Long-term outcomes of hemostatic therapy for variceal bleeding and the challenge pending in the post-direct-acting antivirals era

K. Shibata, K. Yokoyama, R. Yamauchi, K. Matsumoto, S. Himeno, T. Nagata, T. Higashi, T. Kitaguchi, H. Fukuda, N. Tsuchiya, A. Fukunaga, K. Takata, T. Tanaka, Y. Takeyama, S. Shakado, S. Sakisaka, F. Hirai

Department of Gastroenterology and Medicine, Fukuoka University Faculty of Medicine, 7-45-1 Nanakuma, Jonan-ku, Fukuoka-shi, Fukuoka 814-0180, Japan.

Abstract

Background and study aims: **This study evaluated the long-term outcomes of mainly endoscopic hemostatic therapy for gastrointestinal variceal bleeding and of the transition of hemostatic therapy.**

Patients and methods: **Among 1,163 patients treated for gastrointestinal varices between April 2006 and June 2020, a total of 125 patients who underwent emergency hemostatic therapy were enrolled. Survival rates and secondary evaluation points were analyzed. Additionally, patients were classified into two groups: the previous and latter term. Patients' background, therapeutic method, and treatment results were compared between the groups.**

Results: **94.4% had cirrhosis. The average Child-Pugh score was 8.90. Successful primary hemostasis rate was 98.4%, and 5.6% died within 2 weeks, all with a Child-Pugh score ≥9. The respective 1- and 5-year survival rates for Child-Pugh grade A/B were 81.3% and 55.4%, while those for Child-Pugh grade C were 58.1% and 17.8%. Child-Pugh grade C or hepatocellular carcinoma was significantly associated with poor prognosis. In total, 21.6% experienced variceal re-bleeding; 62.9% of these cases were triggered by continued alcohol consumption. There was no significant difference in survival between patients with and without variceal re-bleeding and in post-treatment survival between the previous and latter terms. In the latter term, the number of cases caused by continued alcohol consumption significantly increased.**

Conclusions: **Multidisciplinary treatment and continuation of proper management after hemostatic therapy for variceal bleeding are crucial. Continued alcohol consumption leads to variceal bleeding and re-bleeding; its proper management, including alcohol abstinence, is one of the major challenges left in the post-direct-acting antivirals era.** (Acta gastroenterol. belg., **2022,** 85, **7-14**).

Keywords: gastrointestinal hemorrhage; endoscopic variceal hemostasis; alcohol consumption; variceal re-bleeding.

Introduction

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 1- and 3-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% (6); variceal bleeding occurs at an annual rate of approximately 15% (1), and the 6-week mortality rate of patients with variceal bleeding is 16%-20% (7,8).

Advances in pharmacological and endoscopic therapies have led to a decrease in acute variceal bleeding-related mortality (9-11). Although primary hemostatic therapy is possible in most cases, there are still few studies reporting a 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

Among 1,163 patients treated for gastrointestinal varices between April 2006 and June 2020, a total of 125 patients who underwent emergency hemostatic therapy for gastrointestinal variceal bleeding were enrolled in this study. Emergency hemostatic therapy was defined as variceal bleeding at the time during endoscopy or bleeding findings such as hematemesis within 24 hours.

The cumulative survival rates after treatment were considered as the primary evaluation point. Secondary evaluation points were as follows; the bleeding site, therapeutic method, as short-term results, the success rate of primary treatment, mortality within 2 weeks after treatment, as long-term outcomes, comparison of survival rates by liver reserve and with and without variceal re-bleeding, recurrence rates, re-bleeding rates, factors associated with prognosis for survival and causes of re-bleeding, respectively.

In addition, patients were classified into two groups in the 14-year analysis period as follows; the first 7

Correspondence to: Keiji Yokoyama MD, Department of Gastroenterology and Medicine, Fukuoka University Faculty of Medicine, 7-45-1 Nanakuma, Jonan-ku, Fukuoka-shi, Fukuoka 814-0180, Japan. Fax: +81-92-874-2663.1
Email: yokotin@fukuoka-u.ac.jp

Submission date: 11/05/2021
Acceptance date: 18/07/2021

years of the 14 years, defined as the previous term (April 2006-March 2013; n=66), and the subsequent 7 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. Balloon-occluded retrograde transvenous obliteration [BRTO] was performed for some of the IGV bleeding cases. Moreover, ectopic variceal bleeding was treated with EIS-CA.

