

Adjusted Blood Requirement Index as Indicator of Failure to Control Acute Variceal Bleeding

Marko Duvnjak, Neven Baršić, Vedran Tomašić, Lucija Virović Jukić, Ivan Lerotić, Tajana Pavić

Department of Internal Medicine,
Division of Gastroenterology and
Hepatology, Sisters of Mercy
University Hospital, Zagreb, Croatia

> **Correspondence to:**

Marko Duvnjak
Department of Medicine
Division of Gastroenterology and
Hepatology
Sestre milosrdnice University
Hospital
Vinogradska cesta 29
10000 Zagreb
Croatia
marko.duvnjak@zg.t-com.hr

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Aim To estimate the clinical value of adjusted blood requirement index (ABRI) in relation to other criteria for failure of variceal bleeding control proposed at Baveno consensus workshops and to evaluate ABRI as an early predictor of occurrence of other Baveno criteria and identification of possible predictors of unfavorable ABRI.

Methods We retrospectively analyzed the data on 60 patients admitted to the hospital due to acute variceal bleeding. Number of treatment failures according to Baveno II-III and Baveno IV definitions and criteria was compared. We tested the ABRI's predictability of other Baveno IV and Baveno II-III criteria. Logistic regression analysis was performed to ascertain independent variables that predict $ABRI \geq 0.75$.

Results Failure to control variceal bleeding occurred in 40 of 60 patients according to Baveno II-III criteria, and in 35 of 60 patients according to Baveno IV criteria. Excluding the criterion of "transfusion of 2 units of blood or more (over and above the previous transfusions)" and ABRI criterion, failure to control variceal bleeding was observed in 17 and 14 of 60 patients, respectively. Congruence of ABRI with other criteria was present in about two-thirds of the cases. $ABRI \geq 0.75$ was associated with increased risk of positive other Baveno criteria, particularly modified Baveno II-III (odds ratio [OR] 4.10; 95% confidence interval [CI], 1.11-15.05) and Baveno IV without ABRI (OR 4.37; 95% CI, 1.04-18.28). Independent predictors of $ABRI \geq 0.75$ identified in logistic regression analysis were male sex ($P < 0.001$) and higher hematocrit values ($P = 0.004$).

Conclusion We found low congruence between ABRI and other Baveno criteria and the incidence of treatment failure in our study was higher than the previously reported frequencies of early rebleeding. It seems that criteria related to the quantity of blood transfusions are not reliable indicators of treatment failure.

Prevalence of esophageal varices in patients with liver cirrhosis is high, as by the time of diagnosis, they are present in up to 40% of compensated patients and up to 60% of those who present with ascites (1-3). Approximately 30% of patients experience an episode of variceal hemorrhage within 2 years of the diagnosis of varices (4,5). Acute bleeding from varices in a patient with portal hypertension often poses a life-threatening medical emergency with a mortality that is, in spite of the recent progress, still around 20% at 6 weeks (6,7). Bleeding-associated mortality is highest in the first 5 days after the first episode of variceal bleeding and returns to baseline after 3-4 months (5,8).

Several definitions and criteria to evaluate failure to control variceal bleeding and failure to prevent variceal rebleeding, as well as prognostic indicators of rebleeding, were developed previously at three Baveno Consensus Workshops (9-13). With application in clinical trials, it has been found that they have a limited clinical value (14). Therefore, new definitions and criteria have been recently proposed at Baveno IV Consensus Workshop (14). Adjusted blood requirement index (ABRI) has been suggested as an independent criterion to define the failure to control bleeding, but it has not been validated yet.

The aims of this study were to evaluate the clinical significance and consistency of ABRI in relation to other criteria of failure to control variceal bleeding proposed at Baveno Consensus Workshops (9-14), to determine if ABRI could be used as an early predictor of occurrence of other Baveno criteria, and to identify predictors of unfavorable ABRI.

