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CORRELATION OF MAGGIC SCORE (META ANALYSIS OF GLOBAL GROUP IN CHRONIC HEART FAILURE RISK SCORE) WITH MAJOR ADVERSE CARDIAC EVENTS (MACE) IN PATIENTS WITH CHRONIC HEART FAILURE AT H. ADAM MALIK MEDAN HOSPITAL

Stefanie Tarigan*[1], Harris Hasan, Anggia C. Lubis, Zulfikri Mukhtar, T Bob Haykal & Yuke Sarastri

[1]Department of Cardiology and Vascular Medicine, Faculty of Medicine, University of North Sumatera, Medan, Indonesia

Abstract

Background: The prevalence of heart failure was raised 1-2% with many severities during the last decade. Patients with cardiovascular diseases have secondary risk of MACE. MAGGIC Score is a comprehensive risk score to predict prognosis heart failure with preserved and reduced EF.

Objective: To determine the correlation between MAGGIC score and one year MACE in patients with chronic heart failure in RSUP. H. Adam Malik Medan.

Methods: A retrospective study including 417 patients, who had hospitalized in RSUP H. Adam Malik Medan between Januari 2019-December 2019 due to chronic heart failure. The outcome of this study was one year MACE.

Results: There are correlation between MAGGIC score with the incidence of MACE, such as mortality and rehospitalization of patients with CHF (p values<0.001). MAGGIC score has a strong correlation and statistically significant with MACE that AUC defined strenght value is 0.804 and p value <0.001. The intersection of the sensitivity and specificity curves resulted a cut off point of the MAGGIC score on the incidence of MACE, which was at a score of 23.5.

Conclusion: There is a correlation between MAGGIC score and MACE, in the form of mortality and hospitalization in patients with chronic heart failure

Introduction

Major Adverse Cardiac Events (MACE) that are often studied include heart failure, non-fatal re-infarction, recurrence of angina, rehospitalization due to heart disease, recurrent PCI, CABG and mortality.[1] Heart failure is one of the major causes of cardiovascular death with vary prognoses.[2] The average heart failure mortality rate for various populations ranges from 10-40%. Estimated 10% of heart failure are >70 years old. One in six people >65 years old who come with complaints of shortness of breath already has heart failure without recognizing previous symptoms. The risk of developing heart failure at 55 years old is 33% for men and 28% for women.[3] The Acute Decompensated Heart Failure Registry (ADHERE) in five hospitals in Java and Bali, 2006, showed the average age of heart failure patients in Indonesia was around 60 years old and the mortality rate for heart failure patients in Indonesia was 6.7%, higher than Asia Pacific.[4] The prevalence of heart failure in the province of North Sumatra was found to be 26,819 people.[5]

According to the guidelines of the European Society of Cardiology (ESC) heart failure is a clinical syndrome characterized by typical symptoms of shortness of breath, pretibial edema and fatigue, signs of increased jugular venous pressure such as wet crackles and peripheral edema. Heart failure is caused by structural and functional disorders of the heart, causing a decrease in cardiac output and increase in intra cardiac pressure at rest and during activities. Abnormalities of heart valves, pericardium, endocardial heart rhythm disturbances, and cardiac conduction can also cause heart failure.[3] Smoking is a high risk factor for heart failure in Indonesia, which is 36.5%.[6]

The European Society of Cardiology (ESC) 2016 guidelines classifies heart failure based on (1)ejection fraction (i.e. preserved ejection fraction (HfpEF, mid-range ejection fraction (HfmrEF, and reduced ejection fraction (HfrEF)), (2)time (NYHA functional capacity), (3)Severity of symptoms (AHA Killip Classification) Terminology based on onset is also known as *de novo* heart failure and Acute Decompensated Heart Failure (ADHF).[3]

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The Global Group Meta-analysis score in Chronic Heart Failure (MAGGIC) is a comprehensive score that can be used to predict prognostically in patients with heart failure, both with low ejection fraction and normal.[2] There are 13 variables used in assessing the MAGGIC score, namely age, sex, systolic blood pressure, BMI, left ventricular ejection fraction, serum creatinine level, NYHA classification, diabetes, smoking, COPD, onset of heart failure <18 months, use of b- blockers, and use of ACE inhibitors/ARBs. Of the thirteen variables, a total score of 0-52 was obtained. A MAGGIC score with a value of <17 provides a low risk, while a score 33 provides a high risk with an expected three-year survival of 30%.[2] The calculation of the MAGGIC score can be done by accessing the online calculator through the website www.heartfailurerisk.org.[7] The ability of the MAGGIC score is known to show significance in predicting mortality and morbidity in patients with heart failure in Europe, Japan, and Korea.[2,7,8] The MAGGIC score is used to assess one-year mortality which is one of the variables in the MACE assessment.[7]

In this study, the authors aimed to determine the correlation between MAGGIC scores and MACE in patients with heart failure at H. Adam Malik Hospital Medan.

