

# Risk Factors for Recurrent Upper Gastrointestinal Tract Bleeding after Esophageal Varices Ligation on Patients with Liver Cirrhosis

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## ABSTRACT

*Background: Upper gastrointestinal tract (GIT) bleeding on liver cirrhosis patients will increase morbidity and mortality. Recurrent bleeding's risk rise after the first episode of variceal bleeding. The mortality risk also rises on each bleeding.*

*Purpose: This study was done in order to identify the risk factors for the first episode of recurrent bleeding of upper GIT on liver cirrhosis patient. Evaluation of risk factors was based on preliminary data prior to ligation.*

*Method: Evaluation of the upper GIT bleeding was done using anamnesis on the patients or their relatives by letter, home visits or telephone. The data on recurrent bleeding was obtained from medical records. They were evaluated on the 3<sup>rd</sup> month then 1<sup>st</sup> year after ligation. This study was a cross sectional study with retrospective data and a consecutive sampling method.*

*Result: Bivariate analysis revealed the 3<sup>rd</sup> month's risk factors for first episode of upper GIT bleeding were ascites, total bilirubin level of > 2 mg/dL, hepatoma, Child-Pugh C classification of the liver function and red color sign on esophageal varices. The risk factors for the first episode of upper GIT bleeding on first year were age ≤ 60 years old, hepatoma, and red color sign (RCS) on esophageal varices. The differences between risk factors on upper GIT bleeding on the 3<sup>rd</sup> month and 1<sup>st</sup> year were likely due to intervention, collateral para-esophageal varices, medication that irritated GIT, physical activities, and differences on variceal obliteration rate related to variceal ligation.*

*Conclusion: Risk factors for recurrent upper GIT bleeding that could be minimized were ascites, total bilirubin level, Child-Pugh classification and RCS. It was expected with paracentesis, diuretics, hepatoprotector medications and drugs that lowers portal hypertension (such as propranolol and isosorbid mononitrate), might improve those risk factors thus decreasing the risk for recurrent upper GIT bleeding.*

**Keywords:** *Upper gastrointestinal tract, esophageal varices, liver cirrhotic.*

## INTRODUCTION

Liver cirrhosis mortality on 38 countries in America, Europe, Africa and Asia from 1985 until 1990 was 3 to 40 /100,000 people. The worldwide prevalence of liver cirrhosis in 1993 was between 25 and 40 cases/100,000 people. About 90% cases of liver cirrhosis resulted in portal hypertension and 1/3 die due to upper gastrointestinal track (GIT) bleeding.<sup>1</sup> A survey conducted by The Indonesian Ministry of Health in 1996 revealed 4.2% of mortality caused by chronic liver disease and liver cirrhosis.<sup>2</sup> Liver cirrhosis and portal hypertension might increase the probability for liver cirrhotic to 35% to 85%. Liver cirrhosis with esophageal varices might increase the risk for bleeding up to 25% to 30%,<sup>3</sup> the risk for recurrent esophageal bleeding in one year increases around 30% to 40%,<sup>4</sup> and death due to recurrent bleeding increase more than 50%.<sup>5</sup>

A study conducted by Djojoningrat in Department of Internal Medicine, Cipto Mangunkusumo hospital, showed mortality from upper GIT bleeding was around 26%. From those, 23% was attributable to hypovolemic shock. Endoscopic examination showed most lesions were esophageal varices (70%).<sup>6</sup> A study by Abdoellah M et al., on Ramelan Navy hospital in Surabaya in 1999 revealed 78% incidence of esophageal varices in patients with hematemesis and melena.<sup>7</sup> In Sardjito Hospital in Jogjakarta, there were 42.1% liver cirrhosis patients died caused by with hepatic coma preceded by GIT bleeding.<sup>8</sup>

Prognosis for a non-variceal bleeding is better than variceal bleeding. The severity of variceal rupture bleeding are attributed to more complications, more blood needed for transfusion, complex management, and higher mortality.<sup>9</sup> Therefore, hematemesis and melena are warning signs, which causes must be searched for, and preventions for recurrent bleeding must be taken.<sup>10</sup>

Factors involve in the first episode of variceal bleeding are Child-Pugh classification, the size of esophageal varices, and red wale marking on esophageal varices wall.<sup>11,12</sup> Other predictors are cherry-red spot, elevated serum bilirubin level, portal vein congestive index (portal vein's diameter and portal blood velocity).<sup>13</sup> Also encephalopathy, ascites and age have correlation to mortality.<sup>11</sup>

