Mortality, kidney disease and cardiac procedures following acute coronary syndrome

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Abstract

Background. Cardiac interventions are underutilized in patients with chronic kidney disease (CKD) following acute coronary syndrome (ACS) partly due to nephrotoxicity concerns.

Methods. We analyzed outcomes of 4631 subjects with ACS enrolled in the Blockade of the Glycoprotein IIb/IIa Receptor to Avoid Vascular Occlusion trial, including time to death, time to reduced renal function (50% reduction in estimated glomerular filtration rate (eGFR) or development of end-stage renal disease (ESRD)) and percent change in eGFR from baseline.

Results. Subjects with a lower baseline eGFR were more likely to be older, female and have diabetes, hypertension, congestive heart failure or peripheral vascular disease (all \( P < 0.0001 \)); they were less likely to be taking aspirin \( \geq 162 \text{ mg} \) or to have undergone a percutaneous coronary intervention (PCI) prior to enrollment (\( P < 0.0001 \)). As eGFR declined, the proportion of subjects experiencing death versus reduced eGFR or ESRD qualitatively increased. In adjusted analyses, every 10 ml/min/1.73 m² decrease in eGFR \( \leq 90 \) was associated with a 15% increased hazard of death (HR 1.15, \( P = 0.01 \)). In adjusted analyses of predictors of percent change in eGFR, catheterization (cath) with or without PCI compared to medical therapy during follow-up was not associated with significant differences in long-term eGFR (\( P = 0.09 \)).

Conclusions. Among CKD subjects in this study, the risk of death greatly outweighed the risk of reduced eGFR or development of ESRD following ACS and the occurrence of cath \( \pm \) PCI was not associated with significant differences in long-term renal function. The presence of CKD should not preclude potentially beneficial interventions and research should focus on reducing the high cardiovascular burden in this population.

Keywords: acute coronary syndrome; cardiac catheterization; cardiac interventions; chronic kidney disease; mortality; outcomes

Introduction

Cardiovascular disease affects \( \sim 71 \) million Americans; in 2003 alone, more than 850 000 individuals were hospitalized for acute coronary syndrome (ACS) [1]. Nearly 40% of patients who present with ACS have some degree of renal dysfunction [2]. Chronic kidney disease (CKD) is a known independent risk factor for cardiovascular disease [3] and is associated with detrimental outcomes among ACS patients [4,5]. Two reasons may explain why CKD is associated with adverse outcomes after cardiovascular events: beneficial therapies appear less likely to be used among patients with CKD as renal function declines [6–10] and percutaneous cardiac procedures may lead to excess toxicity among patients with baseline renal dysfunction [11].

Unfortunately, due to the epidemics of diabetes mellitus and obesity, the prevalence of CKD is expected to exceed 20 million people by 2010, resulting in a large population at risk for cardiovascular events [12]. Appropriate evidence-based therapies for this burgeoning population remain unclear because patients with renal impairment have been systematically excluded from large cardiovascular trials [13]. Thus, treatment decisions for this chronically ill population are difficult and can be affected by a variety of clinical parameters. Further, physicians must often balance the decision to perform diagnostic and therapeutic cardiovascular procedures among CKD patients with the possibility of losing viable renal function.

While it has been clearly demonstrated that the presence of CKD is a risk factor for radiocontrast-associated nephrotoxicity that can result in decreased short- and long-term survival [14–18], the relationship between kidney function, cardiac procedures and long-term renal outcomes is yet to be defined. Herein, we compared renal and patient survival...
Methods