Patients and methods

Data collection

We retrospectively analyzed medical records of a total of 87 patients with acute variceal bleeding admitted to the Interventional Gastroenterology

Unit of the Sisters of Mercy University Hospital between March 1, 2002, and December 31, 2005. All patients who received blood transfusion(s) and survived at least to the end of the first transfusion were eligible for the study. Eighteen patients who did not need a transfusion, 2 patients who died before the start of transfusion, and 7 patients who died in the course of the first transfusion were excluded from the study. Baseline data on demographic and clinical characteristics were collected for the remaining 60 patients (Table 1). Median age of the patients was 56.5 years, ranging from 32 to 83 years. Forty-five patients were men.

Table 1. Demographic and clinical characteristics of 60 patients with acute variceal bleeding

Parameter	No. of patients (n=60)
Age (median, range; years)	56.5 (32.0-83.0)
Men/women	45/15
Child-Turcotte-Pugh class (15):	
A	13
B	25
C	22
Bleeding varices location:	
esophagus	40
gastroesophageal junction	3
cardia	17
Varices grade (16):	
I	1
II	14
II/III	20
III	25
Endoscopic treatment modality:	
N-butyl-cyanoacrylate	36
polidocanol	17
band ligation	4
Treated with octreotide	25

Patient data were entered in a Microsoft Access database (Microsoft Corporation, Redmond, WA, USA). Occurrence of each of Baveno II/III and Baveno IV criteria for the treatment failure was entered separately. For the purpose of data analysis, modified Baveno criteria II-III were defined as Baveno criteria II-III without the "transfusion of 2 or more blood units (above the previous transfusions)" criterion. ABRI values were calculated according to the following formula for each transfusion received: $ABRI = \text{blood units transfused} / [(\text{final hematocrit} - \text{initial hematocrit}) / (\text{initial hematocrit} - \text{normal hematocrit})]$

crit)+0.01] According to Baveno IV criteria, $ABRI \geq 0.75$ at any time point defines failure to control bleeding.

Statistical analysis

Continuous variables were presented as medians and interquartile ranges, and categorical variables as frequencies. Nonparametric Mann-Whitney's test was used to test the significance of difference between quantitative variables. For categorical variables, Fisher exact test was used. Logit analysis was performed to test if ABRI predicted occurrence of other clinical manifestations proposed as the criteria for failure to control bleeding; the results were presented as odds ratios (OR) with 95% confidence interval (95% CI). Patients with $ABRI \geq 0.75$ and those with $ABRI < 0.75$ were compared by all relevant demographic, clinical, and laboratory variables. Logistic regression analysis was performed to ascertain independent variables that predicted $ABRI \geq 0.75$. Criteria for inclusion of variables in the logistic regression models were based on evidence of an association ($P < 0.1$) in the bivariate analysis. The appropriateness of the fitted model and its predictive utility were confirmed. Summary measures of goodness of fit were evaluated using Hosmer-Lemeshow test. Interactions were

assessed by running correlation matrix or logit analysis. $P < 0.05$ was considered statistically significant. All statistical analyses were performed with SAS software 8.0 (SAS Institute Inc., Cary, NC, USA).

Results

There were three times more men than women with acute variceal bleeding (Table 1). Esophagus was the most common localization of bleeding varices (Table 1). In 45 of 60 patients, hemorrhage resulted from varices grade II/III or III. According to Child-Turcotte-Pugh classification, most patients were class B (15). N-butyl-cyanoacrylate was the most frequently used endoscopic treatment modality, applied in more than half of the patients, whereas octreotide was administered in 25 patients.

ABRI vs Baveno criteria

According to Baveno II-III criteria, failure to control acute variceal bleeding occurred in 40 patients (Table 2). The "transfusion of 2 units of blood or more (over and above the previous transfusions)" criterion was present in 36 of these patients, while all other Baveno II-III criteria combined were present in only 17 patients.

