Long-term outcome after endoscopic ligation of acute esophageal variceal bleeding in patients with liver cirrhosis

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Abstract

Endoscopic variceal ligation (EVL) has been the standard treatment for acute variceal bleeding (AVB). However, reports of long-term prognosis after EVL are scarce. Therefore, the current work aimed to investigate the long-term outcome and prognostic modifiers of cirrhotic cases presented with acute esophageal variceal bleeding and managed with EVL.

The current prospective work comprised primarily 276 consecutive grown-up cirrhotic cases presenting with AVB and managed with EVL. Two-hundred patients who completed the study till death or 3-year follow-up were enrolled in final analysis. The primary outcome measure was occurrence of rebleeding and all-cause mortality.

By the end of follow up 56 patients (28%) developed rebleeding and 78 (39%) died. The independent factors associated with rebleeding were lacking follow up EVL (OR: 4.8, 95%CI: 1.9-12.2), BMI > 30 kg/m² (OR: 0.-, 95%CI: 0.2-0.9), Child class C (OR: 3.8, 95%CI: 1.8-7.8), and grade IV varices (OR: 2.6, 95%CI: 1.3-5.3). The independent factors associated with mortality were: Age > 65 years (OR: 32.4, 95%CI: 8.7-120.3), rebleeding (OR: 98.4, 95%CI: 27.9-347.0), coexistence of HCC (OR: 7.4, 95%CI: 2.0-27.4), and lacking follow up EVL (OR: 6.1, 95%CI: 1.2-31.1).

Recurrent bleeding after emergency endoscopic ligation of acute esophageal variceal bleeding in cirrhotic cases is a rather common complication that significantly increases the mortality rate. The liver condition, lack of follow up endoscopy, old age, and severity of esophageal varices are independent prognostic indicator of rebleeding and morality. (Acta gastroenterol. belg., **2020**, 83, **373-380**).

Keywords : endoscopic ligation, variceal bleeding, liver cirrhosis.

Introduction

Acute variceal bleeding (AVB) is associated with an elevated mortality rate in cases with liver cirrhosis. Despite improvement in recent years, it carries a 6-week mortality rate of 15%-20% (1,2). In addition, cases with bleeding esophageal varices have elevated rates of rebleeding, and adverse events than cases with non-variceal bleeding as ulcer bleeding (3). It was reported that early rebleeding rate is about 30% to 40% within the first 6 weeks after the first episode (4). The rate of rebleeding may reach 60% within the first year (5).

Acute variceal bleeding is an emergency situation that necessitates medical management with vasoactive drugs, antibiotics, blood transfusion, combined with variceal ligation (6). A recent meta-analysis reported that endoscopic variceal ligation (EVL) is superior to endoscopic injection sclerotherapy in terms of the decreased rates of rebleeding, adverse outcomes, and the higher rate of variceal eradication (3). The American Society for Gastrointestinal Endoscopy (ASGE) guidelines recommended EVL as the first-line treatment for AVB (7).

Reports of long-term prognosis after endoscopic variceal ligation of acute variceal bleeding are scarce. Therefore, the goal of the current work was to investigate the long-term (3 years) outcome and prognostic modifiers of cirrhotic cases who presented with acute esophageal variceal bleeding and managed with EVL in a large tertiary center in Egypt.

Patient and Methods

The current prospective work comprised primarily 276 consecutive cirrhotic cases presenting with AVB who were managed with EVL between February 2012 and March 2014. Patients who did not complete the follow-up period were excluded. Thus, only 200 completed the study till death or completion of 3 years. All the 200 cases had true AVB (Hematemesis and/or melena)

The steps of the work were in accordance with ethical guidelines of the 1975 declaration of Helsinki and its modifications. The study was confirmed by the institutional review board. All cases signed written informed consents for performance of endoscopy as well as for participation in the study.

According to the local institutional protocol of management, urgent upper gastrointestinal (GI) endoscopy was done in case of suspicion of variceal bleeding within 6 hours of presentation to the emergency department. Patients were eligible to be enrolled in the study if they were adults (> 18 years old) having liver cirrhosis with overt hematemesis and/or melena who were emergently hospitalized and managed for acute esophageal variceal bleeding. Patients with elective or prophylactic EVL, bleeding due to causes other than esophageal varices,

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bleeding from gastric varices, or inpatient onset of GI bleeding were excluded from the study.

