

Prognostic Value of Short-Term Mortality Using BARC Bleeding Classification in Acute Myocardial Infarction Patients

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ABSTRACT

Introduction: Acute myocardial infarction (AMI) treatment involves dual antiplatelet and anticoagulant therapy, which reduces thrombotic risks but increases bleeding risk. The Bleeding Academic Research Consortium (BARC) classification has emerged as a valuable tool for assessing bleeding severity. This study aims to evaluate the short-term mortality predictive value of BARC classification among AMI patients at 115 People's Hospital in Vietnam. **Methods:** This was a prospective cohort study conducted from May to August 2023 involving 289 AMI patients. Data collection included clinical and demographic characteristics, laboratory results, procedural details, and post-treatment outcomes. Bleeding events were categorized using the BARC classification. Statistical analyses determined bleeding incidence, associated risk factors, and short-term mortality predictive value. **Results:** Of the 289 patients, 28.4% experienced bleeding, and 7.6% had major bleeding (BARC 3-5). The mean age was 64.61 years, with 62.98% being male. The main bleeding sites included procedural access points (28%) and gastrointestinal locations (23%). Factors associated with major bleeding included elevated BMI, chronic kidney disease, and higher creatinine levels. The BARC classification showed moderate predictive ability for 30-day mortality (AUC = 0.647, $p = 0.002$). BARC 3A had high specificity (97.5%) but lower sensitivity (34.8%). **Conclusion:** The BARC classification is a valuable predictor of short-term mortality among AMI patients. Enhanced utilization of this tool may aid clinicians in balancing anticoagulant therapy risks, improving patient outcomes. Further studies are recommended to refine bleeding risk assessments and broaden applicability in varied clinical settings.

INTRODUCTION

Anticoagulation and dual antiplatelet therapy are important treatments for patients with acute myocardial infarction (AMI) [1-3]. In addition to reducing the risk of thrombosis and ischemia, anticoagulation and antiplatelet therapy increases the risk of bleeding in this group of patients. Recent studies have shown that bleeding complications are as dangerous as recurrent AMI [4-12]. Bleeding events during both inpatient and post-discharge treatment are associated with an increased risk of mortality [6,7,9]. Furthermore, post-discharge bleeding is more challenging to detect and manage than in-hospital bleeding. Therefore, in the treatment of patients with AMI, clinicians need to consider the risk of thrombosis and the risk of bleeding. Therefore, predicting bleeding and assessing the classification when bleeding events occur are necessary to select and adjust the most appropriate dual anticoagulation and antiplatelet treatment strategy for this group of patients. To date, multicenter trials have not been consistent in their choice of definitions or classifications of bleeding events in patients with AMI. Therefore, comparing results between studies leading to conclusions regarding bleeding risk or bleeding events is difficult.[13] The Thrombolysis in Myocardial Infarction scale (TIMI), Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO), and Bleeding Academic Research Consortium score (BARC) are commonly used definitions and classifications of bleeding events and have been validated in recent follow-up studies. [14,15] BARC was developed to overcome the limitations of TIMI, GUSTO, and several other bleeding classification criteria. The advantage of BARC is that it uses both clinical and paraclinical information to classify bleeding, paying attention to minor bleeding events with major clinical significance [16].

There are very few studies using the BARC definition to assess bleeding in AMI patients in Vietnam to date. A few studies in Vietnam, on AMI patients, have recorded bleeding rates based on different definitions including GRACE (Global Registry of Acute Coronary Events), CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the ACC/AHA Guidelines scale), TIMI, GUSTO and BARC ranging from 1% to 9% [16]. In this context, contributing another survey to assess bleeding events and prognosis based on the BARC bleeding definition in AMI patients in Vietnam will be necessary in clinical practice.

Based on the above thoughts, we designed a study to survey bleeding events in AMI patients at People's Hospital 115. The study aims to determine the bleeding rate according to the BARC definition and related factors and initially evaluate the short-term mortality prognostic value of this bleeding definition.

We hope that the study results will provide evidence of a reliable bleeding rate according to the BARC definition, and at the same time indicate factors related to bleeding in AMI patients, indicating the prognostic value of in-hospital mortality and 1 month post-discharge with bleeding events according to the BARC definition compared with TIMI and GUSTO in AMI patients. Thereby helping medical staff to be able to apply the BARC bleeding classification more widely in the context of Vietnam to serve the monitoring and treatment, appropriate monitoring management strategies, especially for AMI patients.

