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Original article

MORTALITY AND RISK FACTORS AFTER ENDOSCOPIC VARICEAL BAND LIGATION

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Abstract

Background Bleeding from esophageal varices is the major complication of portal hypertension and is associated with a high mortality rate. Despite advances in the management, the mortality rate remains at 30%-80%. Endoscopic variceal band ligation (EVL) is a new technique designed to manage esophageal varices and become the optimal first-line treatment for acutely bleeding varices. Variceal rebleeding, which occurs in 6%-36% of patients, is common during the treatment period before variceal obliteration is achieved, and mortality from esophageal variceal hemorrhage increases with Child-Pugh's classification.

Methods Thirty-one patients with a history of esophageal variceal bleeding, who were endoscopically confirmed between Feb 1999 and Feb 2001, received regular EVL until variceal disappearance was reviewed retrospectively.

Results Variceal bleeding was controlled in 96.8% with the remaining 3.2% dying because of massive hemorrhage. There was no major complication. The rebleeding rate was 23.33%. In portal hypertensive-sources of rebleeding, gastric varices and portal hypertensive gastropathy were the most common. Ten fatalities occurred during this study (32.2%). Deaths caused by rebleeding accounted for 50% of cases, whereas, 10% were from failure to control hemorrhage, 10% from hepatoma, 10% from heart failure and 90%-20% from renal failure. Age, sex and other measures such as hematocrit, platelet count, prothrombin time, serum albumin, SGOT, SGPT, alkaline phosphates, serum bilirubin and Child-Pugh's score were not found to be closely related to patients survival ($p > 0.05$). Mortality was significantly high in the rebleeding group ($p = 0.006$) and exsanguination was the major cause of death.

Conclusion Failure to control early rebleeding of varices in an important determinant of mortality. We sugest that long-term follow-up is required. **Chiang Mai Med Bull 2003; 42(2):61-67.**

Key words : variceal bleeding, endoscopic ligation, mortality, risk factor

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Liver cirrhosis is the result of repeated longterm hepatocellular injuries. Alcoholism and viral hepatitis B and C are the most common causes. The liver tissue becomes damaged and is replace with fibrosis. This causes obstruction of the blood flow from abdominal organs to the liver and portal hypertension. The venous return from the abdominal cavity bypasses through portosystemic collaterals. This pathological change causes development of esophageal varices, hypersplenism, ascites and encephalopathy.

While esophageal varices increase in size, they may rupture and cause massive hemorrhage and contribute to death. The incidence of bleeding is reported at 25% within two years after diagnosis.[1] Rebleeding occurs in 90% of patients who bleed spontaneously and do not receive treatment within two years. The mortality rate of bleeding episode is 30%-50%.[2] Formerly, the treatment for bleeding esophageal varices was balloon tamponade and vasoconstrictive agents. This regimen could control bleeding temporarily. Direct injection of sclerosing agent via an endoscope (Endoscopic injection sclerotherapy – EIS was another technique. This procedure could control bleeding esophageal varices immediately and the injection could be repeated severals times in a certain period of time. This technique became widely accepted as the standard treatment of choice. The success rate was over 85%, but severe complication such as stricture or perforation of the esophagus might occur. Furthemore, rebleeding in the first year was as hight as 50%.[3]

Endoscopic variceal band ligation (EVL) was developed in 1950. This procedure was adopted in 1986 when Stiegmann *et al*.[4-6] reported the effectiveness of controlling hemorrhage with few complications. However, rebleeding still occurred in 6% to 36% of cases[7] The factors that contribute to death were related to the severities of liver pathology according to Child-Pugh's classification.[8] This was the grading system calculated from the level of ascites, encephalopathy, serum albumin, serum bilirubin and prolonged prothrombin time. The total scores of 5-6, 7-9 and 10-15 represent class A, B and C, respectively.

