (37.93)
C	25	4 (16.00)	3 (12.00)	6 (24.00)	2 (8.00)	0 (0.00)	10 (40.00)
D	23	4 (17.39)	2 (8.70)	5 (21.74)	1 (4.35)	1 (4.35)	10 (43.48)
χ^2		0.032	0.326	0.266	0.705	2.016	0.166
P-value		0.999	0.955	0.966	0.872	0.569	0.983

Table IV. Position and detection rate of bleeding among the 61 patients with active bleeding under gastroscopy [n (%)]

Group	N	GV rupture bleeding		EV rupture bleeding			Bleeding from portal hypertensive gastropathy	Detection rate
		Cardiac region	Other parts of stomach	Upper segment	Middle segment	Lower segment		
A	15	2 (13.33)	3 (20.00)	1 (6.67)	2 (13.33)	5 (33.33)	2 (13.33)	13 (86.67)
B	18	2 (11.11)	4 (22.22)	1 (5.56)	4 (22.22)	5 (27.78)	2 (11.11)	13 (72.22)
C	15	2 (13.33)	3 (20.00)	1 (6.67)	4 (26.67)	5 (33.33)	0 (0.00)	10 (66.67)
D	13	1 (7.69)	2 (15.38)	1 (7.69)	2 (15.38)	5 (38.46)	2 (15.38)	6 (46.15)
χ^2/Z		0.287	0.227	0.057	1.071	0.399	2.329	5.472
P-value		0.962	0.973	0.996	0.784	0.940	0.507	0.140

Table V. Success rate of haemostasis, rebleeding rate, 6-month mortality rate, and incidence rate of short-term complications [n (%)]

Group	N	Success rate of haemostasis	Rebleeding rate		6-month mortality rate	Incidence rate of short-term complications
			Early rebleeding	Delayed rebleeding		
A	25	20 (80.00)	2 (8.00)	4 (16.00)	0 (0.00)	0 (0.00)
B	29	18 (62.07)	4 (13.79)	5 (17.24)	0 (0.00)	1 (3.45)
C	25	13 (52.00)	4 (16.00)	5 (20.00)	0 (0.00)	2 (8.00)
D	23	11 (47.83)	3 (13.80)	5 (21.74)	0 (0.00)	2 (8.70)
χ^2		6.322	0.775	0.329	0.000	2.645
P-value		0.048	0.855	0.955	1.000	0.450

Table VI. Hospitalization- and transfusion-related indicators (mean ± SD)

Group	N	Length of hospital stay [days]	Red blood cell transfusion volume [U]	Plasma transfusion volume [ml]
A	25	11.65 ±2.35[a]	2.41 ±0.32[a]	121.62 ±25.65[b]
B	29	15.63 ±3.67	4.65 ±0.44	268.52 ±21.05
C	25	15.98 ±4.52	5.69 ±0.41	403.62 ±40.65
D	23	16.85 ±3.87	8.52 ±1.16	782.32 ±62.02
F		15.635	135.659	256.354
P-value		0.000	0.000	0.000

[a]P < 0.05 vs. Groups B-D.

tion ($p > 0.05$). After treatment, the levels of serum MDA and LHP declined, but the levels of GSH-Px and SOD rose in all groups as compared to those immediately after hospitalization ($p < 0.05$), and these indicators were improved more significantly in Group A ($p < 0.05$) (Table VII).

Discussion

With the increasing advance of gastrointestinal endoscopic techniques, emergency gastroscopy has been widely applied in the diagnosis and treatment of UGIB in liver cirrhosis. Emergency gastroscopy has advantages over surgery in terms of less trauma, fewer complications, and the ability to clearly observe the mucosal state of the oesophagus, duodenal bulb, and stomach. Moreover, cytological examination and *in vivo* pathological examination can be performed in gastroscopy, and a satisfactory haemostatic effect can be achieved [14, 15]. However, the timing of gastrointestinal endoscopy and endoscopic treatment for UGIB remains controversial.

