

Clinical Study on the Timing of Emergency Gastroscopy in Liver Cirrhotic Patients with Esophageal Variceal Bleeding

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Abstract Esophageal variceal bleeding is a common complication of liver cirrhosis, and gastroscopic therapy has gradually become a significant clinical treatment for it. However, the timing of treatment with gastroscopy in liver cirrhotic patients with upper gastrointestinal bleeding is still controversial. In this study, 138 cases of liver cirrhotic patients with esophageal hemorrhage were retrospectively analyzed and followed up. Patients were divided into 4 groups based on whether they underwent gastroscopy and the first timing of gastroscopy, including group A with emergency gastroscopy within 12 hours, group B with emergency gastroscopy within 12-24 hours, group C with emergency gastroscopy within 24-48 hours and group D with conservative treatment. Gastroscopy at different time points and results of treatment were analyzed, and the bleeding detection rate, success rate of hemostasis, early recurrent bleeding rate, mortality rate within a year and average hospital stay were followed up in order to further explore the best time-window and value of treatment in liver cirrhotic patients with esophageal variceal bleeding by emergency gastroscopy. The results of this study showed that the success rate of hemostasis, mortality rate within a year and average hospital stay of patients in group B were superior than that of group A, C and D. This study also demonstrates that emergency gastroscopy can effectively reduce the early recurrent bleeding rate, mortality rate within a year and average days in hospitalization in liver cirrhotic patients with esophageal variceal bleeding, but have no effect on the success rate of hemostasis. This study indicates that emergency gastroscopy is an efficient and effective method to diagnose and treat liver cirrhotic patients with esophageal variceal bleeding at present, and the best time-window of treatment with emergency gastroscopy should be within 12h-24h after admission.

Keywords: liver cirrhosis, portal hypertension, esophageal variceal bleeding, emergency gastroscopy

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1. Introduction

Liver cirrhosis (LC) is a common chronic liver disease, and hepatocytes can be damaged by one or more factors, which can lead to its degeneration and necrosis. Then liver cells are regenerated and fibrous connective tissues are proliferated, which results in liver fibrosis and eventually liver cirrhosis [1,2]. There are many pathogenies to cause liver cirrhosis including viral hepatitis, chronic alcoholism, drug and damage of industrial poison, cryptogenic cirrhosis, liver congestion, genetic metabolic diseases, schistosomiasis and so on. Posthepatitis B cirrhosis is dominant in our country while in other countries, especially North America and Western Europe, alcoholic cirrhosis is the most common seen [3,4,5]. The study of global disease burden (GDB) in 2010 showed that more than 1 million people died of liver cirrhosis and liver

disease is one of the main reasons of global morbidity and mortality [6]. Liver cirrhosis is the 12th cause of death in the United States [7], while it's the 1st in the middle-aged in South Korea since its mortality rate of liver cirrhosis has reached 13.8/100,000 [8]. There is still no accurate statistics on the incidence and mortality of liver cirrhosis in our country at present. However, liver cirrhosis is a common digestive disease in our country and also has serious consequences, which brings heavy financial burden to families and society.

There is no significant manifestation in the early stage of liver cirrhosis. Complications including esophageal variceal bleeding, spontaneous peritonitis, portal vein thrombosis and hepatic encephalopathy arise in the decompensation stage, esophageal variceal bleeding is the most serious one, mainly due to increased portal blood flow and resistance caused by visceral arterial vasodilation, which leads to increased portal pressure. Since the lower esophageal submucosal vein is lack of support from

connective tissue, hemorrhage will happen because of the most direct and continuous influence by portal hypertension and the fatality rate was 32% [9,10,11]. It is reported that about 5% of patients with liver cirrhosis occurred esophageal varices within a year and about 10%-20% small varicosity developed to large varicosity after a year. The risk of bleeding within 2 years was 20%-30% and the mortality of first bleeding within one week was 25%-30% [12]. The risk of bleeding in liver cirrhosis patients with esophageal varices was 19%-40%, of which 40%-70% patients died of first bleeding. The proportion of recurrent bleeding rate was about 50% in the early mortality rate. Esophageal variceal bleeding has acute onset and rapid progression, and patients often accompanied by massive bleeding which led to hemorrhagic shock [13], therefore, it is particularly important to prevent the first bleeding of esophageal varices.

So far, there has not been a recognized and effective treatment. Surgical treatment, especially portosystemic shunt, is effective in controlling bleeding but not in increasing the survival rate which can cause side effects as hepatic encephalopathy. Beta-blockers like propranolol, which is reported to have the ability to prevent recurrent bleeding, considered as unsatisfied effect and more side effects in majority. In recent years, the development and application of endoscopic technology have obtained a certain effect [14,15,16]. Esophageal variceal ligation (EVL) is one of the effective methods for the treatment of esophageal variceal bleeding because of simple equipment, easy operation, safe use, fewer complications, exact effect and low cost of treatment. It has become the preferred treatment of esophageal varices [17]. Gastroscopy and hemostasis are relatively safe and effective measures for liver cirrhotic patients with upper gastrointestinal bleeding. According to UK guidelines on the management of variceal haemorrhage in cirrhotic patients [18], severe and unstable liver cirrhotic patients with upper gastrointestinal bleeding should undergo gastroscopy immediately after resuscitation, and other patients should be examined within 24-48h after admission. However, several studies have also shown that about 0.2% of patients might develop serious complications after gastroscopic hemostasis with a mortality rate of about 1/10000. Therefore, it is still controversial for liver cirrhotic patients with upper gastrointestinal bleeding to undergo endoscopy and the timing of treatment [19]. There are emergency and general gastroscopy based on different timing of examination. Emergency gastroscopy refers to gastroscopy performed within 24h-48h after admission [20]. Emergency gastroscopy is very important for liver cirrhotic patients with esophageal variceal bleeding, which is the gold standard to diagnose liver cirrhosis with esophageal varices and the reliable method of treating acute bleeding [21,22]. This study

retrospectively studied the data of 138 cases of liver cirrhotic patients with esophageal variceal bleeding who were treated in our hospital from January 2015 to December 2016 in order to analyze different timing of gastroscopy and results of treatment. The early recurrent bleeding rates and hospitalization days of patients were also followed up to further explore the best time window and the therapeutic value of emergency gastroscopy for the diagnosis and treatment of esophageal variceal bleeding in liver cirrhosis.

