



## Comparison Between Door to Wire Time and Grace Score to Predict Major Adverse Cardiovascular Event in ST Segment Elevation Myocardial Infarction

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### ABSTRACT

**Background:** Primary percutaneous coronary intervention (PPCI) is the mainstay of treatment for ST segment elevation acute myocardial infarction (STEMI) patients. Delays in terms of Door to Wire will affect the outcome of STEMI, one of which is MACE. Risk stratification screening with Global Registry of Acute Coronary Event (GRACE) scores is important to assess Major Cardiovascular Events (MACE) in STEMI patients. The purpose of this study was to assess the correlation of Door to Wire time and GRACE score with MACE in STEMI patients, especially in Manado, North Sulawesi.

**Methods:** This study is an observational study, using a cohort design, data were collected from medical records for analysis.

**Results:** A total of 218 STEMI patients who underwent PPCI contributed to this study. Correlation analysis using all cases did not show a correlation between Door to Wire time and GRACE scores, but in a subpopulation analysis with Door to Wire time of up to 600 minutes (10 hours) found a weak but significant positive correlation ( $r = 0.26$ ;  $p < 0.001$ ), which changed to a moderately positive relationship in the subgroup without MACE ( $r = 0.56$ ;  $p < 0.001$ ). A stronger correlation was seen in the analysis involving only samples with GRACE scores  $\leq 154$  and still limiting the Door to Wire time to 600 minutes. The Correlation disappeared again after the analysis was further reduced to cases with a GRACE score  $\leq 125$  even though a significant correlation was still seen in the subgroup without MACE ( $r = 0.43$ ;  $p = 0.034$ ). The optimal cut-off point for the GRACE score was obtained at a value of 127, where the sensitivity, specificity and accuracy of MACE predictions are around 86%, 75%, and 84%, respectively. For Door to Wire time, the optimal point is around 179.5 minutes where the sensitivity, specificity and accuracy of MACE predictions are around 69%, 56%, and 67%, respectively.

**Conclusion:** The GRACE score is superior to Door to Wire for predicting MACE in STEMI patients.

### Introduction

ST Segment Elevation Acute Myocardial Infarction (STEMI) is a medical emergency where there is sudden occlusion of a coronary artery causing ischemia and necrosis of cardiac tissue. Based on data from the European STEMI Registry in Sweden in 2015 it was found that the incidence of STEMI was 58 per 100,000 population per year, while in other European countries the incidence of STEMI was reported to range from 43 to 144 per 100,000 population per year<sup>1</sup>. In America, there was a decrease in incidence from 133 per 100,000 in 1999 to 50 per 100,000 in 2008<sup>2</sup>. Research conducted by Dharma S et al (Jakarta Acute Coronary Syndrome Registry) in Indonesia in the period October 2014-July 2015 obtained data for Acute Coronary Syndrome (ACS) as many as 3015 cases and 1024 of them were cases of

STEMI.<sup>3</sup> Reperfusion therapy is the mainstay of treatment for STEMI, most effective if given early. Primary percutaneous coronary intervention (PPCI) is the preferred reperfusion option for STEMI<sup>4-6</sup>. Door to wire time refers to calculating the time interval from the patient's arrival at the hospital for STEMI to the time of crossing wire with the aim of reopening the blocked artery. Reduction of this delay can shorten total ischemic time and is considered an important strategy to reduce the risk of permanent myocardial damage that affects patient outcome and mortality<sup>7</sup>. Studies on Door to Wire time are still very limited, generally assessing door to balloon time as conducted by Long Li et al, showed data that among Asian countries only Taiwan, Singapore and Israel had a door to balloon time of  $< 90$  minutes<sup>8</sup>. In Indonesia, it is difficult to achieve a door to balloon time

of < 90 minutes. Based on research by Dharma S et al (Jakarta Acute Coronary Syndrome Registry) in the period 2008-2009 the median door to balloon time was 94 minutes and the hospital mortality rate was 9.6%. After the introduction of a system called the Regional STEMI Network in 2010, in the 2015-2016 period, the median door to balloon time decreased to 82 minutes and the hospital mortality rate was 7.1%<sup>9</sup>. Interestingly, in a study conducted by Kim HK et al, in Korea for 4 years from 2008-2011, involving 8040 patients undergoing PPCI, data showed that although there was an improvement in door-to-balloon time, there was no parallel decrease in total ischemic time and observed mortality rates.<sup>10</sup> Risk stratification screening is important to guide the management of STEMI cases. One way of risk stratification is by assessing the Global Registry of Acute Coronary Event (GRACE) scores which are easy to apply and have advantages over other risk scores.<sup>11</sup> An initial study on the GRACE score was initiated in 1999 involving 123 hospitals in 14 countries. countries in North America, South America, Europe, Australia and New Zealand followed by a study in 154 hospitals in Europe, North America, South America, China, Australia<sup>11</sup>. D'Ascenzo et al, who conducted a meta-analysis of TIMI, GRACE and other alternative risk scores in Acute Coronary Syndrome, consisting of 40 derivation studies and 42 validation studies. In STEMI patients, 15 derivation studies and 22 validation studies were performed, the data showed that the Area Under Curve (AUC) for TIMI was 0.77 (95% CI = 0.71-0.83) in short-term and long-term outcomes, while the GRACE score was 0.82 (95% CI=0.81-0.83) at short-term outcome and 0.81 (95% CI=0.81-0.83)<sup>12</sup>. Major Cardiovascular Events are a composite of clinical events and are generally used as clinical outcomes in cardiovascular research<sup>13</sup>. Door to Wire time data as well as the GRACE score on MACE in IMAEST patients in Indonesia is still very lacking so the authors are interested in examining the relationship between Door to Wire time delay and GRACE scores on MACE in IMAEST patients, especially at Prof. Dr. RD Kandou Hospital, Manado, North Sulawesi.

