

Effect of Modified Global Risk Classification on Prognosis at Patients Undergoing Bypass Surgery and Percutaneous Coronary Intervention with Multi-vessel Disease

Çoklu Damar Hastalığı Olan Baypas Cerrahisi ve Peruktan Koroner Girişim Yapılan Hastalarda Modifiye Global Risk Skorunun Prognoz Üzerindeki Etkisi

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ABSTRACT

Objective: The aim of this study was to compare mortality and myocardial infarction in patients with multi-vessel disease using "Modified Global Risk Classification" (mGRC).

Methods: We divided 579 patients into low, intermediate risk with a high EuroSCORE (IE), intermediate risk with a high SYNTAX score (IS), and high Modified Global Risk groups. Patients were evaluated for death, myocardial infarction, cerebrovascular events, need for re intervention, and a primary endpoint, which denotes the occurrence of any one of the four events.

Results: Comparing the bypass surgery and percutaneous coronary intervention groups using mGRC showed significantly better prognostic results in the bypass surgery patients for the rate of the occurrence of the myocardial infarction for the IS group (p=0.047). In terms of the primary endpoint, the EuroSCORE, SYNTAX score, and Global Risk Classification (GRC) were found to be independent risk factors in logistic regression analysis. The ability of GRC to discriminate for the 1-year mortality was found to be better than that of the EuroSCORE and SYNTAX score.

Conclusion: With the evaluation of the EuroSCORE and SYNTAX score together, the modified GRC, which includes both anatomical and clinical risk factors, provides an additional benefit for predicting the prognosis and decision of treatment in patients with multi-vessel disease.

Keywords: Modified global risk score, coronary artery bypass surgery, percutaneous transluminal coronary angioplasty

ÖZ

Amaç: Bu çalışmanın amacı, "Modifiye Global Risk Sınıflaması" kullanarak çok damar hastalığı olan hastalarda mortalite ve miyokard enfarktüsünü karşılaştırmaktır.

Yöntemler: EuroSCORE ve SYNTAX Skoru değerleri göz önüne alınarak 579 hasta; düşük, yüksek EuroSCORE'lu orta, yüksek SYNTAX Skoru orta ve yüksek modifiye Global Risk gruplarına ayrıldı. Hastalar ölüm, miyokard enfarktüsü, serebrovasküler olay gelişimi, tekrar girişim ihtiyacı ve bu dördünden herhangi birinin gelişmesi anlamına gelen bileşke sonlanım noktası açısından taburculuk öncesi, 1. ay, 6. ay ve 12. ayda değerlendirildi.

Bulgular: Modifiye Global Risk skorlamasına göre bypass cerrahisi ve perkutan koroner girişim yapılan hasta grupları karşılaştırıldığında yüksek SYNTAX skorlu orta risk grubunda miyokard enfarktüsü gelişimi oranında (p=0,047) bypass cerrahisi yapılan hastalarda daha iyi prognostik sonuçlar elde edildi. Logistik regresyon analizinde bileşke sonlanım noktasına ulaşma için EuroSCORE, SYNTAX Skoru ve Global Risk Skoru bağımsız risk faktörü olarak saptanmıştır. mGRC'nin 1 yıllık mortalite için diskriminasyon yeteneğinin EuroSCORE ve SYNTAX skorundan daha iyi olduğu bulunmuştur.

Sonuç: Çoklu damar hastalığına sahip hastalarda EuroSCORE ve SYNTAX skorunun beraber değerlendirilmesiyle oluşturulan, anatomik ve klinik risk faktörlerine birleştiren bir risk skorlaması olan modifiye Global Risk Skoru prognozun öngörülmesinde ve tedavi seçiminde ek fayda sağlamaktadır.

Anahtar kelimeler: Modifiye global risk skoru, koroner arter bypass cerrahisi, perkutan translüminal koroner anjiyoplasti

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INTRODUCTION

Historically, coronary artery bypass grafting (CABG) has been the preferred method of revascularization in patients with complex coronary artery disease (CAD); however, recent evidence indicates that percutaneous coronary intervention (PCI) can offer a safe and suitable alternative in specific groups of patients (1). With the increasing use of PCI, a systematic approach is needed to stratify these complex patients for choosing the appropriate revascularization option for each patient.