Selection of subjects

A total of 9190 subjects who completed the Blockade of the Glycoprotein IIb/IIIa Receptor to Avoid Vascular Occlusion (BRAVO) trial were potentially available for this analysis. The methods and results of BRAVO have previously been described [19,20]. Briefly, BRAVO was a randomized double-blind trial comparing lotrafiban (an oral glycoprotein IIb/IIIa inhibitor) or matching placebo plus aspirin in patients with documented acute cardiovascular or cerebrovascular disease. Subjects enrolled in BRAVO were followed for 1 year (median follow-up 366 days). Subjects qualified for the BRAVO study if they had (1) a myocardial infarction (MI) within 14 days of baseline evaluation; (2) a diagnosis of unstable angina within 14 days of baseline evaluation; (3) an ischemic stroke confirmed by history, physical examination and computed tomographic (CT) or magnetic resonance (MR) imaging scan to be entered into the study no sooner than 5 days before and no later than 30 days after the acute event; (4) a transient ischemic attack (TIA) within 30 days of baseline evaluation, confirmed through positive history and/or physical examination in the absence of any significant findings on CT or MR imaging scan or (5) evidence of peripheral vascular disease combined with evidence of either cardiovascular or cerebrovascular disease. Subjects were excluded from the original trial if they had severe CKD (creatinine clearance <30 ml/min by Cockcroft–Gault formula) or concomitant severe disease, such as neoplasm that was likely to limit life expectancy or study participation to <2 years.

Study measurements and definitions

At enrollment, the following parameters were obtained and were available for our analyses: age; gender; race; body mass index (BMI); baseline heart rate; tobacco use; history of diabetes mellitus, hypertension, congestive heart disease, peripheral vascular disease and stroke; history of cardiac catheterization (cath) ± percutaneous coronary intervention (PCI); aspirin dose ≥162 mg/day and treatment arm (lotrafiban versus placebo). Serum creatinine was measured at baseline, at 72 h or hospital discharge, at 7, 10, and 14 days; at month 3 and every 3 months subsequent to enrollment in the absence of any significant findings on CT or magnetic resonance (MR) imaging scan to be entered into the study no sooner than 5 days before and no later than 30 days after the acute event; (4) a transient ischemic attack (TIA) within 30 days of baseline evaluation, confirmed through positive history and/or physical examination in the absence of any significant findings on CT or MR imaging scan or (5) evidence of peripheral vascular disease combined with evidence of either cardiovascular or cerebrovascular disease. Subjects were excluded from the original trial if they had severe CKD (creatinine clearance <30 ml/min by Cockcroft–Gault formula) or concomitant severe disease, such as neoplasm that was likely to limit life expectancy or study participation to <2 years.

Primary outcome

The primary outcomes of interest included reduced renal function (50% decrement in eGFR or development of end-stage renal disease (ESRD) and the occurrence of death. Secondary outcome measurements included percent change in eGFR during follow-up.

Statistical methods

Our analysis was restricted to subjects enrolled in BRAVO with the diagnosis of unstable angina or acute MI within 14 days of baseline evaluation (N = 4634). Demographic and clinical factors were summarized and compared between groups of subjects stratified on the basis of renal function. Continuous variables were compared using the Spearman correlation test and binary categorical variables were compared using the Wilcoxon rank sum test. Univariate survival probabilities were compared among groups of subjects based on the category of eGFR using Kaplan–Meier methodology with the log-rank test.

Cox proportional hazards regression was used to model the association between eGFR, cardiac procedures (cath ± PCI) and the hazard of reduced renal function or the hazard of death while controlling for other predictors. Proportional hazards assumptions and linearity assumptions for continuous variables were assessed by restricted cubic splines. When the relationship was found to be nonlinear, appropriate transformations were applied. Due to a nonlinear association between eGFR and log hazards ratio, a two-piece-wise linear spline was used to represent the eGFR effect. Cardiac procedures and eGFR were both treated as time-dependent covariates in the model predicting death. Baseline eGFR was used in models predicting the hazard of reduced renal function. Due to presumed non-proportional hazards following coronary artery bypass grafting (CABG), subjects who underwent CABG after enrollment were censored in the time-to-event analyses at the time of CABG.
Table 1. Baseline characteristics among subjects characterized by eGFR (ml/min/1.73 m²) categories

