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# Can GRACE Risk Score Predict the Coronary Anatomy in Non-ST Elevation Acute Coronary Syndrome?

## GRACE Risk Skoru ST Akut Koroner Sendromda Koroner Anatomiyi Öngörebilir Mi?

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Abstract / Özet

**Objective:** The Global Registry of Acute Coronary Events (GRACE) risk score; a commonly used risk scoring system; predicts hospital and 6-month survival rates of patients with acute coronary syndrome (ACS). The purpose of this study was to evaluate whether the GRACE risk score could also predict the extent of diseased coronary vessels in patients with non-ST elevation acute coronary syndrome.

**Methods:** We evaluated 95 patient data retrospectively who were hospitalized with a diagnosis of non-ST elevation ACS between 2005-2006 at the Istanbul University Cardiology Institute. All the patients' GRACE risk scores were calculated and coronary angiograms were re-analysed. We further divided the patients into three groups according to risk score (Low risk score: <108, medium risk score: 109-140, high risk score: >141) and evaluated the association between the GRACE risk score and the number of diseased coronary arteries.

**Results:** After GRACE risk score calculation; the number of low risk, medium risk and high risk patients were 38 (%40), 44 (%46.4) and 13 (%13.6) respectively. Three-vessel disease was insignificantly higher in low and medium risk groups but statistically significant in high risk group. ($p<0.01$). Patients with low ejection fraction (<40%) were more numerous in the high risk group than medium and low risk groups ($p<0.05$). number of patients with estimated glomerular filtration rate (eGFR) less than 60 mL/dk/1.73 $m^2$ was higher in medium and high risk groups than the low risk group ($p<0.001$).

**Conclusion:** As the GRACE risk score calculated in emergency room for ACS patients can predict in-hospital mortality and clinical events, it may also predict coronary anatomy, low ejection fraction and low eGFR.

**Key Words:** GRACE risk score, non-ST elevation acute coronary syndrome, coronary anatomy

**Amaç:** Sıkça kullanılan risk skorlarından 'Global Registry of Acute Coronary Events' (GRACE) risk skorlama sistemi akut koroner sendrom ile başvuran hastalarda hastane-içi ve 6-aylık mortaliteyi öngörebilir. Bu çalışmanın amacı ST-elevasyonsuz akut koroner sendromlarda (AKS) GRACE risk skorunun koroner arter hastalığı yaygınlığını da öngörüp öngöremeyeceğinin belirlenmesidir.

**Yöntemler:** İstanbul Üniversitesi Kardiyoloji Enstitüsünde 2005-2006 yılları arasında ST-elevasyonsuz AKS tanısı ile yatırılarak tedavi görmüş 95 hastanın dosyası retrospektif olarak incelendi. Tüm hastaların GRACE risk skorları hesaplandı ve koroner anjiyografileri incelendi. GRACE risk skoruna göre hastalar 3 gruba ayrıldı (düşük <108, orta 109-140, yüksek >141) ve gruplara göre damar tutulum sayıları belirlendi.

**Bulgular:** GRACE risk skoru hesaplamasına göre düşük, orta, yüksek risk rubundaki hasta sayıları sırasıyla 38 (%40), 44 (%46,4) ve 13 (%13,6) idi. Tutulan damar sayısına göre 3-damar hastalığı istatistiksel olarak anlamsız olsada düşük ve orta risk grubunda yüksek saptanırken yüksek risk grubunda istatistiksel olarak belirgin şekilde daha yüksekti ($p<0,01$). Düşük ejeksiyon fraksiyonu (<%40) yüksek risk grubunda orta ve risk grubuna göre daha fazla saptandı ($p<0,05$). Tahmini glomeruler filtrasyon hızı (eGFR) 60 mL/dk/1,73$m^2$'dan düşük olan hasta sayısı orta ve yüksek risk grubunda düşük risk grubuna göre daha fazla idi ($p<0,001$).

**Sonuç:** Acil servise ST-yükselmesiz AKS öntanısı ile başvuran hastalarda mortalite ve klinik olayları öngörebilen GRACE risk skoru aynı zamanda koroner anatomiyi, düşük ejeksiyon fraksiyonunu ve eGFR'ıda öngörebilir.