Various risk scores with various risk factors have been developed to decide the choice of treatment and to predict the short- and long-term prognosis in CAD.

The EuroSCORE is the most widely used clinical risk score. It is a prognostic scoring system developed for patients undergoing cardiac surgery and has gained wide popularity over time because its performance has been validated in several local populations (2, 3). The EuroSCORE can also reasonably stratify PCI population into risk categories because most of its variables are derived from the clinical status of the patient (4). However, one common concern of using clinical risk scores in the setting of PCI is that they do not incorporate any comprehensive information regarding the anatomy and extent of CAD.

The SYNTAX score is the most widely used anatomic risk score. It has been developed as a combination of several previously validated angiographic classifications aiming to grade the coronary anatomy with respect to the number of lesions and their functional impact, location, and complexity (5). Higher SYNTAX scores, indicative of a more complex condition, are likely to represent a bigger therapeutic challenge and to have a potentially worse prognosis in patients undergoing contemporary revascularization with PCI.

In order to improve its performance to determine the procedural risk and to detect the appropriate treatment for patients who had multi-vessel CAD, the parallel use of a clinical score, such as the EuroSCORE that determines the procedural risks, was thought to be a better option than the use of the SYNTAX score alone. A new tool called Global Risk Classification (GRC), which includes both angiographic and clinical information contained in the SYNTAX score and EuroSCORE, respectively, was developed as a combined risk model.

For better identification of patients who would benefit greatly from CABG treatment, we developed the "Modified Global Risk Classification" (mGRC) with a slight change in GRC. The aim of this study was to compare mortality, myocardial infarction, and a primary endpoint in patients undergoing CABG and PCI with multi-vessel disease using mGRC, which includes both anatomical and clinical risk factors.

METHODS

Patient Population

We included 579 patients who underwent coronary angiography at the coronary angiography units of the Çukurova University

Hospital and Adana Numune Training and Research Hospital in this retrospective cohort study. Patients with stable angina pectoris, unstable angina, non-ST segment elevation myocardial infarction, and those undergoing bypass surgery and PCI were included in this study. The local ethics committee approved the study protocol, and written informed consent obtained from each participant.

Patients with left main coronary artery (LMCA) lesion (>50%), three-vessel disease (3VD) (>50%), left anterior descending artery diagonal I, diagonal II bifurcation lesion (>50%), proximal left anterior descending, and circumflex or right coronary artery 2-vessel disease (>50%) were included. Patients with ST-elevation myocardial infarction, a history of severe liver disease, neutropenia, thrombocytopenia with contraindications or intolerance to aspirin and clopidogrel, a history of previous CABG, non-cardiac disease limiting the life expectancy, severe valvular disease requiring surgical treatment, and those requiring non-cardiac surgery in a short time were excluded from the study.

The treatment strategy (CABG or PCI) was determined by the responsible clinician independently from the study.

Definition of scoring systems

Each coronary lesion with a diameter stenosis $\geq 50\%$ in vessels ≥ 1.5 mm was scored with the SYNTAX score as originally described (6). The EuroSCORE was calculated based on the original methodology (2). GRC was created by a combination of the SYNTAX score and EuroSCORE strata (7).

