Long-Term Outcomes of Hemostatic Therapy for Gastrointestinal Variceal Bleeding and the Transition of Hemostatic Therapy: A Retrospective Study

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Abstract

BACKGROUND Gastrointestinal varices are dilated submucosal veins in the gastrointestinal lumen associated with portal hypertension and represent important complications of liver cirrhosis (LC). Gastrointestinal variceal bleeding has serious life-threatening outcomes; although hemostatic therapy is possible in many cases, there are only a few studies reporting the detailed course of patients with variceal bleeding after hemostatic therapy and the transition of hemostatic therapy. This study aimed to evaluate the long-term outcomes of endoscopic hemostatic therapy for gastrointestinal variceal bleeding and of the transition of hemostatic therapy.

METHODS A total of 125 patients who underwent emergency hemostatic therapy for gastrointestinal variceal bleeding between April 2006 and June 2020 were included. Data on the bleeding site, therapeutic method, primary therapeutic success rate, cumulative survival rates, factors associated with prognosis, recurrence rates, re-bleeding rates after treatment, and causes of re-bleeding were analyzed. Additionally, patients were classified into two groups: the previous term and the latter term. Patients’ background, therapeutic method, and treatment results were compared between the groups.

RESULTS Overall, 94.4% had cirrhosis. The average Child-Pugh (CP) score (CPS) was 8.90. The rate of successful primary hemostasis was 98.4%, and 5.6% died within two weeks, all with a CPS ≥9. The respective one- and five-year survival rates for CP grade A/B were 81.3% and 55.4%, while those for CP grade C were 58.1% and 17.8%. CP grade C or hepatocellular carcinoma was significantly associated with poor prognosis. In total, 21.6% experienced variceal re-bleeding, and 62.9% of variceal re-bleeding cases were triggered by alcohol consumption. There was no significant difference in survival between patients with and without variceal re-bleeding. There was no significant difference in post-treatment survival between the previous and latter terms. In the latter term, the number of cases caused by alcohol consumption increased.

CONCLUSIONS The hemostasis rate for variceal bleeding was high. Multidisciplinary treatment and continuation of proper management after treatment are crucial. Alcohol consumption increased variceal re-bleeding in the post-direct-acting antivirals era.

Background

Gastrointestinal varices, which are dilated submucosal veins in the gastrointestinal lumen, are one of the serious complications of liver cirrhosis (LC) associated with portal hypertension, which can lead to variceal bleeding and have serious life-threatening consequences[1]. Without therapeutic endoscopy, more than 60% of patients with variceal bleeding have a risk of re-bleeding within a year, and the mortality is reported to increase by 33%[2]. The one- and three-year incidences of esophageal varices in patients with LC were approximately 5% and 28%, respectively[3]. The prevalence of gastrointestinal varices is known to increase proportionally with the severity of LC[4,5]. In
addition, the incidence of gastrointestinal varices increases at an annual rate of 10%–12%\cite{6}; variceal bleeding occurs at an annual rate of approximately 15%\cite{1}, and the six-week mortality rate of patients with variceal bleeding is reported to be 16%–20%\cite{7,8}.

In previous studies, it has been reported that advances in pharmacological and endoscopic therapies have led to a decrease in acute variceal bleeding-related mortality\cite{9-11}. Although primary hemostatic therapy is possible in most cases, there are still few studies reporting the more detailed course of patients with variceal bleeding after hemostatic therapy and the transition of hemostatic therapy in the post-direct-acting antivirals (DAA) era as the hepatitis C virus (HCV) is being progressively eradicated.

We are actively pursuing the treatment of cases of variceal bleeding to improve survival rates. This study aimed to evaluate the long-term outcomes of hemostatic therapy for gastrointestinal variceal bleeding, mainly with endoscopic therapy and the transition of hemostatic therapy methods.

**Methods**

A total of 125 patients who underwent emergency hemostatic therapy for gastrointestinal variceal bleeding from April 2006 to June 2020 were enrolled in this study.

The cumulative survival rates after treatment were considered as the primary evaluation point. The bleeding site, therapeutic method, success rate of primary treatment, factors associated with prognosis, recurrence rates, re-bleeding rates after treatment, and causes of re-bleeding were considered secondary evaluation points. In addition, patients were classified into two groups: the first seven years of the 14-year analysis period, defined as the previous term (April 2006–March 2013; n=66), and the subsequent seven years, defined as the latter term (April 2013–June 2020; n=59). Patients’ backgrounds, treatment methods, and treatment results were compared between the two groups as secondary evaluation points.