**Anahtar Kelimeler:** GRACE risk skor, ST-yükselmesiz akut koroner sendrom, koroner anatomi

## Introduction

Non-ST elevation acute coronary syndrome (ACS) is divided into unstable angina pectoris (USAP) and non-ST elevation myocardial infarction (NSTMI). As ACS patients are heterogenous, death and cardiac event development is also a very broad spectrum, so determining the status of cardiac event risk in these patients with a quick and reliable method is of great importance (1, 2). Many investigators have developed risk scoring systems that could predict the outcome of patients delivered to hospitals with ACS diagnosis (3-6). The GRACE (global registry of acute coronary events) risk scoring system's ability to predict in-hospital, 6-month and even longer term mortality and cardiac events in ACS patients has been shown by many studies (5, 6). We investigated the possibility of the GRACE risk score to predict the number of diseased coronary vessel when it is applied at first contact in emergency room.

## Methods

We evaluated retrospectively consecutive 178 patient files hospitalised in the Istanbul University Cardiology Institute, Cardiology department during 2005-2006 with a diagnosis of unstable angina pectoris and non-ST elevation myocardial infarction. Patients were grouped as USAP/NSTMI according to their presenting chest pain, electrocardiogram (ECG) properties and cardiac marker levels. Patients younger than 21 years-old, ST-elevation MI, non-cardiac chest pain, survivors of sudden cardiac death, incessant malignant arrhythmias, severe chronic obstructive airway disease, severe liver

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failure, severe renal failure, malignity, chronic inflamatory disease, previous cerebrovascular disease and active infection were excluded from the study. 95 appropriate patients, who did not have exclusion criteria, enrolled in the study. Each patient's individual GRACE risk score at admission was calculated from the patient files retrospectively using the published risk score calculator from the GRACE registry (7). Full details of the design and methods of the GRACE risk score have been previously published (8). This score is calculated from eight individual variables:- the age of the patient, admission systolic blood pressure, heart rate, Killip score, baseline creatinine level, cardiac arrest on admission, ST segment deviation on initial ECG and elevation of cardiac biomarkers. From these variables, estimated risk of death or myocardial infarction can be calculated using the GRACE ACS Risk Model 0,36 (7, 8).

After risk score calculation, patients were divided into 3 groups as; low (<108 points), medium (109-140 points) and high risk (141-372 points) (7). Every patient's estimated glomerular filtration rate (eGFR) was calculated according to Modification of Diet in Renal Disease MDRD formula (9). Weobtained the coronary angiography (CAG) compact discs from the hospital archive and re-examined every patient's CAG CD in order to determine the number of vessels with significant stenosis. Coronary arteries with >50% stenosis were considered as having significant stenosis. Echocardiography reports were reviewed and left ventricular ejection fractions (EF) were recorded. Therapeutic strategies and in-hospital major adverse cardiac events (death, myocardial infarction (MI), recurrent ischemia and stroke) were also recorded. Written infrormed contest was obtained from all patients.

**Statistical analysis**

Calculations were performed using the SPSS (Statistical Package for Social Sciences) software for Windows 10.0 programme. Kolmogorov- Smirnov test was used for suitability of normally distributed data. One way ANOVA test was used for comparison of parametric data suitable for normal distribution between groups and when a significance was detected; the Tukey test; one of the post hoc tests; was used. Comparison of qualitative data was done by qi-square and Fisher Exact Qi-square test. Results were evaluated with 95% confidence intervals, statistical significance was considered for $p<0.05$.