**Methods**

This research is an observational study where data collection uses a retrospective cohort design. STEMI patients whose data was recorded during their stay at the study hospital formed a cohort of research subjects. Medical Records containing information on these patients from hospital admission until 6 months after discharged were evaluated retrospectively. Demographic information, medical history, physical examination and complete blood count at admission, relevant clinical and angiographic data (including Door to Wire time and GRACE risk score) and presence or absence of Major Cardiovascular Events during the treatment period were collected from medical records for analysis. For mortality predictions in hospitals, patients with GRACE risk scores ≤ 108 were considered to have a low risk (mortality risk < 1 %), while patients with GRACE risk scores of 109 - 140 and >140 respectively had an intermediate (1-3%) and

high mortality risk (> 3 %). For mortality predictions within 6 months after discharged, patients with GRACE risk scores of < 88 were considered to have a low risk (mortality risk < 3 %), while patients with GRACE risk scores of 89-118 and > 118 respectively had a medium (3-8%) and high (>8%) mortality risk<sup>16</sup>. Central General Hospital. Dr. R.D. Kandou Manado. Retrieval of information from Medical Records began after the researcher obtained approval from the Ethics Committee of the Manado Hospital. According to the planned time allocation, sample selection and research data collection took place over a full three months or until the minimum samples required for analysis was reached. The data time period is from January 1, 2017 to December 31, 2020.

**Study Population**

STEMI patients undergoing PPCI in the Heart and Blood Vessel Disease Section of the Manado Hospital are the target population in the study. The diagnosis of STEMI is based on the presence of typical angina symptoms for more than 20 minutes, persistent ST segment elevation in two adjacent leads on the ECG and an increase or decrease in cardiac biomarker values, especially high sensitivity cardiac troponin where at least one of them is above the 99th percentile threshold value. Samples were selected for those whose medical records were available from the Manado Hospital database and met the study criteria. Retrospective patient recruitment was carried out until the minimum sample size was reached. Inclusion criteria include:

- a. Patients with a diagnosis of STEMI
- b. Performed reperfusion therapy with PPCI

Those who met the inclusion criteria were forced to be excluded from the list of candidate study sample if it has at least one of the following conditions:

- a. Using a pacemaker
- b. Have a history of bypass surgery
- c. Information for calculating GRACE scores or door to wire times is not available
- d. The presence or absence of a major cardiovascular event cannot be determined

The basis for calculating the minimum sample size in this study is to see the relationship between door to balloon time and the GRACE score on major cardiovascular events. To simplify calculations, only values for the GRACE score (on a numerical scale) for which sufficient data are available in the literature are used in determining the sample size. In this case, the number of n1 patients needed is: 14,15

$$n_1 = 4\sigma^2 \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2}{\Delta^2}$$

where for the two-way test and the level of significance 5% then  $Z_{1-\alpha/2} = 1.96$  while for power  $1-\beta = 90\%$  large  $Z_{1-\beta} = 1.28$ . As for 2 in the context of this study is the variance of the GRACE score in patients with major cardiovascular events. The literature mentions the value of between 45.9 and 69.149 if the value of 2 is taken as

69 while or the difference in the mean GRACE score of patients with and without major cardiovascular events is set at 45 for a meaningful result, both follow the literature mentioned above, then large the sample required at the bivariate level is at least:

$$n_1 = 4(69)^2 \frac{(1.96+1.28)^2}{45^2} =$$

98,8 or 99 patients after rounding up

In multivariate analysis, this study was prepared to analyze data where the partial correlation coefficient R2 between the independent variables is a maximum of 0.20. That is, the required sample size approximately 124 STEMI patients after rounding up.

**Definition and Endpoints**

Complete PPCI is defined as complete revascularization strategy in patients being treated with PPCI who have multivessel disease presenting with STEMI.

Major Adverse Cardiovascular Events is the presence of cardiovascular complications during the treatment period since the time of the first hospitalized until 6 months after discharged, such as mortality (both cardiovascular and non-cardiovascular), cardiogenic shock, major arrhythmias, heart failure, recurrent infarction, rehospitalization for causes related to cardiovascular disease, recurrent PCI and stroke<sup>13</sup>.

GRACE Score is the Assessment of patient's risk of morbidity and mortality based on age, systolic blood pressure, heart rate, creatinine level, KILLIP classification of heart failure, presence or absence of cardiac arrest during hospitalization, cardiac enzyme levels, and ST segment deviation<sup>16</sup>.