Factors associated to early upper GIT bleeding (< 6 weeks) are severity of first bleeding period, age > 60 years old, severity of hepatic function, ascites, encephalopathy, and disturbance on kidney function, active bleeding on first time endoscopic examination, stigmata on varices, platelet clot in varices, and the size

of varices.<sup>14,15</sup> Factors involved in late recurrent bleeding (> 6 weeks) are severity of liver function, ascites, hepatoma, active alcohol drinker and red sign on endoscopy.<sup>15</sup> Other study revealed factors for recurrent bleeding such as albumin < 3 g/dL and active variceal bleeding on endoscopy index.<sup>16</sup> Another study found age, cirrhotic etiology, ascites, variceal size and Child-Pugh classification had no correlation on recurrent variceal bleeding.<sup>16,17</sup>

Other methods for predicting variceal bleeding is variceal pressure. North Italian Endoscopic Club (NIEC) index plus variceal pressure measurement will increase prediction of variceal bleeding incidence.<sup>18</sup> These conclude that clinical findings and endoscopic data are valuable information for estimating the risk of bleeding.<sup>19</sup>

Standard treatments on esophageal varices might prevent recurrent bleeding. Those treatments would be ligation, sclerotherapy and/or medications.<sup>20</sup> Study in Cipto Mangunkusumo hospital in 1989 showed variceal sclerotherapy could lower the incidence of recurrent bleeding.<sup>21</sup> Recently ligation is more popular than sclerotherapy because sclerotherapy have higher incidence for recurrent bleeding than ligation.<sup>16,17,22</sup> Also one meta-analysis study showed the complication of ligation was lesser than sclerotherapy.<sup>23</sup> Three studies conducted by Hata et al., Lo et al., and Hou et al., showed there were no difference in the incidence of recurrent bleeding in ligation and sclerotherapy.<sup>24-26</sup> Bleeding from gastric varices was more common in sclerotherapy than in ligation. Bleeding incidence also tends to be higher in unobliterated varices.<sup>26</sup> Ligation can control 94% of acute variceal bleeding<sup>22</sup> and also prevents recurrent variceal esophageal bleeding up to 25%.<sup>14</sup>

This study was done to obtain the prevalence of the first episode of recurrent upper GIT bleeding after the first ligation of esophageal varices in the 3 month and 1 year period after the treatment and to have knowledge of the risk factors for the recurrence of upper GIT bleeding after first ligation of esophageal varices in liver cirrhotic patient. Risk factors were observed from clinical signs and upper GIT endoscopic before ligation.

## METHOD

This was a cross sectional study with recurrent upper GIT bleeding as outcome variable, which would be evaluated in 3 months and 1 year after the first ligation of esophageal varices.

### Population and sample

Target populations were patients with esophageal varices due to liver cirrhosis with history of upper GIT bleeding, who had not had any variceal ligation. Population within reach: liver cirrhosis patients who had been performed esophageal varices ligation. Sample was patients who had been performed esophageal varices.

### Data collection

Inclusion criteria were liver cirrhosis patients who had esophageal varices with upper GIT bleeding before ligation of the varices.

Exclusion criteria were patient whose medical record was damaged or lost, no clinical/laboratory data before esophageal varices ligation, patient died due to non-bleeding cause during evaluation period, incomplete address hindered communication through letters, telephone or home visits.

Baseline data before ligation were retrospective, including age, gender, physical examination (level of consciousness and ascites), laboratory data (serum albumin level, total bilirubin level, prothrombin factor, and thrombocyte count), Child-Pugh classification, abdominal ultrasonography (cirrhosis appearance, ascites, portal hypertension, hepatoma) and esophagogastroduodenoscopy (RCS appearance, esophageal varices size, cardia/fundal varices and PHG). Data collected after the first ligation were recurrent upper GIT bleeding (description of hematemesis or melena). These data based on anamnesis on patients or family members by telephone, letters, home visits, and medical records. Data on upper GIT bleeding then evaluated in 3 months time and in 1 year time.