2. Materials and Methods

2.1. Materials

Gastroscope: Olympus GIF-H260 electronic gastroscope (Japan Olympus Corporation); Ligator: Cook Ligator (U.S Cook Corporation), INJI.A1.07.

180 type endoscopic injector (produced by Medwork medical products and services GmbH); Hardener is Lauromacrogol injection (10ml/branch, produced by Shaanxi Tianyu Pharmaceutical Co., Ltd.); Body tissue adhesive: (Trade name: Compont, 0.5ml/branch, produced by Beijing Suncon Medical Adhesive Co., Ltd.).

2.2. General Information

During the period from January 2012 to December 2016, 138 cases of patients with esophageal variceal bleeding diagnosed and treated by emergency gastroscopy were selected in the Department of Gastroenterology, integrated Chinese and Western medicine hospital in Baoshan district, Shanghai. All patients were confirmed by biochemical, imageological test and Endoscopic diagnosis of esophageal varices. There were 81 males and 57 females, aged from 24 to 60 years old, with an average age of years (45.62±16.38). All patients included 93 cases (67.39%) of patients with hepatitis B cirrhosis, 34 cases (24.64%) of patients with hepatitis C cirrhosis and 11 cases (7.97%) of patients with alcoholic cirrhosis.

Patients were divided into 4 groups based on whether they underwent gastroscopy and the timing of first gastroscopy, including 15 cases in group A with emergency gastroscopy within 12 hours, 46 cases in group B with emergency gastroscopy within 12-24 hours, 49 cases in group C with emergency gastroscopy within 24-48 hours and 28 cases in group D with conservative treatment. Gastroscopy or conservative treatment for 8 weeks was acted as the endpoint. There is no significant difference in the sex ratio, age and course of disease among the four groups ($P>0.05$). The informed consent was signed before the operation by patients or their relatives. The results are shown in Table 1.

Table 1. Comparison of general information of treatment and control group

Group	N	Gender (Male/Female)	Age (Years)	course of disease (month)
A (emergency gastroscopy, 12h)	15	9/6	45.12±16.23	15.82±9.32
B (emergency gastroscopy, 12-24h)	46	26/20	43.33±18.56	16.65±10.72
C (emergency gastroscopy ,24-48h)	49	30/19	46.65±19.73	16.65±10.72
D (conservative treatment)	28	16/12	44.80±18.29	16.65±10.72

2.3. Standards of Selected Cases

2.3.1. All Cases Were Accorded with the Following Diagnostic Criteria for Liver Cirrhosis [23]

(1) 20 years old ≤ age ≤ 80 years old (unlimited gender); (2) relative medical history which may lead to liver cirrhosis such as viral hepatitis, long-term and high alcohol consumption; (3) clinical manifestations of hypohepatia and portal hypertension; (4) liver function tests with decreased serum albumin, increased serum bilirubin, prolonged prothrombin time and other indicators of liver decompensation; (5) or patients who was definitely diagnosed as liver cirrhosis by liver biopsy; (6) patients with initial endoscopic treatment who had examination of presence of esophageal varices and history of active bleeding or who was assessed for bleeding potential and treated by endoscope; (7) patients who agreed to be treated by endoscope and signed the relevant informed consents.

2.3.2. The Clinical Manifestations of Esophageal Hemorrhage Are Presented in All Cases [23]

(1) hematemesis, melena or circulatory failure; (2) vomitus or fecal occult blood test positive; (3) decreased hemoglobin concentration, erythrocyte number and hematocrit; (4) causes of bleeding outside the digestive tract have been excluded: including bleeding from the respiratory tract, mouth, nose and throat; (5) melena caused by dietary factors has been excluded.

2.4. Exclusion Criteria

(1) patients with acute non-variceal upper gastrointestinal bleeding; (2) age < 20 years old and age > 80 years old; (3) combined with serious internal medical diseases (cerebral infarction, coronary heart disease and myocardial infarction, liver and kidney dysfunction, etc.); (4) combined with gastric varices bleeding or gastritis bleeding associated with portal hypertension confirmed by gastroscopy; (5) severe and excessive bleeding, shock cannot be corrected; (6) narcotic allergy; (7) combined with malignant tumors of other systems except liver cancer at or during admission; (8) patients with poor general condition or combined with other serious diseases which can affect survival time such as cardiac insufficiency, chronic renal insufficiency (uremia), respiratory failure and hepatic encephalopathy; (9) patients with ligation contraindications: diameter of varicose vein is greater than 2cm, latex allergy, cricopharyngeal or esophageal stenosis or perforation; (10) patients who cannot tolerate endoscopy and treatment.

2.5. Treatment

All patients were given treatments including oxygen, fasting, fluid resuscitation, proton pump inhibitors, anti-infection, nutritional support, monitoring of vital signs after admission. Patients at shock stage were given applications of blood transfusion, dilation and vasoactive drugs. Endoscopy were treated when patients were with stable vital signs.