Objectives:

1. Determine the bleeding rate according to BARC classification in acute myocardial infarction patients.
2. Determine the relationship between risk factors and major bleeding according to BARC classification in acute myocardial infarction patients.
3. Determine the short-term mortality prognostic value of BARC bleeding classification in acute myocardial infarction patients

RESEARCH SUBJECTS AND METHODS

Subjects: This study involved patients with AMI admitted to the 115 People's Hospital's Cardiology Department from May 2022 to August 2023. Inclusion criteria required that patients be diagnosed with AMI and provide informed consent for participation. Patients were excluded if they had incomplete clinical or laboratory data or significant coagulation disorders that might confound bleeding assessment.

Study Design: This was a prospective cohort study focusing on the prognostic value of bleeding events categorized using the BARC classification for short-term mortality in AMI patients.

Data Collection: Data were gathered on demographic information, clinical characteristics, medical history, and laboratory values (e.g., hemoglobin, platelet count, and creatinine levels). All data on bleeding events and outcomes, both in-hospital and up to 30 days post-discharge, were documented based on the BARC classification criteria.

Statistical Analysis: Statistical analysis involved descriptive statistics to outline patient characteristics, bleeding incidence, and outcomes. The association between variables and bleeding severity was assessed using logistic regression models, while Cox regression models were used to estimate the hazard ratio (HR) for mortality. Statistical significance was determined with a p-value <0.05.

RESULTS

3.1. Patient Demographics and Baseline Characteristics

During the period from May to August, 2023, at the Interventional Cardiology Department of Hospital 115, we selected 289 patients with AMI who met the selection criteria to participate in the study. Among the patients participating in the study, 182 patients were male, accounting for 62.98%, and 107 patients were female, accounting for 37.02%. The male/female ratio was 1.70/1. The mean age of the study was 64.61 ± 11.47 years.

The oldest and youngest patients were 94 and 32 years old, respectively. The patients in the study had a mean body mass index of $23.68 \pm 3.36 \text{ kg/m}^2$. The most common risk factors in the study were hypertension, diabetes and smoking. Hypertension was the most common risk factor in 243 patients, accounting for 84.1%. Another common risk factor was diabetes, accounting for 25.3%. There were 147 patients who smoked, most of whom were men (95.2%). The number of patients with a history of previous bleeding was low, only 0.7%. More than one-third of patients had tachycardia at admission. Six patients were noted to have systolic blood pressure $<90 \text{ mmHg}$.

Lab test results: platelets, creatinine, troponin I levels, aPTT, PT, INR, left ventricular diameter, PAPs did not have a normal distribution. There were 126 anemic patients (43.59%). The number of patients with estimated glomerular filtration rate below $30 \text{ mL/min/1.73m}^2$ was 15 people, accounting for 5.19%. Meanwhile, 38 patients had ejection fraction below 40%, corresponding to 13.14%, 210 patients were recorded to have regional movement disorders on echocardiography (72.66%). In the study, 169 patients were hospitalized for NSTEMI, accounting for the majority at 58.5%. Treatment with dual anticoagulation and antiplatelet therapy in patients with AMI in the study accounted for almost all, over 95%. Clopidogrel is the P2Y₁₂ receptor inhibitor commonly chosen to combine with aspirin. Only 1 case was treated with unfractionated heparin. No patients treated with vitamin K antagonists/NOACs were recorded. Of 289 patients admitted for myocardial infarction, 114 underwent coronary angiography with arterial access primarily via the radial artery, of whom 78 underwent PCI, mostly using drug-eluting stents.