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total cohort</th>
<th>eGFR &lt; 45</th>
<th>45 ≤ eGFR &lt; 60</th>
<th>60 ≤ eGFR &lt; 75</th>
<th>75 ≤ eGFR &lt; 90</th>
<th>eGFR ≥ 90</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years (SD)</td>
<td>60.1 (11.1)</td>
<td>68.4 (9.3)</td>
<td>66.2 (10.0)</td>
<td>62.3 (10.2)</td>
<td>59.8 (11.0)</td>
<td>55.1 (10.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male gender, No. (%)</td>
<td>3540 (76%)</td>
<td>126 (53%)</td>
<td>365 (66%)</td>
<td>841 (75%)</td>
<td>990 (81%)</td>
<td>1218 (81%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>White race, No. (%)</td>
<td>4390 (95%)</td>
<td>73 (31%)</td>
<td>103 (19%)</td>
<td>148 (13%)</td>
<td>125 (10%)</td>
<td>130 (9%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Tobacco user, No. (%)</td>
<td>1258 (27%)</td>
<td>31 (13%)</td>
<td>108 (20%)</td>
<td>244 (22%)</td>
<td>317 (26%)</td>
<td>558 (37%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mean BMI, kg/m² (SD)</td>
<td>28.2 (5.7)</td>
<td>29.4 (10.5)</td>
<td>27.9 (4.5)</td>
<td>28.0 (4.6)</td>
<td>28.1 (4.8)</td>
<td>28.5 (6.3)</td>
<td>0.65</td>
</tr>
<tr>
<td>Mean heart rate, beats/min (SD)</td>
<td>67.7 (10.8)</td>
<td>69.4 (11.2)</td>
<td>67.8 (10.9)</td>
<td>66.9 (10.7)</td>
<td>67.2 (10.7)</td>
<td>68.2 (10.7)</td>
<td>0.18</td>
</tr>
<tr>
<td>Diabetes mellitus, No. (%)</td>
<td>1000 (22%)</td>
<td>190 (81%)</td>
<td>412 (74%)</td>
<td>739 (66%)</td>
<td>730 (60%)</td>
<td>875 (58%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hypertension, No. (%)</td>
<td>2946 (64%)</td>
<td>190 (81%)</td>
<td>412 (74%)</td>
<td>739 (66%)</td>
<td>730 (60%)</td>
<td>875 (58%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Baseline aspirin dose ≥ 162 mg, No. (%)</td>
<td>2096 (45%)</td>
<td>84 (16%)</td>
<td>201 (36%)</td>
<td>463 (41%)</td>
<td>558 (46%)</td>
<td>790 (53%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

P-values: Spearman correlation test used for P-values for age, BMI and heart rate. All other P-values obtained using the Wilcoxon rank sum test.

All P-values reported are two-sided, and all confidence intervals (CI) reported are 95% intervals. All analyses were performed using SAS (version 8.2, SAS Institute Inc., Cary, NC, USA).

Results

Study population

A total of 4634 subjects with unstable angina or acute MI were enrolled in BRAVO and were included in this analysis (baseline characteristics based on eGFR can be seen in Table 1). In general, subjects with a lower baseline eGFR were significantly more likely to be older, white, female and have a history of diabetes mellitus, hypertension, congestive heart failure or peripheral vascular disease. Subjects with a lower baseline eGFR were also significantly less likely to have undergone a cath ± PCI previously or at baseline, to have smoked tobacco or to be taking daily aspirin therapy ≥162 mg at baseline.

Outcomes based on stage of kidney disease

In univariate analysis, subjects with a lower baseline eGFR had a shorter time to a composite endpoint of a 50% reduction in eGFR, development of ESRD or death (P = 0.007). However, the relative number of subjects who developed reduced eGFR, progressed to ESRD or died varied based on baseline kidney function (Table 2). Among all and were excluded in other event rate analyses. The aforementioned baseline variables that were candidates for risk factor adjustment were first included in the model and retained using P = 0.05 as the inclusion criterion. Interactions between clinically relevant variables such as eGFR and the occurrence of cath ± PCI were tested in separate models.

