Usefulness of the SYNTAX Score to Predict Acute Kidney Injury After Percutaneous Coronary Intervention (from the Acute Catheterization and Urgent Intervention Triage Strategy Trial)

Mahesh V. Madhavan, BA[a], Philippe Généreux, MD[a,b,c,*], Jonah Rubin, BA[a], Tullio Palmerini, MD[d], Adriano Caixeta, MD, PhD[e], Ke Xu, PhD[b], Giora Weisz, MD[a,b], Roxana Mehran, MD[b,f], and Gregg W. Stone, MD[a,b]

The synergy between percutaneous coronary intervention (PCI) with Taxus and cardiac surgery (SYNTAX) score (SS) has prognostic utility for ischemic outcomes in patients undergoing PCI. Acute kidney injury (AKI) after PCI has been demonstrated to be associated with adverse outcomes. However, the relation between the SS and AKI after PCI has yet to be fully investigated. We therefore sought to study this relation in the formal angiographic substudy of the large Acute Catheterization and Urgent Intervention Triage Strategy trial. We stratified 2,268 patients who underwent PCI for non−ST-segment elevation acute coronary syndromes by postprocedural AKI status and by SS tertiles (SS <7, 7 to 12, and >12). We also assessed rates of in-hospital, 30-day, and 1-year adverse outcomes. A total of 226 patients (10%) developed AKI, and rates in the highest Acute Catheterization and Urgent Intervention Triage Strategy SS tertile (>12) were significantly greater than those in the intermediate (7 to 12) and lowest tertiles (<7; 13% vs 8.9% vs 7.7%, respectively, p = 0.002). By multivariable analysis, the SS was independently associated with AKI (odds ratio per 10 SS points 1.22, 95% confidence interval 1.04 to 1.43, p = 0.02. Rates of major adverse cardiovascular events and net adverse clinical events increased significantly by SS tertile and were more common in patients who developed AKI. Patients who developed AKI experienced higher in-hospital, 30-day, and 1-year rates of mortality. In this large study, the SS was independently associated with AKI after PCI for non−ST-segment elevation acute coronary syndromes, and patients who developed AKI experienced worse short-term and long-term outcomes. **(Am J Cardiol 2014;113:1331−1337)**

Acute kidney injury (AKI) is a frequent complication of percutaneous coronary intervention (PCI). AKI after PCI, which is most often attributed to contrast exposure, has been repeatedly demonstrated to be associated with increased rates of adverse events, including death, myocardial infarction, and end-stage renal disease.[1−4] Previous studies have attempted to develop risk scores for postprocedural AKI based principally on clinical predictors.[5,6] Although angiographic variables have prognostic utility for the development of adverse cardiovascular events after PCI, their relation with the development of AKI has yet to be definitively established. The synergy between PCI with Taxus and cardiac surgery (SYNTAX) score (SS), a tool developed to assess the extent and burden of coronary artery disease, has demonstrated prognostic utility in patients with both stable coronary artery disease and acute coronary syndromes undergoing PCI.[7−9] Recent reports have suggested that the SS has an association with the development of AKI after primary PCI for ST-segment elevation myocardial infarction.[10,11] However, these studies were limited by small sample sizes, single center design, and/or lack of blinded core lab assessment. Moreover, the association between the SS and AKI after PCI for non−ST-segment elevation acute coronary syndrome (NSTEACS) has yet to be evaluated. We therefore sought to assess this relation in the large Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) trial.[12]

Methods

The ACUITY trial design and primary results have been previously described in detail.[12,13] Briefly, ACUITY was a multicenter, prospective, randomized trial of 13,819 patients with moderate- and high-risk NSTEACS who were treated with an early invasive strategy. Major inclusion criteria were age ≥18 years with symptoms of unstable angina lasting ≥10 minutes duration within 24 hours of randomization and ≥1 of the following: new ST-segment depression or transient elevation of at least 1 mm, cardiac biomarker elevations, known coronary artery disease, or all 4 other variables as part of the thrombolysis in myocardial

[a]NewYork-Presbyterian Hospital and the Columbia University Medical Center, New York, New York; [b]Cardiovascular Research Foundation, New York, New York; [c]Hôpital du Sacré-Coeur de Montréal, Université de Montréal, Montréal, Canada; [d]Istituto di Cardiologia, University of Bologna, Italy; [e]Hospital Israelita Albert Einstein and Escola Paulista de Medicina, Universidade Federal de Sao Paulo, Brazil; and [f]Mount Sinai Medical Center, New York, New York. Manuscript received August 25, 2013; revised manuscript received and accepted December 30, 2013.

Mahesh V. Madhavan and Dr. Philippe Généreux contributed equally to this article.

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*Corresponding author: Tel: (646) 434-4383; fax: (646) 434-4464.

E-mail address: pg2295@columbia.edu (P. Généreux).

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Table 1
Baseline clinical characteristics according to the development of postprocedural acute kidney injury (AKI)