Management protocol of cases

Cases received blood transfusion guided by the standard guidelines which advised starting transfusions if Hb levels declined below 7 g/dL, and the aimed level is 7 to 9 g/dL (8). Besides, all cases were given Intravenous (IV) ceftriaxone at a dose of 1 g per day for a maximum of one week.

An IV vasoconstrictor was started immediately because early infusion may result in better outcome. Two IV vasoconstrictors were employed depending on availability: terlipressin and octreotide. These drugs were maintained up to 5 days after the endoscopy. Terlipressin was given at a dose of 1-2 mg IV every 4-8 hours. Octreotide was given at a dose of initial IV bolus 50 mcg, followed by continuous IV infusion of 50 mcg/hour for 2 to 5 days. (9).

Data registry

Physicians and nurses registered initial vital signs and laboratory work-up when cases came with acute overt GI bleeding in the emergency department. The following clinical characteristics were recorded: body mass index (BMI), lifestyle factors, comorbidities (diabetes mellitus, hypertension, or hepatocellular carcinoma "HCC'), vital signs, laboratory data, etiology of cirrhosis, and red cell concentrate demand during hospital stay. In addition, discharge medications were recorded. Also, the number of endoscopies and number of EVL during the follow-up period was determined for each participant.

Endoscopic findings at initial presentation included presence or absence of red color sign and grade of varices. The grading system was based on Paquet's classification of varices that was released in 1982, employing a four-point Likert scale to identify four grades of varices. Grade I: Microcapillaries situated in distal esophagus or esophago-gastric junction and grade II: One or two small varices situated in the distal esophagus and grade III: Medium-sized varices of any number & Grade IV: Large-sized varices in any part of esophagus (10).

All patients were followed-up to 3 years after their initial presentation or up to death. The primary outcome measure was occurrence of rebleeding and all-cause death. Rebleeding was determined as considerable overt GI bleeding after discharge with unstable vital signs (systolic blood pressure $\leq$ 90 mmHg or pulse $\geq$ 110 bpm), substantial decrease (of 2 points) in hemoglobin, requirement of blood transfusion, or endoscopically verified overt GI bleeding.

Because clinical suspicion of rebleeding should necessitate another endoscopy whenever possible and be managed based on endoscopic assessment, we enrolled other sources of GI bleeding in the definition of rebleeding, such as gastric varices, peptic ulcer disease, esophageal ulceration, and Mallory-Weiss syndrome (11).

Statistical analysis

Statistical analysis was performed employing IBM© SPSS© Statistics version 22 (IBM© Corp., Armonk, NY, USA). Numerical variables were presented as mean and standard deviation or median and range as appropriate. Qualitative variables were presented as frequency and percentage. Chi-square test (Fisher's exact test) was employed to assess the relation between qualitative variables. Relative risk (PR) with it 95% confidence interval (CI) were employed for risk estimation. Multivariate analysis was performed using logistic regression models. A p value < 0.05 was considered significant.

Results

The current study included 200 cirrhotic cases who presented with AVB. Of these cases, 74 presented with hematemesis only, 55 with melena only and 71 with hematemesis and melena. During endoscopy, 25 % (50) patients were actively bleeding.

A total number of 155 (77.5 %) patients received blood transfusion. The amount of blood transfusion ranged from 1 to 7 units, with a mean of 4 units. One-hundred twelve cases were given terlipressin and the rest were given octreotide.

Table (1) demonstrates the baseline data at presentation of the 200 patients enrolled in the work.

Follow-up

Rebleeding

Within the follow-up period, 56 patients (28%) developed rebleeding for difference causes (Table 2).

Regarding the time of bleeding, group I included patients who rebled within the first 30 days (three patients, two of them were referred to TIPS), group 2 who rebled within three months included 10 patients, group 3 who rebled with 3-6 months included 11 patients, group 4 who rebled with 6-12 month included 18 patients, group 5 who rebled within 12-24 months included 12 patients, group 6 who rebled within 24-36 months included 2 patients.

