Original Article

Risk Factors for Early Re-bleed following Endoscopic Variceal Band Ligation and Assessing Utility of Dedicated Score (BICAP Score) to Identify High Risk Groups

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Background : Endoscopic Variceal Band Ligation (EVBL) is a universally accepted and approved treatment for bleeding esophageal varices. Re-bleed is the most common complication following EVBL. Ours is a prospective study analyzing risk factors for Early Re-bleed (ERB) and for creating a laboratory based BICAP score (Bilirubin, INR, Creatinine, Albumin, Platelet) for detecting high-risk groups for re-bleed.

Materials and Methods : The study period was between March, 2021 to March, 2022 when 111 patients underwent EVBL in our department. Patients were followed by telephone or direct visits weekly for 6 weeks. ERB was defined by active variceal hemorrhage presenting as hematemesis in a patient following EVBL within 6 weeks. Endoscopy was done for all patients after re-bleed to confirm.

Results : Among 111 patients, 26 patients developed ERB with an incidence of 23.4%. ERB was higher in emergency EVBL than elective (29.3% *versus* 6.9%, p=0.014). Platelet count of < 50,000 and INR > 2.0 were associated with high ERB risk (52.4%, p>0.002) and (60%, p = 0.001). Overt encephalopathy was associated with 42.3% risk of ERB (p = 0.009). Usage of high number of bands (>6) were associated with increased risk of ERB (56.3%, p>0.001). Child Pugh C patients had high risk of ERB (37.5%, p = 0.001). BICAP score >7 was associated with increased risk of ERB (80%, p = 0.002).

Conclusion : Child-Pugh score and BICAP score both can predict high risk groups for ERB, but BICAP score is a dedicated score and can be used even in non-cirrhotic patients. BICAP score is found to have high sensitivity in detecting patients with high risk for early Re-bleed.

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Key words **: Endoscopic Variceal Band Ligation, Early Re-bleed, BICAP Score, Child-Pugh Score.**

Variceal bleeding especially from esophageal varices is the most devastating complication of portal hypertension and is always a medical emergency. This complication is associated with a mortality rate of 24%[1] and leads to further complications such as ascites, spontaneous bacterial peritonitis, hepatic encephalopathy and hepatorenal syndrome. Following stabilisation upper GI Endoscopy is mandated early to assess and take action to prevent further bleeding. Endoscopic Variceal Band Ligation (EVBL) is the most accepted and used technique to ligate the large esophageal varices which are the most common cause of variceal bleed[2].

Re-bleed is one of the life-threatening complications of EVBL and can lead to significant morbidity and mortality. Many studies have identified causes for the high risk of re-bleed. Re-bleed can be classified into very early re-bleed which occurs within 5 days, Early Re-bleed (ERB) which occurs between 7th day and 6 weeks and late re-bleed, which occurs beyond 6 weeks[3].

Editor's Comment :

- BICAP score is useful in predicting high risk groups with increased risk for early re-bleed.
- A larger study is needed to validate its utility, especially for comparison with other indices like MELD score.

Our study focuses on ERB and the factors affecting it in our patients. We included both cirrhotic and non-cirrhotic causes of portal hypertension and subsequently variceal bleed or high-risk esophageal varices. In our study, we also used Child- Pugh score, MELD score and our own newly created BICAP score and assessed their utility in identifying high risk patients for ERB.

Materials and Methods

Study Design :

This was a case-control study that took place in our Department of Medical Gastroenterology and

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hepatology, Tirunelveli Medical College, Tirunelveli from March, 2021 to March, 2022. The Tirunelveli Medical College Scientific and Advisory Committee and Institutional Ethics Committee approved the study.