## Results

The study group consisted of 95 patients (26 women, 69 men, mean age: 66.9±8.1). After GRACE risk score calculation; the number of low risk, medium risk and high risk patients were 38 (40%), 44 (46.4%) and 13 (13.6%) respectively. Patients with diabetes were 21% (8/38), 43.1% (19/44) and 36.4% (5/13), hyperlipidemia 34.2% (13/38), 15.9% (7/44) and 23% (3/13) and hypertension 57.8% (22/38), 72.7% (32/38) and 76.9% (10/13) in low, medium and high risk groups respectively. Patients with a history of previous MI were significantly lower in the low-risk group (5.2%(2/38))mid- and high risk groups (40.9%(18/44) and 30.7%(4/13)) ($p<0.001$) (Table 1). 11\38 (28.9%) of low-risk, 11\44 (25%) of medium-risk and 1\13 (7.6%) of high risk patients had 1-vessel disease.10\38 (26.3%) of low-risk, of medium-risk and 1\13 (7.6%) of high-risk patients had 2-vessel disease). Although 3-vessel disease was insignificantly higher in the low and medium risk groups (15\38 (39.4%), 15\44 (34%) respectively); it was statistically significantly higher in the high risk group (10\13 (76.9%)) ($p<0.01$). ) The left main coronary artery (LMCA) was detected in 2\38 (5.2%), 3\44 (6.8%) and 1\13 (7.6%) of low-,medium- and high- risk patients respectively. Number of diseased vessels according to groups are given in Table 2. In-hospital clinical events, ejection fractions and eGFR values are given in Table 3. Patients with low EF (<40%) were more numerous in the high-risk group (5\38 (13.1%) than medium- and low-risk groups (5\38 (13.1%) and 5\44 (11.3%) respectively)($p<0.05$). While in-hospital recurrent ischemia/MI ratios were not different among groups (7\38 (18.4%), 15\44 (34%) ad 4\13 (30.7%) in low-, medium- and high- risk patients respectively), in-hospital death was significantly higher in the high-risk group (2\13 (15.3%)) than low- and medium-risk groups (0/38(0%) and 1\44 (2.3%) ($p<0.05$). None of the patients had experienced in-hospital stroke.

Another finding was that the number of patients with eGFR less than 60 mL/dk/1.73m$^2$ was higher in the medium and high risk groups (11\44 (25%) and 4\13 (30.7%)) than the low risk group (2\38 (5.2%)) ($p<0.001$) (Table 3). Treatment strategy chosen by the physician responsible for the patient; shown in Table 4; were not statistically different among groups.

## Discussion

The necessity of identifying individual cardiac event/death risk of ACS patients is accepted worldwide and consequently many risk scoring systems have been developed by investigators (10, 11). The most wellknown of these; Thrombosis In Myocardial Infarction (TIMI), Platelet glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy (PURSUIT) and Fast Revascularisation in Instability in Coronary (FRISC) disease scoring systems; separate patients into low-medium-high risk groups according to qualitative assessment (12-14). However, a scoring system that may predict the quantitative clinical risk exactly has not yet been de-

**Table 1. Demographic characteristics according to risk groups**

| Characteristic | Low risk (n=38) | Medium risk (n=44) | High risk (n=13) | p value |
|---|---|---|---|---|
| Age (years) | 55.4±8.4 | 69.6±8.2 | 75.6±7.7 | p>0.05 |
| W/M | 5\3 | 15\29 | 8\5 | p>0.05 |
| DM | 8\38 (21%) | 19\44 (43.1%) | 5\13(36.4%) | p>0.05 |
| LDL > 100 mg/dL | 13\38 (34.2%) | 7\44 (15.9%) | 3\13 (23%) | p>0.05 |
| HT | 22\38 (57.8%) | 32\44 (72.7%) | 10\13 (76.9%) | p>0.05 |
| Previous MI | 2\38 (5.2%) | 18\44 (40.9%) | 4\13 (30.7%) | p<0.001 |

*W/M: women/men, DM: diabetes mellitus, LDL: low density lipoprotein, HT: hypertension, MI: myocardial infarction

**Table 2. Diseased vessels according to risk groups**

| Number of diseased vessels | Low risk (n=38) | Medium risk (n=44) | High risk(n=13) | p value |
|---|---|---|---|---|
| 1 vessel disease | 11\38 (28.9%) | 11\44 (25%) | 1\13 (7.6%) | p>0.05 |
| 2 vessel disease | 10\38 (26.3%) | 11\44 (25%) | 1\13 (7.6%) | p>0.05 |
| 3 vessel disease | 15\38 (39.4%) | 15\44 (34%) | 10\13 (76.9%) | p<0.01 |
| LMCA disease | 2\38 (5.2%) | 3\44 (6.8%) | 1\13 (7.6%) | p>0.05 |