Of the total 56 cases who experienced rebleeding, 41 (73.2 %) cases had rebleeding due to esophageal varices. There were 13 (23.2 %) patients with more than one attack of rebleeding. Three (5.4%) cases rebled due to post-EVL ulcers.

Twenty-six cases did not undergo follow-up endoscopy as their varices looked small with no risky signs of bleeding at the initial endoscopy.

During the study period, 5 patients were transplanted with uneventful post-transplantation course. Three of these 5 cases had rebleeding before transplantation with no reported further rebleeding attacks post transplantation.

Table 1. — **Initial data of the studied cases at presentation (n=200)**

Parameter	Value
Age (years)	54.3±10.2
Age≥65 years	43 (21.5%)
Sex (male/female)	142/58
Body mass index (kg/m²)	27.2±3.9
Child-Pugh class (A/B/C)	26/91/83
Chronic kidney disease	38 (19.0%)
Loss of consciousness	40 (20.0%)
Hypotension (systolic blood pressure < 90 mmHg)	128 (64.0%)
Hepatocellular carcinoma	34 (17.0%)
Discharge medications	
NSAIDs	18 (9.0%)
Antithrombotic drugs	6 (3.0%)
Proton pump inhibitors	142 (71.0%)
β-blockers	20 (10.0%)
Nitrate	8 (4.0%)
Laboratory data at presentation	
Hemoglobin (gm/dL)	8.4±0.8
Hematocrit value (%)	26±2
Platelet count (x10³/mm³)	83.0± 22.0
International Normalized Ratio (INR)	1.9±0.4
Serum Albumin (g/dL)	2.6±0.6
Serum Creatinine (mg/dL)	1.9±0.4
Total bilirubin (mg/dL)	2.4±0.7
Etiology of cirrhosis	
HCV	102 (51.0%)
HBV	31 (15.5%)
Autoimmune Hepatitis	16 (8.0%)
Alcoholic	11 (5.5%)
Primary Sclerosing Cholangitis	10 (5.0%)
Primary Biliary Cholangitis	8 (4.0%)
Other Causes*	11 (5.5%)
Unknown	11 (5.5%)
Endoscopic findings	
Red color sign	90 (45.0%)
Grade (I/II/III/IV)	18/40/62/80
Transfusion requirement	155 (77.5%)
Total transfused units	4 (1-7)

NSAIDs : non-steroidal anti-inflammatory drugs, HCV : hepatitis C virus, HBV : hepatitis B virus. Data are expressed as mean±SD, median (range), or number (%). * Other causes included HIV + any hepatitis virus (n=2); alcoholic liver cirrhosis + any virus (n=3); primary biliary cirrhosis + HCV (n=1); primary biliary cirrhosis + autoimmune hepatitis (n=3); and hemochromatosis (n=2).

As to other strategies for secondary prevention of variceal bleeding, 20 were maintained on beta-blockers. All of them underwent additional follow-up endoscopy, and of these cases only 6 cases experienced rebleeding attacks. Only 2 patients had TIPS during the follow-up period with no reported adverse events after the procedure.

Table 2. — **Rebleeding and mortality and their causes during the 3-year follow up period of the studied group**

	Value
Rebleeding	56 (28%)
Esophageal varices	41 (73.2%)
Duodenal ulcer	4 (7.1%)
Gastric ulcer	3 (5.4%)
Post-EVL ulceration	3 (5.4%)
Mallory-Weiss syndrome	2 (3.6%)
Esophageal erosion	1 (1.8%)
Unknown	2 (3.6%)
Death	78 (39%)
Esophageal variceal bleeding	20 (25.6%)
Hepatocellular carcinoma	19 (24.4%)
Liver failure	17 (21.8%)
Malignancies other than hepatocellular carcinoma	8 (10.3%)
Non-malignant diseases*	14 (11.5%)

* Non-malignant diseases included interstitial pneumonia (n=2), diffuse alveolar damage (n=1), pulmonary embolism (n = 1), sepsis due to spontaneous bacterial peritonitis (n = 3), myocardial infarction (n = 2), cerebral hemorrhage (n= 4), and cyroglobinemic vasculitis (n=1).