Sclerotherapy for gastroesophageal varices: Hardeners are injected via intravenous injection (Lauromacrogol

injection), which can damage vascular endothelium, accelerate thrombosis and block blood vessels; fibrosis can be formed around varicose veins after paravenous injection while varicose veins are compressed. Lauromacrogol injections were applied to the intravascular or para vascular injection of gastroesophageal varices, especially intravascular injection. Each injection dose of intravascular injection is 10-15ml and each injection dose of para vascular injection is 1-2ml. A total dose of hardening injection does not exceed 35ml.

Ligation for gastroesophageal varices: Wilson-cook multi-band ligators are applied from esophagogastric junction to ligate esophageal varices as spiral or ligate gastric varices directly. Each vein is ligated by multiple ligation rings according to the need and the interval between the two rings is about 1.5cm with a total of 6 to 12 rings.

Tissue adhesive embolization for gastroesophageal varices: Under the action of anions in the blood and tissue fluid, tissue adhesive is cured rapidly so that it seals the blood vessels and blocks the blood flow to achieve the purpose of embolization to stop bleeding. Tissue adhesive is injected by endoscopic layered injection method (sandwich method). Three branches of 2 ml syringes are taken while two of them are extracted with iodide oil 2ml (or 50% dextrose or Lauromacrogol) and another is extracted with tissue adhesive. Selected target vein is pricked under endoscope and tissue adhesive is injected rapidly at each point. Dose is selected according to the size of the varicose vein, mostly 1.0-2.0ml.

Group A, B and C were treated with emergency gastroscopy with a total of 110 cases. Patients were examined under intravenous anesthesia (tracheal intubation if necessary) or local anesthesia at bedside or endoscopy room. 61 cases of patients were confirmed with esophageal variceal bleeding and excluded gastric varices bleeding or gastritis bleeding associated with portal hypertension. 39 cases of patients were treated with ligation, 15 cases of patients were treated with tissue adhesive embolization and 7 cases of patients were sprayed thrombin or injected hardener. Another 49 cases were unable to be treated under the gastroscopy because of the patient's intolerance and the occurrence of active bleeding. All patients were observed in the ward after emergency gastroscopy and given conservative therapy continuously.

28 cases of group D patients who were not treated with gastroscopy within 48h after bleeding, and conservative treatment were applied with vasoactive drugs. Octreotide 0.1mg was injected intravenously and it was changed to 0.6mg/12h plus liquid 250ml to maintain intravenous infusion. The course of treatment was 3-5 days. Some patients with terlipressin 1-2mg/4-6h was pushed by slow intravenous injection in the course of 3-5 days.

2.6. Efficacy Criteria

2.6.1. Endoscopic Diagnosis of Variceal Bleeding

According to the endoscopic diagnosis and treatment pilot program of varices and bleeding in the digestive tract in 2009 [24]: patients with varicose veins can be seen esophageal varices, mild bleeding or jet-like massive bleeding happens when varicose veins are acute bleeding,

visible white spots can be seen on the surface of varicose veins with attached blood clots.

2.6.2. Bleeding Detection Rate

A positive result is considered as signs of active bleeding including pulsatile bleeding, errhysis, white thrombus or red thrombus confirmed by emergency gastroscopy.

2.6.3. Success rate of Hemostasis

A positive result is considered as signs of controlled bleeding points, disappeared symptoms of hematemesis or hematochezia, stable blood pressure and normal hemoglobin levels.

2.6.4. Early Recurrent Bleeding Rate

Gastroscopy or conservative treatment for 8 weeks was acted as the end point.

A positive result is considered as signs of recurrent variceal bleeding within 8 weeks.

2.6.5. Average Days in Hospitalization

Total days of each group/number of patients in this group=total days of average days in hospitalization of patients with gastroscopy/number of patients in group A+B+C= days in hospitalization of patients with gastroscopy.

2.7. Observation Index

(1) Gastroscopy time; (2) performance of patients under gastroscopy, reason of bleeding and detection rate of bleeding sites; (3) endoscopic treatment and selection of methods; (4) observation of success rate of hemostasis, hospital mortality, early recurrent bleeding rate, delayed recurrent bleeding rate and mortality rate within one year.

2.8. Statistical Methods

SPSS21.0 software was used for statistical methods. Measurement data were expressed as mean±standard deviation by t-test or rank sum test for comparison between groups. Enumeration data were described by the composition ratio and chi-square test was used for

comparison between groups. $P < 0.05$ was considered statistically significant.

3. Results

3.1. Bleeding Characteristics of Patients

Among 110 cases of patients with gastroscopy, all patients showed the sign of active bleeding. 30 cases (27.27%) of patients showed acute endoscopic bleeding, 23 cases (20.82%) of patients showed red thrombus on the surface of varicose veins, 42 cases (38.46%) of patients showed white thrombus on the surface of varicose veins and 15 cases (13.45%) of patients showed ulcer or erosion on the mucosa of varicose veins. Bleeding characteristics are shown in [Table 2](#).

3.2. Patients' Conditions of Gastroscopic Treatment

Of the 110 cases of patients with gastroscopy, 61 cases (54.45%) of patients had gastroscopy and the remaining 49 cases (45.55%) of patients had not receive gastroscopy. 12(10.91%) of them refused the gastroscopy due to intolerance and 37(33.64%) of them were treated with conservative treatment due to active bleeding. The results are shown in [Table 3](#).

3.3. Comparison of Patients' Condition after Treatment

3.3.1. Bleeding Detection Rate

The total detection rate was 92.7%(102/110) in 48 hours, of which the detection rate was 100%(15/15) in group A, 97.8%(45/46) in group B and 85.7%(42/49) in group C.