Endoscopic follow-up was performed at 1, 3, and 6 months after emergency hemostatic treatment and every 3-12 months afterward, depending on the endoscopic findings of gastrointestinal varices. Preventive therapeutic indications for exacerbations of gastrointestinal varices after emergency hemostatic therapy exhibited a rapid increase in variceal size compared to previous endoscopic findings or the presence of red wale marks on varices (12-14).

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 c^2 test and Student *t*-test. 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 the 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 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 causes of 7 patients without liver cirrhosis were secondary extra-hepatic portal obstruction due to other carcinoma in 3 cases, drug-induced sinusoidal obstruction syndrome due to oxaliplatin in 2 cases, portal vein thrombosis in 1 case and idiopathic portal hypertension in 1 case. The main causes of cirrhosis were viral hepatitis (51 cases, 40.8%) and alcohol consumption (68 cases, 54.4%). The number 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 17 patients (13.6%) with a previous preventive treatment of varices before their episode of variceal bleeding. There were 27 patients (21.6%) with hepatocellular carcinoma [HCC], and seven patients with advanced portal vein tumor thrombus [PVTT] that progressed proximally to the primary branch of the portal vein.

Table 1. — **Clinical characteristics of patients**

Number of patients	125	
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	
History of previous preventive treatment for varices		
presence	17	13.6%
absence	108	86.4%
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.

Table 2. — **Bleeding sites and therapeutic methods**

Bleeding sites		
Esophagus	96	76.8%
Stomach	25	20.0%
Duodenum	3	2.4%
Rectum	1	0.8%
Therapeutic methods		
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.

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). Ectopic variceal bleeding was treated with EIS-CA in all four patients.

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 2 weeks after treatment (Fig. 1). Among the seven patients who died within 2 weeks, five patients had CP grade C, and two patients had CPS B9 within CP grade B.

Long-term outcomes

The 1-, 2-, 3-, and 5-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 (Fig. 2a). 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 1-, 2-, 3-, and 5-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) (Fig. 2b).

The univariate and multivariate analyses of prognostic factors for survival show ed 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 survival (Table 3).

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 (Fig. 1), with an average period until re-treatment of 331 days. In addition, 27 patients (21.8%) had variceal re-bleeding (Fig. 1), with an average period until variceal re-bleeding of 358 days. Moreover, five patients (4.0%) had recurrent variceal re-bleeding (Fig. 1). The 1-, 2-, 3-, and 5-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),