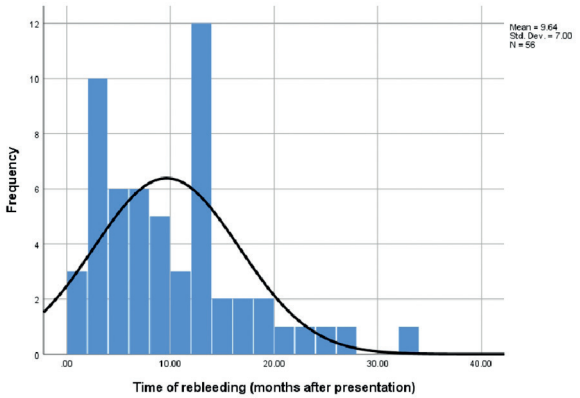

Figure 1. — Histogram for time of rebleeding.

Adherence to beta blockers was quite low in this study because a considerable number of cases experienced intolerance and/or advanced decompensated cirrhosis.

As shown in (table 3), the occurrence of rebleeding within the 3-year follow up period was significantly linked to older age (p = 0.008), male sex (p = 0.030), BMI < 30 kg/m² (p = 0.019), Child class C (p < 0.001), grade IV varices (p < 0.001), and lack of follow up endoscopy (p < 0.001) or EVL (p < 0.001). On multivariate analysis, lacking follow up EVL, BMI < 30 kg/m², Child class C, and grade IV varices were the independent factors associated with rebleeding (Table 4).

Deaths

Within the follow-up period, 78 patients (39%) died because of different causes (Table 2).

Table 3. — **Risk factors for rebleeding in the whole studied group (n=200)**

		Rebleeding	No Rebleeding	p value
Age≥ 65 years	Yes	19 (44.2%)	24 (55.8%)	0.008*
	No	37 (23.6%)	120 (76.4%)	
Sex	Male	46 (32.4%)	96 (67.6%)	0.030*
	Female	10 (17.2%)	48 (82.8%)	
Cause of cirrhosis	Viral	32 (24.1%)	101 (75.9%)	0.080
	Non-viral	24 (35.8%)	43 (64.2%)	
HCC	Yes	8 (23.5%)	26 (76.5%)	0.524
	No	48 (28.9%)	118 (71.1%)	
BMI (kg/m^2)	≥ 30	11 (17.2%)	53 (82.8%)	0.019*
	< 30	45 (33.1%)	91 (66.9%)	
Child score	A	2 (7.7%)	24 (92.3%)	< 0.001**
	B	16 (17.6%)	75 (82.4%)	0.232
	C	38 (45.8%)	45 (54.2%)	0.003*
Child score	A + B	18 (15.4%)	99 (84.6%)	< 0.001**
	C	38 (45.8%)	45 (54.2%)	
Chronic kidney disease	Yes	10(26.3%)	28 (73.7%)	0.797
	No	46(28.4%)	116 (71.6%)	
Loss of consciousness	Yes	12(30.0%)	28 (70.0%)	0.753
	No	44(27.5%)	116 (72.5%)	
Systolic pressure < 90	Yes	36 (28.1%)	92 (71.9%)	0.958
	No	20 (27.8%)	52 (72.2%)	
Transfusion requirement	Yes	43 (27.7%)	112 (72.3%)	0.880
	No	13 (28.9%)	32 (71.1%)	
INR	> 1.5	45 (28.1%)	115 (71.9%)	0.937
	Normal	11 (27.5%)	29 (72.5%)	
Albumin	< 3	39 (28.7%)	97 (71.3%)	0.756
	Normal	17 (26.6%)	47 (73.4%)	
Red color sign	Yes	23 (25.6%)	67 (74.4%)	0.486
	No	33 (30.0%)	77 (70.0%)	
Grade of varices	I	0 (0.0%)	18 (100.0%)	0.001**
	II	9 (22.5%)	31 (77.5%)	
	III	13 (21.0%)	49 (79.0%)	
	IV	34 (42.5%)	46 (57.5%)	
Grade IV	IV	34 (42.5%)	46 (57.5%)	< 0.001**
	I, II, III	22 (18.3%)	98 (81.7%)	
Follow-up endoscopy	Yes	43 (23.8%)	138 (76.2%)	< 0.001**
	No	13 (68.4%)	6 (31.6%)	
Follow-up EVL	Yes	37 (21.5%)	135 (78.5%)	< 0.001**
	No	19 (67.9%)	9 (32.1%)	

*P value < 0.05 significant, ** P value < 0.001 highly significant. HCC : hepatocellular carcinoma, BMI : body mass index, INR : international normalized ratio, EVL : esophageal variceal ligation, RR : Risk ratio, CI : Confidence interval.