3.3.2. Success Rate of Hemostasis

The total success rate of hemostasis was 86.9% (53/61), of which the success rate was 80% (4/5) in group A, 88.5% (23/26) in group B and 86.7% (26/30) in group C.

Table 2. Analysis of bleeding characteristics of patients by gastroscopy

bleeding characteristics of patients by gastroscopy	Case(n)	Group(n)			Percentage(%)
		A	B	C	
Acute bleeding	30	10	9	11	27.27
Red thrombus on the surface of varicose veins	23	6	6	11	20.91
White thrombus on the surface of varicose veins	42	21	11	10	38.18
Ulcer or erosion on the surface of varicose veins	15	7	2	6	13.64
Total	110	44	28	38	100

Table 3. Patients' Conditions of Gastroscopic Treatment

patients' conditions of gastroscopic treatment	Case(n)	Group(n)			Percentage(%)
		A	B	C	
with gastroscopy	61	25	17	19	54.45
without gastroscopy	49	16	27	6	45.55
refuse gastroscopy	12	4	7	1	10.91
conservative treatment	37	12	20	5	33.64
Total	110	41	44	25	100

3.3.3. Early Recurrent Bleeding Rate (within 8 Weeks)

The total early recurrent bleeding rate of patients with emergency gastroscopy was 13.6% (15/110), of which the recurrent bleeding rate was 20% (3/15) in group A, 13.1% (6/46) in group B and 12.2% (6/49) in group C.

3.3.4. Mortality Rate within a Year

According to the follow-up, there are two cases of death within a year and the total mortality rate was 1.8% (2/110), of which the mortality rate was 6.67% (1/15) in group A, 0% (0/46) in group B and 2.0% (1/49) in group C.

3.3.5. Average Days in Hospitalization

The total days of hospitalization was 738 days and average days of hospitalization was 6.71 ± 0.69 days in patient with emergency gastroscopy. The total days of hospitalization was 102 days and average days of hospitalization was 6.8 ± 0.28 days in group A; the total days of hospitalization was 280 days and average days of hospitalization was 6.1 ± 0.27 days in group B; the total days of hospitalization was 356 days and average days of hospitalization was 7.3 ± 0.32 days in group C.

In order to compare differences of bleeding detection rate, success rate of hemostasis, early recurrent bleeding rate, mortality rate within a year and average days in hospitalization in group A, group B and group C, chi-square was performed with the test level of $\alpha=0.05$.

Bleeding detection rate was compared: comparison between group A and group B, $P=0.565 > 0.05$, which indicates that there were no significant differences between group A and group B; Comparison between group A and group C, $P=0.121 > 0.05$, which indicates that there were no significant differences between group A and group C; Comparison between group B and group C, $P=0.034 < 0.05$, which indicates that there were significant differences between group B and group C and the bleeding detection rate of group C was less than that of group B.

The success rate of hemostasis was compared, comparison between group A and group B, $P=0.605 > 0.05$, which indicates that there were no significant differences between group A and B; comparison between group A and group C, $P=0.693 > 0.05$, which indicates that there were no significant differences between group A and group C; comparison between group B and group C, $P=0.03 < 0.05$, which indicates that there were significant differences between group B and group C, and the success rate of hemostasis of group C was less than that of group B.

The early recurrent bleeding rate was compared, comparison between group A and group B, $P=0.509 > 0.05$, which indicates that there were no significant differences between group A and group B; comparison between group A and group C, $P=0.45 > 0.05$, which indicates that there were no significant differences between group A and group C; comparison between group B and group C, $P=0.97 > 0.05$,

which indicates that there were no significant differences between group B and group C and the early recurrent bleeding rate of group C was less than that of group B.

The mortality rate within a year was compared, comparison between group A and group B, $P=0.077 > 0.05$, which indicates that there were no significant differences between group A and group B; comparison between group A and group C, $P=0.359 > 0.05$, which indicates that there were no significant differences between group A and group C; comparison between group B and group C, $P=0.335 > 0.05$, which indicates that there were no significant differences between group B and group C, and the mortality rate of group C was higher than that of group B.

The average days in hospitalization was compared, comparison between group A and group B, $P=0.000 < 0.05$, which indicates that there were significant differences between group A and group B, and the average days in hospitalization in group A was higher than that of group B; comparison between group A and group C, $P=0.194 > 0.05$, which indicates that there were no significant differences between group A and group C; comparison between group B and group C, $P=0.000 < 0.05$, which indicates that there were significant differences between group B and group C, and the average days in hospitalization in group C was higher than that of group B.

The results in this study showed that the bleeding detection rate (97.8%, 45/46), success rate of hemostasis (91.3%, 42/46), mortality rate within a year (0%, 0/46) and average days in hospitalization (6.1 ± 0.27) in group B were superior to group A and group C. The early recurrent bleeding rate in group B (13.1%, 6/46) was higher than that of group C (12.2%, 6/49), but there were no significant differences between the two groups ($p > 0.05$). Therefore, this study shows that emergency gastroscopy is of great significance in liver cirrhotic patients with esophageal variceal bleeding, and the best time-window of treatment should be within 12h-24h after admission. The results are shown in Table 4.

3.4. Outcome in Group D (Conservative Treatment)

In this study, 28 cases of patients without gastroscopy (in group D) were given the vasoactive drug octreotide, and some patients were combined with terlipressin for 3-5 days of treatment course. Among them, 21 cases were discharged after improvement, 2 cases were transferred to surgery, 2 cases were transferred to other hospitals, 1 case was discharged automatically and 2 cases died. The success rate of hemostasis was 75% (10/28). The early recurrent bleeding rate was 35.7% (10/28). The mortality rate within a year was 7.14% (2/28). The total days of hospitalization were 304 days and average days in hospitalization were 10.9 ± 0.92 days.