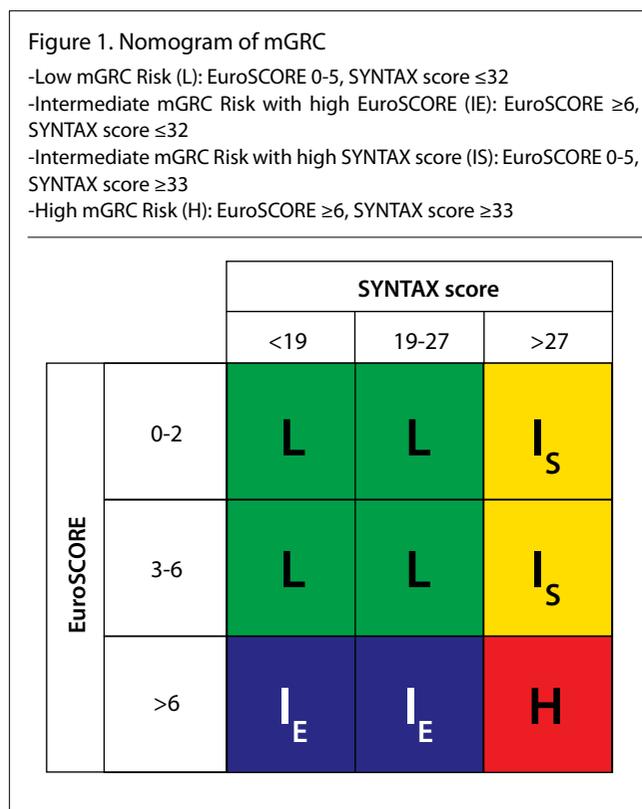
A low mGRC risk is defined as a EuroSCORE of 0-5 and SYNTAX score of ≤ 32 , an intermediate mGRC risk with a high EuroSCORE (IE) is defined as a EuroSCORE of ≥ 6 and SYNTAX score of ≤ 32 , an intermediate mGRC risk with a high SYNTAX score (IS) is defined as a EuroSCORE of 0-5 and SYNTAX score of ≥ 33 , and high mGRC risk is defined as a EuroSCORE of ≥ 6 and SYNTAX score of ≥ 33 . In our study, the intermediate risk group is divided into two groups for the first time. The reason of this implementation is to separate the patient population with high SYNTAX score and low EuroSCORE, and this could benefit more from CABG treatment (Figure 1).

Echocardiography

The standard 2-dimensional and Doppler echocardiography were performed for all patients. Left ventricle (LV) end-diastolic diameters (LVDd), end-diastolic interventricular septal thickness, and end-diastolic left ventricular posterior wall thickness were measured at end-diastole according to the established standards of the American Society of Echocardiography. LV ejection fraction (EF) was determined using the biplane Simpson's method.

Follow-up of patients

Patients were evaluated before discharge and at 1, 6, and 12 months for death, myocardial infarction, cerebrovascular accident, need for re-intervention, and a primary endpoint, which denotes the occurrence of any one of the four events. The primary endpoint of the study was the occurrence of mortality. Patients were followed up through phone calls.



Statistical Analysis

The Statistical Package for Social Sciences (SPSS) 17.0 (SPSS Inc.; Chicago, IL, USA) program was used for statistical analysis. Continuous variables were presented as mean±standard deviation (SD) or as median and interquartile range; categorical variables were presented as number and percentage.

The chi-square test or Fisher’s exact test was used to compare categorical variables. Continuous variables with normal distribution were compared using ANOVA and Student’s unpaired *t* test. Continuous variables without normal distribution were compared using the Kruskal-Wallis or Mann-Whitney rank sum test. The normality assumption for continuous variables was evaluated using the Kolmogorov-Smirnov test.

A logistic regression analysis was used to find independent predictors of mortality, myocardial infarction, and the primary endpoint. The discrimination of GRC, SYNTAX score, and EuroSCORE was first assessed using the areas under the receiving operator characteristic curves (AUROC). The level of statistical significance was set at 0.05 for all tests.

RESULTS

Baseline Characteristics

The percentage of male patients was significantly higher in the PCI group (*p*<0.05). The percentage of peripheral artery disease history and presence of a LMCA lesion were found to be significantly higher in the CABG group (*p*<0.05, for all). There were no significant differences in other demographic data (Table 1).

