Sdü Sağlık Bilimleri Enstitüsü Dergisi / Cilt 9 Sayı 2 / 2018

Combined Value of Left Ventricular Ejection Fraction and HAS-BLED Score for Predicting Mortality in Patients with St-Elevation Myocardial Infarction Who Were Undergoing Primary Percutaneous Coronary Intervention

Primer Perkütan Koroner Girişim Uygulanan ST Yükselmeli Miyokart Enfarktüslü Hastalarda Sol Ventrikül Ejeksiyon Fraksiyonu ve HAS-BLED Skoru Kombinasyonunun Mortaliteyi Öngördürücü Değeri

Tuncay Kırıs[1], Eyup Avci[2], Aykan Celik[1]

[1]Physician in Cardiology, Department of Cardiology, Izmir Katip Celebi University, Ataturk raining and Research Hospital, Izmir, Turkey.

[2]Physician in Cardiology, Department of Cardiology, Balikesir University, Balikesir, Turkey.

Abstract

Objective: The HAS-BLED score and left ventricular ejection fraction(LVEF) can both independently predict clinical outcomes in patients having acute coronary syndromes. We studied the predictive value of LVEF as well as HAS-BLED score for mortality in ST segment elevation myocardial infarction (STEMI) patients undergoing primary percutenous coronary intervention (PPCI).

Material-Method: We investigated 588 sequential STEMI patient undergoing PPCI. For each patients, HAS-BLED scores were calculated and the stipulated ability for mortality was analysed by means of area under curve (AUC). The patients were considered in four different groups in terms of the their HAS-BLED score. Their groups of HAS-BLED score were very/low risk= 0, low risk= 1, moderate risk= 2, high risk ≥ 3. Primary endpoint was total mortality.

Results: By multivariate cox regression analysis, HAS-BLED score ($p < 0.001$) and LVEF($p < 0.001$) were independent predictors of total mortality. When HAS-BLED score was used singly, AUC for total mortality was 0.71 [95%CI= 0.66-0.76]. The AUC for total mortality increased to 0.77 ($p < 0.001$) after adding LVEF. The incremental predictive value of combining LVEF and HAS-BLED score was significantly improved, also shown by the the net reclassification improvement (NRI = 27.2%, $p < 0.001$) and integrated discrimination improvement (IDI = 0.061, $p < 0.001$).

Conclusions: Adding LVEF to HAS-BLED score independently improved the estimated value for all mortality in STEMI patients undergoing PPCI.

Keywords: HAS-BLED Score, Left Ventricular Ejection Fraction, Mortality, STEMI

Özet

Amaç: HAS-BLED skoru ve sol ventrikül ejeksiyon fraksiyonu (SVEF), akut koroner sendromlu hastalarda her ikiside klinik sonuçları bağımsız olarak öngörebilir. Primer percutan koroner girişim (PKG) ile tedavi edilen ST segment yükselmeli miyokard infarktüsü (STEMI) hastalarında SVEF ve HAS-BLED skoru kombinasyonlarının mortaliteyi öngördürücü değerini araştırdık.

Materyal-Method: Primer PKG uygulanan 588 ardışık STEMI hastasını araştırdık. Her hasta için HAS-BLED skorları hesaplandı ve mortalite için öngörü değeri, eğri altındaki alan (AUC) kullanılarak analiz edildi. Hastalar HAS-BLED skorlarına göre dört gruba ayrıldı. Onların HAS-BLED skorları çok düşük risk: 0, düşük risk: 1, orta risk: 2, yüksek risk: ≥ 3 idi. Birincil son nokta toplam mortaliteydi.

Bulgular: Çok değişkenli cox regresyon analizi ile HAS-BLED skoru ($p <0,001$) ve SVEF ($p <0,001$) toplam mortalitenin bağımsız öngördürücüleriydi. Sadece HAS-BLED skoru için toplam mortalitede AUC 0,71 (95% CI: 0,66-0,76) idi. SVEF eklendikten sonra 0,77'ye ($p <0,001$) yükseldi. SVEF ve HAS-BLED skorlarının birleştirilmesinin artan prediktif değeri, net yeniden sınıflandırma iyileştirmesi (NRI =27,2%, $p <0.001$) ve entegre ayrımcılık iyileştirmesi (IDI = 0,061, $p <0,001$) ile de gösterildi.

Sonuç: SVEF'nin HAS-BLED skoru ile birleştirilmesi, primer PKG uygulanan STEMI hastalarında tüm nedenlere bağlı mortalite için öngördürücüydü.