Table 4. Comparison of time-window by emergency gastroscopy

Group	bleeding detection rate(%)	success rate of hemostasis(%)	early recurrent bleeding rate(%)	mortality rate within a year(%)	average days in hospitalization(d)
Group A(12h)	100	80	20	6.67	6.8 ± 0.28
Group B(12-24h)	97.8	91.3	13.1	0	6.1 ± 0.27
Group C(24-48h)	85.7	87.8	12.2	2.0	7.3 ± 0.32
Group D	-	75	35.7	7.14	10.9 ± 0.92

The group D was used as the control group. The difference of hemostatic success rate, early rebleeding rate, 1 years mortality rate and average hospitalization days were compared between the group A, group B, group C and the control group D. Chi square test was used to test the level of $\alpha=0.05$.

The success rate of hemostasis was compared, comparison between group A and group D, $P=0.810>0.05$; comparison between group B and group D, $P=0.203>0.05$; comparison between group C and group D, $P=0.257>0.05$, which indicates that there were no significant differences between the group A, group B, group C and the control group D, but the success rate of hemostasis in group B was higher than that of the other three groups.

The early recurrent bleeding rate was compared, comparison between group A and group D, $P=0.285>0.05$; comparison between group B and group D, $P=0.022<0.05$; comparison between group C and group D, $P=0.15<0.05$, which indicates that there were significant differences between the group A, group B, group C and the control group D, that is, the early recurrent bleeding rate in group D was higher than that of the other two groups.

The mortality rate within a year was compared, compared group D with A, B and C, P values were respectively 0.953, 0.066 and 0.266 >0.05 , which indicates that there were no significant differences between group D and the other three groups. However, the mortality rate within a year in group B was less than that of the other three groups.

The average days in hospitalization was compared, compared group D with A, B and C, P values were all $0.000<0.05$, which indicates that there were significant differences between group D and the other three groups, and the average days in hospitalization of group D was higher than that of the other three groups.

This study shows that gastroscopy can effectively decrease early recurrent bleeding rate, mortality rate within a year and average days in hospitalization of liver

cirrhotic patients with esophageal variceal bleeding, but there was no effect on the success rate of hemostasis. The results are shown in Table 4.

3.5. Outcome of 138 Cases of Patients

In this study, there were 110 cases of patients treated with emergency gastroscopy (group A, B and C) and the successful rate was 100%. There was 0 patient died during the operation. Another 49 cases failed to complete the gastroscopy due to intolerance and other factors. All patients were transferred to the ward for observation after gastroscopy, and further treated with internal conservative treatments. Among them, 97 cases were discharged after improvement and the total success rate of hemostasis was 88.2% (97/110). 6 cases were transferred to surgery, 4 cases were transferred to other hospitals, 1 case was discharged automatically and 2 cases died. The early recurrent bleeding rate in follow-up patients (within 8 weeks): the total recurrent bleeding rate in patients with emergency gastroscopy group was 13.6% (15/110) and 2 cases of three groups died within a year. The total mortality rate was 1.8% (2/110). The total days of hospitalization were 738 days and average days in hospitalization were 6.71 ± 0.28 days.

28 cases of patients with conservative treatment (group D), who did not receive gastroscopy, were given the vasoactive drug octreotide, and some patients were combined with terlipressin for 3-5 days of treatment course. Among them, 21 cases were discharged after improvement and the success rate of hemostasis was 75% (10/28). 2 cases were transferred to surgery, 2 cases were transferred to other hospitals, 1 case was discharged automatically and 2 cases died. The early recurrent bleeding rate in follow-up patients (within 8 weeks) was 35.7% (10/28). The total days in hospitalization were 304 days and average days in hospitalization were 10.9 ± 0.92 days.

Table 5. Comparison of Outcome of 138 patients

Group	success rate of hemostasis (%)	early recurrent bleeding rate (%)	mortality rate within a year (%)	average days in hospitalization (d)
Emergency gastroscopy group (A+B+C)	88.2 (97/110)	13.6(15/110) *	1.8(2/110) *	6.71±0.28 *
conservative treatment group(D)	75 (21/28)	35.7(10/28)	7.14(2/28)	10.9±0.92

Compared with conservative treatment group(D), * $P<0.05$.

In brief, the success rate of hemostasis in group D (conservative treatment) was significantly lower than that of the emergency gastroscopy group. However, there were no significant differences between the two groups ($p>0.05$); the early recurrent bleeding rate, mortality rate within a year and average days in hospitalization were also significantly higher than that of emergency gastroscopy group. There were significant differences between the two groups ($p<0.05$). The results are shown in Table 5.

4. Discussion

Esophageal and gastric varices bleeding (EGVB) is the most common complication, and one of the major causes of death in liver cirrhotic patients. The incidence of

cirrhosis at compensated stage is 0-40% and that at decompensated stage is 70%-80% [25]. The mortality rate of small esophageal variceal bleeding is 5% each year, and that of large esophageal variceal bleeding is 15%-20%. The mortality rate of bleeding after a week is 20%-25% [26]. With the continuous development of digestive endoscopy, endoscopic treatment has gradually become the main method to prevent and cure liver cirrhosis with gastroesophageal varices. At present, main methods of treating EGVB by endoscope include esophageal varices ligation (EVL), endoscopic injection sclerotherapy (EIS), tissue adhesive injection therapy and combination therapy. A large number of reports [27-36] have affirmed that esophageal varices treated with EVL have a satisfied clinical effect. Compared with conventional drug treatment, the recurrent bleeding rate decreased significantly. The

operation of EVL therapy is simple, and the time required for treatment is only about 3 minutes. The clinical effect of emergency hemostasis is ideal, and effect of elimination of varicose veins is also significant. Therefore, it is a relatively effective non-surgical method for the prevention and treatment of gastrointestinal bleeding. Scholars in china have summarized the current status of treatment esophageal and gastric variceal bleeding by gastroscopy. For emergency bleeding, the rate of hemostasis with ligation was 90%-95%, and complications were less. The rate of hemostasis with sclerotherapy was up to 90%. Complications are mainly perforation, esophageal stricture and so on. For gastric varices bleeding, the rate of emergency hemostasis with tissue adhesive injection therapy was up to 100%, and pulmonary embolism and portal vein embolism are its main complications [30].