Table 1. Baseline and procedural characteristics of patients

Variable	PCI (n=282)	CABG (n=297)	Total (n=579)	p value
Age, years±SD	63.6±9.9	62.5±8.9	63.1±9.4	0.193
Male sex n (%)	200 (86.2)	180 (66.7)	380 (75.7)	<0.001
Diabetes n (%)	88 (37.9)	112 (41.5)	200 (39.8)	0.655
Smoking history n (%)	135 (58.2)	140 (51.9)	275 (54.8)	0.177
Hypercholesterolemia n (%)	46 (19.8)	70 (25.9)	116 (23.1)	0.112
Family history n (%)	50 (21.6)	78 (28.9)	128 (25.5)	0.065
Hypertension n (%)	87 (37.5)	108 (40.0)	195 (38.8)	0.583
Previous MI n (%)	55 (23.7)	72 (26.7)	127 (25.3)	0.472
Previous PCI n (%)	34 (14.7)	55 (20.4)	89 (17.7)	0.102
Previous CVA n (%)	1 (0.4)	4 (1.5)	5 (1.0)	0.380
Previous PAD n (%)	2 (0.9)	31 (11.4)	33 (6.6)	<0.001
LMCA lesion n (%)	23 (9.9)	44 (16.3)	67 (13.3)	0.048
EF (%)±SD	48.7±23.2	51.8±8.6	50.4±17.1	0.037
Creatinine (mg/dL) ±SD	1.0±0.3	1.1±0.7	1.1±0.6	0.010
LDL (mg/dL)±SD	108.2±36.5	117.6±40.2	113.2±38.7	0.007
HDL (mg/dL)±SD	37.9±28.3	36.2±21.8	37.0±25.1	0.446
EuroSCORE	3.23±2.47	3.45±2.35	3.34±2.41	0.70
SYNTAX score±SD	25.1±6.9	25.5±6.9	26.6±7.5	0.441

MI=myocardial infarction, CVA=cerebrovascular event; LMCA=left main coronary artery; PAD=peripheral arterial disease, SD=standard deviation, PCI=percutaneous coronary intervention, EF=ejection fraction. LDL=low-density cholesterol, HDL=high-density cholesterol

Compared with the PCI group, EF, creatinine, and low-density cholesterol levels were found to be significantly higher in the CABG group (*p*<0.05, for all). There were no significant differences in other laboratory data. (Table 1). Baseline characteristics of the patients with and without mortality are shown in Table 2.

Independent Predictors of Mortality, Myocardial Infarction, and the Primary Endpoint

Age (odds ratio [OR]=1.19, *p*=0.001), presence of a LMCA lesion (OR=11.90, *p*=0.001), smoking history (OR=20.34, *p*<0.001), family history of CAD (OR=29.80, *p*=0.017), EuroSCORE (OR=1.55, *p*=0.049), SYNTAX score (OR=1.21, *p*=0.002), and intermediate- (OR=5.42, *p*=0.048) and high-risk mGRC (OR=18.28, *p*=0.033) were found to be independent predictors of mortality in the logistic regression analysis (Table 3).

The EuroSCORE (OR=1.18, *p*=0.040), SYNTAX score (OR=1.186, *p*<0.001), and intermediate- (OR=8.08, *p*=0.006) and high-risk mGRC (OR=18.69, *p*=0.004) were found to be independently associated with the occurrence of new myocardial infarction in the logistic regression analysis. EF (OR=0.93, *p*=0.006) was found to be inversely associated with the occurrence of myocardial infarction.

Table 2. Baseline characteristics of patients with and without mortality

Variable	Patients without mortality (n=547)	Patients with mortality (n=32)	p value
Age, years±SD	70.9±7.1	62.8±9.2	<0.001
Male sex n (%)	417 (76.2)	27 (84.4)	0.290
Diabetes n (%)	227 (41.5)	18 (56.2)	0.112
Smoking history n (%)	296 (54.1)	25 (78.1)	0.008
Hypercholesterolemia n (%)	131 (23.9)	7 (21.9)	0.789
Family history n (%)	138 (25.2)	1 (3.1)	0.004
Hypertension n (%)	209 (38.2)	13 (40.6)	0.785
Previous MI n (%)	137 (25.0)	12 (37.5)	0.117
Previous PCI n (%)	89 (16.3)	7 (21.9)	0.407
Previous CVA n (%)	5 (0.9)	0 (0)	0.380
LMCA lesion n (%)	73 (13.3)	10 (31.3)	0.005
EF (%)±SD	50.4±16.4	42.4±13.4	0.007
Creatinine (mg/dL)±SD	1.0±0.5	1.3±0.4	0.007
LDL (mg/dL)±SD	114.3±38.1	118.2±48.3	0.581
HDL (mg/dL)±SD	36.8±23.9	32.0±9.3	0.251
EuroSCORE	3.23±2.37	5.25±2.39	<0.001
SYNTAX score±SD	26.3±7.5	32.3±4.6	<0.001
Revascularization type PCI n (%)	265 (48.4)	17 (53.1)	0.607