**Hemostatic procedures**

In most cases of acute gastrointestinal variceal bleeding, endoscopic treatments were performed, which included endoscopic variceal ligation (EVL), endoscopic injection sclerotherapy with 5% ethanolamine oleate (EIS-Eo), and endoscopic injection sclerotherapy using cyanoacrylate (EIS-CA).

Esophageal variceal bleeding was treated with either EVL or EIS-Eo. After endoscopy was performed to identify whether the bleeding site was in the fundus or gastroesophageal junction, bleeding of isolated gastric fundal varices (IGV) was treated with EIS-CA, while gastroesophageal junctional variceal bleeding was treated with EVL or EIS-Eo. EVL is not recommended for IGV. If the varix and contralateral wall cannot be captured by band ligation, blood flow remains uninterrupted, which may lead to massive bleeding. The standard therapy for IGV is to administer a sclerotizing substance in the form of a cyanoacrylate injection. Cyanoacrylate therapy uses 75% n-butyl-2-cyanoacrylate and the fatty contrast agent Lipiodol. Following administration, cyanoacrylate is polymerized and exerts its effects instantly\cite{12–14}.
Balloon-occluded retrograde transvenous obliteration (BRTO) was performed for some of the IGV bleeding cases. BRTO was first described by Kanagawa et al. in 1991 as a treatment for IGV [15]. It has been reported to be successful in treating 76.9% to 100% of IGV bleeding cases [16–18]. However, BRTO could not be performed immediately when variceal bleeding was confirmed by endoscopy, and endoscopic therapy is often prioritized over BRTO for preventing bleeding more rapidly. Therefore, EIS-CA was performed in most cases of variceal bleeding at our department. Moreover, ectopic variceal bleeding was treated with EIS-CA in four patients.

Endoscopic follow-up was performed at one, three, and six months after emergency hemostasis treatment and every 3-12 months afterwards depending on the endoscopic findings of gastrointestinal varices. Preventive therapeutic indications for exacerbations of gastrointestinal varices after emergency hemostatic therapy were a rapid increase in variceal size compared to previous endoscopic findings or the presence of red wale marks on varices [19-21].

**Statistical analyses**

Results are presented as mean±standard deviation. The cumulative survival, recurrence, and re-bleeding rates after treatment were calculated using the Kaplan-Meier method, while the log-rank test was used for comparing each curve. Differences between the two groups were analyzed using the $\chi^2$ test and Student t-test. The multivariate analysis was performed using the Cox proportional hazards model. A p-value of <0.05 was considered statistically significant. All analyses were performed using the JMP version 13.0 software (SAS Institute, Charlotte, NC).

**Ethical statement**

The study protocol was approved by the ethics committee of Fukuoka University Hospital (approval number: H20-07-006) and was conducted in compliance with the principles of the Declaration of Helsinki and the Ethical Guidelines for Medical Research of the Ministry of Health, Labor, and Welfare. The information obtained was kept strictly anonymous. This was a retrospective study using past medical information, and it was impossible to obtain consent from the target patients in advance. Therefore, the waiver for the informed consent was obtained from the ethics committee. This clinical study has been outlined on our website (http://www.med.fukuoka-u.ac.jp/research/life_med_ethic/).

**Results**

**Clinical characteristics of patients**

The clinical characteristics of the patients are presented in Table 1. The study included 93 male patients and 32 female patients with a mean age of 62.3±12.2 years, and 118 of the 125 patients (94.4%) had cirrhosis. The main causes of cirrhosis were viral hepatitis (51 cases, 40.8%) and alcohol consumption (68 cases, 54.4%). The numbers of patients with Child-Pugh (CP) grades A, B, and C were 9, 62, and 47, respectively, with an average CP score (CPS) of 8.90±2.0. There were 27 patients (21.6%) with
hepatocellular carcinoma (HCC), and seven patients had advanced portal vein tumor thrombus (PVTT) that progressed proximally to the primary branch of the portal vein.

