# Proteinuria predicts postcardiotomy acute kidney injury in patients with preserved glomerular filtration rate

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**Objective:** Acute kidney injury is a common and serious problem after cardiac surgery. Postoperative acute kidney injury is independently associated with in-hospital mortality and long-term morbidity, even after adjustment for comorbid diseases. Chronic kidney disease has been recognized as a strong risk factor of acute kidney injury after cardiac surgery. The association between proteinuria and postcardiotomy acute kidney injury in patients with preserved glomerular filtration rate remains uncertain.

**Methods:** Patients with an estimated glomerular filtration rate greater than 60 mL/min/1.73 $m^2$ who underwent cardiac surgery between January 2003 and December 2007 in a tertiary medical center were retrospectively analyzed. Dipstick urinalysis was performed before surgery. Proteinuria was categorized into negative, trace, 1+, 2+, or 3+. Postoperative acute kidney injury was defined by the Acute Kidney Injury Network criteria. Multinomial logistic regression was used to clarify whether proteinuria is an independent risk factor of postoperative acute kidney injury.

**Results:** A total of 1246 patients were included in this study, with a mean estimated glomerular filtration rate of 80 ± 13 mL/min/1.73 $m^2$. Proteinuria was present in 290 patients (23.4%). Postoperative acute kidney injury developed in 434 patients (34.8%), and 36 patients (2.9%) required renal replacement therapy. Proteinuria was independently associated with all stages of postcardiotomy acute kidney injury and dialysis-requiring acute kidney injury. The crude risk of acute kidney injury was greater in patients with a higher grade of proteinuria. In subgroup analysis for gender, diabetes, and surgical type, preoperative proteinuria remains a strong risk factor of acute kidney injury after cardiac surgery.

**Conclusions:** Urine analysis is usually neglected before cardiac surgery despite the fact that proteinuria is the earliest manifestation of kidney dysfunction. In the current study, we show that urine protein is strongly and independently associated with postoperative acute kidney injury in subjects with preserved estimated glomerular filtration rate. These data suggest that such a relatively simple and clinically easy to use tool as a urinary dipstick may be useful to identify patients at high risk of acute kidney injury before cardiac surgery. (J Thorac Cardiovasc Surg 2015;149:894-9)

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See related commentary on pages 900-1.

Acute kidney injury (AKI) is a common and serious complication after cardiac surgery. It is independently associated with not only short-term but also long-term adverse outcomes.[1-4] Emerging evidences have suggested that even small changes in serum creatinine levels after cardiac surgery are associated with significant effects on mortality.[5-7] Therefore, identification of the high-risk patients followed with appropriate intervention plays a critical role in improving the clinical outcome of cardiac surgery. Preoperative renal dysfunction usually is the most important determinant of postoperative AKI, and serum creatinine is routinely measured as a marker of renal function.[8,9] Although clinicians have long recognized proteinuria to be the earliest manifestation of kidney dysfunction, the prognostic significance of the presence and severity of proteinuria was hindered among patients with preserved glomerular filtration rate (GFR).

Community-based studies by James and colleagues[10] and Grams and colleagues[11] have shown that the presence of proteinuria is associated with an increased risk of subsequent AKI among patients with estimated glomerular filtration rate (eGFR) greater than 60 mL/min/1.73 $m^2$. Both studies confirmed the prognostic value of proteinuria in the development of AKI despite normal serum creatinine. In addition, the association among proteinuria, adverse renal outcomes, and mortality in patients undergoing

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**Abbreviations and Acronyms**
AKI = acute kidney injury
AKIN = Acute Kidney Injury Network
eGFR = estimated glomerular filtration rate
GFR = glomerular filtration rate
IABP = intra-aortic balloon pump
RRT = renal replacement therapy

percutaneous coronary intervention[12] and coronary artery bypass surgery[13] has been reported. However, the prognostic significance of proteinuria on postcardiotomy AKI in patients with preserved eGFR has remained unknown. The current study assesses the impact of preoperative proteinuria on AKI after cardiac surgery in subjects with eGFR greater than 60 mL/min/1.73 $m^2$.