In this study, 61 cases of patients who were confirmed with esophageal variceal bleeding and excluded gastric varices bleeding or gastritis bleeding associated with portal hypertension, were all given the corresponding endoscopic treatment, 39 cases of patients were treated with ligation for hemostasis, of which 37 patients were successful and the success rate of hemostasis was 94.9% (37/39); 15 cases of patients were treated with tissue adhesive embolization for hemostasis, of which 11 patients were successful and the success rate of hemostasis was 73.3% (11/15); 7 cases of patients were sprayed thrombin or injected hardener, of which 4 patients were successful and the success rate of hemostasis was 71.4% (5/7). This study shows that ligation therapy is safer and more effective to control acute variceal bleeding compared with sclerotherapy.

The follow-up results of this study also displayed that patients in group D who did not receive gastroscopy and treatment but with conservative medical treatment had a lower success rate of hemostasis. It is only 75%, lower than that of other three groups, there was no significant difference; and the early recurrent bleeding rate is 35.7%, which is significantly higher than that of other three groups, there was no significant difference. In addition, the average days in hospitalization, 10.9 ± 0.92 days, is higher than that of other three groups, with significant differences. Patients of the other three groups who underwent gastroscopy to early determine sites and causes of bleeding provide a strong basis for the disease in order to choose a reasonable therapeutic regimen. The results of this study illustrate that gastroscopy can effectively decrease the early recurrent bleeding rate, mortality rate within a year and average hospitalization of liver cirrhotic patients with esophageal variceal bleeding, but no effect on the success rate of hemostasis.

It is always controversial for the timing of emergency gastroscopy with esophageal variceal bleeding. It is mostly recommended by current expert consensus and guidelines that timing of gastroscopy and treatment is within 12 hours after admission since it has advantage of early diagnosis of variceal bleeding and elimination of other causes such as ulcer disease. The risk of recurrent bleeding can also be assessed on the basis of endoscopy, and treatment can be performed simultaneously. However, this proposal is lack of stronger evidence-based support, mainly from experts' personal experience. A retrospective cohort study by Cheung, et al. [31] demonstrated that the timing of endoscopic therapy did not affect the case-fatality rate

(OR 1.0, 95% CI 0.92~1.08, $P = 0.91$). However, the study of Hsu, et al. [32] showed that the case-fatality rate of patients with delayed endoscopic therapy (>15 hours) was higher than that of patients with emergency endoscopy within 15 hours of onset (OR = 3.67, 95% CI 1.27 ~ 10.39). Therefore, it is an extremely complicated issue to choose the best time point for endoscopic treatment. We cannot simply think that earlier is better.

It has been reported that, bleeding lesions could be found by gastroscopy within 24 hours of bleeding in 77.0% patients in acute upper gastrointestinal bleeding, 57.6% within 48 hours and 38.2% within 72hours [33]. In this study, the bleeding detection rate of gastroscopy within 12 hours (group A) was 100% and that of gastroscopy within 24 hours (group B) was 97.8%, which were significantly higher than the bleeding detection rate (85.7%) of gastroscopy within 48 hours (group C). The study of Chen PH, et al [33] showed that for liver cirrhotic patients with esophageal variceal acute bleeding who manifested as hematemesis, the recurrent bleeding rate within 6 weeks and mortality rate of early gastroscopy group (12h after admission) were lower than that of delayed gastroscopy group (more than 12h). For those who did not manifest as hematemesis, there were no significant difference on the recurrent bleeding rate within 6 weeks and mortality rate between early gastroscopy group (12h after admission) and delayed gastroscopy group (more than 12h). However, Cheung J, et al. [34] considered that there was no effect on mortality rate for timing of gastroscopy for hemodynamically stable acute variceal bleeding. Another study by Hsu YC, et al. [35] showed that for liver cirrhosis with acute variceal bleeding patients, the mortality rate of those who underwent gastroscopy for bleeding within 15h was lower than that of those who underwent gastroscopy for bleeding >15h. In this study, there were no significant differences on the success rate of hemostasis, early recurrent bleeding rate and mortality rate within a year between patients with gastroscopy within 24 hours (group B) and those with gastroscopy within 12 hours (group A) after bleeding. The average days in hospitalization of group B was significantly less than that of group A, which had significant differences. However, the early recurrent bleeding rate of group A in this study was significantly higher than that of group B. There were no significant differences on the early recurrent bleeding rate and mortality rate within a year between patients with gastroscopy within 24 hours (group B) and those with gastroscopy within 48 hours (group C) after bleeding. The average days in hospitalization of group B was significantly less than that of group C, and the success rate of hemostasis of group B was significantly higher than that of group C, which had significant differences. This study demonstrates that liver cirrhotic patients with esophageal variceal bleeding must be diagnosed and treated as early as possible by emergency gastroscopy, and the best time-window of treatment should be within 12h-24h after admission.

