Original Paper

Clinical SYNTAX Score Can Predict Acute Kidney Injury following On-Pump but Not Off-Pump Coronary Artery Bypass Surgery

Mete Gursoy^a Abdulkadir Faruk Hokenek^a Egemen Duygu^b
Mehmet Atay^d Asuman Yavuz^c

Departments of ^aCardiovascular Surgery and ^bCardiology, Acibadem International Hospital, and ^cDepartment of Nephrology, Acibadem University, Istanbul, and ^dDepartment of Cardiovascular Surgery, Karaman State Hospital, Karaman, Turkey

Key Words

Clinical SYNTAX score · Coronary bypass · Off-pump coronary artery bypass grafting · Acute kidney injury · RIFLE criteria

Abstract

Background: The complexity of coronary artery disease is usually a neglected factor in risk stratification systems. We aimed to analyze the discriminative ability of the clinical SYNTAX score (CSS) for acute kidney injury (AKI) following on- and off-pump coronary artery surgery. **Methods:** A total of 193 patients were reviewed in this study. Patients were divided into two groups according to the surgical procedure (group I: off-pump coronary artery bypass grafting, n = 89; group II: on-pump coronary artery bypass grafting, n = 104). Preoperative demographic data, the CSS and postoperative renal functions were evaluated. The postoperative AKI classification was made using the RIFLE (Risk, Injury, Failure, Loss of function, and End-stage renal disease) criteria. **Results:** Postoperative AKI occurred in 14 of 89 patients (15.7%) in group I and in 29 of 104 patients in group II (27.8%; p = 0.046). The CSS did not vary much between the groups (31.52 ± 13.08 vs. 29.89 ± 15.70; p = 0.638). In group I, the CSS was not different between patients with AKI and those without AKI (30.167 ± 3.93 vs. 31.91 ± 14.75; p = 0.78). In group II, the CSS was 36.85 ± 18.33 in patients with AKI and 28.02 ± 12.32 in those without, and the difference was significant (p = 0.02). The discriminative ability of the CSS for postoperative AKI using the AUC analysis was 0.500 in group I and 0.840 in group II. **Conclusion:** The CSS may be a simple and successful means of risk prediction of postoperative AKI in on-pump coronary artery surgery.

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Mete Gursoy, MD
Acibadem International Hospital Istanbul, Cad. No. 82
TR-34149 Yesilkoy, Istanbul (Turkey)
E-Mail metegursoy35@gmail.com

Introduction

Postoperative acute kidney injury (AKI) is one of the most common and potentially life-threatening complications of cardiac surgery, with an incidence between 8.9 and 39% [1–5]. AKI and even subclinical creatinine changes increase mortality following coronary artery bypass grafting [6].

The SYNTAX score (synergy between percutaneous coronary intervention with taxus and cardiac surgery) is a risk stratification tool that evaluates the complexity and prognosis of patients undergoing percutaneous coronary intervention [7–9]. Recently, some authors have used SYNTAX scores to predict major adverse cardiac and cerebrovascular events following coronary artery bypass grafting [10, 11]. The clinical SYNTAX score (CSS) is a combination of age, ejection fraction, decrease in creatinine clearance and classic SYNTAX score. The CSS has been found to be superior in predicting the 30-day and 1-year clinical outcome, compared to the SYNTAX scores by Jou et al. [11].

In this study, we aimed to analyze the validity of the CSS in predicting the incidence and severity of AKI and other risk factors in patients who underwent off- and on-pump coronary artery bypass grafting.

Materials and Methods

The Institutional Review Board approved the present study. We retrospectively analyzed 272 patients who underwent cardiac surgery between December 2013 and December 2014. A total of 79 patients were excluded, and we reviewed the laboratory, echocardiographic, angiographic, operative and clinical data of the remaining 193 patients. The criteria for excluding patients are shown in a flow diagram (fig. 1). Patients who underwent off-pump coronary artery surgery were enrolled in group I (n = 89), and patients who underwent on-pump coronary artery surgery were enrolled in group II (n = 104).

The total SYNTAX score was derived from the summation of the individual scores for each separate lesion (defined as >50% stenosis in vessels >1.5 mm). Full details on the SYNTAX score calculation are reported elsewhere [7]. All angiographic variables related to the SYNTAX score were evaluated by 2 experienced cardiologists who were blinded to the procedural data and the clinical outcome on angiograms. In cases of disagreement, the opinion of a third observer was obtained, and the final decision was made by consensus [12].