Study Participation :

111 patients who underwent EVBL were included in the study. Cases were patients who had early re-bleed and controls were patients without re-bleed. Inclusion criteria were patients between age group 18 to 70 years, who underwent emergency or elective EVBL. Patients with common etiologies of portal hypertension including ethanol, chronic viral hepatitis, NAFLD, EHPVO and PSVD (pre-hepatic) were included in the study. Exclusion criteria were Pregnant and lactating mothers, patients with other causes of upper GI bleeding like gastric or duodenal ulcers, gastric varices and patients with upper GI malignancies.

All patients gave informed consent and our Institute's Ethics Committee approved the study.

Study Intervention :

All the criteria fulfilled patients had blood work done including Complete Blood Counts, liver and renal biochemistry, viral screening tests for Hepatitis B,C and ultrasound abdomen during their course in the hospital. During EVBL the grading of the varices (Japanese classification) as well as number of bands applied were noted. The patients were kept on follow-up for 6 weeks either by hospital visits or through telephone for history of any re-bleed. Patients with re-bleed underwent urgent endoscopy.

Outcome Measures :

The primary objective was identification of all the risk factors for ERB. The secondary objective was using the Child – Pugh score, MELD score and BICAP score as means to detect patients with high risk of ERB.

Statistical Analysis :

Data were analysed with SPSS version 24. Quantitative variables were expressed as median and interquartile range and qualitative variables as frequency and percentage. The association of categorical variables was analysed by Chi-square test. A p-value of <0.05 was considered statistically significant.

Results

Among 111 patients who underwent EVBL, 26 patients developed early Re-bleed with an incidence rate of 23.4%. Early Re-bleed was highest in age less than 40-year-old (40%) probably because of increased re-bleed in pre-hepatic cases which are mostly young age population. Low Platelet Count <50,000 and elevated PT-INR >2.0 were associated with 52.4% and 60% cases of ERB (p = 0.002 and 0.001 respectively). 29.3% patients in emergency EVL had re-bleed compared to only 6.9% with elective EVL (p = 0.014). 43.2% of patients with overt encephalopathy had ERB compared to 17.6% in covert group (p = 0.009). In patients who had more than 6 bands applied, 56.3% of them developed an ERB (p = 0.001).

MELD score of more than 20 had higher ERB, but it was not found to be statistically significant. Child–Pugh score C category patients had 37.5% of them developing an ERB and this was found to be statistically significant. BICAP score was calculated for all patients and categorized into 3 groups ≤3 (low), 4-6 (mid) and 7-10 (high). 80% of patients with high BICAP score (7-10) had ERB while only 14.9% in low BICAP score (≤3) group (p = 0.002) (Tables 1-4).

Discussion

The study had higher than expected incidence of Early Re-bleed (ERB) cases (23.4%). The previous studies with early Re-bleed incidence was between 4.8% and 20.54%[4-6]. We believe the high re-bleed cases is due to higher number of emergency cases in the study. Many of these cases had elevated bilirubin or low platelets or high PT-INR which put them at increased risk of an ERB.

Majority of patients with early re-bleed were young patients in our study and this finding was also found by Grothaus, *et al*[7] in his study. The reason for this finding in our study is probably because of a greater number of young patients especially with pre-hepatic portal hypertension and alcoholics with severe alcoholic hepatitis both are high risks for early Re-bleed. Our study did not find a correlation between early Re-bleed among men and women and this finding was also published by Xu, *et al*[8] showing gender did not have a significant outcome in early re-bleed. Emergency EVBL was associated with more risk of Re-bleed in our study compared to elective cases and this observation was also noted by Petrasch, *et al*[9]. Very low platelet count was associated with higher risk of re-bleed in our study and this finding was mentioned by MS Faisal, *et al*[10].