Variable	AKI		p Value
	Yes (n = 226)	No (n = 2,042)	
Age (yrs)	63.2 ± 12.9	60.3 ± 11.5	0.002
Women	103 (46)	627 (31)	<0.0001
Diabetes mellitus	91/225 (40)	557/2,030 (27)	<0.0001
Insulin treated	39/225 (17)	140/2,030 (6.9)	<0.0001
Hypertension*	176 (78)	1,301/2,036 (64)	<0.0001
Hyperlipidemia†	115/221 (52)	1,115/2,012 (55)	0.35
Current smoker	65/224 (29)	742/2,035 (37)	0.03
Previous myocardial infarction	68/222 (31)	572/2,000 (29)	0.53
Previous PCI	87/225 (39)	909/2,040 (15)	0.10
Renal insufficiency‡	43/225 (19)	312/2,040 (15)	0.15
Left ventricular ejection fraction (%)	62 ± 13	65 ± 12	0.002
White blood cell count (10^9/L)	8.8 ± 3.1	8.6 ± 3.2	0.25
Hemoglobin (g/dl)	13.5 ± 1.8	14.0 ± 1.6	<0.0001
Platelet count ($\times 10^3$/mm^3)	247.3 ± 69.7	239.2 ± 68.2	0.10
Cardiac biomarker elevation	154/216 (71)	1,157/1,949 (59)	0.0007
ST-segment deviation ≥1 mm	64 (28)	517 (25)	0.34
TIMI risk score			
Low (0–2)	27/181 (15)	282/1,651 (17)	0.53
Intermediate (3–4)	101/181 (56)	974/1,651 (59)	0.43
High (5–7)	53/181 (29)	395/1,651 (24)	0.12
Mehran risk score	6.1 ± 4.1	4.7 ± 3.5	<0.0001

Data are presented as mean ± SD, n (%), or median (IQR).
eGFR = estimated glomerular filtration rate; IQR = interquartile range; TIMI = thrombolysis in myocardial infarction.
* Hypertension is defined as on antihypertensive medication on admission.
† Hyperlipidemia is defined as on lipid-lowering medication on admission.
‡ Renal insufficiency is defined as eGFR <60 ml/min/1.73 m^2 by the Cockcroft-Gault equation.

infarction risk score for unstable angina.[14] Exclusion criteria included acute ST-segment elevation myocardial infarction or shock; bleeding diathesis or recent major bleeding episode; thrombocytopenia; estimated glomerular filtration rate by the Cockcroft-Gault equation of <30 ml/min/1.73 m^2; recent antithrombotic or thrombolytic agent administration; and allergy to study drugs or iodinated contrast medium not amenable to pretreatment.

Before coronary angiography, patients were randomly assigned to heparin (unfractionated or low molecular weight) plus a glycoprotein IIb/IIIa inhibitor, bivalirudin plus a glycoprotein IIb/IIIa inhibitor, or bivalirudin monotherapy. Angiography was performed within 72 hours of randomization, and depending on coronary anatomy, patients were triaged to PCI, coronary artery bypass graft (CABG) surgery, or medical therapy. In patients who underwent PCI, stent choice (bare metal or drug eluting) was per operator discretion. Aspirin and clopidogrel were recommended for at least 1 year. An independent clinical events committee, blinded to treatment assignment, adjudicated all major adverse events.

Our primary objective was to assess the relation between SS and risk of developing AKI within 48 hours after PCI for NSTEACS. We included only patients in whom quantitative coronary angiography was performed by experienced core laboratory technicians, blinded to randomization and clinical outcomes (Cardiovascular Research Foundation, New York, New York), as part of the formal ACUITY angiographic substudy.[15] Because the SS had only been validated for native coronary arteries at the time of our angiographic analysis,[16] patients with previous CABG were excluded.

Three experienced interventional cardiologists (P.G., T.P., and A.C.), who were also blinded to randomization and clinical outcomes, assessed the SS for each angiogram. Lesions causing ≥50% reduction in luminal diameter in vessels with a minimal diameter of 1.5 mm were scored using the SS algorithm as described elsewhere.[17] The Fleiss kappa statistic[18] (tertile partitioning), determined by each of the 3 readers independently reading 50 films, was 0.57. This value signifies a moderate level of interobserver agreement comparable with what was achieved in the SYNTAX trial.[19] Additionally, in an effort to determine the association between the completeness of revascularization, the SS, and rates of postprocedural AKI, the previously described residual SS (assessed after PCI) was determined for each group.[20]

Rates of AKI were assessed using 2 definitions, based on severity of postprocedural renal dysfunction. First, we applied the most widely adopted definition: a rise in serum creatinine from baseline by ≥0.5 mg/dl or ≥25% within 48 hours post-PCI.[1] Additionally, severe AKI was defined as a serum creatinine increase of ≥1 mg/dl or ≥50% within 48 hours after PCI.[1] We also determined rates of death (cardiac and noncardiac), myocardial infarction, ischemia-driven target vessel revascularization (TVR), non-CABG major and minor bleeding, major adverse cardiovascular events (MACE), and net adverse clinical events (NACE), for which definitions have been previously reported.[13] MACE was defined as any death, myocardial infarction, or unplanned ischemia-driven TVR. NACE was defined as any MACE or non-CABG major bleeding. Non-CABG major bleeding was defined as intracranial or intraocular bleeding, access site hemorrhage requiring intervention, hematoma ≥5 cm in diameter, reduction in hemoglobin levels ≥4 g/dl without an overt bleeding source or ≥3 g/dl with an overt source, reoperation for bleeding, or any blood product transfusion.

We stratified patients by SS based on true tertile cutoffs from the ACUITY trial population (<7, 7 to 12, and >12). We also divided patients by tertile cutoffs from the original SYNTAX trial (<23, 23 to 32, and >32).[7] Score ranges will be referred to as $SS_{<7}$, $SS_{7\ to\ 12}$, and $SS_{>12}$ and $SS_{<23}$, $SS_{23\ to\ 32}$, and $SS_{>32}$, respectively. To assess how the purely angiographic SS compared with clinical scores for AKI, the Mehran risk score[5] was determined using the following variables: age >75 years, anemia, chronic kidney disease, diabetes, intra-aortic balloon pump, and contrast volume. Continuous data are presented as mean ± SD and were compared using the Student *t* test or analysis of variance, as appropriate. Binary variables (including in-hospital outcomes) are presented as n (%) and were compared between groups with the chi-square test. Thirty-day and 1-year event