Table 2. Treatment failure of acute variceal bleeding according to different criteria

Treatment failure criteria	No. of patients (n = 60)
Baveno II-III (12):*	40
transfusion of 4 units of blood or more within the first 6 h	1
inability to achieve an increase in systolic blood pressure of 20 mm Hg or to 70 mm Hg or more within the first 6 h	0
inability to achieve a pulse reduction of 20/min from baseline or to <100/min within the first 6 h	0
occurrence of hematemesis	7
reduction in blood pressure of more than 20 mm Hg from the 6-h point	13
increase in pulse rate of more than 20/min from the 6-h point on 2 consecutive readings 1 h apart	3
transfusion of 2 units of blood or more (over and above the previous transfusions) required to increase the hematocrit to above 27% or hemoglobin to above 90 g/L	36
Baveno IV (14):*†	35
fresh hematemesis ≥ 2 h after the start of treatment	7
30-g drop in hemoglobin ($\approx 9\%$ drop in hematocrit) if no transfusion is administered	8
death	2
adjusted blood requirement index (ABRI) ≥ 0.75 at any time point	32
Modified Baveno II-III‡	17
Baveno IV without ABRI‡	14
Overall incidence of treatment failure	46
Endoscopic reintervention	6

*Occurrence of any single criterion signifies failure to control variceal bleeding.

†The time frame for the acute bleeding episode is 120 h.

‡Baveno II-III criteria excluding "transfusion of 2 units of blood or more (over and above the previous transfusions)" criterion and Baveno IV criteria without ABRI criterion, as defined by authors.

Table 3. Relation of adjusted blood requirement index (ABRI) and other Baveno criteria in 60 patients with acute variceal bleeding

Criteria*	ABRI (No. of patients)		P	congruity	sensitivity (%)	specificity (%)
	<0.75 (n=28)	≥0.75 (n=32)				
Baveno II-III (12):						
positive	15	25	0.057	38	62.5	65.0
negative	13	7				
Modified Baveno II-III:						
positive	4	13	0.043	37	76.5	55.8
negative	24	19				
Baveno IV without ABRI:						
positive	3	11	0.037	36	78.6	54.4
negative	25	21				

*Modified Baveno II-III criteria excluding "transfusion of 2 or more blood units (above the previous transfusions)" criterion, and Baveno IV criteria without ABRI criterion, as defined by authors.

According to Baveno IV criteria, failure to control acute variceal bleeding occurred in 35 patients (Table 2). ABRI≥0.75 as the only criterion occurred in 21 of these patients.

Congruence between ABRI and other Baveno criteria was present in over half of the patients, with ABRI sensitivity ranging between 62.5% and 78.6% and ABRI specificity between 54.4% and 65.0% (Table 3). Baveno II-III criteria excluding the "transfusion of 2 units of blood or more (over and above the previous transfusions)" criterion were congruent with Baveno IV criteria excluding ABRI criterion in 49 patients (Table 3).

Predictive value of ABRI

Logit analysis showed that ABRI≥0.75 was associated with increased risk of other Baveno criteria, particularly modified Baveno II-III criteria and Baveno IV criteria excluding ABRI criterion (Table 4) In a group of 25 patients where ABRI and other criteria were both present, ABRI had occurred before other criteria in 8 patients.

Predictors of unfavorable ABRI

Bivariate analysis to test predictors of ABRI≥0.75 included age, sex, varices localization and grade, Child B and Child C classes, prothrombin time expressed as international normalized ratio (INR), first hemoglobin and hematocrit value, and treatment modalities (Table 5). Only 2 of these variables, male sex and higher hematocrit values, were identified as predictors of poor out-

come based on the evaluation of ABRI. Logistic regression analysis using ABRI≥0.75 as the outcome variable identified male sex (OR, 14.0; 95% CI, 2.9-111.9, P=0.003) and higher hematocrit values as independent predictors. Increase in hematocrit by 1% increased the risk of unfavorable ABRI by 10% (OR per unit change, 1.10; 95%

Table 4. Logit analysis of the dependence of Baveno criteria on adjusted blood requirement index (ABRI)

Criteria*	Odds ratio (95% confidence interval)	P
Baveno II-III (12)	3.10 (0.99-9.71)	0.052
Modified Baveno II-III	4.10 (1.11-15.05)	0.034
Baveno IV without ABRI	4.37 (1.04-18.28)	0.044

*Modified Baveno II-III criteria excluding "transfusion of 2 or more blood units (above the previous transfusions)" criterion, and Baveno IV criteria without ABRI criterion, as defined by authors.