Anahtar kelimeler: HAS-BLED Skoru, Sol Ventrikül Ejeksiyon Fraksiyonu, Mortalite, STEMI

DOI: 10.22312/sdusbed.423517
Müracaat tarihi: 14.05.2018
Kabul tarihi: 20.06.2018

Yazışma Adresi / Corresponding: Eyup Avci,
Balikesir University, Medical Faculty Cardiology Department, Balikesir, Turkey.
Tel: 0266 612 10 10
Fax: 0266 612 30 10
E-mail: e-mail: dreyupavci@gmail.com

Introduction

Different risk scores have been proposed to classify STelevation myocardial infarction (STEMI) patients in terms of theirmortality risk (low or high). Initially, The risk score of Thrombolysis in Myocardial Infarction (TIMI) was created for prediction of 30-day mortality(1). Thereafter, it was validated for prediction of one-year mortality when the percutaneous coronary intervention (PCI) was applied to the patients having STEMI(2). The Zwolle score was used in predicting 30-day mortality(3). The Primary Angioplasty in Myocardial Infarction (PAMI) score was developed to determine the mortality of 180 days(4). The Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) and the Global Registry of Acute Cardiac Events (GRACE) risk scores are also used to predict the mortality in the STEMI patients(5,6).

The HAS-BLED score is commonly used to evaluate bleeding risk of patients having Atrial Fibrillation(AF) taking anticoagulant treatment(7). This score based on various parameters [abnormal liver/renal function, hipertension, stroke, labile international normalized ratio, bleeding predisposition/history, alcohol/drugs use, elderly]. Furthermore, there are some studies representing clinical invastigation based on HAS-BLED score in STEMI patients undergoing PPCI(8,9). In addition, each component of this score is associated with mortality in STEMI patients(10-13).

The study including statistical evaluations showed that left ventricular ejection fraction (LVEF) was correlated with mortality thereafter myocardial infarction(14,15). However, The value of LVEF and HAS-BLED score for STEMI patients undergoing PPCI had never been combined for the estimating mortality. This study was planned to explore the incremental prognostic important LVEF combined by HAS-BLED score in these patients.

Material-Method

612 sequential STEMI patients undergoing PPCI between May 2010 and May 2015 were considered in the scope of study. The total of 24 patients were removed from the study because of missing data. The remaining of 588 STEMI patients were evaluated in the scope of study. The STEMI was described as chest pain within the last 30 minutes but no mone than 12 hours with ST-segment eleva¬tion grather than 1 mm in ≥2 sequential leads, new left bundle branch block and increased cardiac biomarkers [troponins,CK-MB](16).

The patient population considered in the study was divided into different risk categories in terms of patients` admission HAS-BLED score [very low risk= 0 low risk= 1 moderate risk= 2 high risk ≥ 3]. The study protocol was approved by the ethics committee of the authors' hospital.

Patients` data

The demographic and clinical properties of patients; various risk factors e.g, (hypercholesterolemia, diabetes mellitus, hypertension, smoking, ischemic attack, anemia or bleeding, and alcohol usage) were collected. The HAS-BLED score was calculated so that each of one point presence of HT, old age (> 65), liver dysfunction (alanine aminotransferase level higer than 100 mg/dl, chronic hepatic disease), renal dysfunction (a serum creatinine level higer than 2mg/dl,dialysis treatment), history of stroke, anemia (lower than 13mg/dL for men, lower than 12mg/dL for women),labile international normalized ratio (higer than 1.3), or bleeding predisposition, alcohol comsuption , and non-steroidal anti-inflammatory drug usage (NSAIDS).

Blood Sampling

All biochemical parameters such as INR, sCr, and alanine aminotransferase (ALT) were measured before the coronary angiography. INR was measured by means of the reagent HemosIL RecombiPlasTin 2G.

Echocardiographic Analysis

Echocardiographic analysis was performed within 24 h after admission. LVEF was computed after measuring the end-diastolic and end-systolic left ventricul (LV) volumes in the apical four-chamber and two-chamber views using the modified method of Simpson.

Coronary Angiography, and Intervention

The chewable aspirin of 300 mg and clopidogrel of 600 mg were given patients before coronary angiography (CAG). The cardiac catheterization laboratory data were used to obtain the patients' angiographic history . All CAG and PCI procedures were conductedby means of the transfemoral approach. The infract related artery (IRA) was determined based on the ECG and TIMI flow classification(17). Once arterial anatomy was visualized, the heparin of 100 U/kg was given. Angiographic evaluatations were visual performed. Based on lesion anatomy the PPCI was conducted for only IRA. It can be noted that interventional success was obtained for the acute phase in case of the obstruction and stenosis of artery having TIMI of 2 or 3 flow were decreased under <50% just after PPCI. After intervention, all patients taken aspirin of 100 mg and clopidogrel of 75 mg in every day.

Definitions

As it known, one formation of antihypertensive medications usage, systolic pressure over 140 mmHg and diastolic pressure over 90 mmHg was defined as hypertension. However, Diabetes mellitus consisted of one of insulin/antidiabetic agents uses or a fasting glucose level over 126 mg/dL. Heart failure (HF) was accepted LVEF decreases under 40%. Hypercholesterolemia was defined as total cholesterolof at least 200 mg/dL.