The CSS was calculated retrospectively for each patient using the following formula: CSS = SYNTAX score × modified ACEF (age, creatinine clearance, ejection fraction) score. The modified ACEF score (ACEF_{CrCl}) was calculated using the following formula: age/ejection fraction + 1 point for every 10 ml/min reduction in CrCl <60 ml/min/1.73 m² (up to a maximum of 6 points) [13].

The patients' biochemical analysis was done using the kinetic method with a COBAS Integra[®] 400 plus (Roche Diagnostics GmbH, Mannheim, Germany). Hemograms were done using the flow cytometry method with a SUSMEX XT1800i (Siemens, Erlangen, Germany).

Statistical Analysis

Data were analyzed with the Statistical Package for the Social Sciences version 17.0 (SPSS Inc., Chicago, Ill., USA). All data were expressed as means ± standard deviations. The Kolmogorov-Smirnov test was used to analyze the results with respect to normal distribution. Student's t test and the Mann-Whitney U test were used to compare quantitative data, and the χ^2 test was used to compare categorical data. The receiver operating characteristic (ROC) test was used to determine the discriminative ability of the CSS for postoperative AKI. A p value of 0.05 was considered statistically significant.

AKI Definition

AKI was diagnosed and categorized according to the RIFLE (Risk, Injury, Failure, Loss of function, and End-stage renal disease) criteria. A patient was categorized in the risk stage when the postoperative serum creatinine value increased by 1.5–2 times the baseline, in the injury stage when the creatinine value increased 2–3 times the baseline, and in the failure stage in the presence of a >3-fold increase or a >4 mg/dl creatinine

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Fig. 1. Flow diagram of the study. LVEF = Left ventricular ejection fraction.

value. Complete loss of renal function (requiring dialysis) lasting more than 4 weeks was termed 'loss of function', and 'ESRD' (end-stage renal disease) was the term for the loss of renal function for >3 months [14].

Surgical Technique

Patients were operated under general anesthesia and with full median sternotomy. Operations were performed by 2 surgeons with expertise in off- and on-pump coronary artery surgery. Operative procedure selection was done with the consensus of the surgeons preoperatively. In patients with thinner, tortuous, intramural or severely calcified target coronary arteries, the on-pump procedure was preferred. A predicted bypass graft count was not accepted as criteria in the decision making. In patients with a severely calcified aorta, the no-touch off-pump procedure was preferred. Anesthesia was achieved with midazolam, remifentanyl, pancuronium and sevoflurane. The left internal thoracic artery was used in all patients regardless of the patient's age and comorbidities. A radial artery graft was preferred as a second arterial graft, particularly in diabetics (22 in group I, 19 in group II). In group I, positioning of the heart was achieved with a stabilizer, an apex holder and a posterior pericardial stitch. Distal anastomosis was done using an intracoronary shunt. In group II, aorta two-stage cannulation was done and cardiopulmonary bypass was performed with a Stöckert roller pump system (Stöckert Instrumente GmbH) and a Sorin-Dideco Masterflow D-703 hollow-fiber oxygenator. Periodic antegrade blood cardioplegia was used for myocardial protection. Operations were done under mild hypothermia (32°C). Proximal anastomosis was completed with the aid of a side

Table 1. Demographic features of the patients

Parameter	Group I	Group II	p value
Patients	89	104	
Age, years	62.85 ± 10.52	63.04 ± 10.39	0.911
Males, %	71.90	68.20	0.738
Diabetes mellitus, %	41	37	0.213
Hypertension, %	36	31	0.23
Hyperlipidemia, %	23	26	0.175
Smoking history, %	39	36	0.11
Peripheral artery disease, %	11	9	0.187
EuroSCORE II	0.92 ± 0.05	1.09 ± 0.07	0.002
SYNTAX	24.46 ± 8.92	20.92 ± 7.31	0.019
Left atrium diameter, mm	36.08 ± 0.48	37.62 ± 0.94	0.172
Ejection fraction, %	54.33 ± 1.61	52.92 ± 1.11	0.051

clamping of the aorta. In patients whose aorta was calcified, proximal anastomosis was done to the left internal thoracic artery. Heparinization was planned to take 300 s for activated coagulation time in group I and 450 s in group II. The postoperative target hematocrit value was 30 mg/dl in group II.