### RESULTS

There were 72 cases satisfying the inclusion criteria in the 3<sup>rd</sup> month evaluation period. In one year evaluation period there were only 71 cases because one patient died due to non hemorrhagic cause. The remaining cases then analyzed for recurrent upper GIT bleeding based on clinical and laboratory data prior to ligation. Forty three data on recurrent upper GIT bleeding were obtained from anamnesis on the patients or family members and 29 cases obtained from medical records. Data on risk factors and upper GIT recurrent bleeding then were analyzed using univariate and bivariate models. Analysis of those data then divided into 2 parts.

### Analysis on the data from the 3<sup>rd</sup> months after ligation

#### a. Clinical and endoscopic feature of esophageal variceal ligation

From 72 ligated esophageal varices cases, 14 cases (19.4%) experienced recurrent upper GIT bleeding within 3 months. There were 45 cases (62.5%) of male patients and 27 cases (37.5%) of female patients with mean age 55.5 years old. Child-Pugh classification A and B were 67 cases and Child-Pugh C was 5 cases. Hepatoma patients were 10 people. Endoscopic findings prior to ligation were 4 people with grade one and two esophageal varices, and 68 people with grade 3 and 4. There were 21 people with esophageal varices and RCS, and 4 people with esophageal varices along with cardia/fundal varices. There were 49 people with esophageal varices with portal hypertensive gastropathy (PHG.)

#### b. Risk factors for recurrent upper GIT bleeding from clinical and endoscopy features during 3<sup>rd</sup> month evaluation period.

Bivariate analysis on 3<sup>rd</sup> month group found some variables that act as risk factors for recurrent GIT bleeding had  $p \leq 0.05$ . They were:

- Total bilirubin  $> 2$  mg/dL, increased the risk for having recurrent upper GIT bleeding by 4.7 times compared to total bilirubin of  $\leq 2$  mg/dL [OR = 4.688 and CI = 1.284-17.117]
- The presence of ascites, increased the risk for having recurrent upper GIT bleeding by 4.5 times compared to no ascites [OR = 4.513 and CI = 1.138-17.893]
- The presence of hepatoma, increased the risk for having recurrent upper GIT bleeding by 18 times compared to no hepatoma [OR = 18.33 and CI = 3.835-87.645]
- Child-Pugh C classification, increased the risk for having recurrent upper GIT bleeding by 7.6 times compared to Child-Pugh A and Child Pugh B classification [OR = 7.636 and CI = 1.139-51.117]
- The presence of RCS, increased the risk for having recurrent upper GIT bleeding by 4.6 times compared to no RCS [RR = 4.615 and CI = 1.355-15.716]

The analysis also showed variables that were not act as risk factors for recurrent GIT bleeding ( $P > 0.05$ ), they were age  $\leq 60$  years old, thrombocyte  $< 100,000 \mu\text{L}$ , albumin  $< 3.5$  g/dL, PT  $> 17$  seconds, esophageal varices grade 3 & 4, presence of fundal/cardial varices and PHG degree moderate & severe.

**Table 1. Clinical and Endoscopic Characteristic of Ligated Esophageal Varices Patients During 3<sup>rd</sup> Month Evaluation Period**

Variable	N	Mean	Median	SD	Minimum	Maximum
Age		55.5	58	10.3	28	71
= 60	47					
> 60	25					
Thrombocyte (per $\mu$ L)		120,947	96,500	79,414	31,000	520,000
< 100,000	37					
= 100,000	35					
Total bilirubin (mg/dL)		2.0	1.3	3.0	0.2	24.5
= 2	14					
> 2	58					
Albumin		3.1	3	0.7	1.8	5
< 3.5	56					
= 3.5	16					
Prothrombin (second)		14	13.6	2.3	10	20
> 17	8					
= 17	64					
Ascites						
Positive	37					
Negative	35					
Child-Pugh score						
Child C	5					
Child A and B	67					
Hepatoma						
Positive	10					
Negative	62					
Red color sign						
Positive	21					
Negative	51					
Esophageal varices size						
Grade 3 and 4	68					
Grade 1 and 2	4					
Cardia/fundal varices						
Positive	4					
Negative	68					
PHG						
Moderate/severe	49					
Mild	23					