MI=myocardial infarction, CVA=cerebrovascular event, SD=standard deviation, PCI=percutaneous coronary intervention, EF=ejection fraction. LDL=low-density cholesterol, HDL=high-density cholesterol

The EuroSCORE (OR=1.38, $p=0.018$), SYNTAX score (OR=1.13, $p=0.001$), and high-risk mGRC (OR=8.01, $p=0.008$) were found to be independent risk factors to reach the primary endpoint in the logistic regression analysis (Table 3).

Comparison of Mortality, Myocardial Infarction, and the Primary Endpoint Rates for All Patients with GRC

The mortality rates were 1.9%, 7.7%, and 14% for the low-, medium-, and high-risk mGRC groups, respectively. There were statistically significant differences between the low-to-moderate ($p=0.016$) and low-to-high ($p=0.001$) risk groups.

The rates of the occurrence of new myocardial infarction were 3.9%, 9.3%, and 14% at the low-, medium-, and high-risk mGRC groups, respectively. There were statistically significant differences between the low-to-moderate ($p=0.041$) and low-to-high ($p=0.004$) risk groups.

The primary endpoint rate was 7.7%, 14.2%, and 25.6% at low, medium-, and high-risk groups, respectively. There were statistically significant differences between the low-to-moderate

($p=0.034$), low-to-high ($p=0.001$), and medium-to-high ($p=0.027$) risk groups.

Comparison of Mortality, Myocardial Infarction, and the Primary Endpoint Rates According to mGRC in Patients Undergoing CABG and PCI

With regard to the mortality rates of CABG and PCI groups with mGRC, the prognostic results were better with CABG in the IS group and with PCI in the IE group. However, there was no statistically significance ($p>0.05$, for all). The prognostic results were better with CABG in the IS group and with PCI in the IE group for primary endpoint rates. However, there was no statistically significance ($p>0.05$, for all). The prognostic results for the rate of occurrence of myocardial infarction in the IS group were significantly better in CABG patients ($p=0.047$; Table 4).

Discrimination Analysis

The ability of GRC to discriminate for 1-year mortality was found to be better than that of the EuroSCORE and SYNTAX score. The AUROC was 0.712 (95% confidence interval [CI]: 0.62-0.80, $p<0.001$) with mGRC, 0.705 (95% CI: 0.62-0.78, $p<0.001$) with the SYNTAX score, and 0.690 (95% CI: 0.60-0.77, $p<0.001$) with the EuroSCORE (Table 5).

DISCUSSION

To the best of our knowledge, this is the first description of mGRC that represents a risk score combining both clinical and angiographic variables. The main findings from this study are that mGRC has an ability superior to either the SYNTAX score or EuroSCORE alone for predicting the 1-year mortality in patients with multi-vessel disease undergoing PCI and CABG. Furthermore, mGRC is found to have the ability to isolate patients with a high SYNTAX score and with low or intermediate EuroSCORE (IS group), who can potentially benefit greatly from surgical treatment.

The SYNTAX score is a reliable risk score for predicting the cardiac mortality in CAD, and it was created using angiographic risk factors (6-9). The EuroSCORE, Mayo Clinic score, Personnet score, ACEF score, and NCDR CathPCI score can be considered as clinical risk scores. There was a need to create a new diagnostic tool that combines the angiographic and clinical risk factors for a more precise prediction of cardiac mortality and for better guidance in deciding treatment modalities.