Methods

Research Population
This study is an analytic study conducted in a retrospective cohort. Determination of the sample was carried out by total sampling consisting of all patients with chronic heart failure who were hospitalized at H. Adam Malik Hospital Medan in the period January 2019 – December 2019 who met the inclusion criteria. All samples will be contacted to assess the outcome, which is MACE, after one year of treatment by conducting interviews during the study period carried out in November 2020 - December 2020. The inclusion criteria were age >18 years old, diagnosed with chronic heart failure who was hospitalized in 2019, complete medical records, and can be interviewed by telephone or face to face.

The study involved 730 patients with chronic heart failure and as many as 417 patients met the inclusion criteria. Patients with incomplete medical records, congenital heart defects, valve structural abnormalities, genetic disorders, died during the treatment period, and could not be connected/interviewed, were excluded from the study subjects.

MAGGIC Score and Major Adverse Cardiac Event (MACE) Assessment
The MAGGIC score will be calculated based on data taken from medical records when the patient was treated, there are laboratory data, ECG, and echocardiography. Outcomes after 1 year, MACE, on research subjects were obtained from interviews via telephone or face-to-face with patients or patients' families who could be connected.

Statistical analysis
Data were analyzed using the SPSS version 23 program. The correlation between MAGGIC scores and patients experiencing MACE would be analyzed by bivariate test with comparison of numerical data tested by independent-T test or Mann Whitney. Variables with categorical data were tested by Chi-square test. Then to assess the correlation of each variable with the incidence of MACE using logistic regression analysis (odds ratio (OR) and 95% confidence interval (CI). To find out the cut-off value of the MAGGIC score on the incidence of MACE, an analysis was carried out using the Receiver Operating Characteristic (ROC) curve, and it will be presented in the form of AUC (95%).

Results and Discussion

Characteristics of Research Subjects
From 417 subjects, 184 patients (44.1%) experienced a major adverse cardiac event (MACE) and rehospitalization was the most MACE (102 patients; 24.5%), followed by death (44 patients; 10.6%). Patients with chronic heart failure in this study were dominated by male than female, with ratio of 3:1. Of all types of heart failure, mostly experienced HFrEF as many as 104 patients (58.1%). There was statistically significant difference between the types of heart failure and the incidence of MACE.

From the results of the analysis, there was a significant correlation between diastolic blood pressure, heart rate, haemoglobin, haematocrit, sodium, urea, and creatinine levels on the incidence of MACE (p<0.05), where the

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median levels of haemoglobin, haematocrit, and sodium in patients experiencing MACE were lower and the median levels of urea and creatinine were higher than patient without MACE. Based on the ECG examination, QRS duration was statistically significantly related to the incidence of MACE with p value = 0.002. Analysis of heart failure classification based on NYHA category found the most patients in NYHA class II, namely 177 patients (42.4%), NYHA class III 174 patients (41.7%), and NYHA class IV 66 patients (15.8%) . The highest proportion who experienced MACE was found in patients with NYHA class IV 43 people (65.2%; p<0.05). The basic characteristics of the research subjects are presented in table 1.