All-cause mortality occurrence determined end point of primary study during the median follow-up of 27.4 months. Additionally, stroke/transient ischemic attack (TIA), myocardial reinfarction, cardiac death, target-vessel revascularization (TVR), and heart-failure admission were considered as secondary end points. Patiet`s data were obtanied from hospital records or by personal interviewss or telephone with their families or physicians.

Statistical Analysis

Quantitative variables were indetified by mean value ± standard deviation whereas qualitatives were in

percentage(%). Comparisons of parametric valuesbetween groups were made using a one-way ANOVA. Categorical variables were compared with a likelihood ratio x2 test or Fisher's exacttest. Bonferroni test was used for pairwise post-hoc tests. Multivariate Cox regresion analyses with $p < 0.1$, was conducted to describe predictors of all-cause mortality. Comparing the areas under the receivers operating characteristic (ROC) curve, a combination of LVEF and HAS-BLED score were estimated. DeLong's test was used to compare the AUC from each of models(18). Also, Net Reclassification Improvement (NRI) and Integrated Discrimination Improvement(IDI)(19) were taken into account to estimate discriminitive value. By using Kaplan-Meier method where differences were evaluated by the log-rank test, the cumulative survival curves were generated for all-cause mortality. It could be noted that the results were statistically significant if the p value was less than 0.05. All statistical calculations were performed by SPSS v16.0 (SPSS Inc. Chicago, IL, USA).

Results

The average population age 62 ±12 years, and 75.3% were male. 117 patients (19.9%) died median follow-up period of 28.1 months. The clinical and angiographics characteristics are listed for all patients in Table 1. Based on HAS-BLED score, patients were subdived four groups. Baseline characteristics between these four groups are presented Table 2. Patients having high riskgroup (≥ 3) were generally older and female, with HT and stroke histories, but less frequently current smokers than the other subgroups. The high risk group had higher impaired renal function and abnormal liver function than those of other groups. The rate of patients taking beta blockers and angiotensin receptor blokers/angiotensin converting enzyme inhibitors was lower for the high risk group.

Univariate and multivariate analysis of total mortality are provided in Table 3. For the patients having lower risk HAS-BLED score, the mortality rate was fewer than those of the high (HR:5.64, 95% CI: 2.17-14.63, p< 0.001) and moderate (HR:3.94, 95% CI: 1.52-10.12, p = 0.005) HAS-BLED score althoug the mortality rate was not different from the low HAS-BLED score (HR:2.19, 95% CI: 0.82-5.84, p = 0.118) when multivariable risk analyses was performed. Also, HAS-BLED score (HR:1.63, 95% CI: 1.35-1.97, p < 0.001) as continues variable and LVEF (HR:0.96, 95% CI: 0.94-0.98, p < 0.001) were correlated with total mortality in multivariate analysis(Table 3). In Kaplan-Meier survival curves, survival rates generally decreased with a higher HAS-BLED score (Figure 2)

As both LVEF and HAS-BLED score were independent risk factors for all-cause mortality, we evaluated their combined value for predicting mortality. When HAS-BLED score was considered singly, the AUC was calculated 0.71 (95% CI: 0.66-0.76). On the other hand, in case of the LVEF was added to HAS-BLED score, in this instance, the AUC was 0.77 (95% CI:0.72-0.81, p < 0.001; Figure 1). Patients reclassification for all-cause mortality is shown Table 4. This combination procedure was correlated with both the NRI with 27.2% (p < 0.001), and the IDI 0.061 (p < 0.001).