One of the studies with a combined risk classification approach was the Clinical SYNTAX Score (CSS) (10). CSS was calculated retrospectively for each of the 512 patients undergoing PCI with complex CAD using the formula $CSS=[SYNTAX\ Score] \times [modified\ ACEF\ score]$. The modified ACEF score (ACEF creatinine clearance [CrCl]) was calculated retrospectively using the formula $age/EF+1$ point for every 10 mL/min reduction in CrCl below 60 mL/min per 1.73 m² (up to a maximum of 6 points). The clinical outcomes in terms of major adverse cardiac and cerebrovascular events (MACCE) and mortality at 1- and 5-year follow-ups were stratified according to the CSS tertiles: $CSS_{LOW} \leq 15.6$ (n=170), $15.6 < CSS_{MID} < 27.5$ (n=171), and $CSS_{HIGH} \geq 27.5$ (n=171). At

Table 3. Predictors of mortality and primary endpoint in the logistic regression analysis

Variable	Mortality		Primary endpoint	
	OR	p value	OR	p value
Age, years	1.19 (1.07-1.32)	0.001	1.01 (0.97-1.06)	0.456
Male sex	1.78 (0.26-12.02)	0.550	1.14 (0.47-2.75)	0.763
Diabetes	0.85 (0.20-3.47)	0.823	1.30 (0.61-2.74)	0.485
Smoking history	20.34 (4.30-96.21)	0.001	1.85 (0.93-3.68)	0.078
Family history	29.80 (1.84-482.66)	0.017	1.06 (0.46-2.45)	0.880
Hypercholesterolemia	2.62 (0.50-13.69)	0.254	0.88 (0.40-1.93)	0.756
Hypertension	1.02 (0.29-3.51)	0.970	1.38 (0.72-2.63)	0.319
Previous MI	4.635 (0.82-26.19)	0.083	1.31 (0.49-3.48)	0.589
Previous PCI	3.539 (0.50-24.95)	0.205	1.01 (0.32-3.15)	0.983
EF	1.01 (0.95-1.07)	0.761	0.99 (0.96-1.02)	0.663
Creatinine	2.09 (0.89-4.88)	0.086	1.25 (0.72-2.16)	0.422
LMCA lesion	11.90 (2.71-52.27)	0.001	1.91 (0.87-4.17)	0.105
Revasc. type (CABG)	1.00 (0.39-2.55)	0.985	1.53 (0.84-2.79)	0.159
EuroSCORE	1.55 (0.99-2.42)	0.049	1.38 (1.05-1.80)	0.018
SYNTAX score	1.21 (1.07-1.37)	0.002	1.13 (1.06-1.21)	0.001
GRC (Int. Risk)	5.425 (0.82-35.61)	0.048	2.60 (0.89-7.52)	0.078
GRC (High Risk)	18.289 (1.25-266.47)	0.033	8.01 (1.71-37.38)	0.008

MI=myocardial infarction, LMCA=left main coronary artery, OR=odds ratio, EF=ejection fraction, CABG=coronary artery bypass graft, GRC=Global Risk Classification, Revasc=revascularization, PCI=percutaneous coronary intervention

Table 4. Comparison of mortality, myocardial infarction, and the primary endpoint rates according to mGRC in patients undergoing CABG and PCI

		IE (n=79)	IS (n=104)	p value
Mortality (%)	PCI (n=93)	5.4	10.7	0.48
	CABG (n=90)	9.5	4.2	0.28
	<i>p</i>	0.43	0.26	
MI (%)	PCI (n=93)	8.1	16.1	0.10
	CABG (n=90)	7.1	4.2	0.77
	<i>p</i>	0.40	0.047	
Primary endpoint (%)	PCI (n=93)	13.5	16.1	0.19
	CABG (n=90)	16.7	10.4	0.34
	<i>p</i>	0.35	0.46	