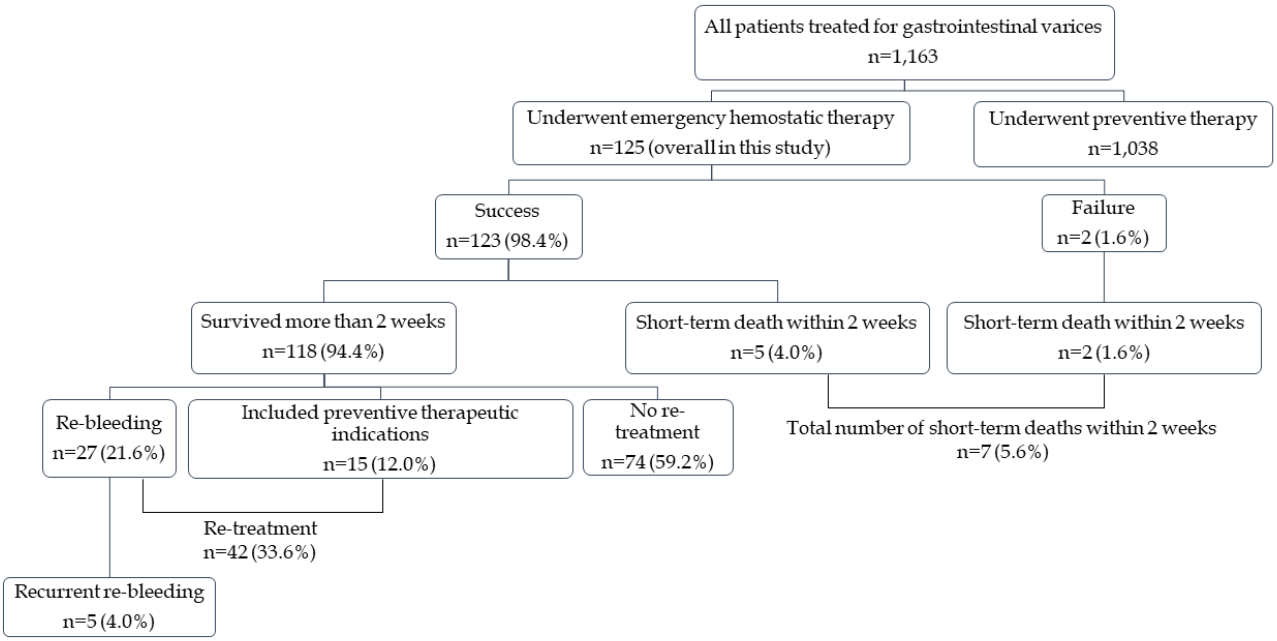

Fig. 1. — Flowchart of progress after hemostatic therapy.

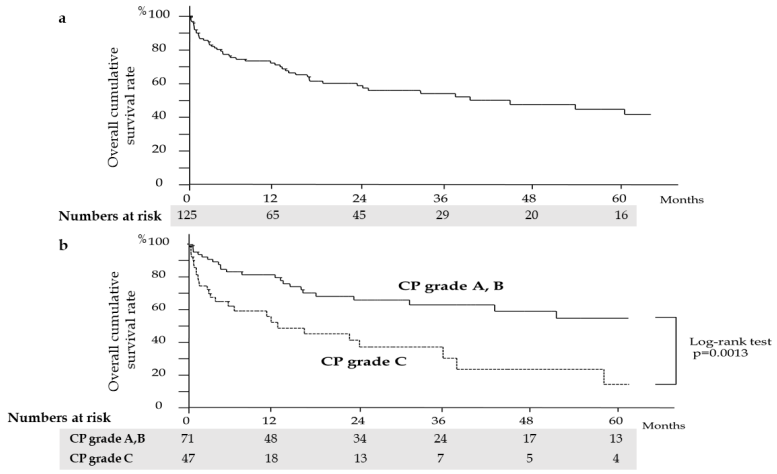

Fig. 2. — Overall cumulative survival rates after treatment (image A). Cumulative survival rates after treatment for CP grades A and B vs. CP grade C (image B). CP: Child-Pugh.

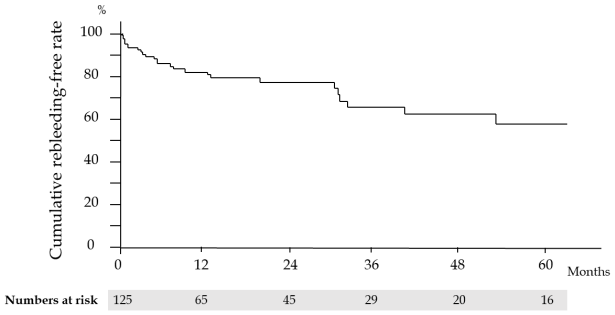

Fig. 3. — Cumulative re-bleeding-free rates after the first variceal eradication.

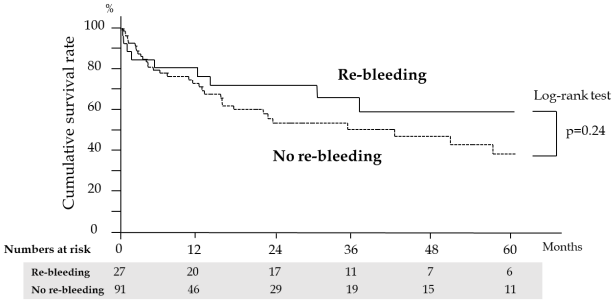

Fig. 4. — Cumulative survival rates in patients with and without variceal re-bleeding. [1]Except for seven patients who died within 2 weeks.