3.2. Bleeding events

Bleeding events occurred in 82 patients, corresponding to 28.4%. In 114 patients undergoing coronary angiography/intervention, 48 patients had bleeding, accounting for 42.11%. Most of the bleeding occurred at the site of the procedure, the skin, soft tissue, musculoskeletal system, and the gastrointestinal tract. There were only 4 cases of intracranial bleeding and 2 cases of nasopharyngeal bleeding. The majority of bleeding cases were mild bleeding (BARC type 1 and type 2) with 60 patients, accounting for 20.8%. There were 22 cases of severe bleeding according to the BARC definition, corresponding to 7.6% of the total number of patients, including: 17 patients with type 3a bleeding (3.9%), 4 patients with type 3b bleeding (1.4%), 1 patient with type 3c bleeding (0.4%), 0 patients with types 4, 5A, 5B (0%). In the group of patients undergoing coronary angiography/intervention, there were 5 cases of severe bleeding, accounting for 4.4%. Most cases of severe bleeding were located in the gastrointestinal tract (72.7%). There were 3 cases of intracranial bleeding, 1 case of severe bleeding in soft tissue, nasopharynx and surgical access. There were no cases of respiratory, genitourinary or intracavitary bleeding. Of the 22 patients with severe bleeding, 5 patients required blood transfusion, equivalent to 22.7%, and 8 patients had hemodynamic instability, accounting for 36.4%. Nearly half of the bleeding patients required temporary or permanent discontinuation of both antithrombotic drugs (anticoagulants and DAPT). During the study period, a total of 46 patients died from all causes within 30 days, of which 35 patients died in-hospital and were seriously ill and asked to go home, accounting for 12.1%, and 11 patients died after discharge, equivalent to 3.8%. In the bleeding group, out of 82 patients, there were 13 in-hospital deaths, accounting for 15.9%, while the non-bleeding group had 22 deaths out of 207 patients, corresponding to a rate of 10.6%. Notably, in the group of 22 patients with severe bleeding, the number of in-hospital deaths was 12, accounting for 54.5%, compared to only 23 deaths out of 267 patients without severe bleeding, corresponding to a rate of 8.6%. Similarly, when considering the all-cause mortality rate within 30 days, the bleeding group recorded 21 deaths out of 82 patients, reaching a rate of 25.6%, higher than the 25 deaths out of 207 patients without bleeding, equivalent to 12.1%. Notably, the group with severe bleeding had 16 deaths out of 22 patients, accounting for 72.7%, while the group without severe bleeding had 30 deaths out of 267 patients, accounting for 11.2%.

3.3. Risk factors associated with major bleeding according to BARC classification

Table 1. Association between severe bleeding and risk factors

Variables	Severe bleeding	p
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	Yes (n=22)	No (n=267)	
Age, Mean $\pm$ SD	64.64 $\pm$ 2.62	64.60 $\pm$ 0,70	0.990 [#]
Female, n (%)	10 (45.5)	97 (36.3)	0.396 [*]
BMI, Mean $\pm$ SD	22.32 $\pm$ 3.17	23.79 $\pm$ 3.36	0.048^t
Smoking, n (%)	8 (36.4)	139 (52.1)	0.158 [*]
Hypertension, n (%)	18 (81.8)	225 (84.3)	0.764 [*]
Diabetes, n (%)	7 (31.8)	66 (24.7)	0.463 [*]
Chronic Kidney disease, n (%)	5 (22.7)	20 (7.5)	0.014[*]
Heart failure, n (%)	3 (9.1)	30 (11.2)	0.735 [*]
PCI/CABG, n (%)	1 (4.5)	17 (6.4)	0.735 [*]
Old Myocardial Infraction, n (%)	3 (13.6)	37 (13.9)	0.977 [*]
Old Ischemic Stroke, n (%)	2 (9.1)	17 (6.4)	0.622 [*]
Bleeding, n (%)	0 (0)	2 (0.7)	0.685 [*]
Anticoagulants, n (%)	0 (0)	2 (0.7)	0.685 [*]
Gastric and duodenal ulcers, n (%)	5 (22.7)	33 (12.4)	0.168 [*]
Heart rate, bpm, Mean $\pm$ SD	88.23 $\pm$ 12.4	82.63 $\pm$ 12.5	0,044[#]
Systolic Blood pressure, mmHg Mean $\pm$ SD	110.91 $\pm$ 20.7	114.78 $\pm$ 19.4	0,372 [#]
Diastolic Blood pressure, mmHg Mean $\pm$ SD	65.45 $\pm$ 10.1	68.69 $\pm$ 9.9	0.144 [#]
STEMI, n (%)	8 (36.4)	112 (41.9)	0.611 [*]
Atrial fibrillation, n (%)	1 (4.5)	10 (3.7)	0.851 [*]
Red blood cell (M/ μ L), Mean $\pm$ SD	4.07 $\pm$ 0.75	4.43 $\pm$ 0.65	0.014[#]
Hemoglobin (g/dL), Mean $\pm$ SD	11.2 $\pm$ 2.28	13.07 $\pm$ 1.96	<0.001[#]
Hematocrit (%), Mean $\pm$ SD	33.88 $\pm$ 6.31	38.98 $\pm$ 5.53	<0.001[#]
Platete (K/ μ L), (25 th – 75 th)	292.50 (239 – 327)	255.00 (211 – 300)	0.031[@]
aPTT (second)	102.6 $\pm$ 5,2	118.5 $\pm$ 1,3	0.433 [#]
PT (second), (25 th – 75 th)	14.6 (13.08 – 16.98)	13.9 (13.10 – 14.80)	0.045[@]
INR, (25 th – 75 th)	1.19 (1.01 - 1.31)	1.05 (0.06 – 1.12)	0.068 [@]
Creatinin (mg/dL), (25 th – 75 th)	107.5 (85.83 – 149.25)	91.70 (78.90 – 107.0)	0.002[@]
eGFR (ml/min/1.73)	106.2 $\pm$ 5.9	121.6 $\pm$ 1,3	0.002[#]
Na ⁺ (mmol/L), Mean $\pm$ SD	137.05 $\pm$ 4.43	139.38 $\pm$ 3.46	0.003[#]