The patients in Sawanpracharak Hospital, with bleeding esophageal varices for over two years from Feb 1999 until now, were treated by endoscopic variceal band ligation. Rebleeding and death were common problems. The mortality rate and associated risk factors were unknown and could be the same as in previous reports. Other risk factors may be important such as platelet count and prothrombin time, which are involved in the clotting mechanism and directly related to liver function. We found no such in reviews of literature report. Therefore, we designed this study to identify the mortality rate after treatment and the risk factors that contribute to death.

Methods

Cirrhotic patients, admitted to Sawanpracharak Hospital with hematemesis and received variceal rubber band ligation from Feb 25, 1999 to Feb 25, 2001 were reviewed retrospectively. Medical records and endoscopic findings were collected. Endoscopy was performed in every patients for confirmation of diagnosis. One of the following four findings was the criterion for diagnosis :

active bleeding from varices, varices that were larger than one third of the diameter of the esophageal lumen, evidence of previous bleeding (Red color signs), and no other evidence of a bleeding site. All patients received variceal band ligations every two weeks until bleeding was completely eradicated. Interval endoscopy every 3-6 months was carried out as a follow up.

The data of all patients were fixed in on the record forms that consisted of 3 parts. The first part comprised the demographic and personal data such as gender, age, associated diseases and drinking habit. The second one consisted of physical examination and laboratory reports such as ascites, encephalopathy, platelet count, prothrombin time and liver function test. The last part comprised endoscopic findings such as the site of bleeding, size of esophageal and gastric varices, and portal hypertensive gastropathy.

Thirty-one records were analyzed using SPSS for Windows software. Frequency, percentage and mean of the survivors and those patients who died were calculated. The correlation of death and associated factors were analyzed by the Chi-square test and Studen's t-test. Stastistical significance was considered if the p value was below 0.05.

Results

During the period of this study, thirty-one cirrhotic patients with hemorrhage was treated by endoscopic variceal band ligation. Most of the patients were male (25 cases or 80.6%) with ± mean age of 49 years and 10 months 11 years and 5 months (range 31-80 years). More than a half (54.8%) was in the age group of 41 to 60 years (Table 1). The patients were habitual drinkers in 74.2%. Positive viral hepatitis B and C antigens were fond at 19.4% and 12.9%, respectively. Associated diseased were detected in 9.7% with Diabetes Mellitus, 3.2% with hyptertension and 3.2% with hepatoma. The patients were classified as Child-Pugh's A, B and C at 6.45%, 61.29% and 32.26%, respectively. The period of follow up varied between 12 days and 1 year and 8 months and 21 days, with a mean period of 7 months and 22 days ± 5 months and 19 days. Failure rate of hemorrhage control was 32% (1 case). Opera tions were performed in 6.45% of cases for large gastric varices and severe portal hypertensive gastropathy. The rate of complete eradication was 26.67% (8 cases). The recurrent rate was 6.5%. Severe compli-cations were not found. The rebleeding rate was 23.33% (7 cases), and in 28.57% of them (2 cases) the hemorrhage ceased sponta- neously before admission to the hospital. The remaining 71.43% (5 cases) all died from massive hemorrhage. Portal hypertensive gastropathy was found at 42.86% of rebleeding, 14.28% had gastric varices and 42.86% did not undergo endoscopic examination (Table 2).

The mortality rate was 32.3%. The deaths were classified as Child-Pugh's B and C at 60% and 40%, respectively. The causes of death were failure of the rubber band ligation

Table 1. Age distribution of cirrhotic patients with bleeding esophageal varices.

Age	Male	Female	Numbers (%)
21-40	6	-	6 (19.35)
41-60	15	2	17 (54.84)
61-80	4	4	8 (25.81)
Total	25	6	31 (100)

Table 2. Sites of rebleeding after endoscopic variceal band ligation.