N = Number of patient; SD = standard deviation

**Table 2. Risk Factors for Recurrent Upper GIT Bleeding during 3<sup>rd</sup> Month Period**

Variable	Recurrent Bleeding		Prevalence (%)	P	OR	95% CI	
	Positive	Negative				Lower	Upper
Age				0.758			
= 60	10	37	21.3		1.419	0.396	5.089
> 60	4	21	16.0		1		
Thrombocyte (per $\mu$ L)				0.191			
< 100,000	5	32	13.5		0.451	0.135	1.513
= 100,000	9	26	25.7		1		
Total bilirubin (mg/dL)				0.014			
= 2	6	8	42.9		4.668	1.284	17.117
> 2	8	50	13.9		1		
Albumin				0.497			
< 3.5	10	46	17.9		0.652	0.174	2.447
= 3.5	4	12	25.0		1		
Prothrombin (second)				0.648			
> 17	2	6	25		1.444	0.259	8.058
= 17	12	52	18.8		1		
Ascites				0.036			
Positive	11	26	29.8		4.513	1.138	17.893
Negative	3	32	8.6		1		
Child-Pugh score				0.047			
Child C	3	2	60.0		7.636	1.139	51.11
Child A and B	11	56	16.4		1		
Hepatoma				0.000			
Positive	7	3	70.0		18.33	3.835	87.645
Negative	7	55	11.3		1		
Red color sign				0.010			
Positive	8	13	38.1		4.615	1.355	15.716
Negative	6	45	11.8		1		
Esophageal varices size				1.000			
Grade 3 and 4	13	55	18.8		0.709	0.068	7.380
Grade 1 and 2	1	3	25.0		1		
Cardia/fundal varices				1.000			
Positive	1	3	25.0		1.410	0.136	14.677
Negative	13	55	18.8		1		
PHG				0.525			
Moderate/severe	11	38	22.5		1.930	0.482	7.722
Mild	3	20	13.0		1		

Note: CI = confidence interval, OR = odds ratio, N = number of patient

### Analysis on the data from 1<sup>st</sup> year after ligation

a. Clinical and endoscopic feature of patients with ligated esophageal varices (see table 3.)

On the first year evaluation, there were 71 ligation cases which met inclusion and exclusion criteria, 28 people (39.4%) experienced first episode of recurrent bleeding during 1 year after ligation. Clinical characteristics of this group were 45 people (63.4%) male and 26 people (36.6%) were female. Mean age was 55.4 years old, Child-Pugh A & B classification were 66 people, Child-Pugh C classification were 5 people. Endoscopic characteristics before esophageal varices ligation were grade 3 and 4 esophageal varices were 68 people and grade 1 and 2 were 3 people.

b. Risk factors for recurrent upper GIT bleeding from clinical and endoscopy features during 1<sup>st</sup> year evaluation period.

There were some variables acting as risk factors for recurrent GIT bleeding with  $P \leq 0.05$  are follow as:

- Age  $\leq 60$  years old increased the risk for bleeding by 2.9 times compared to  $> 60$  years old [OR = 2.903 and CI = 0.981-8.590]
- Hepatoma increased the risk for bleeding by 4.4 times compare to non hepatoma [OR = 4.444 and CI = 1.040-18.985]
- RCS increased the risk for bleeding by 3.8 times compared to no RCS [RR = 3.792 and CI = 1.303-11.037]

**Table 3. Clinical and Endoscopic Characteristic of Ligated Esophageal Varices Patients During 1<sup>st</sup> Year Evaluation Period**

Variable	N = 71	Mean	Median	SD	Minimum	Maximum
Age		55.4	58	10.33	28	71
= 60	46					
> 60	25					
Thrombocyte (per $\mu$ L)		122,157	98,000	79,307	31,000	520,000
< 100,000	36					
= 100,000	35					
Total bilirubin (mg/dL)		2.0	1.3	3.1	0.2	24.5
= 2	14					
> 2	57					
Albumin		3.1	3.0	0.7	1.8	5
< 3.5	55					
= 3.5	16					
Prothrombin (second)		14	13.7	2.2	10.0	20
> 17	8					
= 17	63					
Ascites						
Positive	37					
Negative	34					
Child-Pugh score						
Child C	5					
Child A and B	66					
Hepatoma						
Positive	10					
Negative	61					
Red color sign						
Positive	21					
Negative	50					
Esophageal varices size						
Grade 3 and 4	68					
Grade 1 and 2	3					
Cardia/fundal varices						
Positive	4					
Negative	67					
PHG						
Moderate/severe	48					
Mild	23					