Table 3. — **Univariate and multivariate analyses of prognostic factors for survival**

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		

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

63.7% (n=21), and 55.3% (n=11), respectively (Fig. 3). In addition, 27 patients with variceal re-bleeding had 1-, 2-, 3-, and 5-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 2 weeks) had 1-, 2-, 3-, and 5-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) (Fig. 4). The causes of variceal re-bleeding are shown in Table 4. Variceal re-bleeding was triggered by continued alcohol consumption in 17 of the 27 patients (62.9%). Moreover, recurrent variceal re-bleeding was caused by continued alcohol consumption in all five patients.

Table 4. — **Causes of variceal re-bleeding and recurrent variceal re-bleeding**

	re-bleeding n=27		recurrent re-bleeding n=5	
Continued alcohol consumption	17	62.9%	5	100%
Viral hepatitis	3	11.1%	0	0%
Cryptogenic	5	18.5%	0	0%
Obstruction of splenic vein	1	3.7%	0	0%
PVTT	1	3.7%	0	0%

PVTT: portal vein tumor thrombus

Combination with drug therapy

Regarding the combination with EVL and 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. On the other hand,14 patients with and 60 patients without variceal re-bleeding were only repeated EVL in secondary prophylaxis. There was no statistically significant difference in the presence of variceal re-bleeding regardless of NSBB administration (p=0.84).

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 time period.

Transition of hemostatic therapy for variceal bleeding

Comparison between clinical characteristics of patients in the previous and latter terms (except for seven patients who died within 2 weeks) are shown in Table 5.

Compared to the previous term group, the number of cases with variceal bleeding caused by continued alcohol consumption increased from 29 cases in the previous term group to 42 cases in the latter term group (p=0.003). As for the therapeutic methods in the full cohort, 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.

The 1-, 2-, 3-, and 5-year cumulative survival rates after treatment for the 63 patients in the previous term group (median follow-up, 1552 days) were 78.5%

Table 5. — **Comparison between clinical characteristics of patients in the previous and latter terms**

	Previous term	latter term	p value
Number of patients	63	55	
Male/female	42/21 (66.7%/33.3%)	44/11 (80.0%/20.0%)	0.11
Age, years (mean ± SD)	64.5 ± 11.5	60.4 ± 12.2	0.067
Liver cirrhosis			
presence/ absence	60/3 (95.2%/4.8%)	52/3 (94.5%/5.5%)	0.86
Etiology			
viral hepatitis	27 (42.9%)	24 (43.6%)	0.93
alcohol consumption	29 (46.0%)	42 (76.4%)	0.003
others	15 (23.8%)	6 (10.9%)	0.056
Child-Pugh grade			
grade A	6 (9.5%)	3 (5.5%)	0.41
grade B	30 (47.6%)	32 (58.2%)	0.25
grade C	27 (42.9%)	20 (36.4%)	0.47
Child-Pugh Score (mean ± SD)	9.13 ± 1.9	9.09 ± 2.0	0.92
Therapeutic methods			
EVL	30 (47.6%)	49 (89.1%)	<0.0001
EIS-Eo	21 (33.3%)	1 (1.8%)	<0.0001
EIS-CA	11 (17.5%)	9 (16.4%)	0.80
BRTO	3 (4.8%)	0 (0%)	0.095
History of previous preventive treatment for varices			
presence/ absence	7/56 (11.1%/88.9%)	7/48 (12.7%/87.3%)	0.79
HCC			
presence/ absence (unknown)	13/47 (20.6%/74.6%) (3)	11/40 (20.0%/72.7%) (4)	0.85
PVTT			
presence/ absence	3/60 (4.8%/95.2%)	4/51 (7.3%/92.7%)	0.56

SD: standard deviation; CP: Child-Pugh; 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; HCC: hepatocellular carcinoma; PVTT: portal vein tumor thrombus.

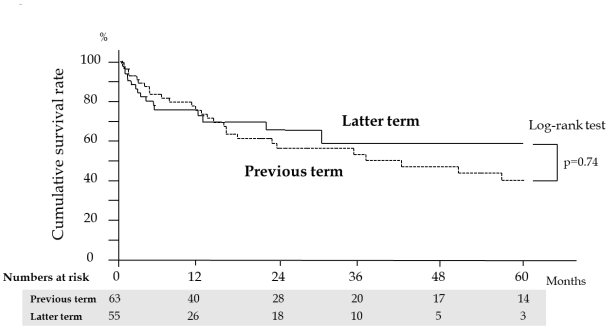

Fig. 5. — Cumulative survival rates in the previous and latter terms. [1]Except for seven patients who died within 2 weeks.