Hemodynamic Management

In group I, we aimed to protect normotension and the normal heart rate. Low-dose (0.01 mg/kg/min) intravenous noradrenalin perfusion, volume support and table positioning were used as required. In group II, the perfusion rate was planned to achieve 2.4 liters/m² flow and 60–70 mm Hg mean pressure under cardiopulmonary bypass. Dopamine was the first choice in patients who needed inotropic support. Adrenalin infusion and an intra-aortic balloon pump were used according to surgeons' and cardiac anesthetists' decisions.

Results

A total of 193 patients were included in the study (n = 89 in group I and n = 104 in group II). Their mean age was 62.85 ± 10.52 years in group I and 63.04 ± 10.39 years in group II (p = 0.91). Gender distribution was similar. Hypertension, hyperlipidemia, diabetes mellitus, smoking and peripheral artery disease history were also similar between groups. Although the incidence of diabetes mellitus was similar (41 vs. 37%), the mean hemoglobin A_{1c} (HbA_{1c}) value was found to be higher in group I (6.32 ± 0.46 vs. 5.84 ± 0.29%; p = 0.035). The patients' demographic features are summarized in table 1.

The patients' operative risk was calculated with the EuroSCORE II system and was found to be significantly higher in group II (0.92 ± 0.04 vs. 1.09 ± 0.07; p = 0.002). Quantification of the complexity of coronary artery disease was measured with the SYNTAX system and found to be significantly different between groups (24.46 ± 8.92 vs. 20.92 ± 7.31; p = 0.019).

The mean number of bypass grafts was 2.43 ± 0.92 in group I and 2.65 ± 0.82 in group II (p = 0.189). In group I, the mean number of bypass grafts was similar between patients with and those without AKI (2.57 ± 0.97 vs. 2.40 ± 0.92; p = 0.677). In group II, the mean number of bypass grafts was 2.72 ± 0.75 in patients with AKI and 2.62 ± 0.86 in those without AKI (p = 0.660). In an analysis of patients with AKI, the difference was insignificant between groups (p = 0.721).

Postoperative AKI occurred in 14 of the 89 patients (15.7%) in group I and in 29 of the 104 patients in group II (27.8%; p = 0.046). RIFLE categories of these patients are summarized in figure 2. Postoperative changes in creatinine are shown in figure 3.

Fig. 2. RIFLE categories of patients in both groups. **Fig. 3.** Postoperative creatinine change in patients.

The mean transfused red blood cell package was 1.27 ± 0.92 units in group I and 2.38 ± 1.47 units in group II ($p = 0.035$). No difference was found between patients with and those without AKI in either group.

The CSS was similar for both groups (31.52 ± 13.08 vs. 29.89 ± 15.70 ; $p = 0.638$). In group I, the CSS was not different between patients with AKI and those without (30.167 ± 3.93 vs. 31.91 ± 14.75 ; $p = 0.78$). In group II, the CSS was 36.85 ± 18.33 in patients with AKI and 28.02 ± 12.32 in patients without AKI; the difference was significant ($p = 0.02$).

The discriminative ability of the CSS for postoperative AKI using the AUC was 0.500 in group I and 0.840 in group II (fig. 4, 5).

Advanced age, a lower hematocrit level, and higher EuroSCORE II, C-reactive protein, HbA_{1c} and blood urea nitrogen values were found to be significant risk factors for AKI in group I. In group II, female gender, advanced age, a lower hematocrit level, and higher HbA_{1c} and EuroSCORE II values were found to be significant risk factors for postoperative AKI. In this group, cardiopulmonary bypass time and aortic cross-clamp time were compared and, although both of them were higher in patients with AKI, the difference was not statistically significant between patients with and those without AKI (cardiopulmonary bypass time:

Fig. 4. ROC of the CSS for AKI in group I patients.

Color version available online

Fig. 5. ROC of the CSS for AKI in group II patients.

Color version available online

79.39 ± 35.39 vs. 70.92 ± 25.57 min, $p = 0.373$, and aortic cross-clamp time: 47.17 ± 32.71 vs. 39.97 ± 15.48 min, $p = 0.271$).

Preoperative risk factors were compared between the groups for patients who had postoperative AKI. Hematocrit, hyperlipidemia and smoking history were significantly different between groups ($p = 0.029$, $p = 0.048$ and $p = 0.048$, respectively). A lower preoperative hematocrit level was the strongest risk factor for AKI following coronary artery bypass grafting.