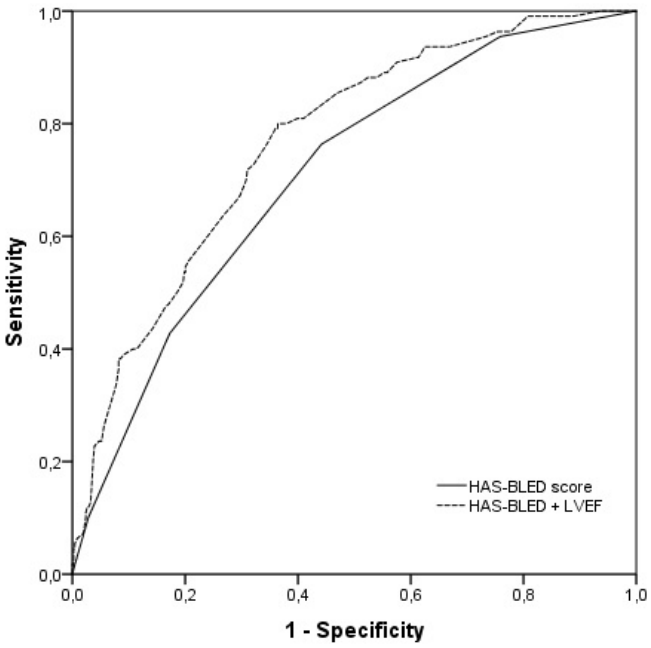

Figure 1. ROC analysis of HAS-BLED score and HAS-BLED+LVEF

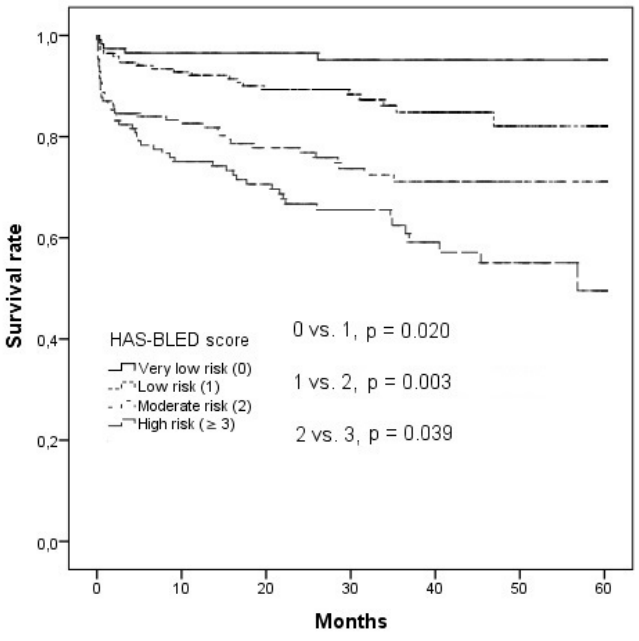

Figure 2. Survival rates of patients who categorized according to HAS-BLED score

Table 1. Baseline characteristics of the study population

Past medical history	Survivors (n = 471)	Non-survivors (n = 117)	p - value
Age > 65, n (%),(years)	166 (35)	67 (57)	< 0.001
Female, n (%)	107 (23)	38 (33)	0.029
Diabetes mellitus, n (%)	107 (23)	41(35)	0.007
Hypertension, n (%)	190 (41)	57 (49)	0.104
Current smoker, n (%)	146 (31)	28 (23)	0.085
Stroke history, n (%)	12 (3)	13 (11)	< 0.001
Hyperlipidemia, n(%)	53 (11)	19 (16)	0.148
Anemia or bleeding history, n (%)	247 (53)	88 (75)	< 0.001
Pre-usage NSAID, n (%)	9 (2)	2 (2)	0.879
Alcohol consumption, n (%)	3 (1)	0 (0)	0.385
Prior CAD, n (%)	92 (20)	28 (24)	0.281
Clinical presentation			
Killip ≥ 2, n (%)	22 (5)	45 (38)	< 0.001
LVEF (%)	45.3 ± 9	39.7 ± 10	< 0.001
Multi-vessel disease, n (%)	201(43)	65 (56)	< 0.001
Final TIMI flow 0-2, n (%)	54 (12)	18 (15)	0.250
Renal impairment, n (%)	7 (2)	13(11)	< 0.001
Abnormal liver function, n (%)	23 (5)	18 (15)	< 0.001
INR > 1.3, n (%)	8 (2)	7 (6)	0.009
HAS-BLED score	1 (1-2)	2 (2-3)	< 0.001
Angiographic characteristics			
Infarct related artery			0.317
LAD, n (%)	218 (46)	57 (49)	
CX, n (%)	67 (14)	10 (9)	
RCA, n (%)	167 (36)	47 (39)	
Others, n (%)	19 (4)	3 (3)	
Stent use, n (%)	452 (97)	114 (95)	0.385
DES, n (%)	38 (8)	4 (4)	0.193
Stent diameter (mm)	3.5 ± 0.6	3.5 ± 0.5	0.553
Stent lentgh, (mm)	25 (18-48)	28 (20-51)	0.292
Tirofiban use, n (%)	204 (43)	51 (43)	0.938
Medication at discharg			
Beta-blockers, n (%)	412 (88))	82 (70)	< 0.001
ACE/ARB, n (%)	393 (83)	73 (62)	< 0.001
Statin, n (%)	377 (80)	92 (79)	0.758
Clinical outcomes			
In-hospital major bleeding, n (%)	10 (2)	8 (7)	0.026
In-hospital death, n (%)	0 (0)	34 (29)	< 0.001
Cardiac death, n (%)	0 (0)	52 (44)	< 0.001
Heart failure admission, n (%)	18 (4)	18 (15)	< 0.001
Repeated stroke, n (%)	10 (6)	6 (5)	0.074
Myocardial reinfarction, n (%)	43(9)	10 (9)	0.839
TVR, n (%)	49 (10)	10 (9)	0.545

HAS-BLED: Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalized ratio, Elderly, Drugs or alcohol use, NSAID: non-steroidal anti-inflamatory drugs, CAD: coronary artery disease, LVEF: left ventricular ejection fraction, TIMI: thrombolysis in myocardial infarction, INR: international normalized ratio, LAD: left anterior desending artery, Cx: circumflex coronary artery, RCA: right coronary artery, ACE/ARB: angiotensin-converting enzyme inhibitors/ angiotensin-reseptor blocker, TVR: target vessel revascularization.