Sites of rebleeding	Number (%)
Portal hypertensive-related bleeding :	
Portal hypertensive gastropathy	3 (42.86)
Gastric varices	1 (14.28)
No data	3 (42.86)
Total	7 (100)

Table 3. Causes of death

Causes of deaths	Number (%)
Massive hemorrhage:	
Failue to control hemorrhage	1 (10)
Rebleeding	5 (50)
Heart failure	1 (10)
Acute renal failure	2 (20)
End state hepatoma	1 (10)
Total	10 (100)

in 10%, rebleeding in 50% and others causes in 40%, i.e. 10% from heart failure, 20% from acute renal failure and 10% from end stage hepatoma (Table 3).

Statistical analysis with a t-test at the p value of < 0.05 was used to identify any difference between the mean values of hematocrit, platelet count, prothrombin time, serum albumin, SGOT, SGPT, alkaline phosphatase and serum bilurubin among the deaths and survivors. We found no statistically significant difference (Table 4).

In the statistical analysis, with a Chi-square test at the $p < 0.05$, we found no correlation between Child-Pugh's score and mortality rate ($p = 0.54$). The rebleeding group had a mortality rate of 71.43% compared to 17.39% in the no rebleeding group ($p = 0.006$).

Discussion

Male to female ratio of 31 patients was 4:1. This may be due to more common drinking habits in males. Three quarters of these patients were habitual drinkers and males drank about 5 times more than females. More than half of the patients were 41-60 years old. The failure rate of endoscopic variceal band ligation was only 3.2%. The complete eradifcation of varices was achieved in only one forth of cases, due to the in experience of endoscopists at the beginning of this study. Ligations of the small vessels are limited to EVL. Some reports accepted small varices that were resistant to ligation as eradication. Therefore, the eradication rate increased to more than two third.[2] The recurrent rate of varices rate of varices was 6.5% and this may be due to the short period of foloow up.

The rebleeding rate was 23.33%. At least 50% were portal hypertensive-related bleeding, and classfied as 14.28% of gastric varices and 42.86% of hypertensive gastropathy sites. These figures were similar to other reports in which the rates of rebleeding were 6-36%.[7] The difference was, other reports found that 41.67% were posttreatment esophageal ulcer bleeding.[9] There were two postulations, the first was that the former endoscope had an overtube and could apply only one rubber band at a time. If we need repeated ligations, the ednoscope must be reinserted and this causes trauma to the esophagus. New models of endoscopes allow multiband ligation at the same time and no overtube is necessary. The second postulation came from the result of variceal ligation obstructing the blood flow from the abdominal cavity to the heart and causing in-

creasing portal pressure. Massive blood loss was the major cause of death (60%), in this report, while other reports found that hepatic failure was a major cause of death (93%).[9] The difference may be due to the short period of follow up in this study. If we follow up the patients for a longer period of time, the major cause of death should be due to the severity of liver pathology.

We found no correlation of sex, age, hematocrit, platelet count, prothrombin time, serum albumin, SGOT, SGPT, alkaline phosphatase, serum bilirubin and Child-Pugh's Classification (Table 4 and 5). The patients with rebleeding had a higher mortality rate compared to the no rebleeding group, which was significant ($p < 0.05$). If we can reduce the rate of rebleeding, the mortality rate may decrease. Especially during the first two years after onset.

In conclusion, rebleeding was the main problem of variceal rubber band ligation. It was also the major cause of death. Long-term follow up should be carried out for a further one or two years. Finally, new cases should be added to this study to provide a larger sample size.

Table 4. Risk factors related to mortality.