To assess for changes in eGFR that may have occurred in association with undergoing cath ± PCI, percent changes in eGFR following these procedures were compared between groups undergoing and not undergoing these procedures. Subjects who had undergone cath ± PCI were included in the analyses only if they had an eGFR measured both before and after the procedures (N = 406); the post-cath ± PCI eGFR must have been taken within 7–180 days after the procedure(s), while the pre-cath ± PCI eGFR was the last eGFR measure taken before the procedure(s). Subjects were excluded from the analysis if the only available pre-cath ± PCI eGFR for a subject was taken at baseline and the procedure(s) did not occur within 30 days after baseline. For each subject undergoing cardiac catheterization or PCI, three subjects were selected randomly from subjects who did not undergo cath ± PCI (i.e., the medication-only subjects) and who had serum creatinine measured within a 30-day window of both the pre- and the postprocedure eGFR of the cath ± PCI patient. Percent changes in eGFR were compared using the ANOVA test, adjusting for the timing of the first eGFR taken. In multivariable analyses, a general linear model was used that controlled for baseline eGFR, timing of eGFR and the above-mentioned baseline variables.
categories of subjects based on eGFR, with the exception of subjects whose eGFR $\geq$ 90 ml/min/1.73 m$^2$ at baseline, death accounted for a greater proportion of the events than did reduction of eGFR or progression to ESRD. Additionally, the relative proportion of subjects experiencing death as compared to those experiencing a 50% reduction of eGFR or progression to ESRD qualitatively increased as the categories of kidney function declined.

In adjusted analyses predicting the hazard of reduced renal function, subjects with a higher baseline eGFR were more likely to experience reduced renal function during follow-up (Table 3). Other variables associated with an increased hazard of reduced renal function included increasing age, congestive heart failure and higher BMI.

In multivariable models predicting death, every 10 ml/min/1.73 m$^2$ decrease in time-varying eGFR $<90$ was associated with a 15% increase in hazard of death (HR = 1.15, $P = 0.01$) (Table 4). Other significant predictors of increased mortality included increasing age, the presence of diabetes mellitus, the occurrence of cardiac cath $\pm$ PCI during the period of study and history of congestive heart failure. A history of cath $\pm$ PCI prior to enrollment and use of aspirin $\geq 162$ mg were associated with decreased mortality.

Table 3. Multivariable model of predictors of time to 50% decrease in eGFR or development of end-stage renal disease

<table>
<thead>
<tr>
<th>Variable</th>
<th>Wald $\chi^2$</th>
<th>Hazard ratio (95% CI)</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline eGFR ($\leq 90$ ml/min/1.73 m$^2$, per 10 decrease)</td>
<td>4.43</td>
<td>0.78 (0.62–0.98)</td>
<td>0.04</td>
</tr>
<tr>
<td>Baseline eGFR ($&gt;90$ ml/min/1.73 m$^2$, per 10 decrease)</td>
<td>107.1</td>
<td>0.70 (0.65–0.75)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age (per 1 year increase)</td>
<td>11.9</td>
<td>1.05 (1.02–1.07)</td>
<td>0.0006</td>
</tr>
<tr>
<td>History of CHF</td>
<td>9.8</td>
<td>2.60 (1.43–4.73)</td>
<td>0.002</td>
</tr>
<tr>
<td>BMI (per 1 unit increase)</td>
<td>7.8</td>
<td>1.03 (1.01–1.05)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

The following baseline variables were tested for significance in the model: age; gender; race; body mass index; baseline heart rate; tobacco use; baseline eGFR $>90$; baseline eGFR $\leq 90$; history of diabetes mellitus, hypertension, congestive heart failure, peripheral vascular disease, and stroke; history of cath $\pm$ PCI; time-varying occurrence of cath $\pm$ PCI during the course of the study; aspirin dose $\geq 162$ mg/day and treatment arm (lotrafiban versus placebo).

Change in eGFR over time was compared among a subset of the entire cohort to include all subjects who underwent a cath $\pm$ PCI and subjects not undergoing these procedures but having serum creatinine measurements available during similar time periods (Table 5, Figure 1). Subjects who underwent a cath $\pm$ PCI during the study were younger, were less likely to be taking $\geq 162$ mg of aspirin and were less likely to have a history of congestive heart failure or peripheral vascular disease. Subjects who underwent cath $\pm$ PCI were more likely to have had a prior cath $\pm$ PCI and have a history of stroke. Subjects who underwent cath $\pm$ PCI during the study also had higher eGFR compared to subjects treated with medical therapy.

In unadjusted analyses, subjects who underwent cath $\pm$ PCI had a mean percent change in eGFR of 0.4% ($\pm 22.4$) compared to 2.5% ($\pm 24.0$) among subjects treated medically ($P = 0.13$).