Table (5) shows that death within the 3-year follow up period was significantly linked to older age ($p < 0.001$), non-viral causes of cirrhosis ($p = 0.016$), coexistence of HCC ($p < 0.001$), occurrence of rebleeding ($p < 0.001$), BMI < 30 kg/m^2 ($p = 0.031$), Child class C ($p < 0.001$), grade IV varices ($p < 0.001$), and lack of follow up endoscopy ($p < 0.001$) or EVL ($p < 0.001$). On multivariate analysis, age ≥ 65 years, presence of HCC, rebleeding, and lacking follow up EVL were the independent factors associated with death within 3 years (Table 6).

Data on the underlying liver disease

More than half of the cases had HCV-related cirrhosis (no 102, 51.5 %). Of these 102 patients, 43 were given direct antiviral agents (DAA) with sustained virological response (SVR) achieved in 23 patients.

Table 4. — **The results of multivariate analysis of factors associated with rebleeding**

	B	p value	OR	95% C.I. for OR	
				Lower	Upper
Follow-up EVL	1.571	0.001**	4.81	1.90	12.18
BMI > 30	-0.953	0.024*	0.38	0.17	0.88
Child class C	1.331	< 0.001**	3.79	1.84	7.79
Grade IV	0.950	0.010*	2.59	1.28	5.32

*P value < 0.05 significant, ** P value < 0.001 highly significant. EVL : esophageal variceal ligation, BMI : body mass index, B : regression coefficient, OR : Odds ratio, CI : Confidence interval.

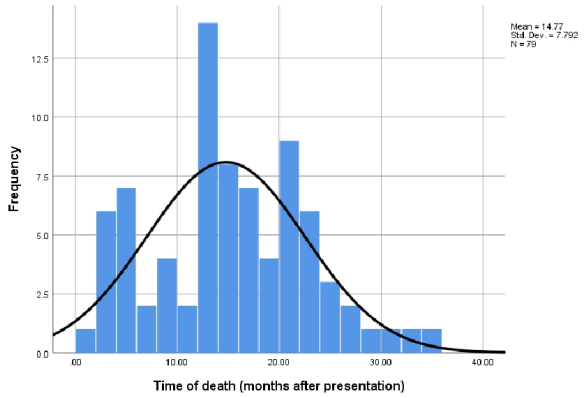

Figure 2. — Histogram for time of death.

Rebleeding occurred in 25 cases of HCV-related cirrhosis, (of them, only 13 cases were given DAA; 8 cases did not achieve SVR and 5 achieved SVR). Mortality occurred in 38 cases of HCV-related cirrhosis. (Of these cases, only 21 cases were given DAA; 15 cases did not achieve SVR, and 6 only achieved SVR).

Another 15.5 % (no 31) were due to HBV-related cirrhosis. All HBV cases were on oral drugs, 17 on tenofovir, and 14 on entecavir. Rebleeding occurred in seven patients and morality occurred in six patients of HBV-related cirrhosis

Ten cases of autoimmune hepatitis were on steroids only and 6 were on steroids and azathioprine. Three of those on steroids, and one on combination therapy experienced rebleeding. There were four cases of mortality within the cases on steroids, and one case on combination therapy.

Two of the cases with alcohol-related cirrhosis had ongoing alcohol consumption, both rebled with one reported case of mortality within the study period. Of the other nine cases of alcohol-related cirrhosis, three experienced rebleeding, and two died.

Additionally, of the ten cases with primary sclerosing cholangitis, three experienced rebleeding and four died, while within the cases of primary biliary cholangitis, two experienced rebleeding, and two died.