#: T test

*: χ^2 test

@: Mann-Whitney U test

Comments: variables that were statistically different between the major bleeding and non-major bleeding groups included: BMI, history of chronic kidney disease, heart rate on admission, red blood cell, hemoglobin concentration, hematocrit, platelet, glomerular filtration rate and serum sodium concentration.

3.4. Short-term mortality prognostic value of BARC bleeding classification

ROC curve analysis showed that the BARC classification of major bleeding in predicting 30-day mortality had an area under the curve AUC = 0.647 (95% CI 0.546-0.748) with $p = 0.002$. Results were showed in **Figure 1** and **Table 2**.

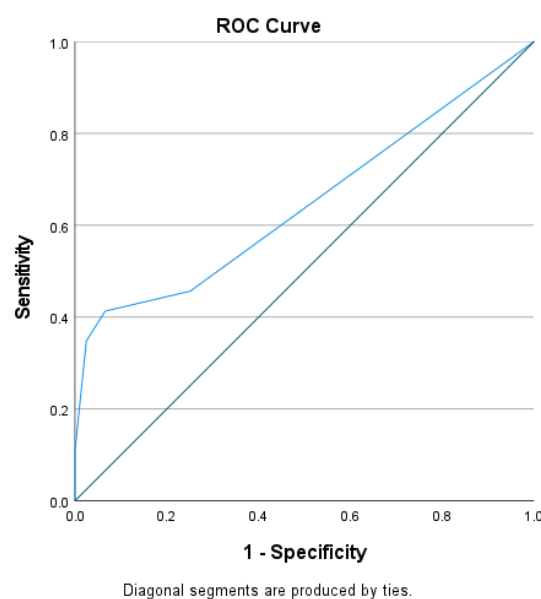


Figure 1. ROC curve of BARC major bleeding classification in predicting 30-day mortality

Table 2. Value of BARC major bleeding classification in predicting 30-day mortality

Cut-off point	AUC	Sensivity	Specificity	PPV	NPV	Accuracy
3A	0.662	0.348	0.975	0.727	0.888	0.875
3B	0.554	0.109	1	1	0.856	0.858
3C	0.511	0.022	1	1	0.844	0.844

DISCUSSION

Short-term mortality in patients with myocardial infarction varies widely across studies, depending on the type and severity of myocardial infarction and the treatment method. This rate for ST-elevation myocardial infarction ranges from 4-6%, if early coronary intervention is performed using percutaneous coronary intervention. However, for patients who do not receive timely intervention, especially the elderly or those with risk factors such as cardiogenic shock or heart failure, the risk of mortality can be as high as 45% [17,18]. For non-ST-elevation myocardial infarction (NSTEMI), the short-term mortality risk is generally lower than STEMI (about 2-5%)[17]. In our study, 46 patients with myocardial infarction died within 30 days of admission, equivalent to 15.92%, approximately the same as the result of author Mai Thanh Hai at 14%, and lower than the study of author Murali at 24.7% [19]. Meanwhile, authors Hironori Hara and Pascal Vranckx recorded short-term mortality rates of 6.25% and 1.5%, respectively [20,21]. This is explained by the fact that the research subjects of the two authors were myocardial infarction patients who had undergone percutaneous coronary intervention. When analyzing factors affecting all-cause 30-day mortality by Cox multivariate