Table VII. Stress response (mean ± SD)

Group	N	MDA [µmol/l]		LHP [µmol/l]		GSH-Px [U/ml]		SOD [U/ml]	
		Immediately after hospitalization	After treatment	Immediately after hospitalization	After treatment	Immediately after hospitalization	After treatment	Immediately after hospitalization	After treatment
A	25	60.84 ±4.87	21.38 ±4.65[ab]	21.06 ±5.64	7.69 ±2.65[ab]	17.65 ±4.25	36.98 ±4.25[ab]	20.25 ±3.58	44.62 ±4.15[ab]
B	29	61.28 ±5.11	28.65 ±5.32[a]	22.08 ±4.98	9.45 ±2.35[a]	17.15 ±3.65	33.25 ±5.21[a]	18.98 ±4.52	40.58 ±5.21[a]
C	25	60.57 ±5.68	38.64 ±6.02[a]	21.36 ±5.22	10.52 ±1.85[a]	18.25 ±4.02	28.15 ±4.65[a]	19.68 ±4.02	37.25 ±4.86[a]
D	23	59.86 ±6.02	41.11 ±5.86[a]	22.19 ±4.98	12.65 ±3.32[a]	17.84 ±4.16	26.74 ±5.11[a]	20.02 ±3.98	34.62 ±3.86[a]
F		0.251	32.584	0.421	30.285	0.415	21.365	0.402	42.365
P-value		0.987	0.000	0.795	0.000	0.725	0.000	0.811	0.000

[a]$P < 0.05$ vs. the same group immediately after hospitalization. [b]$P < 0.05$ vs. Groups B-D.

As reported by Spiegel, the detection rate of bleeding foci was 77.0%, 57.6%, and 38.2%, respectively, among acute UGIB patients who received gastroscopy within 24 h, 48 h, and 72 h of the first bleeding [16]. Similarly, in this study, the detection rates of bleeding in Groups A–D were 86.67%, 72.22%, 66.67%, and 46.15%, respectively, but there were no statistically significant differences among the 4 groups. The possible reason is the small sample size, so both sample size and sample source should be expanded for further analysis in the future. Also, Group A had a higher success rate of haemostasis, a lower plasma transfusion volume, and a lower rebleeding rate than those of the other 3 groups, and the 6-month mortality rate and the incidence rate of short-term complications showed no statistically significant differences among the 4 groups. It can be seen that gastroscopy performed within 12 h of the first bleeding is more conducive to improving the haemostatic effect, shortening the length of hospital stay, and reducing the blood transfusion volume, without a significant impact on the mortality rate. Kumar *et al*. reported that no significant relationship was found between gastrointestinal endoscopy being performed within 12 h and the mortality rate of patients with UGIB (OR = 0.93, 95% CI: 0.77–1.13, $p = 0.47$) [17], being consistent with the findings of this study. In addition, it was found in this study that GOV and EV were the major types of varices among the 102 patients receiving gastroscopy, and the 61 patients with active bleeding under gastroscopy mainly had EV and GV rupture bleeding. The results once again demonstrate that GOV rupture bleeding is the major cause of UGIB in liver cirrhosis.

UGIB in liver cirrhosis may restrain the normal operation of the peripheral circulatory system. Excessive bleeding can cause acute failure of many tissues and organs, and metabolic acidosis and ischaemia/hypoxia can lead to massive fluid accumulation in peripheral loose connective tissues, spleen, and other abdominal organs, further causing peripheral vasodilatation and seriously affecting the blood supply to vital organs. When many tissues and organs are in the state of hypoxia and ischaemia, a large number of oxygen free radicals will be generated to activate lipid peroxidation, and oxidative metabolites are accumulated, resulting in tissue and organ dysfunction [18, 19]. Nucleic acids, proteins, and lipids in cells are vulnerable to the attack of oxygen free radicals, which will produce corresponding oxidative stress products while leading to functional damage and cell structural changes. GSH-Px and SOD have an anti-oxidation effect, the former of which can eliminate lipid hydroperoxides and alleviate the damage of organic hydroperoxides to the body, and the latter can catalyse the production of hydrogen peroxide and molecular oxygen by superoxide free radicals, and eliminate excessive oxygen free radicals. MDA and LHP are oxidative metabolites, whose levels are increased in many hypoxic diseases. According to the study of Dong *et al*., children with UGIB had an increased level of serum MDA and a decreased level of SOD, and the oxidative stress was relieved after successful haemostasis [20]. The above findings suggest that oxidative stress and bleeding form a vicious circle and create a cause and effect with each other. Therefore, close monitoring of the changes in oxidative stress may

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help dynamically reflect the haemostatic effect. In this study, after treatment, the levels of serum MDA and LHP declined but the levels of GSH-Px and SOD rose in all groups compared to those immediately after hospitalization, and these indicators were improved more significantly in Group A. It can be inferred that gastroscopic examination and treatment performed within 12 h of the first bleeding can better restore the oxidative/antioxidant balance and reduce the systemic oxidative stress. These results may come from the strong haemostatic effect of this treatment protocol, which can indirectly prove the ability of gastroscopic diagnosis and treatment performed within 12 h of the first bleeding to improve the haemostatic effect.