Door to Wire time is the time interval between an arrival in hospital and when the balloon is inflated to open a blocked artery, in minutes<sup>4</sup>.

**Statistical Analysis**

Descriptive analysis to see the distribution of research variables was carried out univariate or bivariate. Univariate analysis includes an assessment of the distribution of each variable, including the normality of the numerical variables. This evaluation was carried out using graphs such as histograms, boxplots, and density curves, in addition to the Shapiro Wilk normality test. For categorical variables, distribution assessment is carried out through a frequency table. For numerical variables with a normal distribution, values are given in terms of the mean and standard deviation (SD). If a distribution abnormality can be proven, the median and interquartile range (IQR) values are given instead.

For categorical variables, the value of the proportion is displayed on each. The differences in each variable according to gender (or other variables determined later) are then given and tested using the t test or Mann-Whitney U for numerical variables and the chi-square test or Fisher's Exact for categorical variables. The ability to

discriminate risk of major cardiovascular events from door to balloon time and GRACE score was evaluated using a receiver operating characteristics (ROC) curve in which sensitivity, specificity, accuracy, and positive and negative predictive values were measured for each variable. The area under the curve (AUC) is expressed as the c statistic along with a 95% confidence interval. Comparison of AUC for GRACE scores and door-to-balloon time was performed using the DeLong method which takes into account the dependencies due to measurements in the same patient. Cox regression analysis was then used to determine the independent relationship between door to wire time and GRACE score on the risk of major cardiovascular events. Univariate and multivariate models were used to see whether there was a confounding effect from other variables in the data. The results of the regression analysis are shown as the estimated value of relative risk (RR), 95% confidence interval, and p value < 0.05<sup>14,15</sup>.

**Results**

**Patient Characteristics, Presentation**

A total of 218 STEMI patients who had PPCI treatment contributed to the data in this study. Table 1 shows that male sufferers dominate the study subjects (83%). The patients were, on average, slightly under 60 years old (SD 10.3 years). Most of the patients had comorbid hypertension (72%), while dyslipidemia was found in almost half of the cases (41%) and a history of diabetes in about a quarter of cases in the study (27%), while patients who were current or past smokers accounted for 22% of the whole case. In characteristics involving routine blood tests, the median values of the variables were generally still within normal limits, except for the leukocyte level which showed a tendency to leukocytosis. Renal function markers such as urea and creatinine do not indicate a problem. Meanwhile, lipid profiles such as total cholesterol, HDL, LDL, and triglyceride levels were still within normal limits. Three quarters of cases had a GRACE score between 128 and 157 at CVCU admission, with a median score of 143. According to the conventional division of risk of death for STEMI cases, more than 75% of patients were in the moderate (score 126-154) and high (score > 154) risk groups. The median door to wire time is 210 minutes (three hours) with a distribution between quartiles between 161 and 282 minutes. The median infarct onset and total ischemic time are approximately 7 and 11 hours, respectively. Half of the patients underwent complete PPCI. The length of stay of patients at the CVCU is about 3 days, as is the median period of treatment in the usual care room. The majority (83%) patients experienced MACE while in hospital, with the most types of events being congestive heart failure (62%) and arrhythmias (13%). A total of 13 (6%) patients died during hospitalization. More than half (58%) of patients had rehospitalization within six months, and three patients (1%) were found to have died during this period. A total of 58% of patients had rehospitalization within six months, and three patients (1%) were found to have died during this period.

**Table 1.** Patients Characteristics

Characteristic	Mean ± SD	Median (Q1; Q3)	n (%)
Age	57,2± 10,3		
Sex			
Male			182 (83)
Female			36 (17)
Smoker			49 (22)
Diabetes Mellitus			58 (27)
Hypertension			57 (27)
Dyslipidemia			89 (41)
<i>Blood Laboratory</i>			
Haemoglobin (g/dL)	14,3(13,2 - 15,4)		
Leucosit (×10 <sup>3</sup> /μL)	12,4(10,4 - 15,1)		
Trombosit (×10 <sup>3</sup> /μL)	235,0(196,0 - 280,0)		
Eritrosit (×10 <sup>6</sup> /μL)	4,8(4,5 - 5,1)		
Haematokrit (/dL)	41,8(39,0 - 45,0)		
HbA1C (%)	5,9(5,5 - 8,1)		
Ureum (mg/dL)	30,0(23,0 - 40,0)		
Creatinin (mg/dL)	1,0(0,9 - 1,3)		
Cholesterol (mg/dL)	172,0(148,0 - 208,0)		
HDL (mg/dL)	37,0(33,0 - 44,0)		
LDL (mg/dL)	111,0(91,0 - 143,5)		
Trigliserida (mg/dL)	126,0(90,0 - 150,5)		
Patients Care in Cardiovascular Care Unit (CVCU)			
GRACE Score	143,0 (128,0 - 157,0)		
125 ≤			49 (22)
126-154			103 (47)
> 154			66 (30)
Door to Wire time (minute)	210,0 (161,0 - 281,8)		
Onset of Infarction (hour)	6,8 (4,0 - 10,0)		
Total Iskemik Time(hour)	10,6 (7,9 - 15,2)		
Complete PPCI			106 (49)
Length of Stay			
CVCU (day)	3,0 ( 2,0 - 4,0)		
Regular Ward (day)	3,0 ( 3,0 - 4,0)		
<i>Major Adverse Cardiovascular Event (MACE) at hospital</i>			
Total Patient			182(83)
CHF			135(62)
Aritmia			61(28)
Cardiogenic Shock			10(5)
Acute Lung Oedema			8(4)
All Cause Death			13(6)
<i>Major Adverse Cardiovascular Event (MACE) MACE in 6 month</i>			
Rehospitalized			121 (58)
All Cause Death			3 (1)