In adjusted analyses of predictors of percent change in eGFR, the occurrence of cath $\pm$ PCI compared to medical therapy was not associated with a significant difference in eGFR in the long-term follow-up ($P = 0.09$). Factors associated with greater percent reductions in eGFR over the course of follow-up included higher eGFR at baseline ($P < 0.001$), increasing age ($P < 0.0001$), increased heart
Table 5. Baseline characteristics of subjects undergoing cath ± PCI versus medical therapy

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cath ± PCI (N = 406)</th>
<th>Medical therapy (N = 1218)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years (SD)</td>
<td>57.9 (10.2)</td>
<td>60.4 (11.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male gender, No. (%)</td>
<td>314 (77%)</td>
<td>926 (76%)</td>
<td>0.59</td>
</tr>
<tr>
<td>White race, No. (%)</td>
<td>382 (94%)</td>
<td>1152 (95%)</td>
<td>0.71</td>
</tr>
<tr>
<td>Tobacco user, No. (%)</td>
<td>129 (32%)</td>
<td>289 (24%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Mean BMI, kg/m² (SD)</td>
<td>28.3 (4.9)</td>
<td>28.4 (5.0)</td>
<td>0.66</td>
</tr>
<tr>
<td>Mean heart rate, beats/min (SD)</td>
<td>66.7 (10.5)</td>
<td>67.5 (10.8)</td>
<td>0.16</td>
</tr>
<tr>
<td>Diabetes mellitus, No. (%)</td>
<td>86 (21%)</td>
<td>275 (23%)</td>
<td>0.56</td>
</tr>
<tr>
<td>Hypertension, No. (%)</td>
<td>246 (61%)</td>
<td>800 (66%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Congestive heart failure, No. (%)</td>
<td>32 (8%)</td>
<td>159 (13%)</td>
<td>0.005</td>
</tr>
<tr>
<td>Previous or baseline cath ± PCI, No. (%)</td>
<td>236 (58%)</td>
<td>621 (51%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Peripheral vascular disease, No. (%)</td>
<td>15 (4%)</td>
<td>103 (9%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Baseline ASA dose ≥ 162 mg, No. (%)</td>
<td>177 (44%)</td>
<td>665 (55%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline eGFR ml/min/1.73 m², median (IQR)</td>
<td>81.8 (69.6, 95.8)</td>
<td>79.7 (65.8, 93.8)</td>
<td>0.04</td>
</tr>
<tr>
<td>eGFR prior to procedure, median (IQR)</td>
<td>86.3 (73.8, 101.3)</td>
<td>83.2 (69.0, 98.7)</td>
<td>0.009</td>
</tr>
<tr>
<td>Days after randomization eGFR taken, median (IQR)</td>
<td>14 days (13–89)</td>
<td>14 days (13–90)</td>
<td>0.66</td>
</tr>
<tr>
<td>Long-term eGFR, median (IQR)</td>
<td>85.9 (71.3, 101.4)</td>
<td>83.4 (70.1, 98.5)</td>
<td>0.10</td>
</tr>
<tr>
<td>Days after randomization eGFR taken, median (IQR)</td>
<td>168 days (87, 275)</td>
<td>173.5 days (86, 276)</td>
<td>0.95</td>
</tr>
<tr>
<td>Percent eGFR change, mean (SD)</td>
<td>0.4% (22.4)</td>
<td>2.5% (24.0)</td>
<td>0.13</td>
</tr>
</tbody>
</table>

*Subjects undergoing cath ± PCI were compared with three random subjects who were treated with medical therapy but had serum creatinine measurements in similar time periods.

rate (0.04), baseline aspirin ≥162 mg/day (*P* = 0.03) and treatment arm (*P* = 0.0002).

No interaction was observed between percutaneous cardiac procedures and eGFR (*P* = 0.17) as a predictor of percent change in eGFR among this subcohort. Thus, various levels of eGFR did not alter the association between cardiac procedures and change in eGFR over time (i.e. neither subjects with higher nor with lower eGFR were likely to have a change in renal function with the occurrence of a cardiac procedure).