Table 1 — *BICAP Score*

	0	1	2
Bilirubin	<3mg/dl	3-5mg/dl	>5mg/dl
INR	<1.5	1.5- 2.0	>2.0
Creatinine	<1mg/dl	1-1.5 mg/dl	>1.5mg/dl
Albumin	>3.5g/dl	2.8 – 3.5 g/dl	< 2.8g/dl
Platelet count	>1.5 L	50,000 to 1.5L	<50,000
	Max score is 10		

Table 2 — *Patient baseline Characteristics*

	Total (n=111)	Re-bleed (n=26)	No Re-bleed (n=85)
Age - median (IQR)	49(42-58)	45(35-51)	50(43-61)
Sex - female- n(%)	29(26.1)	6(23.1)	23(27.1)
Platelet count (10^3) -median (IQR)	98(56-149)	60(31.75-98)	107(77.5-163.5)
Bilirubin - median (IQR)	1.2(0.8-3.8)	2.35(1.25-5.95)	1(0.75-3.15)
Albumin - median (IQR)	3.2(3-3.8)	3.05(2.5-3.8)	3.3(3-4)
Creatinine - median (IQR)	0.8(0.7-1.1)	0.85(0.675-1.125)	0.8(0.7-1.1)
INR - median (IQR)	1.3(1.1-1.67)	1.77(1.1675-1.9075)	1.28(1.1-1.54)
MELD score - median (IQR)	11(9-19)	17(9.75-23.25)	11(8-17)
Child Pugh score - median (IQR)	8(6-9)	9(6-10.25)	7(6-9)
BICAP score - median (IQR)	3(2-5)	4(3 - 6)	3(2-4)
UGI bleed - n(%)	82(73.9)	24(92.3)	58(68.2)
Ascites - n(%)	51(45.9)	16(61.5)	35(41.2)
Hepatic encephalopathy Grade>2 - n(%)	19(17.1)	11(42.3)	8(9.4)
Grade of varices>2 - n(%)	88(79.3)	22(84.6)	66(77.6)
Red signs+ - n(%)	80(72.1)	19(73.1)	61(71.8)
Number of bands >4 - n(%)	59(53.1)	12(46.1)	47(55.3)

Table 3 — *Etiology Statistical Analysis*

		Early Re-bleed (ERB) N-26	No-Re-bleed N-85	P-value
Age : years	<40	8(40%)	12(60%)	
	40-60	17(25%)	51(75%)	0.020
	>60	1 (4.3%)	22 (95.7%)	
Sex :	Male	20(24.1%)	63(75.9%)	
	Female	6(21.4)	22(78.6%)	0.773
Etiology :	Alcohol	8(16%)	42(84%)	
	NAFLD	3(10%)	42(90%)	
	Pre-hepatic	10(47.6%)	11(52.4%)	0.002
	Others	5(50%)	5(50%)	
EVBL:	Emergency	24(29.3%)	58(70.7%)	
	Elective	2(6.9%)	27(93.7%)	0.014
Blood transfusion	Restrictive	14(28%)	36(72%)	
	Liberal	10(29.4%)	26(70.6%)	0.888
Platelet count:/mm^3	<50,000	11(52.4%)	10(47.6%)	
	50,000 to 1.5 L	12(18.4%)	54(81.8%)	0.002
	>1.5L	3(12.5%)	21(87.5%)	
Bilirubin mg/dl	<3	15(19.5%)	62(80.5%)	
	3-5	4(28.6%)	10(71.4%)	0.306
	>5	7(35%)	13(65%)	
Albumin g/dl	<2.8	8(34.8%)	15(65.2%)	
	2.8-3.5	9(18.4%)	40(81.6%)	0.308
	>3.5	9(23.15%)	30(76.9%)	
INR	<1.5	8(11.8%)	60(88.1%)	
	1.5-2.0	15(39.5%)	23(60.5%)	0.001
	>2.0	3(60%)	29(40%)	
Creatinine mg/dl	<1.0	16(22.2%)	56(77.8%)	
	1.0-1.5	6(20.7%)	23(79.3%)	0.425
	>1.5	4(40%)	6(60%)	
Ascites	Present	17(15.5%)	35(84.5%)	
	Absent	9(23.6%)	49(76.4%)	0.034
Hepatic Encephalo-pathy	Present	11(42.3%)	15(57.7%)	
	Absent	15(17.6%)	70(82.4%)	0.009
Grade of varices	Grade 2	1(7.1%)	13(92.9%)	
	Grade 3	25(25.8%)	72(74.2%)	0.124
Number of bands	≤3	0(0%)	17(100%)	
	4-6	17(21.8%)	61(78.2%)	0.001
	>6	9(56.3%)	7(43.8%)	

