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Influence of renal dysfunction on mortality after cardiac surgery: Modifying effect of preoperative renal function

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Influence of renal dysfunction on mortality after cardiac surgery: Modifying effect of preoperative renal function.

Background. Acute renal failure (ARF) requiring dialysis is an independent risk factor of mortality after cardiac surgery; the level of preoperative renal function influences the risk of both postoperative ARF and mortality. The relationship between mild renal dysfunction and mortality, and the modifying effect of baseline renal function on this association, is less clear.

Methods. We studied 31,677 patients undergoing cardiac surgery between 1993 and 2002. We used a logistic regression model to assess the relationship between postoperative renal dysfunction and mortality, while adjusting for preoperative renal function, postoperative ARF requiring dialysis, and other risk factors.

Results. The overall postoperative mortality rate was 2.2% (698/31,677). For the entire cohort, a clinically relevant increase in the adjusted risk of mortality occurred beyond 30% decline in postoperative GFR. The mortality rate was 5.9% (*N*, 292/4986) among patients who developed 30% or greater decline in postoperative GFR not requiring dialysis versus 0.4% (*N*, 106/26,136) among those with <30% decline ($P < 0.001$). A significant interaction between preoperative GFR and percent change in postoperative GFR ($P < 0.001$) indicated that at equivalent degrees of renal dysfunction, the mortality risk was greater at a lower preoperative GFR. ARF requiring dialysis was strongly associated with mortality in the model (odds ratio 4.2; 95% CI 3.1–5.7).

Conclusion. Renal dysfunction not requiring dialysis is an independent risk factor of mortality after cardiac surgery. A better preoperative GFR attenuates the effect of postoperative renal dysfunction on mortality; this interaction needs to be considered while defining a clinically relevant threshold of ARF.

Acute renal failure (ARF) is a serious complication after cardiac surgery, with an associated mortality rate in excess of 50% [1–5]. The level of baseline renal function prior to cardiac surgery also influences the risk of both postoperative ARF as well as postoperative mortality [4–6]. ARF was perceived as an unfortunate complication that is proxy to the severity of other medical illnesses; however, it is now apparent that severe ARF requiring dialysis after cardiac surgery is an independent risk factor of death [7]. It is less clear, however, as to whether milder degrees of postoperative renal dysfunction independently influence mortality after cardiac surgery. Furthermore, the modifying effect of preoperative renal function on the association between postoperative renal dysfunction and mortality remains to be examined.

Integral to the association between ARF and mortality is the issue of defining clinically relevant threshold of renal dysfunction. The frequency of ARF varies widely depending upon its definition; when defined in its most severe form as requiring dialysis, the incidence of ARF after cardiac surgery is usually less than 5% [4, 5, 8–10]. This translates into a significant challenge while designing clinical trials because it mandates the enrollment of a large number of patients in order to demonstrate the efficacy of an intervention. Arbitrary definitions of less severe degrees of ARF have been used to circumvent this issue, but they fall short of demonstrating a longitudinal association with "hard" clinical end points such as hospital mortality [11–13].

We aim to study the effect of renal dysfunction not requiring dialysis on mortality, in patients undergoing cardiac surgery; to study the interaction between baseline renal function and postoperative decline in glomerular filtration rate (GFR) for its influence on mortality, after adjusting for other confounding risk factors; and to determine a threshold of clinically relevant renal dysfunction based upon its independent association with mortality. The data indicate that renal dysfunction not requiring dialysis is an independent risk factor of mortality, and that a better preoperative renal function attenuates the

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Table 1. Definitions of risk factors affecting mortality