*LMCA: left main coronary artery

**Table 3. In-hospital other findings**

| Finding | Low risk (n=38) | Medium risk(n=44) | High risk(n=13) | p value |
|---|---|---|---|---|
| EF < 40% | 5\38 (13.1%) | 5\44 (11.3%) | 6\13 (46.1%) | p<0.05 |
| In-hospital recurrent ischemia | 7\38 (18.4%) | 15\44 (34%) | 4\13 (30.7%) | p>0.05 |
| In-hospital death | 0\38 (0%) | 1\44 (2.3%) | 2\13 (15.3%) | p<0.05 |
| In-hospital stroke | 0 | 0 | 0 | NA |
| eGFR <60 ml/dk/1.73m$^2$ | 2\38 (5.2%) | 11\44 (25%) | 4\13 (30.7%) | p<0.001 |

*EF: ejection fraction, NA: not applicable, eGFR: estimated glomerular filtration rate

**Table 4. Therapy strategy according to risk groups**

| Therapy strategy | Low risk (n=38) | Medium risk (n=44) | High risk (n=13) | p value |
|---|---|---|---|---|
| Medical | 12\38 (31.5%) | 10\44 (22.7%) | 6\13 (46.2%) | p>0.05 |
| PCI | 20\38 (52.6%) | 16\44 (36.3%) | 3\13 (23%) | p>0.05 |
| CABG | 6\38 (15.7%) | 18\44 (40.9%) | 4\13 (30.8%) | p>0.05 |

*PCI: percutaneous coronary intervention, CABG: coronary artery by-pass graft operation

veloped. TIMI risk score was developed for use at hospital referral immediately and simply to quantitate the clinical risk and to determine response to treatment (1). Age, at least 3 risk factors for coronary artery disease, known coronary artery disease (>50% stenosis), aspirin usage in last 7 days, angina in last 24 hours, high cardiac markers and ST deviation >0.5 mm are the parameters used to calculate risk in the TIMI scoring system (11, 14). PURSUIT risk score's purpose was to determine 30-day mortality and nonfatal recurrent MI risk. Age, sex, systolic blood pressure, heart failure symptoms, heart rate, presence of ST depression, worsening of Canada Cardiovascular Society class in the previous 6 weeks are parameters looked for in the PURSUIT risk score calculation (12). Investigators of a study comparing PURSUIT and GRACE risk scoring systems found that both models' ability to predict in-hospital mortality is similar however, GRACE is a better method to predict clinical risk for whole ACS subgroups (15). On the other hand, the FRISC risk scoring system is more focused on treatment options. It includes parameters that are clinically important and easy to obtain for early invasive strategy. These parameters are; age, sex, presence of diabetes mellitus, history of MI, ST depression on admission, elevated cardiac markers and elevated IL6 and CRP levels (2).

Besides mortality and morbidity rates; patients' need for referral to tertiary centers, duration of hospital stay and choice of treatment (medical/invasive) may also be determined by risk stratification. A good scoring system should predict short and long term survival, while still containing parameters that can be easily applied at hospital admission (5).

Treatment strategies may also vary according to the risk score. Previously published studies have shown that earlier intervention and more aggressive medical treatment reduces morbidity and mortality rates significantly in patients with high risk scores (5, 14, 16).

The GRACE risk scoring system was performed in 14 countries, 94 hospitals and 22.645 ACS patients. It was designed as a multifactorial model in order to predict in-hospital and 6-month mortality and adverse cardiac events and to determine revascularization strategies according to the patient's risk status (5, 12). The eight independent parameters used in the GRACE scoring system are; age, Kıllip class at hospital admission, systolic blood pressure, heart rate, ST deviation on ECG, high initial cardiac markers, high creatinine level and cardiac arrest at hospital admission (5, 12). All these parameters are scored and the sum is then classified into low, medium and high risk subgroups (4, 5). Results of direct comparison studies between GRACE and other scoring systems establishes GRACE as the recommended risk scoring system at hospital admission and discharge (3, 5, 9). GRACE is separated from other risk scoring systems mainly in three ways: First of all, it may be applied for the whole ACS groups. Secondly, while other scoring systems' data were usually imported from large clinical trials, reflecting specific ACS patient subgroups and not including high-risk patients or patients with comorbidities; GRACE reflects the general