Fig. 1. Change in eGFR percentage among subjects undergoing cath/PCI as compared to subjects receiving medical therapy.
Discussion

Epidemiologic and natural history studies have demonstrated that CKD is a prevalent, independent risk factor for all-cause and cardiovascular mortality. Yet, prior analyses suggest that reduced eGFR is associated with decreased utilization of diagnostic and therapeutic interventions such as cardiac catheterization and PCI [7,8,10,23] likely due to concern about radiocontrast-associated nephrotoxicity and long-term renal dysfunction. However, we have demonstrated that among subjects with CKD, there was no increased risk of a long-term decrease in renal function following cath ± PCI. Further, our study confirms that the presence of CKD is strongly associated with an increased risk of death following ACS [10,24–32].

Prior studies have shown that following cardiac procedures, patients with CKD have an increased risk of acute renal failure [7,17,33], but long-term renal outcomes have not been fully elucidated. In an observational study of 439 CKD patients (serum creatinine > 1.8 mg/dl) who underwent cardiac interventions, <1% required renal replacement therapy on discharge; however, long-term renal outcomes following discharge were not assessed [16]. In our investigation, we found no increased risk of progressive renal failure among patients undergoing a cardiac procedure as compared to medical therapy during follow-up.

Patients with CKD have high mortality rates irrespective of treatments following ACS. In our analysis, there was an ~6% rate of mortality in 1 year among subjects with eGFR < 60, which significantly overshadowed reductions in eGFR or development of ESRD. In similar analyses, 1-year mortality among CKD patients following ACS has been reported to range from ~5% to 25% [26,31,34], emphasizing the need for research aimed at reducing this high cardiovascular burden.

Our study also demonstrates that subjects with CKD are less likely to receive beneficial treatments that may improve cardiovascular outcomes. In our multivariable analyses, subjects treated with ASA ≥ 162 mg, as well as subjects who underwent cath ± PCI upon presentation with ACS prior to enrollment, had improved survival. Unfortunately, subjects with CKD at enrollment were significantly less likely to be treated with these therapies.

Understanding the mechanism that results in poorer prognosis for patients with CKD after ACS is a critical first step in preventing morbidity and mortality in this high-risk population. We have demonstrated that subjects with eGFR ≤ 90 ml/min/1.73 m², subjects undergoing cardiac cath ± PCI during follow-up, older subjects and those with DM or CHF all experienced hastened mortality following ACS. The severity of heart disease, indicated by the need for interventional procedures or marked by the presence of symptoms or comorbid states, is the most likely mechanism determining the prognosis of this population. Patients in this population experience increased rates of vascular calcification as well as the comorbid effects of DM and obesity [35]. In addition, the uremic effects of advanced renal disease provide an increase in oxidative stress that has been proposed as a nontraditional cardiovascular risk factor in this patient population [36].

While this study demonstrates that patients with CKD and ACS are at a greater risk for mortality than reduction in eGFR, its conclusions should be interpreted in the setting of certain limitations. This cohort was recruited for a clinical trial and may therefore not be representative of the general population. Selection biases for subject inclusion may affect our findings and should be considered when generalizing these results to all patients with CKD, particularly with respect to race and to patients with advanced kidney disease, as subjects with an eGFR < 30 ml/min were excluded from the original trial. Indication bias may affect the results of any observational study in that the indication for treatment may affect the likelihood of the outcome. In particular, we are unable to control for unmeasured confounders that may have directed the occurrence of a cardiac catheterization or PCI. Finally, it should be acknowledged that due to the timing and frequency of creatinine measurement, acute renal failure cannot be discerned from progression of underlying kidney disease. Because of the possibility that a subject may have experienced acute renal failure as a preterminal event, no effort was made to differentiate between acute and reversible versus chronic and irreversible kidney disease. Rather, all loss of kidney function was referred to as a reduction in eGFR.

Among subjects with CKD in this study, the risk of death greatly outweighed the risk of further reduction in eGFR or development of ESRD. While it remains unclear whether more accurate assessment of coronary disease by cardiac catheterization or management of existing disease by PCI improves outcomes among CKD patients, our study suggests that cardiac interventions do not significantly worsen long-term renal function. In summary, more aggressive management of the increased cardiovascular risk in CKD patients is clearly needed and the presence of CKD should not preclude the use of potentially beneficial diagnostic and therapeutic interventions.

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References


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