Table 4.1. Characteristics of Research Subjects

Parameter	Total (n=417)	MACE		P value
		Yes (n=184)	No (n=233)	
Age, year	59 (39-87)	59 (42-87)	59 (39-87)	0,619
Sex				
Man	303 (72,7)	134 (44,2)	169 (55,8)	0,947
Woman	114 (27,3)	50 (43,9)	64 (56,1)	
MAGGIC score				
Mortality	373 (89,4)	31,5 (13-41)	22 (7-36)	<0,001
Rehospitalization	315 (75,5)	26 (13-36)	21 (7-41)	<0,001
Ejection Fraction				
HfpEF	158 (37,9)	52 (32,9)	106 (67,1)	<0,001
HFmrEF	80 (19,2)	28 (35,0)	52 (65,0)	
HFrEF	179 (42,9)	104 (58,1)	75 (41,9)	
Smoking	154 (36,9)	61 (39,6)	93 (60,4)	0,155
Dyslipidemia	117 (28,1)	47 (40,2)	70 (59,8)	0,310
Diabetes Melitus	186 (44,6)	92 (49,5)	94 (50,5)	0,049
Hypertension	267 (64,0)	124 (46,4)	143 (53,6)	0,204
CAD	259 (62,1)	104 (40,2)	155 (59,8)	0,037
Pneumonia	37 (8,9)	16 (43,2)	21 (56,8)	0,910
COPD	26 (6,2)	19 (73,1)	7 (26,9)	0,002
CKD	50 (12,0)	38 (76,0)	12 (24,0)	<0,001
ACE	161 (38,6)	76 (47,2)	85 (52,8)	0,315
ARB	149 (35,7)	73 (49,0)	76 (51,0)	0,135
Diuretic	316 (75,8)	143 (45,3)	173 (54,7)	0,412
Beta-bloker	301 (72,2)	132 (43,9)	169 (56,1)	0,858
BSA	1,75 (1,29-17)	1,73(1,29-17,0)	1,77 (1,37-2,24)	0,003
TDS	120 (60-220)	110 (80-200)	120 (60-220)	0,102
TDD	80 (40-140)	70 (44-140)	80 (40-120)	0,046
HR	86 (40-170)	86 (46-170)	84 (40-170)	0,038
Hb	13 (3,5-18,3)	12,4 (6,70-18,3)	13,1 (3,4-18,3)	<0,001
Ht	40 (12-100)	39 (18-100)	42 (12-100)	<0,001
Na	134 (111-150)	134 (111-150)	135 (111-148)	0,047
K	4,1 (1,95-46)	4,1 (1,95-6,5)	4,1 (2,6-46)	0,603
Cl	101 (9,7-195)	101 (80-195)	102 (9,7-195)	0,136
Ur	45 (13-392)	51 (17-392)	34 (13-218)	0,001
Cr	1,27(0,55-10,05)	1,48(0,60-10,05)	1,05 (0,55-7,54)	<0,001
QRS duration	*0,08 (0,06-0,68)*	0,08(0,06-0,68)	0,08 (0,06-0,16)	0,002
NYHA				
I	0 (0,0)	0 (0,0)	0 (0,0)	<0,001
II	177 (42,4)	61 (34,5)	116 (65,5)	
III	174 (41,7)	80 (46,0)	94 (54,0)	
IV	66 (15,8)	43 (65,2)	23 (34,8)	

The MAGGIC score in patients with chronic heart failure in this study had a median score of 23, with the median MAGGIC score of patients experiencing MACE 27 (7-41) higher than the median MAGGIC score for patients not experiencing MACE 19 (8-35). There were significant correlation between MAGGIC scores and the incidence of mortality and rehospitalization with p-values <0.001 each (table 4.1).

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From the echocardiographic examination data, it was found that the median LVEDD 51 (30-72) and LVEDS 38 (7-62) of patients who experienced MACE were higher than the median LVEDD 48 (15-78) and LVEDS 36 (17-62) of patients who did not experience MACE. On the other hand, the median EF score of patients with MACE was 35.5 (15-70) lower than those without MACE 45 (15-70) (p<0.05) (Table 4.2).

Table 4.2 Echocardiographic Characteristics of Research Subjects

Parameter	Total (n=417)	MACE Yes (n=184)	MACE No (n=233)	P value
IVSD	11 (4-22)	11 (4-21)	11 (4-22)	0,490
IVSS	12 (5-24)	12 (5-24)	12 (5-23)	0,175
LVPWD	11 (5,9-22)	11 (5,9-22)	12 (6-22)	0,182
LVEDD	50 (15-78)	51 (30-72)	48 (15-78)	0,007
LVEDS	36 (7-62)	38 (7-62)	36 (17-62)	0,026
EF	44 (15-70)	35,5 (15-70)	45 (15-70)	<0,001
E	6 (0,8-93)	6,5 (0,80-13)	6 (0,80-93)	0,113
A	6 (0,5-78)	6 (0,5-24)	6,3 (0,50-78)	0,510
E/A	1,08 (0,3-7,4)	1,1 (0,3-7,4)	1,08 (0,40-5,0)	0,198
E Septal	6 (2-17)	6 (2-17)	6,0 (3-10)	0,112
E Lateral	8 (3-16)	8 (3-16)	8 (3-13)	0,056
TAPSE	19 (10-28)	19 (10-26)	19 (11-28)	0,015
RAP		8 (5-15)	8 (3-15)	0,144