In study by Mostafa and Mohammad, SBP and ascites was associated with high risk of re-bleed but in our study, due to reasons not clear re-bleed was more in patients without ascites. In our study we made a comparison between increased risk of re-bleed among patients who received restricted transfusion and who received liberal transfusion. Our observations are that there is no statistically significant difference between risk of re-bleed in restrictive and liberal transfusion groups. Current recommendations are however for restrictive blood transfusion targeting a hemoglobin of 7-8 g/dl which in turn prevents wastage and decreases chance of recurrent bleed. Renal insufficiency is an independent risk factor for early Re-bleed and in our study in those with creatinine more than 1.5, Re-bleed was higher although it did not show statistical significance. In our study overt hepatic encephalopathy (West haven 2 and above) patients had higher risk of rebleed (43%).

In our study there was an observation that re-bleed was higher in patients who had received a greater number of EVL bands probably because of increased risk of band ulcers this observation was also explained by Petrasch, *et al*[9]. Comparing MELD score to risk of re-bleed, previous study Bambha, *et al*[11] suggested that rebleed is higher in MELD more than 18 and in our study, re-bleed was higher in MELD more than 15. In previous study by Wipassakornwarawuth, *et al*[12] Child Pugh class C was associated with increased ERB and this was seen in our study where the re-bleed was highest in Child C patients. The BICAP score which is laboratory value-based score of Bilirubin, INR,

Table 4 — *MELD, Child-Pugh class, BICAP score data analysis*

		Early Re-bleed (ERB) N-26	No-Re-bleed N-85	P-value
MELD	<10	6(14.6%)	35(85.4%)	
	10-15	6(20.7%)	23(79.3%)	0.105
	>15	14(34.1%)	27(65.9%)	
Child-Pugh Class	Class A	0(0%)	28(100%)	
	Class B	4(14.3%)	24(85.7%)	0.001
	Class C	12(37.5%)	20(62.5%)	
BICAP Score	≤3 (Low)	10(14.9%)	57(85.1%)	
	4-6 (Mid)	12(30.8%)	27(69.2%)	0.002
	7-10 (High)	4(80%)	1(20%)	

creatinine, albumin and platelet count was found to be as good as Child Pugh score in predicting patients with ERB risk. In an inpatient study of mortality in post variceal bleed patients Krige, *et al*[13] observed that both MELD and Child-Pugh scores were poor measurements of mortality and recommended modified scores for better prediction of mortality[13]. The incidence of ERB was more in patients with high BICAP score. There needs to be more recruitment of patients with high BICAP score for assessing the utility of the score further.

BICAP score in our study was calculated using the laboratory values at the time of presentation, so when it is used as a predictor of ERB, it actually does not take into account the fact an EVBL procedure was done. Also, endoscopic findings and number of bands applied were not included in the score. So, there is a scope for extended BICAP score with endoscopic findings like grade of varices, length of the varices and number of bands applied. Having a dedicated score like BICAP score for identifying individuals with a high risk of re-bleed has the advantage that it can be used across all etiologies of a variceal bleed. BICAP score will be needed to be studied extensively for its applicability in very early Re-bleed, early Re-bleed as well as delayed onset Re-bleed. It is a simple score and easy to use and reproduce. We believe that the BICAP score could be used as a tool of predicting or identifying high-risk patients for early re-bleed.

Conflict of Interest : The authors declared there was no conflict of interest

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