Table 2. Comparison of baseline characteristics based on HAS-BLED score

Variable	HAS-BLED score				
Past medical history	**Score 0, n = 118**	**Score 1, n = 170**	**Score 2, n = 169**	**Score ≥ 3, n=131**	**p - value**
Age > 65, n (%),(years)	0 (0)	25 (15)	93 (55)	115 (88)	< 0.001
Female, n (%)	4 (3)	35 (21)	43 (25)	63 (48)	< 0.001
Diabetes mellitus, n (%)	13 (11)	32 (19)	53 (31)	50 (38)	< 0.001
Hypertension, n (%)	0 (0)	48 (28)	89 (53)	110 (84)	< 0.001
Current smoker, n (%)	42 (36)	74 (44)	37 (22)	21 (16)	< 0.001
Stroke history, n (%)	0 (0)	2 (1)	6 (4)	17 (13)	< 0.001
Hyperlipidemia, n(%)	7 (6)	15 (9)	26 (15)	24 (18)	0.006
Anemia or bleeding history, n (%)	0 (0)	81 (48)	127 (75)	127 (97)	< 0.001
Pre-usage NSAID, n (%)	0 (0)	3 (2)	2 (1)	6 (5)	0.047
Alcohol consumption, n (%)	0 (0)	0 (0)	1 (1)	2 (2)	0.244
Prior CAD, n (%)	23 (20)	38(22)	32 (19)	27 (21)	0.876
Clinical presentation					
Killip ≥ 2 n (%)	3 (3)	16 (9)	23 (14)	25 (19)	< 0.001
LVEF (%)	45.7 ± 9	44.4 ±10	43.0 ± 10	44.2 ± 8	0.130
Multi-vessel disease, n (%)	47 (40)	57 (34)	91 (54)	71 (54)	< 0.001
Final TIMI flow 0-2, n (%)	13 (11)	22 (13)	18 (11)	19 (15)	0.738
Abnormal liver function, n (%)	0 (0)	9 (5)	10 (6)	22 (17)	< 0.001
INR > 1.3, n (%)	0 (0)	1(1)	5 (3)	9 (7)	0.001
Angiographic characteristics					
Infarct related artery					0.005
LAD, n (%)	65 (55)	89 (53)	70 (41)	51 (39)	
CX, n (%)	19 (16)	26 (15)	17 (10)	15 (12)	
RCA, n (%)	29 (25)	49 (29)	74 (44)	62 (47)	
Others, n (%)	5 (4)	6 (4)	8 (5)	3 (2)	
Stent use, n (%)	117 (99)	165 (97)	161 (95)	123 (94)	0.327
DES, n (%)	11(9)	13 (8)	13 (8)	5 (4)	0.136
Stent diameter (mm)	3.5 ± 0.5	3.5 ± 0.5	3.5 ± 0.5	3.5 ± 0.6	0.567
Stent lentgh, (mm)	25 ± 12	25 ± 13	25 ± 14	25 ± 17	0.990
Tirofiban use, n (%)	57 (48)	68 (40)	82 (49)	48 (37)	0.102
Medication at discharge					
Beta-blockers, n (%)	106 (90)	154 (91)	136 (81)	98 (75)	< 0.001
ACE/ARB, n (%)	106 (90)	148 (87)	125 (74)	87 (66)	< 0.001
Statin, n (%)	97 (82)	139 (82)	133 (78)	100 (76)	0.587
Clinical outcomes					
In-hospital major bleeding, n (%)	1 (1)	8 (5)	4 (2)	5 (4)	0.259
In-hospital death, n (%)	0 (0)	4 (2)	18 (11)	12 (9)	< 0.001
Cardiac death, n (%)	1 (1)	8 (5)	23 (14)	20 (15)	< 0.001
All-cause mortality, n (%)	5 (4)	22 (13)	41 (24)	49 (37)	< 0.001
Heart failure admission, n (%)	6 (5)	10 (6)	9 (5)	11 (8)	0.658
Repeated stroke, n (%)	3 (3)	3 (2)	5 (3)	5(4)	0.745
Myocardial reinfarction, n (%)	11(9)	15(9)	18 (11)	9 (7)	0.727
TVR, n (%)	10 (9)	18 (11)	20 (12)	11(8)	0.712

HAS-BLED: Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalized ratio, Elderly, Drugs or alcohol use, NSAID: non-steroidal anti-inflamatory drugs, CAD: coronary artery disease, TIMI: thrombolysis in myocardial infarction, LVEF: left ventricular ejection fraction, INR: international normalized ratio, LAD: left anterior desending artery, Cx: circumflex coronary artery, RCA: right coronary artery, ACE/ARB: angiotensin-converting enzyme inhibitors/ angiotensin-reseptor blocker, TVR: target vessel revascularization.