Analysis of MACE Risk Factors in Chronic Heart Failure Patients

The results of the multivariate logistic regression test on predictors of MACE events in patients with chronic heart failure are shown in Table 4.3. The HR variable had an OR of 1.015 (95% CI 1.003-1.028; p value = 0.012), a history of CKD had an OR of 2.905 (95% CI 1.205 – 7.004; p value = 0.018), and the MAGGIC score had an OR of 1.208 (95% CI 0.788 – 0.956; p value <0.001), meaning that every increase in the MAGGIC score in patients with chronic heart failure will be at risk for CVM. This research is in line with Daniel et al in 2018, which compared the MAGGIC score and 3HC score.[9] Ejection fraction is one of MAGGIC score variable that has constant mortality risk if the ejection fraction above 40%. The interaction of ejection fraction and age will increase in mortality by 4% every 10 years.[2] Interaction of ejection fraction and systolic blood pressure will increase the mortality rate by 1.2% for every 10 mmHg increase in systolic blood pressure. MAGGIC scores were associated with Major Adverse Cardiac Events in patients with chronic heart failure, there is a significant correlation with major cardiovascular event mortality and rehospitalization.[2]

Table 4.3 Multivariate Analysis of MVC Risk Factors in Patients with Chronic Heart Failure

Variables	Coefisien	P value	OR	CI 95% (Min-max)
HR	0,015	0,012	1,015	1,003 –1,028
Cl	-0,017	0,039	0,983	0,983 – 0,999
TAPSE	-0,142	0,004	0,868	0,788 – 0,956
MAGGIC score	0,189	<0,001	1,208	1,150 – 1,270
Smoking (Yes vs No)	-0,679	0,022	0,507	0,284 – 0,906
CKD (Yes vs No)	1,066	0,018	2,905	1,205 – 7,004
RAP	-0,105	0,036	0,900	0,816 – 0,993
Constanta	-2,741			

MAGGIC score cut-off predict MACE

ROC analysis was performed to obtain the cut-off point of MAGGIC score which can estimate the incidence of MACE in patients with chronic heart failure. The MAGGIC score had a strong correlation with the incidence of MACE (AUC 0.804; p<0.001) and MACE mortality (AUC 0.883; p<0.001) (Table 4.4). The intersection of the sensitivity and specificity curves resulted the cut-off point of the MAGGIC score for the incidence of MACE, which was at a score of 23.5. It means that if a patient has a MAGGIC score of 23.5 then the patient can experience

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a major adverse cardiac event (MACE). The score had a sensitivity of 71.2% and a specificity of 75.1% (Figure 4.1).

In previous research in Argentina, the cutoff point was 23.[9] Measurement of biomarkers such as B type Natriuretic Peptide (BNP) has important prognostic value in patient management. In Japan, there is a modification in MAGGIC Score by adding BNP value. The MAGGIC Score is known to be predictor of one year mortality in patients with heart failure, while the addition of BNP value will increase the effectiveness of MAGGIC score for predicting mortality.[10]

Table 4.4. MAGGIC Score ROC Curve in Predicting MACE in Chronic Heart Failure Patients

ROC Curve of MAGGIC-MACE	AUC (CI 95%), p value
Diagonal segments are produced by ties.	0,804 (CI 95% 0,762-0,846; p<0,001) *Cut off point* skor: 23,5 Sensitivity : 71,2 Specificity : 75,1
ROC Curve of MAGGIC-Mortality	
Diagonal segments are produced by ties.	0,883 (CI 95% 0,823-0,944; p<0,001) *Cut off point* skor: 27,5 Sensitivity : 84,1% Specificity :84.5%
ROC Curve of MAGGIC-Rehospitalization	