**Table 1 Clinical characteristics of patients**

| Characteristics          | Number of patients |
|--------------------------|--------------------|
| Number of patients       | 125                |
| Sex (male/female)        | 93/32              |
| Age, years (mean±SD)     | 62.3±12.2 (range 32–83) |
| Liver cirrhosis          |                    |
| presence                 | 118 94.4%          |
| absence                  | 7 5.6%             |
| Etiology                 |                    |
| viral hepatitis           | 51 40.8%           |
| alcohol consumption      | 68 54.4%           |
| others                   | 22 17.6%           |
| Child-Pugh grade         |                    |
| grade A                  | 9 7.6%             |
| grade B                  | 62 52.5%           |
| grade C                  | 47 39.8%           |
| Child-Pugh Score (mean±SD)| 8.9±2.0           |
| HCC                      |                    |
| presence                 | 27 21.6%           |
| absence                  | 89 71.2%           |
| unknown                  | 9 7.2%             |
| PVTT presence            | 7 5.6%             |

SD: standard deviation; HCC: hepatocellular carcinoma; PVTT: portal vein tumor thrombus.

Bleeding sites included the esophagus (76.8%, 96 patients), stomach (20.0%, 25 patients), duodenum (2.4%, three patients), and rectum (0.8%, one patient) (Table 2). Therapeutic methods included EVL (64.0%, 80 patients), EIS-Eo (17.6%, 22 patients), EIS-CA (16.0%, 20 patients), and BRTO (2.4%, three patients) (Table 2).

**Table 2 Bleeding sites and therapeutic methods**
### Bleeding sites

| Site     | Count | Percentage |
|----------|-------|------------|
| Esophagus| 96    | 76.8%      |
| Stomach  | 25    | 20.0%      |
| Duodenum | 3     | 2.4%       |
| Rectum   | 1     | 0.8%       |

### Therapeutic methods

| Method   | Count | Percentage |
|----------|-------|------------|
| EVL      | 80    | 64.0%      |
| EIS-Eo   | 22    | 17.6%      |
| EIS-CA   | 20    | 16.0%      |
| BRTO     | 3     | 2.4%       |

EVL: endoscopic variceal ligation; EIS-Eo: endoscopic injection sclerotherapy with 5% ethanolamine oleate; EIS-CA: endoscopic injection sclerotherapy using cyanoacrylate; BRTO: balloon-occluded retrograde transvenous obliteration.

### Short-term results

Successful primary hemostasis was achieved in 123 patients (98.4%), while fatal bleeding occurred in two patients (1.6%) and seven patients (5.6%) died of liver failure within two weeks after treatment (Figure 1). Of the seven patients who died within two weeks, five patients had CP grade C, and two patients had a CPS ≥ 9 points within CP grade B.

### Long-term outcomes

The one-, two-, three-, and five-year overall cumulative survival rates after treatment (median follow-up, 1389 days) were 72.6% (n=65), 59.4% (n=45), 54.8% (n=29), and 45.6% (n=16), respectively (Figure 2). The death cases consisted of 35 liver-related deaths (68.6%, 24 due to liver failure, 11 due to liver cancer), eight due to other causes, and eight of unknown causes. The one-, two-, three-, and five-year cumulative survival rates for CP grades A and B (median follow-up, 2826 days) were 81.3% (n=48), 68.4% (n=34), 63.4% (n=24), and 55.4% (n=13), respectively, while those for CP grade C (median follow-up, 518 days) were 58.1% (n=18), 44.1% (n=13), 40.1% (n=7), and 17.8% (n=4) respectively (p=0.001) (Figure 3).

The univariate and multivariate analyses showed that CP grade C (hazard ratio (HR), 2.37; 95% confidence interval (CI), 1.05-5.38; p=0.038) and HCC (HR, 4.03; 95% CI, 1.56-11.1; p=0.005) were associated with a poor prognosis (Table 3).

### Table 3 Univariate and multivariate analyses of prognostic factors

| Factor   | HR (95% CI) | p-value |
|----------|-------------|---------|
| CP grade C | 2.37 (1.05-5.38) | 0.038 |
| HCC      | 4.03 (1.56-11.1) | 0.005 |
### Table 4 Causes of variceal re-bleeding

| Factor          | Univariate | Multivariate |
|-----------------|------------|--------------|
|                 | HR (95% CI) | p value      | HR (95% CI) | p value |
| Sex (male)      | 0.19 |  |  |  |
| Age (per year)  | 0.59 |  |  |  |
| Etiology (alcohol) | 0.24 |  |  |  |
| Method (EVL)    | 0.35 |  |  |  |
| CP grade C      | 2.58 (1.23-5.50) | 0.013 | 2.37 (1.05-5.38) | 0.038 |
| Variceal re-bleeding | 0.35 |  |  |  |
| HCC presence    | 4.40 (1.75-11.9) | 0.002 | 4.03 (1.56-11.1) | 0.005 |
| Term (latter)   | 0.23 |  |  |  |

EVL: endoscopic variceal ligation; CP: Child-Pugh, HCC: hepatocellular carcinoma; HR: hazard ratio; CI: confidence interval.