Table 3. Cox regression analyses for all-cause mortality

	Univariate			Multivariate		
Variable	**HR**	**95% CI**	**p-value**	**HR**	**95% CI**	**p--value**
Age* > 65	2,24	1.55-3.23	<0.001			
Female	1,55	1.05-2.28	0.027			
Diabetes mellitus	1,66	1.14-2.43	0.009			
Hipertension*	1,26	0.88-1.81	0.211			
Stroke history*	3,14	1.77-5.60	<0.001			
NSAIDs usage	0,92	0.23-3.71	0.903			
Anemia or bleeding history*	2,39	1.58-3.61	<0.001			
Major bleeding	1,99	0.93-4.27	0.078			
Multi-vessel disease	1,68	1.17-2.43	0.005			
Killip class ≥ 2	8,43	5.77-12.37	<0.001	5,4	3.48-8.38	< 0.001
Renal impairment*	4,99	2.80-8.88	<0.001			
INR* > 1.3	3,54	1.64-7.61	0.001			
Abnormal liver function*	2,82	1.71-4.66	<0.001			
LVEF (%)	0,95	0.93-0.97	<0.001	0.96	0.94-0.98	< 0.001
B-blocker use at follow-up	0,39	0.26-0.58	<0.001	0.47	0.30-0.73	0.001
ACE/ARB use at follow-up	0,36	0.25-0.52	<0.001	0.66	0.43-1.001	0.050
HAS-BLED (continue)	1,7	1.46-1.98	<0.001	1,63	1.35-1.97	< 0.001

HR: hazard ratio, CI: confidence interval, LVEF: left ventricular ejection fraction, INR: international normalised ratio, ACE-I/ARB: angiotensin-converting enzyme inhibitors/ angiotensin-reseptor blocker, HAS-BLED: Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalized ratio, Elderly, Drugs or alcohol use.
*As these parameters are included in HAS-BLED score, they are not entered into the multivariate analysis.

Table 4. Reclassification of acute STEMI patients who died or who were alive at follow-up based on LVEF status

HAS-BLED without LVEF	**HAS-BLED with LVEF**			**Total**
	< 5 % risk	5-20 % risk	>20 % risk	
Patients who died, no.				
< 5 % risk	0	0	0	0
5-20 % risk	4	13	9	26
> 20 % risk	0	14	70	84
Total no.	4	27	79	110
Patients who were alive, no.				
< 5% risk	0	0	0	0
5-20 % risk	103	138	18	259
> 20 % risk	0	79	126	205
Total*	103	217	144	464

STEMI: st elevation myocardial infarction, HAS-BLED:Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalized ratio, Elderly, Drugs or alcohol use, LVEF: left ventricular ejection fraction.
*The total number of patients (n = 574) included in the reclassificaton analysis did not match the total study cohort (n = 588) due to missing LVEF data for 14 patients.

Discussion

The present results demonstrated HAS-BLED score and LVEF were independently associated with total mortality in STEMI patients who were undergoing primary PCI. To our best knowledge, the present study might be first to show that the combined use of HAS-BLED score and LVEF yielded a more accurate predictive value for all-cause mortality in these patients compared with the HAS-BLED score alone.

The HAS-BLED score is used to evaluate the bleeding risk and clinical outcomes for AF patients which should be taken oral anticoagulant therapy. Recent reports investigated for the prediction of clinical outcomes for the patients with/without AF undergoing PCI(8,9,20). Puurunen et al.(8) showed that the HAS-BLED score was not correlated with bleeding risk and major adverse cardiovascular events (MACE) during the follow-up period of 12 months for AF patients undergoing PCI. On the other hand, Capodanno et al.(9) found that MACEs were significantly predicted by this score for non-AF patients undergoing PCI with at 3 years of follow-up.

There were differences for patient population between our study and previous studies. We enrolled only STEMI patients undergoing PPCI with/without DES implantationin this study. However, in the scope of study, these patients were also taken into account regardless of having AF. In another study by Hsieh et al.(20), HAS-BLED score was independently associated with long-term mortality for patients having ACS without AF. The mortality risk showed an increasing tendency as the HAS-BLED score increases in their study. This outcome related to total mortality was a good agreement with our results.

This current study indicated that HAS-BLED score was based on the long-term total mortality. Many mechanisms may account the relationship between HAS-BLED score and mortality. Age parameter is one of good predictor of cardiovascular mortality in STEMI. Thus, it can be note that this parameter is the major component of several risk

scores, such as HAS-BLED, PAMI and TIMI(1,4,7). Another component of the HAS-BLEDscore was anemia, so that it might be considered another important predictor for the mortality after STEMI(10). Renal dysfunction, which is one of the components of this score used in the present study, has high prognostic value for the ACS patients(21). Numerous studies demonstrated that renal dysfunction resulted in higher mortality for ACS patients as parallel to our study(21). The prognostic importance of hepatic dysfunction for STEMI patients has been shown by Abougergi et al(22). In that study, mortality rate for theSTEMI patients with cirrhosis was higher than that of patients without cirrhosis.