Discussion

The results of the current work revealed that rebleeding of esophageal varices after endoscopic ligation of emergency variceal bleeding in cirrhotic cases is a rather common complication (28%). The independent variables linked to rebleeding were lacking follow up EVL, BMI < 30 kg/m^2, Child class C, and grade IV varices. In these patients, mortality is relatively high within 3 years. Rebleeding, old age, presence of HCC, and lack of follow up EVL are the independent variables associated with mortality within 3 years after the primary procedure.

Several studies highlighted the factors related to early rebleeding - or failure - of emergency EVL in cirrhotic patients. However, the long-term prognosis of these cases has not been fully elucidated. The large sample size and long follow up period of this work allowed credibility in finding the incidence and risk factors for rebleeding after EVL.

The rate of rebleeding of esophageal variceal was widely variable in the few previous studies. After a mean follow-up period of 17.3 months of 128 cases, Lopes et al. (12) reported recurrent bleeding in 38.4% of cases. Rebleeding and death were more common among Child C patients. A more recent cohort study of 174 patients treated with emergency EVL, the cumulative rebleeding and death rates at 1 year were 30% and 26.6%, respectively. The mean follow-up period of this study was one and half years. The authors reported that Child-Pugh class C and no follow-up endoscopy were independent risk factors for rebleeding. These two factors in addition to the coexistence of HCC were the independent risk factors for death (13). In a retrospective cohort study, Branch-Elliman et al. found a significantly decreased rate (4.6%) of esophageal variceal bleeding over a period of 2 years after EVL after the primary attack of bleeding.

In the current study, rebleeding itself was an independent mortality risk factor. This finding was previously described in studies of the early outcome of emergency EVL in cirrhotic patients. Zhoa et al. (14) reported that nearly half of the deaths within 6-week follow-up period were caused by uncontrolled EV rebleeding. Early rebleeding is considered a strong predictor of mortality (15,16).

In the present work, Child-Pugh class C cirrhosis was an independent risk factor for both rebleeding and death within 3 years. This finding is concordant with other investigators. In fact, Child-Pugh class was confirmed as a poor prognostic indicator of early treatment failure in previous studies (17,18). Therefore, the severity of liver damage is an important predictor of recurrence of bleeding and mortality. This is supported by the findings

Table 5. — **Risk factors for death within 36 months in the whole studied group (n=200)**

		Dead	Alive	p value
Age > 65 years	Yes	38 (88.4%)	5 (11.6%)	< 0.001**
	No	40 (25.5%)	117 (74.5%)	
Sex	Male	61 (43.0%)	81 (57.0%)	0.073
	Female	17 (29.3%)	41 (70.7%)	
Cause of cirrhosis	Viral	44 (33.1%)	89 (66.9%)	0.016*
	Non-viral	34 (50.7%)	33 (49.3%)	
Presence of HCC	Yes	24 (70.6%)	10 (29.4%)	< 0.001**
	No	54 (32.5%)	112 (67.5%)	
Rebleeding	Yes	51 (91.1%)	5 (8.9%)	< 0.001**
	No	27 (18.8%)	117 (81.3%)	
BMI (kg/m^2)	≥ 30	18 (28.1%)	46 (71.9%)	0.031*
	< 30	60 (44.1%)	76 (55.9%)	
Child score	A	3 (11.5%)	23 (88.5%)	< 0.001**
	B	25 (27.5%)	66 (72.5%)	0.105
	C	50 (60.2%)	33 (39.8%)	< 0.001**
Child score	C	50 (60.2%)	33 (39.8%)	< 0.001**
	A + B	28 (23.9%)	89 (76.1%)	
Chronic kidney disease	Yes	16 (42.1%)	22 (57.9%)	0.663
	No	62 (38.3%)	100 (61.7%)	
Loss of consciousness	Yes	16 (40.0%)	24 (60.0%)	0.885
	No	62 (38.8%)	98 (61.3%)	
Systolic pressure	Yes	49 (38.3%)	79 (61.7%)	0.781
< 90	No	29 (40.3%)	43 (59.7%)	
Transfusion requirement	Yes	60 (38.7%)	95 (61.3%)	0.876
	No	18 (40.0%)	27 (60.0%)	
INR	> 1.5	64 (40.0%)	96 (60.0%)	0.562
	Normal	14 (35.0%)	26 (65.0%)	
Albumin	< 3	47 (34.6%)	89 (65.4%)	0.060
	Normal	31 (48.4%)	33 (51.6%)	
Red color sign	Yes	32 (35.6%)	58 (64.4%)	0.366
	No	46 (41.8%)	64 (58.2%)	
Grade of varices	I	0 (0.0%)	18 (100.0%)	< 0.001**
	II	14 (35.0%)	26 (65.0%)	
	III	17 (27.4%)	45 (72.6%)	
	IV	47 (58.8%)	33 (41.3%)	
Grade IV	IV	47 (58.8%)	33 (41.3%)	< 0.001**
	I, II, III	31 (25.8%)	89 (74.2%)	
Follow-up endoscopy	Yes	64 (35.2%)	118 (64.8%)	
	No	14 (77.8%)	4 (22.2%)	< 0.001**
Follow-up EVL	Yes	59 (33.9%)	115 (66.1%)	
	No	19 (73.1%)	7 (26.9%)	< 0.001**