**Variceal re-bleeding**

After a first variceal eradication with emergency hemostatic therapy and additional treatment, 42 patients (33.9%) required re-treatment owing to recurrent varices or variceal bleeding (Figure 1), with an average period until re-treatment of 331 days. In addition, 27 patients (21.8%) had variceal re-bleeding (Figure 1), with an average period until variceal re-bleeding of 358 days. The one-, two-, three-, and five-year cumulative re-bleeding-free rates after the first variceal eradication (median length of follow-up, 1224 days) were 81.3% (n=55), 76.2% (n=35), 63.7% (n=21), and 55.3% (n=11), respectively (Figure 4). In addition, 27 patients with variceal re-bleeding had one-, two-, three-, and five-year cumulative survival rates (median length of follow-up, 912 days) of 80.9% (n=20), 72.4% (n=17), 66.3% (n=11), and 59.7% (n=6), respectively, while 91 patients without variceal re-bleeding (except for seven patients who died within two weeks) had one-, two-, three-, and five-year cumulative survival rates (median length of follow-up: 1389 days) of 75.3% (n=46), 59.0% (n=29), 54.6% (n=19), and 44.1% (n=11), respectively; however, no statistical significance was observed (p=0.24) (Figure 5). The causes of variceal re-bleeding are shown in Table 4. Variceal re-bleeding was triggered by alcohol consumption in 17 of the 27 patients (62.9%). Moreover, recurrent variceal re-bleeding was caused by alcohol consumption in all five patients.
| Condition                        | Count | Percentage |
|---------------------------------|-------|------------|
| Alcohol consumption             | 17    | 62.9%      |
| Viral hepatitis                  | 3     | 11.1%      |
| Cryptogenic                     | 5     | 18.5%      |
| Obstruction of splenic vein     | 1     | 3.7%       |
| PVTT                            | 1     | 3.7%       |

PVTT: portal vein tumor thrombus.

**Combination with drug therapy**

Regarding the combination with drug therapy, four patients with and 15 patients without variceal re-bleeding were administered nonselective beta-blockers (NSBB) to improve portal hypertension after hemostatic therapy. There was no statistically significant difference in the presence of variceal re-bleeding regardless of NSBB administration (p=0.93).

**Outcomes of cases with advanced PVTT**

In the seven HCC patients with advanced PVTT, only one patient (14.3%) had variceal re-bleeding; however, the average survival time was 60.4±21.4 days, and the majority of the patients died within a short period.

**Transition of hemostatic therapy for variceal bleeding**

Compared to the previous term group, the number of cases with variceal bleeding caused by alcohol consumption increased from 29 cases in the previous term to 42 cases in the latter term (p=0.003) (Figure 6A). As for the therapeutic methods, the number of EVL procedures increased from 30 to 49 cases (p<0.0001), and that of the EIS-Eo procedures decreased from 21 cases to one case (p<0.0001) in the latter term group (Figure 6B).

Except for seven patients who died within two weeks, the one-, two-, three-, and five-year cumulative survival rates after treatment for the 63 patients in the previous term group (median follow-up, 1552 days) were 78.5% (n=40), 62.3% (n=28), 57.5% (n=20), and 45.2% (n=14), respectively, while the rates for the 55 patients in the latter term group (the median follow-up, 729 days) were 75.6% (n=26), 65.5% (n=18), 59.0% (n=10), and 59.0% (n=3), respectively. There was no statistically significant difference between the two groups (p=0.74) (Figure 7). In addition, there was no significant difference in the cumulative survival rates between the EVL and EIS-Eo procedures for esophageal varices (in LC and CP grades A and B) (p=0.25).

**Discussion**
Our study summarized the long-term outcomes of hemostatic therapy for gastrointestinal variceal bleeding and the transition of therapeutic methods. Esophageal and gastric varices accounted for most of the variceal bleeding cases; however, a small number of ectopic varices were observed in approximately 3% of patients. Patients with repeated treatment for esophageal and gastric varices may occasionally develop ectopic varices\textsuperscript{[22–26]}. In addition, extrahepatic portal vein occlusion owing to portal vein thrombosis, pancreatic cancer, or cholangiocarcinoma may cause ectopic varices\textsuperscript{[27,28]}. Therefore, the site of gastrointestinal bleeding should be ascertained in the portal phase of contrast-enhanced computed tomography as much as possible before treatment.

