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Choice of Estimated Glomerular Filtration Rate Equation Impacts Drug-Dosing Recommendations and Risk Stratification in Patients With Chronic Kidney Disease Undergoing Percutaneous Coronary Interventions

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ABSTRACT

BACKGROUND Multiple equations exist to estimate glomerular filtration rate (GFR); however, there is no consensus on which is superior for risk classification in patients with chronic kidney disease (CKD) undergoing percutaneous coronary intervention (PCI).

OBJECTIVES The goals of this study were to identify which equation to estimate GFR is superior for predicting adverse outcomes after PCI and to examine how equation selection would impact drug-dosing recommendations.

METHODS Estimated GFR (eGFR) was calculated with the Cockcroft-Gault, Modification of Diet in Renal Disease Study (MDRD), and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations for 128,805 patients undergoing PCI in the state of Michigan. Agreement between patient pre-PCI eGFR estimates and resultant CKD stage classifications, their ability to discriminate post-procedural in-hospital clinical outcomes, and the impact of equation choice on dosing recommendations for commonly used antiplatelet and antithrombotic medications were investigated.

RESULTS CKD-EPI best discriminated post-PCI mortality by receiver operator characteristic analysis. There was wide variability in eGFR, which persisted after grouping by CKD stages. Reclassification by CKD-EPI resulted in net reclassification index improvement for acute kidney injury and new requirement for dialysis. Equation choice affected drug-dosing recommendations, with the formulas agreeing for only 50.3%, 40.0%, and 34.3% of potentially impacted patients for eGFR cutoffs of <60, <50, and <30 ml/min/1.73 m^2, respectively.

CONCLUSIONS Different eGFR equations result in CKD stage reclassification that has major clinical implications for predicting adverse outcomes after PCI and drug-dosing recommendations. Our results support the use of CKD-EPI for risk stratification among patients undergoing PCI. (J Am Coll Cardiol 2015;65:2714–23) © 2015 by the American College of Cardiology Foundation.

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For patients with acute coronary syndrome who undergo percutaneous coronary intervention (PCI), chronic kidney disease (CKD) and advanced age are associated with an increased risk of adverse outcomes, including in-hospital mortality, bleeding, and acute kidney injury (1–3). Estimated glomerular filtration rate (eGFR), the most common method used to diagnose and stage CKD, can be calculated by several equations, including the Cockcroft-Gault equation, the Modification of Diet in Renal Disease (MDRD) Study equation, and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation (4–6). The Berlin Initiative Study (BIS1) equation was developed recently in adults ≥70 years of age in an attempt to more accurately predict eGFR in this subgroup (7). The 2012 Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommend that clinicians use CKD-EPI because of its superior accuracy (8). The Cockcroft-Gault equation is no longer recommended because it was developed before the standardization of creatinine assays and is less accurate (9); however, the preference for which estimate to use varies widely among institutions, and the Cockcroft-Gault equation is still often used in clinical practice and in pharmacokinetic studies (10).

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Although others have shown that the use of different equations can result in CKD stage reclassification, it is unclear how this would impact prognostication for patients undergoing PCI. We investigated whether the use of different eGFR equations would result in different CKD staging of patients undergoing PCI and examined how reclassification correlates with risk of adverse events after PCI. We then extended our analysis to determine how differences in CKD classification would affect the dosing of commonly used antiplatelet and antithrombotic agents in the catheterization laboratory.

METHODS

We performed a retrospective post-hoc analysis using data from the Blue Cross Blue Shield of Michigan Cardiovascular Consortium, a regional registry of all patients undergoing PCI at nonfederal hospitals in Michigan. A detailed outline of the registry has been described previously (11). To summarize, this is a prospective, multicenter, statewide registry of patients undergoing PCI at 47 participating centers. For our present study, consecutive patients undergoing emergent or elective PCI between January 2010 and March 2014 were included. We excluded all patients who required hemodialysis before PCI, those with incomplete data on serum creatinine levels before or after PCI, and those without both a height and weight recorded. Pre-procedural serum creatinine values were measured within 30 days before PCI, with the value closest to the time of PCI chosen as the baseline value. Peak post-procedural creatinine was defined as the highest value after PCI and before the next procedure or discharge.

ESTIMATION OF GLOMERULAR FILTRATION RATE. For our population of all-comers, we calculated eGFR using the Cockcroft-Gault, MDRD, and CKD-EPI equations. Each equation is provided with a summary of its developmental cohort in Table 1. The Cockcroft-Gault equation calculates creatinine clearance and not eGFR; however, its output has been compared in the literature with the eGFR of other equations, both with and without adjustment for body surface area (12,13). We performed our analysis with the unadjusted Cockcroft-Gault output and an additional analysis with Cockcroft-Gault adjusted for body surface area by normalizing the output per 1.73 m^2 of body surface area (identical to the normalization of the glomerular filtration rate [GFR] measurement) (14). Additionally, because of unclear recommendations for body weight, estimation of eGFR by Cockcroft-Gault was calculated twice, with both actual and ideal body weight (15). For analysis of the subgroup of patients ≥70 years of age, eGFR was also calculated by the BIS1 equation.

STUDY ENDPOINTS. The diagnostic accuracy of candidate eGFR estimates was evaluated with respect to 4 in-hospital clinical outcomes, including the primary endpoint of acute kidney injury (AKI) and secondary endpoints of new requirement for dialysis (NRD), in-hospital mortality, and receipt of transfusion. AKI was defined as a ≥0.5 mg/dl increase in absolute serum creatinine from the baseline pre-procedural value (16,17). NRD was defined as any new, unplanned need for dialysis after PCI. In-hospital mortality was defined as mortality attributable to any cause during the initial hospitalization after PCI. Receipt of transfusion was defined as the transfusion of whole blood or packed red blood cells from the time of PCI to before discharge or death.

STATISTICAL ANALYSIS AND DATA VISUALIZATION. Scatterplots comparing the eGFRs were used to visualize disagreement between eGFR estimates at the patient level. Estimated eGFRs values were winsorized (censored) at 200 ml/min for convenience in graphic representation and to prevent the undue influence of large-value outliers on the analysis. Lin's

ABBREVIATIONS AND ACRONYMS

AKI = acute kidney injury

BIS1 = Berlin Initiative Study

CKD = chronic kidney disease

CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration

eGFR = estimated glomerular filtration rate

GFR = glomerular filtration rate

KDIGO = Kidney Disease Improving Global Outcomes

MDRD = Modification of Diet in Renal Disease

NRD = new requirement for dialysis

NRI = net reclassification index

PCI = percutaneous coronary intervention