In hospital, mortality occurred in 1 patient (group II), and no mortality occurred in the 30-day postoperative period.

Discussion

The present study found that off-pump coronary artery surgery may significantly decrease the incidence of postoperative AKI in patients with a high mean age and of either gender, despite the presence of more complex coronary involvement. The CSS was slightly

higher in group I. In this group, the CSS was not found to be significantly different in patients who had postoperative AKI compared to those who did not. However, in group II, the CSS was significantly higher in patients who had postoperative AKI. The discriminative ability of CSS to predict postoperative AKI by AUC was 0.500 in group I and 0.840 in group II. In this context, CSS can predict the occurrence of postoperative AKI in patients who undergo on-pump coronary artery bypass grafting.

The SYNTAX score shows the complexity and severity of coronary artery disease. Several studies have focused on the peripheral endothelial function and coronary artery disease [15–17]. Kuvin et al. [15] found an association between coronary atherosclerosis and impaired endothelium-dependent vasomotion using high-resolution brachial artery ultrasound imaging. In their study, flow-mediated vasodilation was found to be significantly decreased in patients with positive exercise myocardial perfusion imaging. Matsuzawa et al. [17] reported a correlation between impairment of peripheral finger endothelial function and coronary microvascular function. Recently, Gori et al. [16] found a progressive decline in low flow-mediated vasoconstriction and flow-mediated vasodilation across levels of coronary artery disease which were angiographically measured using SYNTAX.

Atherosclerosis is the most important cause of endothelial dysfunction and damages endothelial integrity; the endothelium has a pivotal role in vasomotor reactions and flow regulation with vasoactive substance release [18]. Endothelium-derived vasoconstrictor agents include superoxide radicals, eicosanoids and endothelin, which may circulate in the bloodstream and can cause vasoconstriction far from where it was released. Endothelium-derived relaxing factor/nitric oxide is a potent vasodilator agent and also inhibits platelet adhesion and aggregation. The release of nitric oxide occurs when the endothelium is intact [18, 19]. This would explain the impaired vasorelaxing response, vasospasm and increased blood coagulation in vascular beds with endothelial lesions. Renal vasoconstriction and increased renal vascular resistance have been shown to be important in AKI pathogenesis. In animal studies, ischemic acute renal failure has been especially associated with abnormal vasomotor responses due to endothelial damage [20].

In on-pump cardiac surgery, various factors effect renal perfusion and stimulate renal vasoconstriction: systemic inflammation, hypoperfusion, ischemia reperfusion injury, acidosis, vasopressor medications, hypothermia, hemolysis, embolism and nonpulsatile flow [21–24]. The release of vasodilator cyclooxygenase metabolites and the formation of nitric oxide following compromised renal circulation are important for the restoration of renal blood flow after ischemia reperfusion injury of the renal vascular bed [25]. This may show the importance of endothelial function for the protection of renal blood flow at the rewarming stage and the weaning from cardiopulmonary bypass. Off-pump surgery may have the advantages of avoiding inflammation related to cardiopulmonary bypass lines, hypothermia and hemodilution, as well as the maintenance of pulsatility. In this context, patients who undergo off-pump coronary artery surgery may be less affected by endothelial dysfunction even if they have more complex coronary atherosclerosis.

The CSS is a combination of modified ACEF and SYNTAX scores. Elements of the modified ACEF score are: advanced age, left ventricle dysfunction and decreased creatinine clearance, which are well-known risk factors for the occurrence of renal impairment [26]. In our study, the modified ACEF and SYNTAX scores failed in the prediction of AKI in both groups separately. However, the CSS was found to be successful in the prediction of AKI in the on-pump group. This result may indicate an association of clinical risk factors and the severity of coronary atherosclerosis and may provide useful information about who has a higher risk of AKI following on-pump coronary bypass.

Our study limitations are the small patient population and retrospective design. The groups were not randomized, and the surgical procedure decision was made with the

consensus of the cardiac surgeons. Prospective randomized studies with a larger sample size are required.

In conclusion, a combination of clinical parameters and the angiographic complexity of coronary atherosclerosis may be a simple and successful system for the risk prediction of postoperative AKI in on-pump coronary artery surgery.

Disclosure Statement

The authors have no conflicts of interest to disclose.

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