Risk factors	Deaths	Survivors	*p* value
Gender :			
Male	9	16	0.363
Female	1	5	
Average age (year)	47.40±7.57	51.00±12.89	0.422
Child-Pugh s :			
A	0	2	0.540
B	6	13	
C	4	6	
Rebleeding :			
Yes	5	2	0.006*
No	4	19	

* statisticaly significant ($p < 0.05$)

Table 5. Hematological and biochemical values of cirrhotic patients before treatment between deaths and survivors

Parameters	Deaths	Survivors	*p* value	95% Cl
Hematocrit (%)	24.50±4.00	24.24±9.74	0.927	-6.31, 6.91
Platelet (K / μL)	140.21±127.88	89.95±63.70	0.318	-58.09, 158.62
Prothrombin time (sec)	36.63±30.31	24.13±7.35	0.361	-19.25, 44.26
Serum albumin (gm/dL)	2.68±0.53	2.37±0.73	0.265	-0.25, 0.86
SGOT (U/L)	83.89±63.27	103.30±139.88	0.696	-120.13, 81.31
SGPT (U/L)	179.44±345.32	61.30±61.18	0.337	-148.04, 384.33
Alkaline phosphatase (U/L)	122.78±66.35	122.0±82.07	0.980	-59.31, 60.93
Serum bilirubin (mg/dL)	5.91±5.77	2.25±1.85	0.097	-0.18, 8.13

Average number ± standard deviation

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อัตราการเสียชีวิตและปัจจัยที่เกี่ยวข้องภายหลังการใช้ยางรัดหลอดเลือดดำโป่งพองในหลอดอาหาร

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บทคัดย่อ

วัตถุประสงค์ เพื่อหาอัตราการเสียชีวิตหลังการรัดยางและหาปัจจัยที่เกี่ยวข้องกับการเสียชีวิตในผู้ป่วยโรคตับแข็งที่มารักษาด้วยเรื่องเลือดออกจากหลอดเลือดดำโป่งพองแตกในหลอดอาหาร

วิธีการ ทำการศึกษาโดยการคัดลอกข้อมูลผู้ป่วยโรคตับแข็งที่มีเลือดออกจากหลอดเลือดดำ ปั่งพองแตกในหลอดอาหาร และได้รับการรักษาด้วยการใช้ยางรัดในโรงพยาบาลสวรรค์ประชารักษ์ตั้งแต่วันที่ 25 กุมภาพันธ์ พ.ศ. 2542 ถึง 25 กุมภาพันธ์ พ.ศ. 2544 ทำการวิเคราะห์ข้อมูลด้วยโปรแกรมสำเร็จรูป SPSS for Windows หาค่าร้อยละ ค่าเฉลี่ย และวิเคราะห์หาค่าความสัมพันธ์ทางสถิติด้วยวิธี Chi-square and Student's t-test กำหนดค่าความเชื่อมั่นไม่น้อยกว่าร้อยละ 95

ผลการศึกษา มีผู้ป่วยจำนวน 31 ราย ที่ได้รับการรัดยางเนื่องจากหลอดเลือดดำโป่งพองแตกในหลอดอาหาร อัตราการเสียชีวิตร้อยละ 32.2 ไม่พบความแตกต่างกันทางสถิติระหว่างเพศ อายุ ค่า Hct, platelet, prothrombin time, serum albumin, SGOT, SGPT, alkaline phosphatase, serum bilirubin และ Child Pugh's score กับอัตราการเสียชีวิตหลังการให้การรักษา ($p > 0.05$) แต่พบว่าภาวะเลือดออกซ้ำมีความ เกี่ยวข้องกับอัตราการเสียชีวิตอย่างมีนัยสำคัญ ($p = 0.006$)

สรุป จากการศึกษาพบว่า เลือดออกซ้ำหลังการรัดยางมีส่วนเกี่ยวข้องกับอัตราการเสียชีวิต ดังนั้นในการรักษาผู้ป่วยกลุ่มดังกล่าวถ้าสามารถลดอัตราการเกิดเลือดออกซ้ำได้ น่าจะทำให้อัตราการเสียชีวิตลดลงด้วย **เชียงใหม่เวชสาร 2546;42(2):61-67.**

คำสำคัญ : อัตราการเสียชีวิต หลอดเลือดดำโป่งพอง หลอดอาหาร