**Table 4. Risk Factors for Recurrent Upper GIT Bleeding during 3<sup>rd</sup> Month Period**

Variable	Recurrent Bleeding (N = 71)		Prevalence (%)	P	OR	95% CI	
	Positive	Negative				Lower	Upper
Age				0.05			
= 60	22	24	47.8		2.903	0.981	8.590
> 60	6	19	24.0		1		
Thrombocyte (per $\mu$ L)				0.561			
< 100,000	13	23	36.1		0.754	0.290	1.957
= 100,000	15	20	42.9		1		
Total bilirubin (mg/dL)				0.367			
= 2	7	7	50		1.714	0.528	5.567
> 2	21	36	36.8		1		
Albumin				0.857			
< 3.5	22	33	40		1.111	0.353	3.498
= 3.5	6	10	37.5		1		
Prothrombin (second)				0.730			
> 17	3	5	37.5		0.912	0.200	4.160
= 17	25	38	39.7		1		
Ascites				0.098			
Positive	18	19	48.7		2.274	0.854	6.056
Negative	10	24	29.4		1		
Child-Pugh score				0.376			
Child C	3	2	60		2.460	0.384	15.756
Child A and B	25	41	37.9		1		
Hepatoma				0.043			
Positive	7	3	70		4.444	1.04	18.985
Negative	21	40	34.4		1		
Red color sign				0.012			
Positive	13	8	61.9		3.792	1.303	11.037
Negative	15	35	30		1		
Esophageal varices size				1.000			
Grade 3 and 4	27	41	39.7		1.317	0.114	15.249
Grade 1 and 2	1	2	33.3		1		
Cardia/fundal varices				0.293			
Positive	3	1	75		5.040	0.497	51.116
Negative	25	42	37.3		1		
PHG				0.971			
Moderate/severe	19	29	39.6		1.019	0.368	2.820
Mild	9	14	39.1		1		

Variables that were not acting as risk factors for upper GIT bleeding ( $P > 0.05$ ) were thrombocyte  $< 100,000/\mu$ L, total bilirubin 2 mg/dL, PT  $> 17$  second, presence of ascites, Child-Pugh C, esophageal varices grade 3 & 4, cardia/fundal varices and mild & moderate PHG

## DISCUSSION

This was a cross sectional study using retrospective data therefore had few limitations such as the presence of interventional therapy, which might interfere with clinical and biochemical manifestations, thus altered the incidence of recurrent GIT bleeding. In order to reduce this bias, the patients were assumed having proportional and equally distributed interventional therapy and upper GIT bleeding data were obtained from anamnesis. Uncontrollable factors yet having significant effects on this study were unidentifiable source of recurrent upper

GIT bleeding, after ligation medications and length of therapy and the presence of esophageal varices obliteration after ligation.

There were 72 cases fulfilling inclusion criteria at 3<sup>rd</sup> month evaluation and 71 cases at 1<sup>st</sup> year evaluation. From those cases, the incidence of recurrent bleeding during 3 months was 19% and during 1 year was 39%. Mean age of the samples was 55 years old, not significantly different from those reported by one meta-analysis which sample's age spread between 46 to 56 years old. This was true for upper GIT recurrent bleeding estimation of 30%.<sup>23</sup>

Risk factors for the first episode of recurrent bleeding were evaluated on the 3<sup>rd</sup> month and 1<sup>st</sup> year time. These evaluation periods were decided in order to evaluate the influence of local factors, or any difference in risk factors for the first episode of recurrent bleeding between evaluation periods. There were other studies

evaluating the recurrent bleeding using period < 6 weeks and > 6 weeks; or on the 1<sup>st</sup> and 2<sup>nd</sup> year. Risk factors that were evaluated include clinical and biochemical features before ligation, such as age, serum albumin level, total bilirubin level, thrombocyte count, prothrombin time, the presence of ascites, Child-Pugh classification, the presence of hepatoma, RCS, measurement of esophageal varices, the presence of cardia/fundal varices, and PHG.

On the 3<sup>rd</sup> month evaluation, age was not a factor for recurrent upper GIT bleeding; on the contrary, on the 1<sup>st</sup> year evaluation age ≤ 60 years old was one of the factors of recurrent upper GIT bleeding. This finding did not correlate with result from other study that showed age > 60 years old as one of the factors for recurrent upper GIT bleeding.<sup>16</sup> A study by Gimson et al., revealed age had no correlation with variceal bleeding.<sup>17</sup> These differences were probably due to variation in post ligation therapy, physical activities, paraesophageal collateral formation that might interfere with portal pressure. All of these circumstances might influence the occurrence of upper GIT bleeding, which warrants further study.