regression, after adjustment, major bleeding events according to BARC classification (HR 11.160; 95% CI 5.078; 24.527, $p<0.001$), previous bleeding/bleeding history (HR 26.114; 95% CI 4.472; 152.492, $p<0.001$), heart failure (HR 3.369; 95% CI 1.317; 8.615, $p=0.011$), INR test results (HR 4.528; 95% CI 1.684; 12.171, $p=0.003$) were variables independently correlated with 30-day mortality. Major bleeding events according to the BARC classification were noted to have a strong impact on the risk of mortality, with a hazard ratio of 11.160, meaning that patients with major bleeding had a 11.16-fold higher risk of death within 30 days than patients without major bleeding. This result is similar to the studies of authors Vranckx (HR 14.25; 95% CI 10.72–18.94, $p<0.0001$) and Hironori Hara (HR 53.11; 95% CI 24.03 -117.37, $p<0.001$) [20,21]. These studies emphasize that major bleeding not only reduces the patient's ability to recover, but also puts additional pressure on the cardiovascular system, making patients more susceptible to severe complications, leading to high mortality. This again confirms that major bleeding is a risk factor for early death in patients with myocardial infarction.

Another important factor is a history of previous bleeding or hemorrhage, indicating that patients with a history of bleeding are at very high risk of death if not carefully controlled during treatment. Patients with a history of bleeding are at higher risk of death, especially in the early period after a myocardial infarction event. Several studies have reported that the risk factor for 30-day mortality in patients with a history of bleeding can range from 2.5 to 6.0, depending on the type of bleeding and the clinical condition of the patient [22]. This confirms the important role of assessing and controlling a history of bleeding before medical interventions after myocardial infarction.

Heart failure is also a poor prognostic factor, indicating that patients with impaired cardiac function are more likely to experience serious events and death [23]. This result is consistent with the international literature. For patients with heart failure after myocardial infarction, mortality may be significantly increased within the first 30 days [24,25]. One study identified heart failure after myocardial infarction (both left and right ventricular dysfunction) as a major risk factor, increasing the risk of death from major cardiovascular events such as hospitalization for heart failure or cardiovascular death [26]. The risk ratios in these studies for patients with heart failure after myocardial infarction may be as high as 2.4 for left ventricular dysfunction and even higher for right ventricular dysfunction [17].

Finally, abnormal INR results reflect that coagulation disorders, especially elevated INR, are closely associated with mortality [27]. Patients with abnormal INRs may experience severe bleeding or complications related to anticoagulation therapy, increasing the risk of short-term mortality. A study in Malaysia also showed similar results, showing that abnormally prolonged INR is a predictor of short-term mortality in patients with ST-elevation myocardial infarction with HR in the range of 4.0-4.5, with p value <0.05 [28].

ROC curve analysis showed that the BARC classification of major bleeding had a predictive value for 30-day mortality with an area under the curve (AUC) of 0.647 (95% CI: 0.546 - 0.748), and achieved statistical significance with $p=0.002$. This showed that the BARC classification had an average predictive ability for mortality.

Our study results showed that the 3A classification had the best predictive value with an AUC of 0.662, indicating an average predictive ability. In particular, the 3A cut-off point had a specificity of 97.5%, but a low sensitivity of only 34.8%. Meanwhile, the 3B classification, although having the maximum specificity and positive predictive value (PPV) (both reaching 1.0), had a very low sensitivity (10.9%). Similarly, the 3C cutoff also had maximum specificity and PPV but the AUC was only 0.511, with a sensitivity of 2.2%. Due to the limited sensitivity of this classification, it should be combined with other prognostic factors to improve the ability to detect patients at higher risk.

Study Limitations:

This study has limitations, including its single-center design, which may limit the generalizability of the

findings. Additionally, some bleeding events may have been under-reported due to the study's reliance on clinical documentation, potentially affecting outcome assessment accuracy.

CONCLUSION

This study demonstrates that the BARC classification is an effective tool for predicting short-term mortality in AMI patients, particularly those with severe bleeding events (grade 3 or higher). The findings suggest that implementing the BARC criteria in clinical settings could aid in optimizing treatment strategies for AMI patients, balancing the risks of bleeding and thrombotic events to improve patient outcomes. Further studies across multiple centers in Vietnam are recommended to validate the use of the BARC classification for AMI patients and to develop standardized bleeding risk assessment protocols tailored to the Vietnamese population.

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