Table 5. Bivariate analysis of independent predictors of adjusted blood requirement index ≥0.75*

Variable	ABRI (No. of patients)		P
	≥75 (n=32)	<75 (n=28)	
Age (median, IQ range, years)	55 (47.5-71.0)	57 (52.0-65.8)	0.138
Men/women	30/2	15/13	0.001
Source of bleeding:			
esophagus	21	19	0.892
gastroesophageal junction	2	1	
cardia	9	8	
Varices grade (16):			
I and II	9	6	0.761
II/III and III	23	22	
Child-Turcotte-Pugh class (15):			
A	7	6	0.613
B	15	10	
C	10	12	
Pretreatment hemoglobin (median, IQ range; g/L)	83 (64.5-99.8)	73 (54.3-84.0)	0.014
Hematocrit (median, IQ range)	25 (18.8-30.0)	21.5 (16.3-24.8)	0.004
Prothrombin time (median, IQ range; INR)	1.47 (1.3-1.7)	1.5 (1.4-1.8)	0.157
Histoacryl treatment	19	17	1
Polidocanol treatment	12	5	0.152
Band ligation	1	3	NE
Octreotide	11	14	0.296

*Abbreviations: ABRI – adjusted blood requirement index; IQ – interquartile range; INR – international normalized ratio; NE – not evaluated.

CI, 1.01-1.28; $P=0.004$). Treatment modalities did not show any influence on ABRI (Table 5).

Discussion

We showed that ABRI has a limited value as an independent predictor of failure to control acute variceal bleeding. In comparison with previously reported early rebleeding rates of 13% (6,7), we observed unusually high proportion of patients in whom control of variceal bleeding failed according to complete Baveno II-III and Baveno IV criteria (66.7% and 58.3%, respectively). Therefore, we separately analyzed the occurrence of treatment failure according to our modification of Baveno II-III criteria, where we excluded the "transfusion of 2 units of blood or more (over and above the previous transfusions)" criterion, and Baveno IV criteria without ABRI. According to these criteria, 28.3% and 23.3% of patients had treatment failure, respectively. These percentages are closer to the rates reported previously (6,7). The proportion of patients who actually underwent endoscopic retreatment was even lower. These results indicated that criteria related to the quantity of blood transfusions, ie, both ABRI and "transfusion of 2 units of blood or more (over and above the previous transfusions)" criterion, were not reliable indicators of treatment failure. The congruence of ABRI with other criteria of treatment failure was low, although we confirmed the possible role of ABRI as a predictor of occurrence of other, clinical criteria included in Baveno IV and Baveno II-III criteria.

When we used ABRI as a dependent outcome variable, we were not able to identify reliable independent predictors of $ABRI \geq 0.75$, although we found that male sex and higher initial hematocrit value were the factors independently associated with high ABRI. The clinical meaning of that finding is elusive.

Our study has several limitations. It is a retrospective, single-center study with a relatively small number of patients. Therefore, the power

of the study is decreased. Due to its retrospective character, the difference in timing of blood drawing cannot be excluded as a possible factor that influenced ABRI. Other factors that could also significantly influence ABRI, such as transfusion-related complications and extravascular hemorrhage (hematoma), were not observed. However, this study is the first one performed to evaluate ABRI in patients with acute variceal bleeding. A multicenter, prospective study with larger number of patients is needed for further validation of ABRI as an independent indicator of treatment failure in patients with acute variceal bleeding.

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