The DM is another fundamental predictor of adverse cardiovascular events for the STEMI patients and this indicator was also taken part as major component in TIMI and PAMI(1,4). During the follow up period of one year, the mortality risk for the DM patients increased twofold comparing nondiabetic patients in the setting of STEMI and other ACS(23). The HT is a well known predictor of STEMI patients` mortality for in-hospital and long term(11). Cooper et al.(13) stated that previous stroke was ralated to short term mortality for the STEMI patients. All HAS-BLED score components predict the mortality for the STEMI patients, and these parameters were correlated with our results. So that, high HAS-BLED score resulted in higher incidence in terms of patients` older age, female gender, HT, anemia, previous stroke, labile INR, renal and hepatic dysfunction.

Prior studies showed a relationship between EF and poor outcomes in the setting of STEMI(24,25). The CADILLAC risk score considers EF and showed it most effective mortality predictor within seven variables included(5). Other research by Liu et al.(15) showed that LVEF was regard to major adverse cardiac events for STEMI patients. Low EF after MI was independently associated with mortality in older patients(14). In that study, an estimated of mortality was determined as 29% for the lowest EF groups (EF $\leq$ 35%). Also, a mildly reduced EF also caused an increased mortality in the related study(14). In agrement with previous studies(14,15), we found that the association between LVEF and mortality remained significant even after confounders adjustment.

Consequently, our findings might be correlated with these well-known predictors with respect to cardiovascular mortality and a reflection of multiorgan dysfunction such asrenal, hepatic, cerebrovascular, cardiovascular, hematological systems and severity of coronary artery disease for STEMI patients. Thus, these findings may explain why the adding LVEF to HAS-BLED score and will be used to predict mortality for STEMI patients undergoing PPCI.

Limitations

Some limitations of our study must be considered. Our study is single center, retrospective study which could contained selection bias. On the otherhand consecutive patients carefully included to the study. Reperfusion markers such as ST resolution or myocardial blush grade did not evaluate. Morever, LVEF wasn't measured at the same time point for all patients.

Conclusion

HAS-BLED score and LVEF are independently predictor of mortality for STEMI patients undergoing PPCI and our results support that information. In this group; combine use of LVEF and HAS-BLED score provides higher predictive value. However, our findings should be supported by further more studies.

References

1. Morrow DA, Antman EM, Charlesworth A, Cairns R, Murphy SA, de Lemos JA et al. TIMI Risk Score for ST-Elevation Myocardial Infarction: A Convenient, Bedside, Clinical Score for Risk Assessment at Presentation An Intravenous nPA for Treatment of Infarcting Myocardium Early II Trial Substudy. Circulation 2000;102(17):2031-2037.

2. Morrow DA, Antman EM, Parsons L, de Lemos JA, Cannon CP, Giugliano RP, et al. Application of the TIMI risk score for ST-elevation MI in the National Registry of Myocardial Infarction 3. JAMA 2001;286(11):1356-1359.

3. De Luca G, Suryapranata H, van't Hof AWJ, de Boer MJ, Hoorntje JC, Dambrink JH,et al. Prognostic assessment of patients with acute myocardial infarction treated with primary angioplasty: implications for early discharge. Circulation 2004;109(22):2737-2743.

4. Addala S, Grines CL, Dixon SR, Stone GW, Boura JA, Ochoa AB, et al. Predicting mortality in patients with ST-elevation myocardial infarction treated with primary percutaneous coronary intervention (PAMI risk score). The American Journal of Cardiology 2004;93(5):629-632.

5. Halkin A, Singh M, Nikolsky E, Grines CL, Tcheng JE, Garcia E, Cox DA, et al. Prediction of mortality after primary percutaneous coronary intervention for acute myocardial infarction: the CADILLAC risk score. J Am Coll Cardiol. 2005;45(9):1397-1405.

6. Granger CB, Goldberg RJ, Dabbous O, Pieper KS, Eagle KA, Cannon CP, et al. Global Registry of Acute Coronary Events Investigators. Predictors of hospital mortality in the Global Registry of Acute Coronary Events. Arch Intern Med. 2003; 163(19):2345-2355.

7. Lip GY, Frison L, Halperin JL, Lane DA. Comparative validation of a novel risk score for predicting bleeding risk in anticoagulated patients with atrial fibrillation: the HAS-BLED (Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly) score. J Am Coll Cardiol. 2011;57(2):173-180.

8. Puurunen MK, Kiviniemi T, Schlitt A, Rubboli A, Dietrich B, Karjalainen P, et al. CHADS2, CHA2DS2-VASc and HAS-BLED as predictors of outcome in patients with atrial fibrillation undergoing percutaneous coronary intervention. Thromb Res. 2014;133(4):560-566.