Correlation analysis using all cases did not show any relationship between Door to Wire time and GRACE score (Figure 1. (I)), but in subpopulation analysis with Door to Wire time of up to 600 minutes (10 hours) a weak but significant positive relationship was found (r = 0.26; p < 0.001), which turned into a moderately positive relationship in the subgroup without MACE (r = 0.56; p < 0.001) (Fig. 1. (II)). A stronger correlation was seen in the analysis involving only samples with GRACE scores classified as mild and moderate risk of STEMI mortality (≤ 154) and still limiting the Door to Wire time to 600 minutes (Figure 1. (III)). On the other hand, the relationship between Door to Wire time variability and GRACE scores disappeared again after the analysis was further reduced to cases with a GRACE score 125 (mild STEMI mortality risk) even though a significant correlation was still seen in the subgroup without MACE (r

= 0.43; p = 0.034) (Figure 1. (IV)). The results of this correlation analysis will be used as a consideration in regression modeling<sup>17-19</sup>. The results of the evaluation of the receiver operating characteristics (ROC) curve of the ability of the two main research variables, namely Door to Wire time and GRACE score, to predict MACE are shown in Figure 2, the GRACE score seems to have a clear advantage with an area under the curve (AUC) 86%, while at the time of Door to Wire its AUC was only around 63%. The difference between the two curves was significant in the DeLong test (p < 0.001).<sup>17-19</sup> The optimal cut off point for the GRACE score was obtained at a value of 127. At that point, the sensitivity of the GRACE score for the prediction of MACE was about 86% with a specificity of 75% and an accuracy of 84%. For Door to Wire time, the optimal point is around 179.5 minutes where the sensitivity, specificity and accuracy of MACE predictions are around 69%, 56%, and 67%, respectively. In all models, only the GRACE score showed a significant relationship with MACE. The relative risk is almost the same regardless of the model used, which is around two. For example, for all cases, STEMI patients with a GRACE score above 127 had a 1.93 fold (95% CI 1.27 to 2.92; p = 0.002) times greater risk of MACE than those with a lower GRACE score. After controlling for Door to Wire time variability, the relative risk was 1.98 (95% CI 1.27 to 3.09; p = 0.003). Quite the opposite was found at the time of Door to Wire. Even in models where the previous correlation analysis (Figure 1) shows a significant relationship between this variable and the GRACE score, the effect of Door to Wire time remains insignificant even though the GRACE score in the same model shows a significant effect<sup>17-19</sup>.

**Table 2.** The Relative Risk of Major Adverse Cardiovascular Event according to Door to Wire time and GRACE Score

	Univariat Model	Multivariat Model
Variable	RR (95% CI) p	RR (95% CI)p
Door to Wire time ≥ 180m	1,20 (0,88 ; 1,65) 0,247	1,04 (0,74 ; 1,45) 0,824
GRACE Score > 127		
Model 2: Door to Wire Time ≤ 600m		
Door to Wire time ≥180m	1,20 (0,87 ; 1,65) 0,265	1,03 (0,74 ; 1,45) 0,848
GRACE Score > 127	1,92 (1,26 ; 2,94) 0,003	1,98 (1,25 ; 3,13) 0,003
Model 3: Door to Wire ≤ 600m dan GRACE Score ≤ 154		
Door to Wire Time ≥180m	1,16 (0,80 ; 1,70) 0,436	1,00 (0,67 ; 1,49) 1,000
Skor GRACE > 127	1,87 (1,20 ; 2,92) 0,006	1,95 (1,21 ; 3,14) 0,006