## MATERIALS AND METHODS

### Study Subjects

This is a retrospective cohort study approved by the institutional review board. All consecutive adult patients who underwent cardiac surgery with cardiopulmonary bypass from January 1, 2003, to December 31, 2008, at Taipei Veterans General Hospital entered this study. Patients who were on maintenance dialysis or who underwent heart transplantation were ineligible for this study. Patients with preoperative eGFR less than 60 mL/min/1.73 $m^2$ were also excluded (Figure 1).

### Data Collection

Demographic and clinical data, such as age, gender, body weight, body mass index, diabetes, and left ventricular ejection fraction, were obtained from medical records. Hemoglobin, serum creatinine, and albumin were measured before surgery. Duration of cardiopulmonary bypass, preoperative treatment of intra-aortic balloon pump (IABP), and types of operation were obtained from surgical records.

### Baseline Urine Protein and Acute Kidney Injury

A urine sample was collected during a 3-day period before surgery. The presence of proteinuria was determined using an automatic dipstick analyzer (CLINITEK Atlas; Siemens Healthcare Diagnostics, Eschborn, Germany). The degree of proteinuria was semiquantified as negative, trace (protein 15-30 mg/dL), 1+ (30-100 mg/dL), 2+ (100-300 mg/dL), or 3+ (>300 mg/dL).

Preoperative eGFR was calculated by the Cockcroft–Gault formula as follows for men: (140 − age) × (body weight in kilograms)/(72 × serum creatinine). In women, the value was multiplied by 0.85.[14] Blood chemistries were checked with a 24-hour interval after operation.

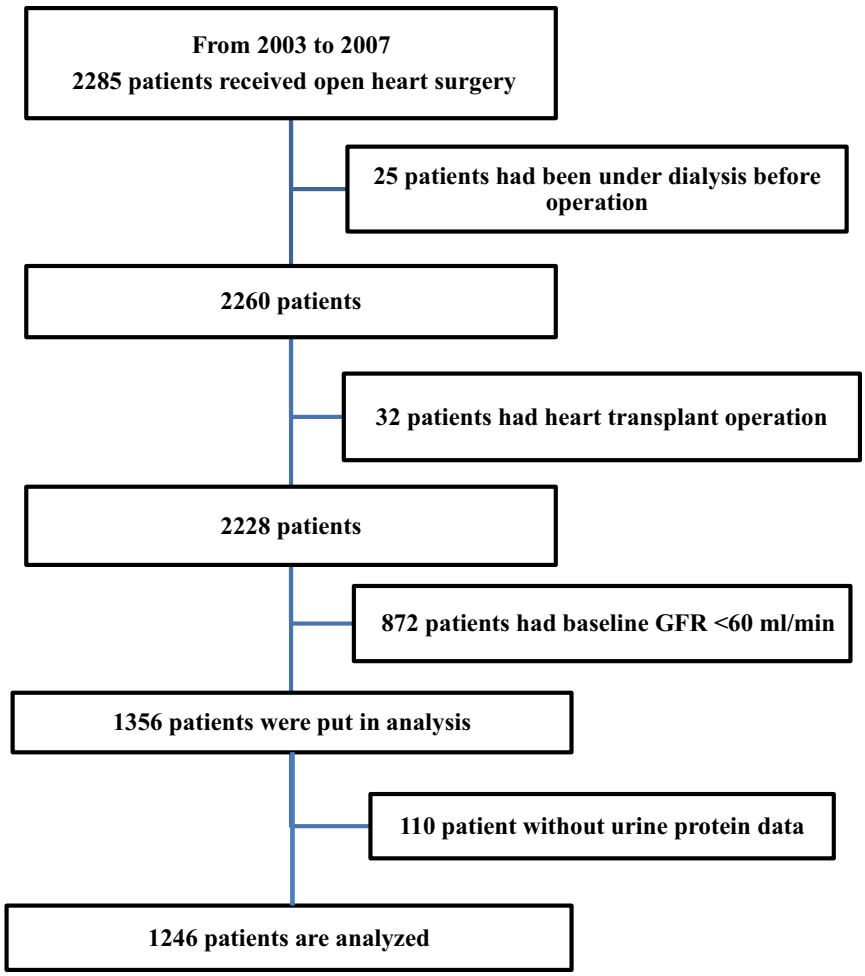


**FIGURE 1.** Patient selection flow. *GFR*, Glomerular filtration rate.

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