On both 3<sup>rd</sup> month and 1<sup>st</sup> year evaluation period thrombocyte count 100,000/μL was not a risk factor for upper GIT bleeding; this was also shown by other study.<sup>14,15,22</sup> On 3<sup>rd</sup> month and 1<sup>st</sup> year evaluation periods, albumin was not a risk for upper GIT bleeding. This did not correspond to other study's finding which showed albumin < 3 g/dL as one factor for recurrent upper GIT bleeding.<sup>22</sup> This difference might be contributed by the difference in cut of point, and the categorization of albumin in this study into < 3.5 g/dL and ≥ 3.5 g/dL and the elevation of albumin level due to intervention.

In this study prothrombin time > 17 seconds was not a risk factor for recurrent upper GIT bleeding, as other study had shown.<sup>14,15,22</sup> Total bilirubin level is a component of Child-Pugh classification for assessing the severity of liver cirrhosis. Siringo et al., showed bilirubin was an independent predictor for first episode of variceal bleeding.<sup>13</sup> This study showed total bilirubin of > 2 mg/dL as risk factor for recurrent upper GIT bleeding in the 3<sup>rd</sup> month evaluation period, but not for 1<sup>st</sup> year evaluation period. This was probably due to intervention and bilirubin level decreasing over time. On 3<sup>rd</sup> month evaluation time, ascites was found as one of risk factors for recurrent upper GIT bleeding, but not on the 1<sup>st</sup> year evaluation period. The finding was concordant to other studies.<sup>15</sup> On the contrary, Gimson

et al., did not find correlation between ascites and recurrent variceal bleeding.<sup>16</sup> The difference between 3<sup>rd</sup> month and 1<sup>st</sup> year findings most likely due to the estimation of ascites used in this study based only on physical examination and ultrasonography and coded as positive and negative without estimating the severity gradation of ascites. Another possibility was intervention given before upper GIT bleeding. If ligation was going to be done on liver cirrhosis patient with ascites, it was preferred treating the ascites before the procedure, because severe ascites might interfere with ligation procedure. The dispersal of ascites might decrease recurrent bleeding. In emergency, variceal ligation can be done regardless ascites status.

In liver cirrhosis, decreased liver function might correlate with the amount of anatomical anomalies of the liver, which influence progression of portal pressure. However, variceal enlargement does not correlate with progression of portal hypertension.<sup>27</sup> On lower grade cirrhosis, this has correlation with anatomical anomalies of the liver, which in turn, increases the risk for bleeding. AASLD suggest endoscopic screening procedure on liver cirrhosis Child-Pugh classification B & C.<sup>28</sup> On third month evaluation period, Child-Pugh C was one of risk factors for recurrent upper GIT bleeding, but not in 1<sup>st</sup> year evaluation period.

The difference in duration and intervention might create variations in risk factors for bleeding between 3<sup>rd</sup> month and 1<sup>st</sup> year evaluation period; this might have relationship to the reduction of Child-Pugh classification.

According to researches by Lo GH and Olmo et al., Child-Pugh classification might have association to recurrent upper GIT bleeding.<sup>22,29</sup> On the contrary, De la Pena et al., found no association between Child-Pugh classification and recurrent variceal bleeding.<sup>17</sup>

Hepatoma was one of the risk factors for recurrent upper GIT bleeding on 3<sup>rd</sup> month and 1<sup>st</sup> year evaluation period. Portal pressure increased in hepatoma with thrombus inside the portal vein. Liver ultrasonography in our study could not find any portal vein thrombus because was not done by the same person. Another study found hepatoma as risk factors for recurrent variceal bleeding in > 6 weeks but not for < 6 weeks.<sup>15</sup> This difference might be attributed to the stadium, location, size, presence of thrombus inside the portal vein and the shape, and therapy given. Our study did not evaluate these terms, thus in order to evaluate the influence of hepatoma on the recurrence of the upper GIT bleeding warrants further study. To estimate the benefit of ligation on hepatoma patients also needs further study.