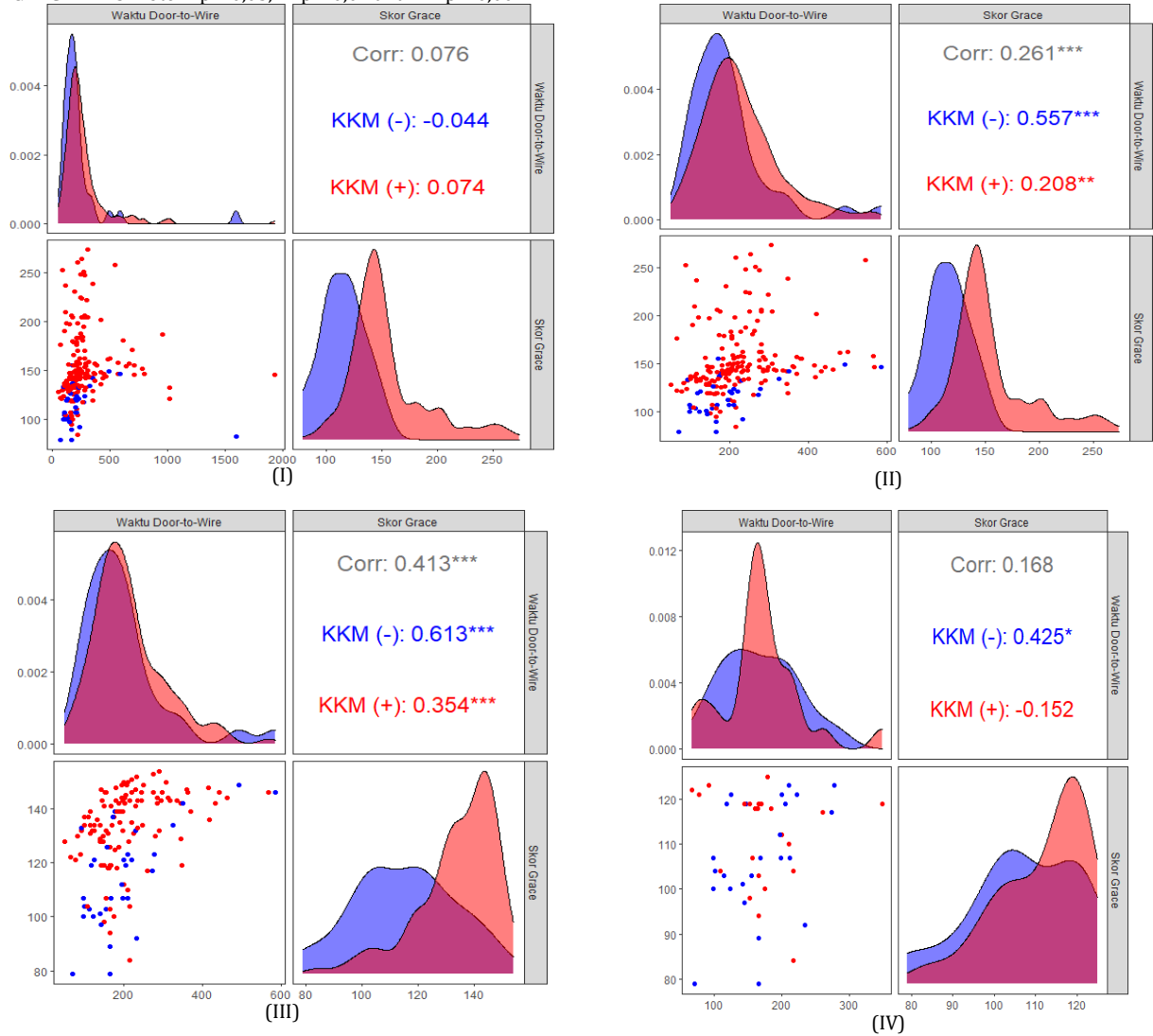
**Discussion**

A number of Poisson regression models were used to assess the relative risk of MACE during hospitalization based on variations in Door to Wire time and GRACE scores. These models were developed from the results of the correlation analysis between Door to Wire time and the previously mentioned GRACE score. In addition, the two predictor variables were converted into binary categories using the results of the ROC curve analysis. This is seen as more helpful in interpreting the results when compared to the use of the original units of the two

variables<sup>17-19</sup>. Correlation analysis using all cases showed no correlation between Door to Wire time and GRACE scores (Figure 1(I)). However, in the analysis of subpopulations with a Door to Wire time of up to 600 minutes (10 hours) a weak but significant positive correlation was found ( $r = 0.26$ ;  $p < 0.001$ ), which turned into a moderate positive correlation in the subgroup without MACE ( $r = 0.56$ ;  $p < 0.001$ ) (Figure 1(II)). A stronger correlation was seen in the analysis involving

only samples with GRACE scores classified as mild and moderate STEMI mortality risk ( $\leq 154$ ) and still limiting the Door to Wire time to 600 minutes (Figure 1(III)). On the other hand, the correlation of Door to Wire time and GRACE scores disappeared again after the analysis was further reduced to cases with a GRACE score  $\leq 125$  (mild STEMI mortality risk) although a significant correlation was still seen in the subgroup without MACE ( $r = 0.43$ ;  $p = 0.034$ ) (Figure 1(IV)).