Conclusions

The timing of emergency gastroscopy is an important influencing factor for the diagnosis and treatment effects on UGIB in liver cirrhosis. Gastroscopy performed within 12 h of the first bleeding is more conducive to improving the haemostatic effect, shortening the length of hospital stay, reducing the blood transfusion volume, and relieving the systemic stress state.

Acknowledgments

Conflict of interest

The authors declare no conflict of interest.

References

1. Scarpellini E, Luigiano C, Svegliati-Baroni G, et al. Liver cirrhosis complications management at the emergency department. Rev Recent Clin Trials 2020; 15: 331-8.
2. Gao Y, Qian B, Zhang X, et al. Prophylactic antibiotics on patients with cirrhosis and upper gastrointestinal bleeding: a meta-analysis. PLoS One 2022; 17: e0279496.
3. Fouad TR, Abdelsameea E, Abdel-Razek W, et al. Upper gastrointestinal bleeding in Egyptian patients with cirrhosis: post-therapeutic outcome and prognostic indicators. J Gastroenterol Hepatol 2019; 34: 1604-10.
4. Zhou YF, Xu Y, Ding YF, et al. Novel nomogram model for predicting 6-week mortality in liver cirrhosis patients with acute upper gastrointestinal bleeding. J Dig Dis 2022; 23: 516-26.
5. Chinese Physicians Association, Emergency Physicians Branch. Expert consensus on the process of emergency diagnosis and treatment of acute upper gastrointestinal bleeding (revised). China Emergency Medicine 2011; 31: 1-8.
6. Saleem SA, Kudaravalli P, Riaz S, et al. Outcomes of upper gastrointestinal bleeding based on time to endoscopy: a retrospective study. Cureus 2020; 12: e7325.
7. Merola E, Michielan A, de Pretis G. Optimal timing of endoscopy for acute upper gastrointestinal bleeding: a systematic review and meta-analysis. Intern Emerg Med 2021; 16: 1331-40.
8. Laursen SB, Leontiadis GI, Stanley AJ, et al. Relationship between timing of endoscopy and mortality in patients with peptic ulcer bleeding: a nationwide cohort study. Gastrointest Endosc 2017; 85: 936-44.e3.
9. Jairath V, Kahan BC, Logan RF, et al. Outcomes following acute nonvariceal upper gastrointestinal bleeding in relation to time to endoscopy: results from a nationwide study. Endoscopy 2012; 44: 723-30.
10. Gralnek IM, Stanley AJ, Morris AJ, et al. Endoscopic diagnosis and management of nonvariceal upper gastrointestinal hemorrhage (NVUGIH): European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2021. Endoscopy 2021; 53: 300-32.
11. Burza MA, Marschall HU, Napoleone L, et al. The 35-year odyssey of beta blockers in cirrhosis: any gender difference in sight? Pharmacol Res 2017; 119: 20-6.
12. Tachezy M, Chon SH, Rieck I, et al. Endoscopic vacuum therapy versus stent treatment of esophageal anastomotic leaks (ESOLEAK): study protocol for a prospective randomized phase 2 trial. Trials 2021; 22: 377.
13. Chinese Society of Gastrointestinal Endoscopy. Consensus on prevention and treatment of esophagogastric variceal bleeding in portal hypertension in liver cirrhosis. Chinese J Liver Dis 2008; 16: 564-9.
14. Kamboj AK, Hoversten P, Leggett CL. Upper Gastrointestinal bleeding: etiologies and management. Mayo Clin Proc 2019; 94: 697-703.
15. Laine L, Barkun AN, Saltzman JR, et al. ACG clinical guideline: upper gastrointestinal and ulcer bleeding. Am J Gastroenterol 2021; 116: 899-917.
16. Spiegel BM. Endoscopy for acute upper GI tract hemorrhage: sooner is better. Gastrointest Endosc 2009; 70: 236-9.
17. Kumar NL, Cohen AJ, Nayor J, et al. Timing of upper endoscopy influences outcomes in patients with acute nonvariceal upper GI bleeding. Gastrointest Endosc 2017; 85: 945-52.e1.
18. Cho SH, Lee YS, Kim YJ, et al. Outcomes and role of urgent endoscopy in high-risk patients with acute nonvariceal gastrointestinal bleeding. Clin Gastroenterol Hepatol 2018; 16: 370-7.
19. Barkun AN, Almadi M, Kuipers EJ, et al. Management of nonvariceal upper gastrointestinal bleeding: guideline recommendations from the International Consensus Group. Ann Intern Med 2019; 171: 805-22.
20. Dong X, Li H, Zhu T. Clinical efficacy of norepinephrine combined with cimetidine in treatment of neonatal upper gastrointestinal hemorrhage and its adverse reactions. Pak J Med Sci 2022; 38: 2215-9.