Risk factor	Definition
Age	In years (per 10-year increase)
Weight	*kg*
Gender	Female vs. male
Race	White (89.1%), black (4%), and other (6.9%)
Albumin	Preoperative serum albumin *g/dL*
Preoperative GFR	Calculated by four-variable MDRD equation *mL/min/1.73m*^{2}
Diabetes mellitus	Insulin requiring diabetes mellitus
COPD	History of chronic obstructive pulmonary disease requiring medical treatment
Peripheral vascular disease	Evidence of peripheral vascular disease by angiography or noninvasive testing, history of vascular surgery, or symptomatic vascular occlusion
Cerebrovascular disease	History of stroke, carotid artery surgery, or >40% stenosis of either carotid artery proven by ultrasound or angiography
LVF <35%	Left ventricular function as determined by echocardiography, left ventriculography, or MUGA scan during the preoperative period
Left main disease	Left main coronary artery disease with >70% occlusion
Congestive heart failure	History of congestive heart failure including history of dyspnea on exertion, orthopnea, or paroxysmal nocturnal dyspnea prior to open-heart surgery
IABP use	Preoperative use of intra-aortic balloon pump
Year of surgery	Calendar year of surgery, 1993 to 2002
Prior surgery	Previous history of open-heart surgery
Emergency surgery	Emergency surgery as indicated by "E" in the anesthesia record sheet as per the criteria of the American Society of Anesthesiology
CPB time	Cardiopulmonary bypass time (minutes)
Surgery type	Coronary artery bypass grafting (CABG), valve surgery, combined CABG and valve procedures, other cardiac surgeries including pericardectomy, septal defect repair, etc.

mortality risk associated with postoperative decline in GFR.

METHODS

Patient population

We studied 33,217 patients who underwent open-heart surgery at the Cleveland Clinic Foundation between April 1993 and December 2002, as recorded in the database of the department of Cardiothoracic Anesthesiology. This on-going registry is approved by the Institutional Review Board to record perioperative information in cardiac surgery patients. There were 34,562 surgeries performed; for the purpose of this analysis, only the first surgical episode was considered. We excluded 1540 patients from the analysis, including those requiring preoperative dialysis, preoperative extra-corporeal membrane oxygenation, preoperative tracheostomy or mechanical ventilation, heart transplant recipients, patients undergoing procedures for automated implantable cardioverter-defibrillator, left ventricular assist devices, sternal work, and those with missing data. One hundred and sixty-four patients met more than one criterion for exclusion. The demographic distribution for the remaining 31,677 patients included 69.5% males (*N*, 22,012) and 31.5% females (*N*, 9665). Racial categories, as recorded in the database, included white (89.1%; *N*, 28,230), black (4%; *N*, 1264), and others (6.9%; *N*, 2183).

Definitions

The primary outcome was all-cause hospital mortality after cardiac surgery. Renal dysfunction was determined by calculating a percent decline in estimated GFR during the postoperative period relative to baseline, but not requiring dialysis. The preoperative GFR was estimated by using baseline serum creatinine, whereas the postoperative GFR was estimated based upon peak serum creatinine during the immediate postoperative period. Both the four-variable MDRD equation [abstract; Levey AS et al, *J Am Soc Nephrol* 11:A0828, 2000; K/DOQI guidelines for chronic kidney disease] and the Cockroft and Gault equation were used to estimate GFR [14].

The preoperative risk factors considered in the analysis for their association with mortality are shown in Table 1. They include demographic factors such as age, gender, race, weight, and clinical risk factors, including preoperative GFR, serum albumin, diabetes mellitus, chronic obstructive pulmonary disease requiring treatment, peripheral vascular disease, cerebrovascular disease, congestive heart failure, left ventricular dysfunction (ejection fraction <35%), greater than 70% occlusion of left main coronary artery, preoperative use of intra aortic balloon pump (IABP), emergency surgery, and the year of surgery. The intraoperative risk factors included cardiopulmonary bypass time and the type of open-heart surgery, including coronary artery bypass graft (CABG) surgery, valve surgery, combined CABG and valve procedures, and other cardiac surgeries, such as ventricular aneurysm repair, septal defect repair, etc. We also considered significant postoperative complications that can affect mortality, including cardiac morbidity, neurologic morbidity, severe ARF requiring dialysis, and serious infection, including sepsis syndrome and septic shock. A detailed account of the variables in the database, the