MI=myocardial infarction, IE=Intermediate mGRC Risk with a high EuroSCORE, IS=Intermediate mGRC Risk with a high SYNTAX score, CABG=coronary artery bypass graft, mGRC=modified Global Risk Classification

the 1-year follow-up, the rates of repeat revascularization and MACCE were significantly higher in the CSSHIGH group. CSSHIGH had significantly higher rates of repeat revascularization and overall MACCE compared with patients in the lower 2 tertiles at

Table 5. Discriminatory measures of mGRC, EuroSCORE, and SYNTAX score for 1-year mortality

Risk measure	1-year mortality AUROC
mGRC	0.712
SYNTAX score	0.705
EuroSCORE	0.690

mGRC=modified Global Risk Classification, AUROC=area under the receiver operator characteristic curved

the 5-year follow-up. The c-statistics for the CSS, SYNTAX score, and ACEF score for the 5-year mortality were 0.69, 0.62, and 0.65 and for the 5-year MACCE were 0.62, 0.59, and 0.57, respectively. As different from our study, only PCI patients were enrolled in the study. The modified ACEF score has limited clinical data (age, EF, and GFR) because it does not contain enough clinical data about the prognosis of a surgical procedure. For this reason, CSS may not be appropriate for the risk classification of CABG patients. For same reason, it may have a limited capacity to help in deciding treatment modalities.

The GRC was first used in a study published by Capodanno et al. (11). In this study, the EuroSCORE and SYNTAX score were used together to estimate the procedural and long-term risks for 255 patients undergoing PCI with a LMCA lesion. When the Euro-

SCORE was added into the SYNTAX score model, the c-statistic increased from 0.681 to 0.732 for the prediction of cardiac mortality. The likelihood ratio test for the significance of adding the EuroSCORE term to the model was $\chi^2=4.109$ ($p=0.043$) with a net re-classification improvement of 26% ($p=0.002$). GRC was found to have the best prediction and discriminative ability in terms of the 2-year cardiac mortality (hazard ratio [HR]: 3.40, $p=0.001$; c-statistic: 0.756) compared with the SYNTAX score (HR:2.87, $p=0.006$; c-statistic: 0.747) and the EuroSCORE (HR:3.04, $p=0.005$; c-statistic: 0.708) alone. In this study, GRC was compared with the EuroSCORE and SYNTAX score for predicting the cardiac mortality for the first time. It has been shown to result in a significant increase in the power to predict mortality. This study had only included LMCA lesion patients treated using PCI. LMCA lesions and their treatment have a different nature because of technical differences. Furthermore, this study had no data about patients with LMCA lesions treated surgically. Therefore, it may not be appropriate to generalize these results to all the multi-vessel disease population.

The Synergy between PCI with TAXUS and Cardiac Surgery (SYNTAX) trial results at 3 years were published recently (12). In this study, at the 36-month period, the all-cause mortality and MACCE were compared using GRC in patients undergoing CABG and PCI treatment with LMCA lesion and 3VD. In this study, the clinical variables (EuroSCORE) were found to be more predictive of the clinical outcomes (all-cause death and MACCE) compared with anatomical variables (SYNTAX score) in the PCI population. In the LMCA lesion PCI population, the Global Risk was found to have greater predictive ability compared with the SYNTAX score or EuroSCORE alone. In the low-risk GRC patient population with LMCA lesion ($n=701$), mortality was significantly lower in the PCI group compared with CABG patients (CABG: 7.5%, PCI: 1.2%, HR: 0.16, $p=0.0054$). Likewise, in the low-risk GRC patient population with LMCA lesion, the MACCE incidence was found to be lower in the PCI group than in the CABG group even if there was no statistical significance (CABG: 23.1%, PCI: 15.8%, HR: 0.64, $p=0.088$). In the low-risk GRC patient population with 3VD ($n=1,088$), there was no significant difference in mortality between CABG and PCI patients (CABG: 5.2%, PCI: 5.8%, HR: 1.14, $p=0.71$). Likewise, in the low-risk GRC patient population with 3VD, there was no significant difference in the MACCE incidence between CABG and PCI patients (CABG: 19.0%, PCI: 24.7%, $p=0.10$). In the 3VD PCI population, the Global Risk improved the risk stratification of patients compared with the SYNTAX score alone by proving that low SYNTAX score patients with a high EuroSCORE had a mortality benefit in undergoing CABG over PCI.