5. Conclusion

Esophageal and gastric varices bleeding (EGVB) is the most common complication and one of the major causes

of death in liver cirrhotic patients. Gastroscopy is not only the main means of diagnosing etiology and site of bleeding, but also the main method of hemostasis and prevention of recurrent bleeding. In this study, 138 cases of liver cirrhotic patients with esophageal hemorrhage were retrospectively analyzed and followed up. The results showed that the detection rate of bleeding site in diagnosing and treating within 12-24h by emergency gastroscopy was higher than the other timing. The success rate of hemostasis could be significantly increased and the early recurrent bleeding rate, mortality rate within a year and average days in hospitalization could be decreased. There were statistical differences compared with patients in the conservative drug group. This study shows that emergency gastroscopy has an important clinical value to diagnose and treat liver cirrhotic patients with esophageal variceal bleeding, and it can be clinically applied as the most direct and reliable means of diagnosis and treatment of acute upper gastrointestinal bleeding.

Abbreviations

LC: liver cirrhosis

EVL: Esophageal variceal

EGVB: ligation esophageal and gastric varices bleeding

EIS: endoscopic injection sclerotherapy

Conflict of Interests

The authors declare that there are no conflicts of interest.

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References

- [1] D. Schuppan, and N.H. Afdhal, "Liver cirrhosis," *Lancet*, vol.371, no.9615, pp.838-851, 2008.
- [2] Y.Lu, J.Liu, C.Lin, H.Wang, Y.Jiang, J.Wang, P. Yang, and F. He, "Peroxiredoxin 2: a potential biomarker for early diagnosis of hepatitis b virus related liver fibrosis identified by proteomic analysis of the plasma," *Bmc Gastroenterology*, vol.10, no.1, pp.115, 2010.
- [3] Y. Yan, J.Y. Yang, Y.H. Mou, L.H. Wang, H Zhang, and C.F. Hu, "Possible metabolic pathways of ethanol responsible for oxidative DNA damage in human peripheral lymphocytes," *Alcoholism-Clinical and Experimental Research*, vol.35, no.1, pp.1-9, 2011.
- [4] C. Fabris, P. Toniutto, E. Falletti, E. Fontanini, A. Cussigh, D. Bitetto, E. Fornasiere, E. Fumolo, C. Avellini, R. Minisini, and M. Pirisi, "MTHFR C677T polymorphism and risk of HCC in patients with liver cirrhosis: role of male gender and alcohol consumption," *Alcoholism-Clinical and Experimental Research*, vol.33, no.1, pp.102-107, 2009.
- [5] J. Chen, and J.D. Jia, "Progress in diagnosis and treatment of liver cirrhosis," *Chinese Journal of Hepatology*, vol.17, no.4, pp.241-243, 2009.
- [6] R. Jürgen, A.V. Samokhvalov, and K.D. Shield, "Global burden of alcoholic liver diseases," *Journal of Hepatology*, vol.59, no.1, pp.160, 2013.
- [7] K.D. Kochanek, J.Q. Xu, S.L. Murphy, and A.M. Minio, "National Vital statistics Report Deaths: Preliminary Data for 2009," *Centers for Disease Control and Prevention*, vol.59, pp.1-51, 2011.
- [8] Korea National Statics Office. Annual Report on the Cause of Death Statics [M]. Korea National Statical Office. 2010.
- [9] S. Augustin, A. Gonzalez, and J. Genesca, "Acute esophageal variceal re-bleeding: Current strategies and new perspectives," *World Journal of Hepatology*, vol.2, no7, pp.261-274, 2010.
- [10] C.H. Zhu, and J.X. Hao, "Endoscopic variceal ligation versus β -blockers plus isosorbide mononitrate in prevention of esophageal variceal re-bleeding: a Meta-analysis," *Chinese Journal of Digestive Endoscopy*, vol.26, no.3, pp.128-133, 2009.
- [11] G.H. Lo, "The role of endoscopy in secondary prophylaxis of esophageal varices," *Clinics in Liver Disease*, vol.14, no.2, pp.307-323, 2010.
- [12] F. Schepis, C. Camma, D. Niceforo, A. Magnano, S. Pallio, M. Cinquegrani, G. D'amico, L. Pasta, A. Craxi, A. Saitta, and G. Raimondo, "Which patients with cirrhosis should undergo endoscopic screening for esophageal varices detection," *Hepatology*, vol.33, no.2, pp.333-338, 2001.
- [13] L. Boyanova, and I. M itov, "Geographic map and evolution of primary Helicobacter pylori resistance to antibacterial agents," *Expert Review of Anti-infective Therapy*, vol.8, no.1, pp.59-70, 2014.
- [14] D. Tripathi, J.W. Ferguson, G. Therapondos, J.N. Plevris, and P.C. Hayes, "Recent advances in the management of bleeding gastric varices," *Alimentary Pharmacology & Therapeutics*, vol.24, no.1, pp.1-17, 2006.
- [15] A.K. Burroughs, "Octreotide in variceal bleeding," *Gut*, vol.35, no. Suppl3, pp.S23-27, 1994.
- [16] K. Stokkeland, L. Brandt, A. Ekbom, and R. Hultcrantz, "Improved prognosis for patients hospitalized with esophageal varices in Sweden 1969-2002" *Hepatology*, vol.43, no.3, pp.500-505, 2006.
- [17] G.V. Stiegmann, "Evolution of endoscopic therapy for esophageal varices," *Surgical Endoscopy & Other Interventional Techniques*, vol.20, no.S2, pp.S467-470.
- [18] H. Deng, X.S. Qi, and X.Z. Guo, "UK guidelines on the management of variceal haemorrhage in cirrhotic patients (2015): an excerpt of recommendations," *Journal of Clinical Hepatology*, vol.31, no.6, pp.852-854, 2015.
- [19] P. Svoboda, M. Konecny, A. Martinek, V. Hrabovsky, V. Prochazka, V. and J. Ehrmann, "Acute upper gastrointestinal bleeding in liver cirrhosis patients" *Biomedical Papers of the Medical Faculty of the University Palacký Olomouc Czechoslovakia*, vol.156, no.3, p.266-270, 2012.
- [20] L. Miu, "The Diagnostic and Therapeutic Values of Emergency Endoscopy in Liver Cirrhotic Patients with Upper Gastrointestinal Bleeding" *Journal of Hunan Normal University (Medical Sciences)*, vol.14, n.6, pp.115-120, 2017.
- [21] Portal hypertension group of Chinese Department of surgery, "Common understanding of diagnosis and treatment of esophageal and gastric variceal bleeding caused by cirrhosis of the portal hypertension (2015 Edition)," *Chinese Journal of General Surgery*, vol.31, no.2, pp.167-170, 2016.
- [22] Chinese Society of Hepatology, Chinese Medical Association, "Guidelines for the diagnosis and treatment of esophageal and gastric variceal bleeding in cirrhotic portal hypertension," *Chinese Journal of Internal Medicine*, vol.55, no.1, pp.57-72, 2016.
- [23] Z.Y. Lu, L.S. Zhong, "Internal Medicine [M], the seventh edition," *Beijing: People's Health Publishing House*, pp.448, 452, 453, 484, 485, 2008.
- [24] Esophagogastric varicosity group of the Chinese Medical Association for digestive endoscopy, "Tentative guidelines for endoscopic diagnosis and treatment of varicosity and variceal bleeding in digestive tract (2009)," *China Continuing Medical Education*, vol.2, no.6, pp.21-26, 2010.
- [25] U. Thalheimer, C. Triamos, J. Goulis, and A.K. Burroughs, "Management of varices in cirrhosis," *Expert Opin Pharmacother*, vol.12, no.5, pp.721-735, 2011.
- [26] J.R. Tafarel, L.H. Tolentino, L.M. Correa, D.R. Bonilha, P. Piauilino, F.P. Martins, R.A. Rodrigues, F.S. Nakao, E.D. Libera, A.P. Ferrari, M.R. da Silveira Röhr, "Prediction of esophageal varices in hepatic cirrhosis by noninvasive markers," *European Journal of Gastroenterology & Hepatology*, vol.23, no.9, pp.754-758, 2011.