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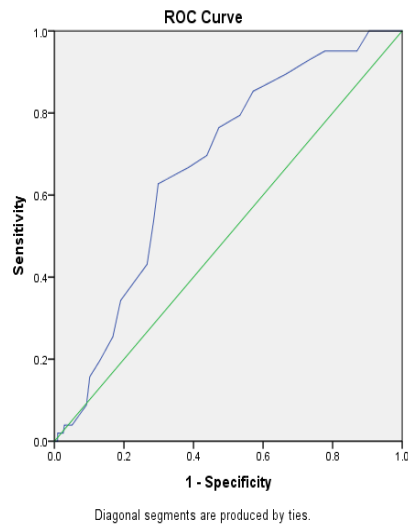
0,670 (CI 95% 0,615-0,726; p<0,001)
Cut off point skor: 23,5
Sensitivity :66,7%
Specificity :61,6%
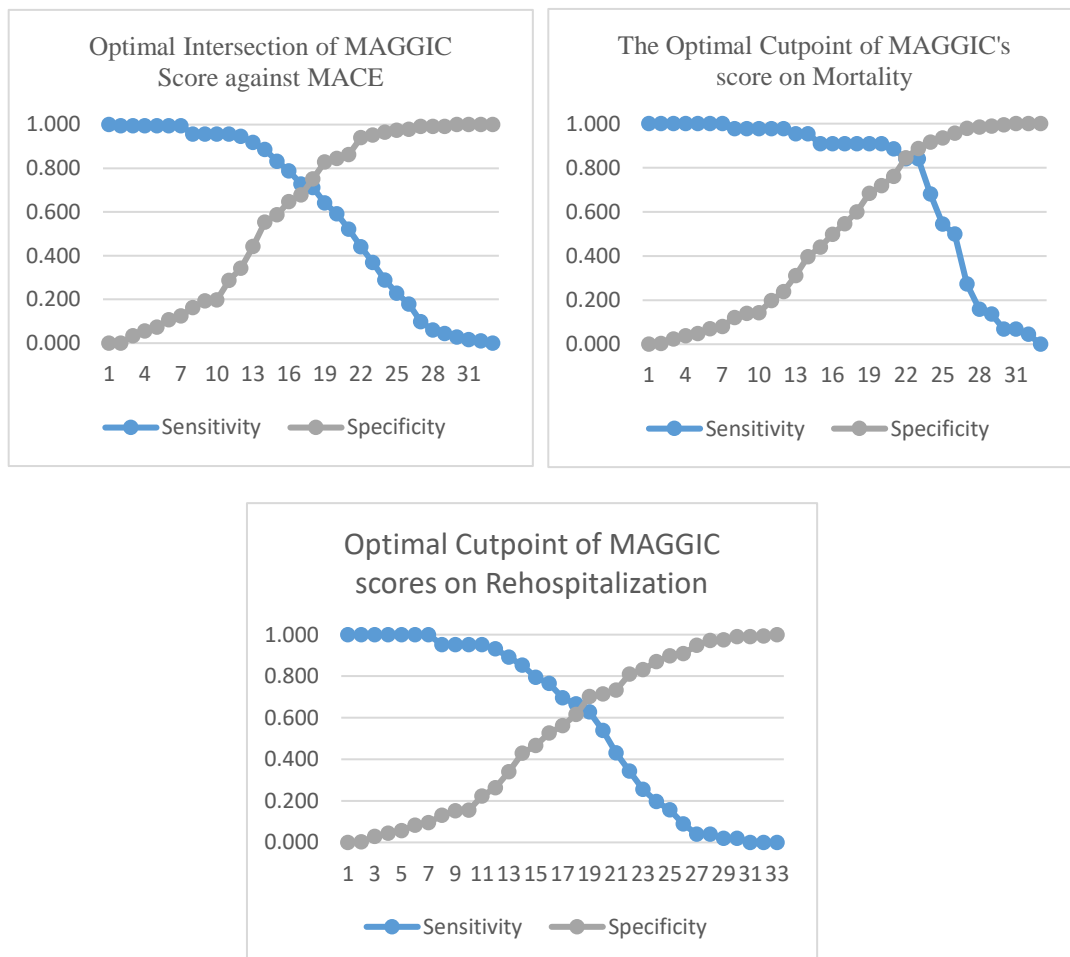
Picture 4. 1 Optimal Cut-off Point of MAGGIC score against : (a) VFD Incidence, (b) Mortality Incidence, and (c) Rehospitalization Incidence

Conclusion

There was a significant correlation between MAGGIC scores and major adverse cardiac events (MACE) in the form of mortality and hospitalization in patients with chronic heart failure (p value <0.001). The median MAGGIC score in patients with MACE was higher than those without (p value < 0.001).

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The MAGGIC Score has an OR of 1.208 (95% CI 0.788 – 0.956; p value < 0.001), meaning that every increase in the MAGGIC SCORE in patients with chronic heart failure will be at risk for MACE. In this study, the cut-off point for the MAGGIC score for MACE was 23.5. The cutoff point for the MAGGIC score on mortality was 27.5 and rehospitalization was 23.5.

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