The main strengths of the Global Risk are that it can be applied across the entire spectrum of the surgical and percutaneous-treated patients and that the addition of the EuroSCORE to the SYNTAX score is a simple non-invasive calculation. Furthermore, it is the first and maybe the best-combined assistance for deciding between CABG and PCI.

In the low-risk mGRC patient population of our study, similar to the 3-year results of the SYNTAX study, there was no statistical significance in mortality (CABG: 1.8%, PCI: 2.1%, $p=0.56$). In the

low-risk mGRC patient population, different from the 3-year results of the SYNTAX study, the rate of reaching the primary endpoint was significantly lower in the CABG group and PCI group (CABG: 6.1%, PCI: 9.7%, $p=0.005$). Patients with a LMCA lesion have not been separated from the complete multi-vessel disease population in the present study because of the small number of patients with pure LMCA lesion.

In the IE mGRC patient population, mortality was higher in patients undergoing CABG compared with PCI but the difference was not statistically significant (CABG: 9.5%, PCI: 5.4%, $p=0.43$). In the IE mGRC patient population, there was no statistically significant difference in the rate of reaching the primary endpoint (CABG: 16.7%, PCI: 13.5%, $p=0.35$). However, in the 3-year results of the SYNTAX study, patient with a low SYNTAX score and a high EuroSCORE have been found to get a mortality benefit in undergoing CABG over PCI.

In the IS mGRC patient population, mortality was higher in the PCI group, though there was no statistically significant difference (CABG: 4.2%, PCI: 10.7%, $p=0.26$). The incidence of myocardial infarction was found to be significantly lower in the CABG group (CABG: 4.2%, PCI: 16.1%, $p=0.047$). The rate of reaching the primary endpoint was significantly lower in the CABG group, although there was no statistically significant difference (CABG: 10.4%, PCI: 16.1%, $p=0.46$). As expected, in the IS patient population, the incidence of myocardial infarction was significantly lower in the CABG group. CABG seems to be more advantageous than PCI in terms of mortality and primary endpoint in this population as expected, but statistical significance was not provided because of the relatively low number of patients in these groups. A greater stent burden and higher complication rates with PCI in patients with a high SYNTAX score can be considered as the reason for this prognostic advantage with CABG in the IS patient population. Furthermore, complete revascularization rates with CABG are likely to be higher than PCI in patients with a high SYNTAX score.

In the high-risk mGRC patient population, there was no statistical significance in mortality (CABG: 14.3%, PCI: 13.6%, $p=0.93$). The rate of reaching the primary endpoint was lower in the CABG group than in the PCI group, although there was no statistically significant difference (CABG: 21.4% PCI: 29.5%, $p=0.38$). These results were similar to those of previous studies.

Intermediate and high GRC were found to be independent predictors of mortality, myocardial infarction, and the primary endpoint in the logistic regression analysis. The ability of GRC to discriminate for the 1-year mortality was found to be better than the EuroSCORE and SYNTAX score. The ability may be improved by converting it to a scoring system with quantitative values.

Limitations

The current study is limited by its post hoc nature. Patients within the PCI and CABG groups have not been randomized because the present study was observational. Thus, the distribution of some of the demographic data was not equal between the groups. In total, 579 patients were included in the study. Although the total

number of patients seems to be sufficient, particularly, the number of patients in the intermediate- and high global risk groups was relatively low. Therefore, a statistical significance could not be obtained, even though there were proportional differences at some parameters.

CONCLUSION

mGRC, which can be applied across the whole spectrum of CABG and PCI patients, improved the risk classification in multi-vessel disease patients with a greater prediction power for cardiac adverse events. More importantly, mGRC should be considered for treatment decisions between CABG and PCI in multi-vessel disease.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Çukurova University. (2012)

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