**Figure 1.** Scatterplot matrix of the correlation between Door to Wire time and Skor GRACE stratified according to presence or absence of Major Adverse Cardiovascular Event (MACE) during hospitalization: (I) All data, (II) Door to Wire time  $\leq 600$  minute, (III) GRACE score  $\leq 154$  nor (IV) Skor GRACE  $\leq 125$ . Note: \*  $p < 0,05$ , \*\*  $p < 0,01$  and \*\*\*  $p < 0,001$



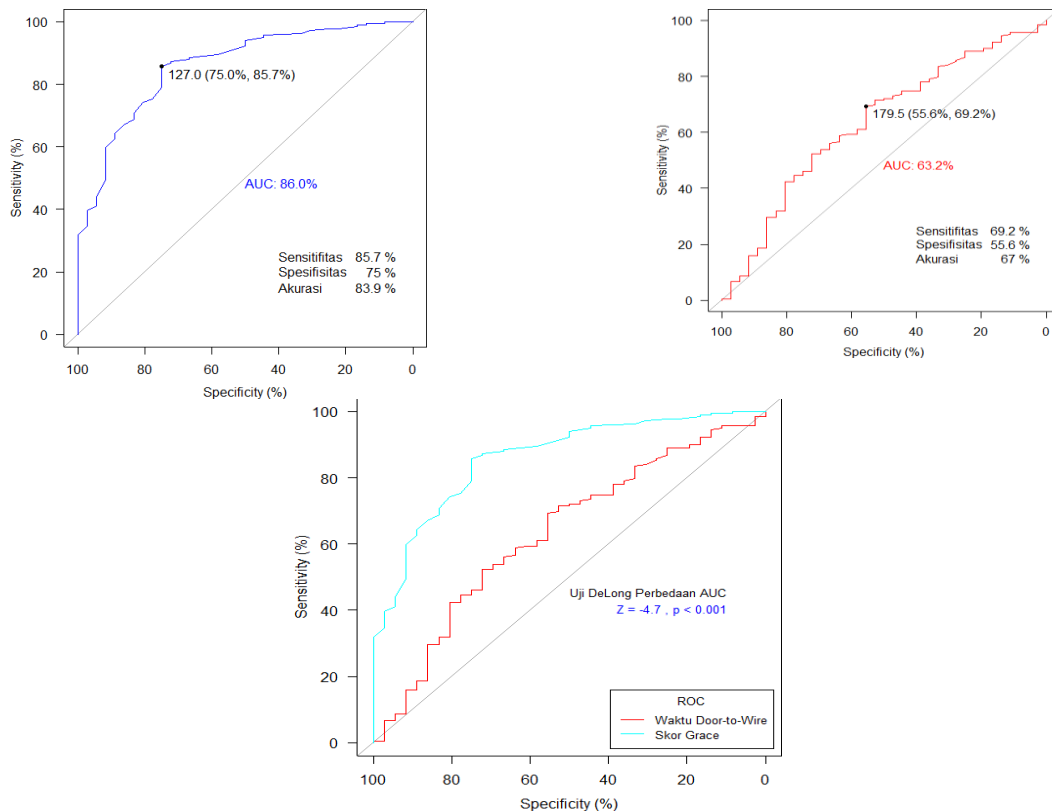
Different results can be caused by differences in the achievement of Door to Wire time which is still far from the target time of  $<60$  minutes in hospitals with PPCI facilities as the European Society of Cardiology (ESC) guidelines. This is because the delay in reperfusion will result in myocardial necrosis, expansion of infarction, increased incidence of heart failure due to reduced contraction function in the infarct area, cardiogenic shock.

Door to balloon  $<3$  hours was associated with a reduced risk of mortality and congestive heart failure at 3 years follow up<sup>20,21</sup>. Reperfusion time is a major factor in post-infarction ventricular amperage instability in STEMI patients undergoing PPCI. Late reperfusion  $> 5$  hours from symptom onset will increase the incidence of ventricular tachycardia 6 times greater than early reperfusion<sup>22</sup>. The Door to Wire time component alone is rarely assessed and

analyzed in detail in a large scale registry study, which includes door-EKG time, ECG-laboratory catheterization time (decision for PPCI, PPCI approval, STEMI team activation, health insurance issues) and laboratory catheterization-wire crossing<sup>23</sup>. Previous studies conducted by Kim et al, in 8040 STEMI patients who were carried out by PPCI in the period 2008-2011 in Korea found an increase in the achievement of Door to Balloon time < 90 minutes from 70.3% in 2008 to 90.2% in 2011, but was not accompanied by a decrease in the number of MACE, which includes 1 month of death, especially in the group that has with high risk<sup>10</sup>. The results of the evaluation of the receiver operating characteristics (ROC) curve of the ability of the two main research variables, namely Door to Wire time and GRACE score, to predict MACE are shown in Figure 2. In all models, only the GRACE score showed a significant correlation with MACE. The relative risk is almost the same regardless of the model

used, which is around two. For example, for all cases, STEMI patients with a GRACE score above 127 had a 1.93-fold (95% CI 1.27 to 2.92; p = 0.002) times greater risk of MACE than those with a lower GRACE score. After controlling for Door to Wire time variability, the relative risk was 1.98 (95% CI 1.27 to 3.09; p = 0.003). Quite the opposite was found at the time of Door to Wire. Even in models where the previous correlation analysis (Figure 15) shows a significant relationship between this variable and the GRACE score, the effect of Door to Wire time remains insignificant even though the GRACE score in the same model shows a significant effect. This result is similar to the previous study conducted by Flynn A et al, on 8771 IMAEST patients who underwent PPCI from 2003-2008 in Michigan, it was found that there was an increase in Door to Balloon time < 90 minutes from 28.5% in 2003 to 67.2% in 2008, but was not accompanied by a decrease in the number of KKM in the form of hospital deaths<sup>24</sup>.