9. Capodanno D, Rossini R, Musumeci G, Lettieri C, Senni M, Valsecchi O, et al. Predictive accuracy of CHA2DS2-VASc and HAS-BLED scores in patients without atrial fibrillation undergoing percutaneous coronary intervention

and discharged on dual antiplatelet therapy. Int J Cardiol. 2015;199:319-325.

10. Nikolsky E, Aymong ED, Halkin A, Grines CL, Cox DA, Garcia E, Mehran R, et al. Impact of anemia in patients with acute myocardial infarction undergoing pri¬mary percutaneous coronary intervention: analysis from the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) Trial. J Am Coll Cardiol. 2004; 44(3):547-553.

11. Richards AM, Nicholls MG, Troughton RW, Lainchbury JG, Elliott J, Frampton C, et al. Antecedent hypertension and heart failure after myocardial infarction. J Am Coll Cardiol. 2002;39(7):1182-1188.

12. Romelsjö A, Allebeck P, Andréasson S, Leifman A. Alcohol, mortality and cardiovascular events in a 35 year follow-up of a nationwide representative cohort of 50,000 Swedish conscripts up to age 55. Alcohol Alcohol. 2012;47(3):322-327.

13. Cooper HA, Domanski MJ, Rosenberg Y, Norman J, Scott JH, Assmann SF, et al. Magnesium in Coronaries Trial Inv stigators. Acute ST-segment elevation myocardial infarction and prior stroke: an analysis from the Magnesium in Coronaries (MAGIC) trial. Am Heart J. 2004;148(6):1012-1019.

14. Sutton NR, Li S, Thomas L, Wang TY, de Lemos JA, Enriquez JR, Shah RU, et al. The association of left ventricular ejection fraction with clinical outcomes after myocardial infarction: Findings from the Acute Coronary Treatment and Intervention Outcomes Network (ACTION) Registry-Get With the Guidelines (GWTG) Medicare-linked database. Am Heart J. 2016;178:65-73.

15. Liu KL, Lin SM, Chang CH, Chen YC, Chu PH. Plasma angiopoietin-1 level, left ventricular ejection fraction, and multivessel disease predict development of 1-year major adverse cardiovascular events in patients with acute ST elevation myocardial infarction - a pilot study. Int J Cardiol. 2015;182:155-60.

16. Steg PG, James SK, Atar D, Badano LP, Blömstrom-Lundqvist C, Borger MA, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC). Eur Heart J. 2012;33(20):2569-2619.

17.Chesebro JH, Knatterud G, Roberts R, Borer J, Cohen LS, Dalen J, et al. Thrombolysis in Myocardial Infarction (TIMI) Trial, Phase I: a comparison between intravenous tissue plasminogen activator and intravenous streptokinase. Clinical findings through hospital discharge. Circulation 1987;76(1):142-154.

18. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics.1998;44(3):837-845.

19. Pencina MJ, D'Agostino RB Sr, Steyerberg EW. Extensions of net reclassificationimprovement calculations to measure usefulness of new biomarkers.Stat Med. 2011;30(1):11-21.

20. Hsieh MJ, Lee CH, Chen CC, Chang SH, Wang CY, Hsieh IC. Predictive performance of HAS-BLED risk score for long-term survival in patients with non-ST elevated myocardial infarction without atrial fibrillation.J Cardiol. 2017;69(1):136-143.

21. Wright RS, Reeder GS, Herzog CA, Albright RC, Williams BA, Dvorak DL,et al. Acute myocardial infarction and renaldysfunction: a high-risk combination. Ann Intern Med. 2002;137(7):563-570.

22.Abougergi MS, Karagozian R, Grace ND, Saltzman JR, Qamar AA. ST Elevation Myocardial Infarction Mortality Among Patients With Liver Cirrhosis: A Nationwide Analysis Across a Decade. J Clin Gastroenterol. 2015;49(9):778-783.

23. Piccolo R, Franzone A, Koskinas KC, Räber L, Pilgrim T, Valgimigli M, et al. Effect of Diabetes Mellitus on Frequency of Adverse Events in Patients With Acute Coronary Syndromes Undergoing Percutaneous Coronary Intervention. Am J Cardiol. 2016;118(3):345-352.

24. Ng VG, Lansky AJ, Meller S, Witzenbichler B, Guagliumi G, Peruga JZ, et al. The prognostic importance of left ventricular function in patients with ST-segment elevation myocardial infarction: the HORIZONS-AMI trial. Eur Heart J Acute Cardiovasc Care. 2014;3(1):67-77.

25. Halkin A, Stone GW, Dixon SR, Grines CL, Tcheng JE, Cox DA, et al.Impact and determinants of left ventricular function in patients undergoing primary percutaneous coronary intervention in acute myocardial infarction. Am J Cardiol. 2005;96(3):325-31.