population because the acquisition of data was from unselected, unbiased patients, not from a certain group of patients (5, 12, 18). And the third distinction is that the GRACE risk score includes different parameters which provides more predictive information about outcome (4). The most important parameter GRACE included is the creatinine level. Although renal impairment is one of the independent predictors of morbidity and mortality in ACS patients, other risk scoring systems not only excluded patients with renal failure from the studies, they also did not score the creatinine levels. Similarly, heart failure; a parameter known to be an important indicator of morbidity and mortality in this group of patients; was not included in the TIMI scoring system (4, 5, 12).

A risk model that may anticipate coronary anatomy has not been developed to date. Only the FRISC scoring system submitted some data about coronary anatomy. The investigators showed a relationship between 3 vessel and LMCA disease and a high FRISC score (2).

Our study showed that the GRACE risk score calculated at hospital admission may also predict coronary anatomy besides mortality and adverse cardiac events. non-ST elevation ACS patients with high GRACE risk score may point out 3-vessel disease.In addition, the GRACE score was found to be higher in patients with low EF. We also observed that frequency of hypertension, diabetes and hyperlipidemia were not statistically different among risk groups, showing that these classical coronary artery disease risk factors are singly insufficient to determine either the risk status or the coronary anatomy.

As mentioned earlier by other studies, renal failure (especially in the geriatric patient group) is one of the most important prognostic indicators (4). As sex, weight, diet, muscle mass and some other situations may affect creatinine levels; glomerular filtration rate (GFR) measurement is more objective and reliable than creatinine levels to determine renal functions and is the recommended method at the present time (19, 20). GRACE investigators included creatinine level measurements and defined it as an independent factor with prognostic value (4). We also searched for a relationship between risk groups and eGFR measurements in subgroup analysis and found that the medium and high GRACE risk groups had more patients with eGFR<60 mL/dk/1.73m$^2$ than the low-risk group. We believe these findings may help physicians in deciding on the treatment strategy and the medications to give to each patient. For example; in patients with high GRACE risk score, if medical therapy is planned, physicians may not choose nephrotoxic drugs or, if invasive therapy is planned, physician would be aware of contrast induced nephropathy because he/she would know that high-risk patients may have impaired renal functions.

Treatment methods were not significantly different among risk groups in our study. This may be because the number of patients included in the study was small. On the other hand, previously published reports have shown that the aggressive treatment which should be performed as current guidelines recommend is administered less often in the high-risk NST-ACS patient group than medium and low risk groups (12, 20). Similarly, we observed that, although statistically not significant; medical strategy was more often the treatment of choice for the high risk group.

### Study limitations

The major limitation of this study is the small sample size. One of the reasons for this is disorganized and insufficient archiving system. We observed that many parameters that should have been evaluated during hospital admission were not recorded in patient files and that was the main reason of excluding patients from the study. Nevertheless, we were able to reach several significant conclusions. A group of patients with premature deaths and complications may have been omitted since our study was based on retrospective diagnosis. Because this was a single-centered study, our study reflects the results of a particular region and the choice of treatment strategies are only based on a single-center. Another limitation is the lack of long-term follow-up of patients.

## Conclusion

As the calculated GRACE risk score in the emergency room for ACS patients can predict in-hospital mortality and clinical events; it may also predict coronary anatomy, low ejection fraction and low eGFR. And so the GRACE scoring system may guide physicians when planning treatment strategies.

**Conflict of Interest**
No conflict of interest was declared by the authors.

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**Ethics Committiee Approval:** Ethics committee approval was received from the ethic committee of İstanbul University Medical Faculty (Protocol no. 8643).

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

**Author Contributions**
Concept - O.K., H.E.G.; Design - Y.D., O.K.; Supervision - Y.S.S., O.K.; Funding - E.Ö., H.B.; Materials - V.T., H.B.; Data Collection and/or Processing - Y.D., E.Ö., N.D.; Analysis and/or Interpretation - H.E.G., O.K., N.D.; Literature Review - Y.D., O.K.; Writing - H.E.G., Y.D.; Critical Review - O.K., Y.D.; Other - V.T.

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