*P value < 0.05 significant, ** P value < 0.001 highly significant. HCC : hepatocellular carcinoma, BMI : body mass index, INR : international normalized ratio, EV L: esophageal variceal ligation.

of other investigators who showed that the Model for End-stage Liver Disease score portended rebleeding (19,20). While these studies were concerned with early failure, there is an agreement with the current study. This indicates that the condition of the liver is a prognostic indicator of recurrent bleeding and mortality on short- and long-term basis.

EVL has been widely accepted as the standard endoscopic management for secondary prevention of esophageal variceal bleeding (21).

Table 6. — **The results of multivariate analysis of factors associated with death**

	B	p value	OR	95% C.I. for OR	
				Lower	Upper
Age > 65 years	3.479	< 0.001**	32.42	8.74	120.28
Rebleeding	4.588	< 0.001**	98.35	27.87	347.04
HCC	1.884	0.003*	7.35	1.97	27.39
Follow-up EVL	1.807	0.300	6.09	1.19	31.09

*P value < 0.05 significant, ** P value < 0.001 highly significant. HCC : hepatocellular carcinoma, EVL : esophageal variceal ligation, B : regression coefficient, OR : Odds ratio, C I: Confidence interval.

Furthermore, combination strategy using beta-blockers and EVL is not uncommon approach for the same purpose. Beta-blockers benefits can also extend to other adverse associations of elevated portal pressure. EVL may result in of rebleeding from post-banding ulcer (22). Besides, TIPS may be used for secondary prophylaxis of variceal bleeding in selected cases as it may increase the probability of hepatic encephalopathy and can lead to shunt dysfunction (23).

An important finding of the current study was the higher rate of rebleeding and death in association with lack of follow up endoscopy. This finding emphasizes the necessity of endoscopic follow up of cirrhotic patients managed with emergency EVL. The current guidelines recommend repeated endoscopy after the control of the acute attack of variceal bleeding until varices have been eradicated (24). Afterwards, endoscopy screening should be done 1-3 months after esophageal variceal eradication and should be repeated at 6-12 months to detect recurrence (7).

The main drawback of this work was the large number of cases that were lost to follow up. Most of these cases were lost too early to include in a statistically sound survival analysis. We decided to limit the analysis to those who completed the 3-year follow-up period. We did not continue for longer period owing to logistic reasons. Additionally, the rebleeding cases were not all confirmed by endoscopy and inclusion of other sources of GI bleeding in the definition of rebleeding. However, points of strength of the work comprise the large sample size and its prospective design.

Future studies should consider major factors that influences portal pressure such as ongoing liver injury, for example continuing alcohol or untreated HCV or the impact of treated HCV on rebleeding and mortality. as these could be major confounders in both for rebleeding as well as death rates.

In conclusion, recurrent bleeding after emergency endoscopic ligation of acute esophageal variceal bleeding in cirrhotic cases is a rather common complication that significantly increases the mortality rate of these patients. The liver condition determined by the Child-Pugh score is an independent prognostic indicator of rebleeding and morality in these patients in addition to lack of follow up endoscopy, old age, and severity of esophageal varices. We recommend close follow up after the initial treatment of bleeding esophageal varices both clinically and endoscopically. Special attention should be provided for older cases with advanced hepatic disease and higher grade varices.

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