**Figure 2.** Receiver Operating Characteristics curve analysis ability to predict cardiovascular events between door to wire time and GRACE score



Menees DS et al, in a study conducted on 96,738 IMAEST patients who underwent PPCI from 2005-2009 showed data on an increase in the achievement of Door to Balloon time < 90 minutes from 59.7% in 2005 to 83% in 2009, but the improvement in this achievement was not related to the improvement in the MACE rate in the form of death in the hospital or 30 days.<sup>25</sup> Study conducted by Wang et al, on 5881 STEMI patients showed that improvement of the median Door to Balloon time from 101 minutes in the period January - December 2005 to 87 minutes in the period July 2006 - July 2007, but the improvement in this

achievement was not accompanied by an improvement in mortality.<sup>26</sup> The GRACE score in the range of values 154 showed a stronger correlation but disappeared again after being depreciated at a value of 125, although a significant correlation was still seen in the subgroup without MACE. This is because STEMI patients with a GRACE score of 125-154 have a complex disease that requires stabilization first, causing delays for immediate reperfusion.<sup>20</sup> The GRACE score appears to have a clear advantage with an area under the curve (AUC) 86%, while at The Door to Wire AUC is only about 63%. The difference between the

two curves was significant in the DeLong test ( $p < 0.001$ ). The optimal cut-off point for the GRACE score was obtained at a value of 127. At that point, the sensitivity of the GRACE score for the prediction of MACE was about 86% with a specificity of 75% and an accuracy of 84%. For Door to Wire time, the optimal point is around 179.5 minutes where the sensitivity, specificity and accuracy of MACE predictions are around 69%, 56%, and 67%, respectively. A study conducted by Jakimov et al, on 200 patients from January to July 2014 obtained data that the GRACE score was superior to the TIMI and RISK PCI scores, to assess the 6-month risk of death and other clinical outcomes.<sup>27</sup> Similar results were also obtained by Ramsay et al, a study conducted on 347 patients, data showed that the GRACE score was superior to the TIMI score for predicting MCC in patients.<sup>28</sup> A study conducted by Littnerova et al, on 593 IMAEST patients who underwent PPCI and was observed for 30 days, 1 year, 2 years and 3 years, obtained data that among 6 risk scoring systems (CADILLAC, PAMI, TIMI, Dynamic TIMI, Zwolle, GRACE), the GRACE score was the best for predicting long-term mortality, followed by CADILLAC, Zwolle, and Dynamic TIMI<sup>6</sup>.

### Limitation of Study

The study did not assess the cause of the delay in Door to Wire time, and further studies need to be carried out to see the long-term clinical outcome of this case.

### Conclusions

Door to Wire time and GRACE scores were able to predict MACE in STEMI patients, but the GRACE score was superior to Door to Wire. Increased Door to Wire time & increased GRACE score will increase the relative risk of MACE in STEMI patients.

