Level of Kidney Function Determines Cardiovascular Fate After Coronary Bypass Graft Surgery

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The traditional risk factors for cardiovascular (CV) disease, ie, hypertension, diabetes, or metabolic syndrome, are also risk factors for chronic kidney disease development. For more than a quarter of a century, the association between late-stage kidney disease, ie, glomerular filtration rate (GFR) <30 mL/min, and higher CV death rate has been recognized. Only recently, however, have studies in the general population and in cohorts with previous CV events linked the continuum of increasing CV risk with decreasing kidney function. This is related in part to the fact that current studies used validated formulas derived from kidney disease outcome trials to find an estimated GFR (eGFR) rather than simply measuring serum creatinine randomly.

All studies published within the last decade indicate that when GFR falls to <60 mL/min (stage 3 nephropathy), a significant increase in CV events occurs. This may relate to the fact that as GFR falls to <60 mL/min, many physiological and regulatory functions of the kidney start to wane; such functions include reductions in 1,25(OH) vitamin D and erythropoietin synthesis. Alterations in these regulatory hormones produce, over time, a vascular environment that promotes increased vascular calcification, reduced oxygen carrying capacity, and thus increased CV risk.1

Subtle changes in calcium/phosphate homeostasis indicated that initial decreases in 1,25(OH) vitamin D and subsequent increases in parathyroid hormone are detectable when GFR is just <60 mL/min and become obvious when GFR is <45 mL/min. A calcium/phosphate product of >55 also can occur at this GFR level and is associated with an increased prevalence of vascular calcification, arteriosclerosis, and CV risk, as well as increased CV mortality.9,10

A second factor that may contribute to a higher CV event rate in these patients is decreased erythropoietin production and resultant anemia. An apparent inverse association also exists between the level of hemoglobin and CV risk. At levels <13 mg/dL, CV events and mortality, especially secondary to heart failure, are increased12; partial correction of hemoglobin levels reduces CV event rate.13

Although coronary artery bypass grafting (CABG) surgery can result in improved quality and prolongation of life in selected patients, several factors have been identified as independent predictors of poor outcomes.14 One of these is renal dysfunction. Several studies indicate that in advanced nephropathy such as stage 5 (end-stage renal disease)15 or stage 4 nephropathy,16,17 an associated increase in morbidity and mortality was present after CABG surgery. Unfortunately, these earlier studies used serum creatinine as a dichotomous rather than as a continuous variable and thus failed to capture the continuum with CV risk.16,18 Furthermore, it is now appreciated that serum creatinine is a relatively imprecise measure of kidney function; older patients (>65 years of age) with eGFR values of 50 to 60 mL/min can have nearly normal creatinine levels and thus higher CV risk.19

In this issue of Circulation, 2 studies provide additional data in this understudied cohort. Cooper et al20 reviewed the Society of Thoracic Surgeons National Adult Cardiac Database starting from July 2000 through December 2003. In the ≈500 000 patients evaluated, 51% had stage 2 nephropathy (GFR of 60 to 90 mL·min⁻¹·1.73 m⁻²), 24% had stage 3 nephropathy (GFR of 30 to 59 mL·min⁻¹·1.73 m⁻²), and 3.5% had stages 4 and 5. Operative mortality increased with declining level of eGFR; it rose from 1.3% in stage 2 nephropathy to >9% for those with stages 4 and 5 nephropathy. This study also confirmed earlier findings of a morbidity and mortality increase among those with stage 5 nephropathy requiring dialysis. Finally, they found that preoperative eGFR was one of the most powerful predictors or CV outcome.

In the second study, Hillis et al21 collected data at the time of CABG on 2067 consecutive patients who did not require preoperative dialysis to evaluate the importance of eGFR on overall mortality. After a median follow-up of 2.3 years, they noted that mean eGFR was significantly lower in patients who died during follow-up compared with survivors. These investigators also noted that the eGFR was an independent predictor of mortality during the follow-up period and that for every 10–mL·min⁻¹·1.73 m⁻²-higher eGFR within the cohort examined, overall mortality was reduced by 20% and 30-day postoperative mortality by 32%.

Although these studies clearly expand our database regarding kidney function and CV outcomes in postsurgical CABG patients, they have limitations. Neither addressed issues of postoperative kidney function or possible differences in eGFR before and after surgery. Neither included information about medications that could affect kidney function. Finally,

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neither measured urine albumin, a well-known marker of CV risk, independently of kidney function.\textsuperscript{22} Nevertheless, these studies expand our armamentarium of data indicating that the level of kidney function is an independent risk factor for CV morbidity and mortality.

In these and other studies, the risk of death and related morbidities rises slowly as the eGFR approaches 60 mL/min; events increase significantly at levels <60 mL/min and are very prominent at eGFR values <45 mL/min. From these data, all patients undergoing CABG surgery should have their eGFR assessed as part of the preoperative laboratory evaluation. Moreover, eGFR should be integrated into clinical risk prediction models for morbidity and mortality after CABG.

Disclosures

None.

References


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