(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 (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) (Fig. 5). 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.

Regarding treatment options for gastric varices, EVL is not recommended for IGV. Because when the varix and the contralateral wall cannot be captured by band ligation, blood flow remains uninterrupted, which may lead to massive bleeding. Therefore, 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 (15-17). On the other hand, BRTO was first described by Kanagawa et al. in 1991 as a treatment for IGV (18). It has been reported to be successful in treating 76.9% to 100% of IGV bleeding cases (19-21). However, BRTO could not be performed immediately when variceal bleeding was confirmed by endoscopy, and endoscopic therapy was often prioritized over BRTO for stopping bleeding more rapidly. Therefore, EIS-CA was performed in most cases of variceal bleeding at our department.

Esophageal and gastric varices accounted for most of the variceal bleeding cases in this study; 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 (22-26). In addition, extrahepatic portal vein occlusion owing to portal vein thrombosis, pancreatic cancer, or cholangiocarcinoma may cause ectopic varices (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 can be considered as an established approach for variceal bleeding (2,29,30). Similar to those reports, in our study, endoscopic therapy using EVL was performed for esophageal variceal bleeding and EIS-CA was performed for IGV bleeding. The success rate of primary hemostasis was exceptionally high. Later, the general condition and hepatic reserve were evaluated and a subsequent policy was planned. There are already several reports on post-treatment survival rates for variceal bleeding (31, 32). In CP grade A and B groups in our study, the results were comparable to those previously reported. Therefore, the outcomes of our study showed the feasibility of our strategy.

Another study reported a 2-year survival rate of 61% in 31 patients with LC and acute variceal bleeding in the pharmacotherapy (vasoactive drugs) + EVL group (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 5-year survival rate of 60%, while no survival benefits were observed in patients with CP grade C (34).

Our findings showed that decreased liver reserve (CPS ≥9) or HCC with advanced PVTT required attention for early liver failure and early cancer death after hemostasis. The 2-year cumulative survival rate of patients with CP grade C has been reported to be approximately 30% (35,36), and a very severe prognosis has been 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 2-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 (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 3 months (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 (40).

The multivariate analysis showed that 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 hypothesized that this occurred because patients with a first bleeding episode were strictly followed up at our hospital and treated quickly and therefore re-bleeding episodes would not go undetected. Therefore, maintaining a strict follow-up schedule was considered crucial for minimizing chances of 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 (41). However, it has also been reported that a significant proportion of patients experience variceal re-bleeding during treatment with NSBB (42). Several reports indicated that NSBB administration is not superior to endoscopic therapy (43-45). In this cohort only a minority got NSBB. In Japan, due to the development of insurance medical care, strict follow-up with an endoscope is relatively possible. Meanwhile, The BAVENO VI guideline advices to start NSBB in all patients to prevent recurrent bleeding, ideally in combination with EV (46). Further examination using the combination of NSBB and endoscopic therapy in a larger sample is needed for investigating their efficacy in preventing re-bleeding.

In the latter term group, it was observed that continued 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 exceedingly high therapeutic effect (47-49). 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 5 years of the analysis period, when treatment with DAA had been generalized, the rate of variceal bleeding owing to continued 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 in recent years (50-52).

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 (53,54). 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 with 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. Fourth, the shorter follow-up period for a substantial number of patients in the latter term group. Therefore, we provided the numbers at risk and numbers censored below each Kaplan-Meier curve. In the future, it is necessary to evaluate with a longer follow-up. 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.

In summary, EVL-based therapy yielded excellent hemostatic results as a hemostatic therapy for gastrointestinal variceal bleeding. Patients with a CPS of ≥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 the chances of death after bleeding or re-bleeding. Continued alcohol consumption leads to variceal re-bleeding and its proper management, including alcohol abstinence, is one of the major challenges to be overcome in the post-DAA era.

Conflict of interest statement

All authors declare that they have no conflict of interests.

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