Endoscopic therapy for variceal bleeding can be considered as established\textsuperscript{[2,29,30]}. Similarly to those reports, in our study, endoscopic therapy using EVL was performed for esophageal variceal bleeding and EIS-CA was performed for IGV bleeding. In addition, the success rate of primary hemostasis was extremely high. There are several reports on post-treatment survival rates for variceal bleeding. According to one study, 287 patients with variceal bleeding caused by alcoholic LC had cumulative overall survival rates of 67%, 42%, and 26% at one, three, and five years, respectively\textsuperscript{[31]}. Moreover, in the analysis of 201 cirrhotic patients with acute variceal bleeding, the one- and three-year survival rates were 65.7% and 60.2%, respectively\textsuperscript{[32]}. Another study reported a two-year survival rate of 61% in 31 patients with LC and acute variceal bleeding in the pharmacotherapy (vasoactive drugs)+EVL group\textsuperscript{[33]}. In addition, according to the examination of the effect of EIS for LC with liver cancer, patients with CP grade A and B had a five-year survival rate of 60%, while no survival benefits were seen in patients with CP grade C\textsuperscript{[34]}

In the CP grade A and B groups in our study, the results were comparable to those previously reported. Primary hemostasis was first performed with EVL for esophageal varices and gastroesophageal junctional variceal bleeding or with EIS-CA for IGV and ectopic varices as a hemostatic therapeutic strategy for gastrointestinal variceal hemorrhage in our facility. Then, the general condition and hepatic reserve were evaluated and a subsequent policy was planned. The outcomes of our study showed the feasibility of our strategy.

Our findings show that decreased liver reserve (CPS $\geq$ 9) or HCC with advanced PVTT required attention for early liver failure and early cancer death after hemostasis.

The two-year cumulative survival rate of patients with CP grade C has been reported to be approximately 30\%\textsuperscript{[35,36]}, and a very severe prognosis was reported. Hepatic ischemia owing to bleeding may promote liver failure immediately. It is also important to clearly inform patients that even if the primary hemostasis is successful, it may lead to a certain degree of liver failure progression and death. In this study, the two-year survival rate of patients with CP grade C was 44.1%, which was a better result than the general cumulative survival rate for these patients. We previously reported that even in patients with end-stage CP grade C LC, multidisciplinary treatment for cirrhosis after invasive treatment such as hemostatic therapy for variceal bleeding may significantly reduce the CPS and improve liver function\textsuperscript{[37]}. Indeed, some
patients were discharged and followed strict systemic management after primary hemostasis and liver supporting therapy, and maintained their daily activities for a longer period, even with a low liver reserve.

In addition, PVTT occurs in approximately 50% of patients with advanced HCC, and the survival rate of patients with HCC and PVTT was reported to be associated with a natural median survival time (MST) of approximately three months\(^\text{[38,39]}\). The MST after hemostatic therapy in our study was 60.4±21.4 days, which was slightly shorter. Therefore, additional treatment such as stereotactic body radiotherapy for the tumor thrombus should be considered according to the general condition after hemostatic therapy\(^\text{[40]}\).

The multivariate analysis showed that a CP grade C or HCC was significantly associated with poor prognosis after treatment. Meanwhile, there was no significant difference in the cumulative survival rate between patients with or without variceal re-bleeding. We considered that this occurred because patients with a first bleeding episode were strictly followed up at our hospital and treated quickly so re-bleeding episodes would not go undetected. Therefore, maintaining a strict follow-up schedule was considered crucial for minimizing early death after re-bleeding.

In our study, there was no statistically significant difference in the presence of variceal re-bleeding between patients with or without NSBB administration. NSBB is known to reduce portal pressure by reducing the heart rate and cardiac output and by contracting visceral blood vessels. The combination of NSBB and EVL has been reported to reduce the risk of variceal re-bleeding and improve survival\(^\text{[41]}\). However, it is also true that a significant proportion of patients experience variceal re-bleeding during treatment with NSBB\(^\text{[42]}\). Several reports indicated that NSBB administration is not superior to endoscopic therapy\(^\text{[43–45]}\); however, further examination using the combination of NSBB and endoscopic therapy is needed for investigating their efficacy in preventing re-bleeding in a larger sample.