The presence of RCS has correlation to the incidence of variceal bleeding.<sup>11,12</sup> In this study, bivariate analysis on 3<sup>rd</sup> month and 1<sup>st</sup> year evaluation period indicate RCS as one of risk factors for recurrent upper GIT bleeding. RCS marks a thinning on variceal wall due to increasing pressure inside. Increasing intra variceal pressure will strain the variceal wall, making it thinner, and easier to bleed. Other study also concur that RCS on esophageal varices was a risk factor for recurrent variceal bleeding.<sup>15</sup>

Several studies demonstrated the size of the varices was a risk factor for recurrent upper GIT bleeding.<sup>14,15,22</sup> However, this study did not reflect those findings. This difference occurred probably due to insufficient cases of low-grade esophageal varices studied (4 of 72). Thus, there should be a case-control study to measure the importance of variceal size on variceal bleeding.

Gastric varices contributed 5% to 10% from all variceal bleeding.<sup>30</sup> This kind of varices was usually more severe compared to esophageal varices.<sup>31</sup> The presence of cardia/fundal varices was an initial prognostic factor for of variceal bleeding.<sup>32</sup> However, in this study cardia/fundal varices did not become one of risk factors for recurrent upper GIT bleeding. This was probably due to insufficient cases of cardia/fundal varices (4 of 72). This also warrants further case-control study. Other study found the prevalence of PHG was between 4% to 98%.<sup>33</sup> Bleeding from PHG was even rare, between 2 to 3%.<sup>30,34</sup> Gastropathy congestive index was a prognostic factor for the first episode of upper GIT bleeding.<sup>32</sup> In this study, PHG was not a risk factor for recurrent upper GIT bleeding which also shown by other studies.<sup>14,15,22</sup>

The overall conclusions from this study were risk factors for recurrent upper GIT bleeding in 3<sup>rd</sup> month evaluation period were ascites, total serum bilirubin > 2 mg/dL, hepatoma, Child-Pugh C classification and RCS. Risk factors that did not have any correlation in 3<sup>rd</sup> month recurrent upper GIT bleeding were age, thrombocyte count, albumin level, PT, esophageal varices size, fundal/cardia varices and PHG. Risk factors for 1<sup>st</sup> year evaluation period of recurrent upper GIT bleeding were age ≤ 60 years old, hepatoma and RCS. Risk factors that did not have any correlation were thrombocyte count, albumin level, PT, total bilirubin, the presence of ascites, Child-Pugh classification, esophageal varices size, cardia/fundal varices and PHG.

The difference in risk factors for recurrent bleeding between the 3<sup>rd</sup> month and 1<sup>st</sup> year evaluation period were probably due to intervention and alteration of risk factors over time. Other factors that might interfere

before recurrent upper GIT bleeding were para-esophageal collateral, drugs that irritate GIT, alteration in physical activity, and obliteration rate of the varices related to ligation therapy. This study did not evaluate those factors, thus warrants further study.

By knowing the risk factors for recurrent upper GIT bleeding on esophageal varices ligation, we could obtain additional information to predict the risk for recurrent bleeding after a ligation procedure. Therefore, by improving or eliminating those risk factors before ligation procedure will reduce the risk for recurrent bleeding after the procedure. Ascites, total serum bilirubin, Child-Pugh classification and RCS are the risk factors that can be improved by diuretics, hepato-protector, and portal pressure lowering drugs (such as propranolol and isosorbide mononitrate).

## CONCLUSION

Risk factors for recurrent bleeding after preliminary ligation of esophageal varices are age ≤ 60 years old, ascites, total serum bilirubin > 2 g/dL, hepatoma, Child-Pugh C and RCS. Further, those factors can be divided into 2 groups, which are:

- Within 3<sup>rd</sup> month evaluation period are total bilirubin > 2 mg/dL have 4.7 times the risk compare to < 2 mg/dL, the presence of ascites have 4.5 times the risk compare to no ascites, the presence of hepatoma have 18 times the risk compare to no hepatoma, Child-Pugh C have 7.6 times the risk compare to Child-Pugh A and B and RCS on varices have 4.6 times the risk compare to no RCS.
- Within 1<sup>st</sup> year evaluation period are age ≤ 60 years old have 2.9 times the risk compare to age > 60 years of age, the presence of hepatoma have 4.4 times the risk compare to no hepatoma and red color sign have 3.8 times the risk compare to no RCS.

## SUGGESTION

Risk for recurrent bleeding could be decreased by improving or eliminating ascites, total bilirubin level, Child-Pugh classification and RCS by means of ascites paracenteses, diuretics, hepato-protectors and portal pressure lowering drugs. Child Pugh B and Child Pugh C needs to have endoscopic procedure and evaluation of risk factors over time. This study should be followed by another study with longer evaluation period and more valid measurement.

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