### References

1. Ibanez B, James S, Agewall S, et al. 2017 ESC Guideline for Management of Acute Myocardial Infarction in Patients Presenting with ST Segment Elevation: The Task Force for the Management of Acute Myocardial Infarction Patients Presenting with ST Segment Elevation of the European Society of Cardiology. *Eur Heart J*. 2018;39(2):119-77.
2. Widimsky P, Wijns W, Fajadet J, et al. European Association for Percutaneous Cardiovascular Intervention. Reperfusion Therapy for ST Elevation Acute Myocardial Infarction in Europe: Description of The Current Situation in 30 Countries. *Eur Heart J*. 2010;31(8):943-57
3. Dharma S, Andriantoro H, Purnawan I, Dakota I, Basalamah F, Hartono B, et al. Characteristics, Treatment and in-Hospital Outcomes of Patients With STEMI in a Metropolitan Area of a Developing Country: an Initial Report of the Extended Jakarta Acute Coronary Syndrome Registry. *BMJ Open*. 2016;1-10
4. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth Universal Definition of Myocardial Infarction. *Eur Heart J*. 2019;40:237-69
5. Brogan RA, Malkin CJ, Batin PD, Simms AD, McLenachan JM, Gale CP. Risk Stratification for ST Segment Elevation Myocardial Infarction in The Era of Primary Percutaneous Coronary Intervention. *World J Cardiol*. 2014;6(8):865-73
6. O'Gara PT, Kushner FG, Ascheim DD, et al. ACCF/AHA Guideline for The Management of ST-Elevation Myocardial Infarction: Executive Summary: A Report of The American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines: Developed in Collaboration with The American College of Emergency Physicians and Society for Cardiovascular Angiography and Interventions. *Circulation*. 2013;127:529-55
7. Park J, Choi KH, Lee JM, et al. Prognostic Implications of Door to Balloon Time and Onset-to-Door Time on Mortality in Patients With ST-Segment- Elevation Myocardial Infarction Treated with Primary Percutaneous. *J Am Heart Assoc*. 2019;8:e012188:1-32
8. Long LI, Man YW, Feng Z, et al. Perspective of Delay in Door to Balloon Time Among Asian Population. *J Geriatr Cardiol*. 2018;15:732-7
9. Dharma S, Andriantoro H, Dakota I, Sukmawan R, Firdaus I, Danny S, et al. Hospital Outcomes in STEMI Patients After the Introduction of a Regional STEMI Network in the Metropolitan Area of a Developing Country. *Asia Intervention*. 2018: 92-7
10. Kim HK, Jeong MH, Ahn Y. Relationship Between Time to Treatment And Mortality Among Patients Undergoing Primary Percutaneous Coronary Intervention According to Korea Acute Myocardial Infarction Registry. *Journal of Cardiology*. 2017;69:377-82
11. Fox KAA, Eagle KA, Gore JM, et al. The Global Registry of Acute Coronary Events, 1999 to 2009-GRACE. *Heart*. 2010 96: 1095-101
12. D'Ascenzo F, Giuseppe BC, Moretti C, Bollati M, Omedè P, Sciuto F, et al. TIMI, GRACE and Alternative Risk Scores in Acute Coronary Syndromes: a Meta-Analysis of 40 Derivation Studies on 216,552 Patients and of 42 Validation studies on 31,625 patients. *Contemp Clin Trials*. 2012:1-9
13. Poudel I, Tejjal C, Rashid H, Jahan N. Major Adverse Cardiovascular Events: An Inevitable Outcome of ST-elevation myocardial infarction? A Literature Review. *Cureus*. 11(7): e5280. 2019:1-11
14. Fleiss JL. The Design and Analysis of Clinical Experiments (Appendix: Sample Size Determination). New York, New York: Wiley; 1986:369-71
15. Hsieh FY, Bloch DA, Larsen MD. A Simple Method of Sample Size Calculation for Linear and Logistic Regression. *Stat Med*. 1998;17(14):1623- 34
16. Pedoman Tatalaksana Sindrom Koroner Akut. Perhimpunan Dokter Spesialis Kardiovaskular Indonesia. 2018:21-50
17. Fleiss J. Appendix: Sample Size Determination. The Design and Analysis of Clinical Trials New York: John Wiley & Sons. 1986;p.369-71

18. Hsieh FY, Bloch DA, Larsen MD. A Simple Method of Sample Size Calculation for Linear and Logistic Regression. *Statistics in Medicine*. 1998;17(14):1623-1634
19. Tasolar H, Cetin M, Balli M, et al. CHA2DS2VASc-HS score in non ST Elevation Acute Coronary Syndrome Patients: Assessment of Coronary Artery Disease Severity and Complexity and Comparison to Other Scoring Systems in Prediction of In Hospital Major Adverse Cardiovascular Events. *Anatolian J Cardiol*. 2016;16(10):742
20. Hochman JS. Acute Myocardial Infarction: Complication. In: Topol ER, Califf RM, Prytowsky EN, Thomas JD, Thompson PD, editors. *Textbook of Cardiovascular Medicine*. 3rd edition. New York: Lippincott Williams & Wilkins; 2007. p.303-26
21. Shiomi H, Nakagawa Y, Morimoto T, Furukawa Y, Nakano A, Shirai S, et al. Association of Onset to Balloon and Door to Balloon Time With Long Term Clinical Outcome in Patients With ST Elevation Acute Myocardial Infarction Having Primary Percutaneous Coronary Intervention: Observational Study. *British Med Journ*. 2012;344:e3257
22. Kumar S, Sivagangabalan G, Thiagalingam A, et al. Effect of Reperfusion Time on Inducible Ventricular Tachycardia Early and Spontaneous Ventricular Arrhythmias Late After ST Elevation Myocardial Infarction Treated with Primary Percutaneous Coronary Intervention. *Heart Rhythm*. 2011;8:493-9
23. Suma MV, Anand G, Vijayakumar S, et al. Door-to-balloon: Where Do We Lose Time? Single Centre Experience in India. *Indian Heart Journal*. 2012; 64:582-7
24. Flynn A, Moscucci M, Share D, et al. Trends in Door to Balloon Time and Mortality in Patients with STEMI Undergoing Primary PCI. *Arch Intern Med*. 2010;170(20):1842-9
25. Menees DS, Peterson ED, Yongfei W, et al. Door to Balloon Time and Mortality among Patients Undergoing Primary PCI. *N Engl J Med*. 2013;369:901-9
26. Wang TY, Fonarow GC, Hernandez AF, et al. The dissociation between door to balloon time improvement in other acute myocardial infarction care processes and patient outcomes. *Arch Intern Med*. 2009; 169(15):1411-19
27. Jakimov T, Mrdovic I, Filipovic B. Comparison of RISK-PCI, GRACE, TIMI Risk Scores for Prediction of Major Adverse Cardiac Events in Patients with Acute Coronary Syndrome. *Croat Med J*. 2017.58(6): 406-15
28. Ramsay G, Podogrodzka M, McClure C, Fox KAA. Risk Prediction in Patients Presenting with Suspected Cardiac Pain: the GRACE and TIMI Risk Scores Versus Clinical Evaluation. *Q J Med*. 2007;100:11-8