In the latter term group, it was observed that alcohol consumption was significantly associated with variceal bleeding. In recent years, there has been a remarkable breakthrough in the treatment of HCV infection using DAA. Combination therapy with DAA (NS5A inhibitor, NS5B inhibitor, or NS3/4a protease inhibitor) has an extremely high therapeutic effect\(^\text{[46–48]}\). Since HCV is rapidly being eradicated after the appearance of DAA, variceal bleeding caused by HCV is expected to decrease in the future. In the last five years, when treatment with DAA was generalized, the rate of variceal bleeding owing to alcohol consumption further increased in this study (72.1%). New medications are being developed for treating alcoholism and the use of nalmefene hydrochloride hydrate has been increasing in Japan recently\(^\text{[49–51]}\).

In a real-world setting, it is difficult to intervene in the daily lives of outpatients. However, patients must be advised of the importance of alcohol abstinence and nutritional support\(^\text{[52,53]}\). In the post-DAA era, it is considered that the importance of instructions pertaining to alcohol abstinence will be increasing in the future.

This study has several limitations. First, the retrospective design of the present study made it difficult to compare the findings to those of prospective studies. Second, this was a single-center study, which may
limit the generalizability of the results. Third, a detailed study of medications other than NSBB, which is expected to reduce portal pressure, could not be performed. However, the promising results obtained provide a valuable evaluation of the long-term outcomes of endoscopic hemostatic therapy for gastrointestinal variceal bleeding and the transition of hemostatic therapy.

**Conclusions**

In summary, as a hemostatic therapy for gastrointestinal variceal bleeding, EVL-based therapy yielded excellent hemostatic results. Patients with a CPS of $\geq 9$ or advanced PVTT should be closely monitored to prevent early death. Multidisciplinary treatment and maintaining a strict follow-up schedule are crucial for minimizing death after bleeding or re-bleeding. Alcohol consumption leads to variceal re-bleeding and its proper management, including alcohol abstinence, is one of the major challenges left in the post-DAA era.

**List Of Abbreviations**

LC, liver cirrhosis; DAA, direct-acting antivirals; HCV, hepatitis C virus; EVL, endoscopic variceal ligation; EIS-Eo, ethanolamine oleate; EIS-CA, endoscopic injection sclerotherapy using cyanoacrylate; IGV, isolated gastric fundal varices; BRTO, balloon-occluded retrograde transvenous obliteration; CP, Child-Pugh; CPS, Child-Pugh score; HCC, hepatocellular carcinoma; PVTT, portal vein tumor thrombus; HR, hazard ratio; CI, confidence interval; NSBB, nonselective beta-blockers; MST, median survival time

**Declarations**

**Ethics approval and consent to participate**

The study protocol was approved by the ethics committee of Fukuoka University Hospital (approval number: H20-07-006) and was conducted in compliance with the principles of the Declaration of Helsinki and the Ethical Guidelines for Medical Research of the Ministry of Health, Labor, and Welfare. The information obtained was kept strictly anonymous. This was a retrospective study using past medical information, and it was impossible to obtain consent from the target patients in advance. Therefore, this clinical study has been outlined on our website (http://www.med.fukuoka-u.ac.jp/research/life_med_ethic/).

**Consent for publication**

Not applicable.

**Availability of data and materials**

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.
Competing interests

The authors declare that they have no competing interests.

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Authors’ contributions

All authors participated in data collection. KS and KY contributed to writing the manuscript. All authors read and approved the final manuscript.

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Figures
Figure 1

Flowchart of progress after hemostatic therapy.

Figure 2

Graph showing overall cumulative survival rate over time.
Figure 2
Overall cumulative survival rates after treatment.

Figure 3
Cumulative survival rates after treatment for CP grades A and B vs. CP grade C. CP: Child-Pugh.

Log-rank test
p=0.0013
Figure 4

Cumulative re-bleeding-free rates after the first variceal eradication.

Figure 5

1 except for 7 patients who died within 2 weeks
Figure 5
Cumulative survival rates in patients with and without variceal re-bleeding. 1Except for seven patients who died within two weeks.

Figure 6A

Figure 6B

Figure 6
Clinical characteristics of patients and transition of therapeutic methods. A: clinical characteristics of patients; B: transition of therapeutic methods. EVL: endoscopic variceal ligation; EIS-Eo: endoscopic injection sclerotherapy with 5% ethanolamine oleate.

**Figure 7**

![](image)

*Cumulative survival rates in the previous and latter terms. 1Except for seven patients who died within two weeks.*