- [27] Z.H. Dong, Q.P. Meng, and L.F. Cheng, "Preventive and Therapeutic Progress of Rebleeding of Esophageal Varices," *Medical Recapitulate*, vol.13, no.12, pp.924-926, 2007.
- [28] S.K. Sarin, M. Wadhawan, S.R. Agarwal, P. Tyagi, and B.C. Sharma, "Endoscopic variceal ligation plus propranolol versus endoscopic variceal ligation alone in primary prophylaxis of variceal bleeding," *American Journal of Gastroenterology*, vol.100, no.4, pp.797-804, 2005.
- [29] D. Jaklewicz, W. Rózański, S. Wojtuń, and J. Gil, "Endoscopic methods of treatment of variceal haemorrhage," *Polski merkuriusz lekarski: organ Polskiego Towarzystwa Lekarskiego*, vol.22, no.131, pp.419-422, 2007.
- [30] Q.Y. Wang, T.S. Liu, W. Jiang, L. Dong, X.Z. Sheng, S.C. Zhang, J.S. Gou, and W.B. Liu, "The prevention and treatment of hepatocirrhosis and its complication," *National Medical Journal of China*, vol.82, no.17, pp.1212-1216, 2002.
- [31] J. Cheung, I. Soo, R. Bastiampillai, Q. Zhu, and M. Ma, "Non-urgent endoscopy in stable acute variceal bleeding," *American Journal of Gastroenterology*, vol.104, no.5, pp.1125-1129, 2009.
- [32] Y.C. Hsu, C.S. Chung, C.H. Tseng, T.L. Lin, J.M. Liou, M.S. Wu, F.C. Hu, and H.P. Wang, "Delarisk factor for in-hospital mortality in acute variceal hemorrhage," *Journal of Gastroenterology & Hepatology*, vol.24, no.7, pp.1294-1299, 2009.
- [33] Z.J. Chen, and M.L. Freeman, "Management of upper gastrointestinal bleeding emergencies: evidence-based medicine and practical considerations," *World Journal of Emergency Medicine*, vol.2, no.1, pp.5-12, 2011.
- [34] P.H. Chen, W.C. Chen, M.C. Hou, T.T. Liu, C.J. Chang, W.C. Liao, C.W. Su, H.M. Wang, H.C. Lin, F.Y. Lee, and S.D. Lee, "Delayed endoscopy increases rebleeding and mortality in patients with hematemesis and active esophageal variceal bleeding: a cohort study," *Journal of Hepatology*, vol.57, no.6, pp.1207-1213, 2012.
- [35] J. Cheung, I. Soo, R. Bastiampillai, Q. Zhu, and M. Ma, "Urgent VS non-urgent endoscopy in stable acute variceal bleeding," *American Journal of Gastroenterology*, vol.104, no.5, pp.1125-1129, 2009.
- [36] Y.C. Hsu, C.S. Chung, C.H. Tseng, T.L. Lin, J.M. Liou, M.S. Wu, F.C. Hu, and H.P. Wang, "Delarisk factor for in-hospital mortality in acute variceal hemorrhage," *Journal of Gastroenterology & Hepatology*, vol.24, no.7, pp.1294-1299, 2009.