Survival After Coronary Revascularization Among Patients With Kidney Disease

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Background—The optimal approach to revascularization in patients with kidney disease has not been determined. We studied survival by treatment group (CABG, percutaneous coronary intervention [PCI], or no revascularization) for patients with 3 categories of kidney function: dialysis-dependent kidney disease, non–dialysis-dependent kidney disease, and a reference group (serum creatinine <2.3 mg/dL).

Methods and Results—Data were derived from the Alberta Provincial Project for Outcomes Assessment in Coronary Heart Disease (APPROACH), which captures information on all patients undergoing cardiac catheterization in Alberta, Canada. Characteristics and patient survival in 662 dialysis patients (1.6%) and 750 non–dialysis-dependent kidney disease patients (1.8%) were compared with the remainder of the 40 374 patients (96.6%). For the reference group, the adjusted 8-year survival rates for CABG, PCI, and no revascularization (NR) were 85.5%, 80.4%, and 72.3%, respectively (P<0.001 for CABG versus NR; P<0.001 for PCI versus NR). Adjusted survival rates were 45.9% for CABG, 32.7% for PCI, and 29.7% for NR in the nondialysis kidney disease group (P<0.001 for CABG versus NR; P=0.48 for PCI versus NR) and 44.8% for CABG, 41.2% for PCI, and 30.4% for NR in the dialysis group (P=0.003 for CABG versus NR; P=0.03 for PCI versus NR).

Conclusions—Compared with no revascularization, CABG was associated with better survival in all categories of kidney function. PCI was also associated with a lower risk of death than no revascularization in reference patients and dialysis-dependent kidney disease patients but not in patients with non–dialysis-dependent kidney disease. The presence of kidney disease or dependence on dialysis should not be a deterrent to revascularization, particularly with CABG. (Circulation. 2004;110:1890-1895.)

Key Words: revascularization • coronary disease • kidney • epidemiology

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in patients with end-stage renal disease1 and begins well before the onset of dialysis.2,3 Once CVD is established, patients with kidney disease are at high risk for subsequent CVD events.4 Although guidelines exist for many aspects of medical care for CVD,5,6 the optimal approach to revascularization in patients with kidney disease has not been determined.

Revascularization approaches available include CABG and percutaneous coronary artery intervention (PCI). Among patients with normal kidney function, randomized trials suggest that compared with PCI, CABG is associated with a lower rate of repeat interventions7–9 and an improved quality of life,10 but other than in a subgroup of diabetic patients,11 it offers no survival advantage.9,12 In contrast, observational data propose that for dialysis patients, CABG may provide a survival benefit.13–16 These reports, however, do not include a reference patient population whose CVD is managed by medical therapy alone, which limits the scope of the findings. Among patients with non–dialysis-dependent kidney disease, a survival benefit for CABG over PCI was reported in some17 but not all14 of the previous studies.

The value, therefore, of coronary revascularization in patients with kidney disease and CVD is uncertain. The purpose of this study was to compare survival by treatment group (CABG, PCI, or no revascularization) for patients with 3 categories of kidney function: dialysis-dependent kidney disease, non–dialysis-dependent kidney disease, and a reference group (serum creatinine <2.3 mg/dL).

Methods

Data were derived from the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH), a prospective data collection initiative that has captured detailed clinical informa-
tion on all patients undergoing cardiac catheterization in Alberta, Canada, since 1995.1,8 All patients enrolled at the time of catheterization are followed up prospectively, thus permitting the outcomes of patients who were not revascularized to also be determined.

The study cohort consisted of all Alberta resident patients undergoing cardiac catheterization from January 1, 1995, to December 31, 2001. At the time of cardiac catheterization, data were collected by laboratory personnel through direct inquiry to patients and the procedure physician and review of medical documentation on clinical risk factors including age, gender, and presence of diabetes, peripheral vascular disease, chronic lung disease, cerebrovascular disease, congestive heart failure, hypertension, hyperlipidemia, liver or gastrointestinal disease, and neoplastic disease. Race was not recorded, although census data indicate that fewer than 1% of the population are reported to be black.19 The results of the cardiac catheterization, specifically left ventricular ejection fraction and coronary anatomy, were also recorded and were used to define severity of coronary artery disease. Patients with normal coronary anatomy or missing data on coronary anatomy were excluded because we wanted to confine this prognostic study to patients with documented coronary artery disease.

The exposure variable of interest, kidney function, was defined within APPROACH as dialysis-dependent kidney disease (on hemodialysis or peritoneal dialysis), nondialysis kidney disease (serum creatinine >2.3 mg/dL [>200 μmol/L] but not on dialysis), and reference patients (the remainder of the cohort). Lack of absolute serum creatinine measurements in APPROACH for all years studied precluded us from estimating glomerular filtration rate.

Patients were followed up through December 31, 2002, for ascertainment of the primary outcome, death due to all causes. Revascularization status (CABG or PCI) was also determined and was defined as the first procedure that occurred within 1 year of the cardiac catheterization. All-cause mortality was determined through semiannual linkage to the Alberta Bureau of Vital Statistics. The ethics review boards of the Universities of Calgary and Alberta approved the APPROACH study protocol.

Statistical Analysis

Patient characteristics for the reference patient population, nondialysis kidney disease patients, and dialysis kidney disease patients were compared with χ² tests. A Cox proportional hazards analysis was used to compute survival within each category of kidney function according to treatment received (CABG, PCI, or no revascularization). The primary outcome variable was all-cause mortality. Survival time was calculated from the date of cardiac catheterization to the date on which the patient was censored (ie, at end of follow-up) or the outcome event occurred. Risk-adjusted survival curves were plotted from the proportional hazards model by the corrected group prognosis method.20 The proportional hazard assumption was evaluated and satisfied for these multivariable survival analyses by examining plots of the log-negative-log within-group survivorship functions versus log-time, examining Schoenfeld residuals, and comparing Kaplan-Meier (observed) with Cox (expected) survival curves.

A multivariable analysis was also performed to control for the propensity1 of being selected for either CABG or PCI compared with no revascularization. This was undertaken by conducting 2 logistic regression analyses to model predictors of undergoing either CABG or PCI. The resulting models (with a c statistic of 0.86 for CABG and 0.80 for PCI) were used to calculate a probability (ie, propensity) of being selected for either CABG or PCI. These 2 propensity scores (1 each for CABG and PCI) were then included in the final multivariable analyses to assess the association between CABG and PCI with no revascularization. Statistical analyses were performed with SAS version 8.1 (SAS Institute).

Results

After excluding 6156 patients (12.7%) with normal coronary anatomy and 520 (1.1%) with missing data, the final study population was 41,786. Of these, 662 (1.6%) were on dialysis (dialysis kidney disease), 750 (1.8%) had serum creatinine >2.3 mg/dL but were not on dialysis (nondialysis kidney disease), and 40,374 (96.6%) had serum creatinine <2.3 mg/dL (reference patients).

The prevalence of clinical risk factors, by treatment group and category of kidney function, are listed in Table 1. Other than known hyperlipidemia, the prevalence of clinical risk factors was significantly higher in patients with kidney disease, both nondialysis and dialysis dependent, than in the reference patient group. Overall, the most common indication for cardiac catheterization was myocardial infarction in the reference and nondialysis kidney disease patients; in the dialysis kidney disease patients, other indications were cited. Other indications most frequently cited were congestive heart failure, suspected silent ischemia, and atypical symptoms.

The majority of dialysis and nondialysis kidney disease patients did not undergo revascularization after their cardiac catheterization despite results of the catheterization showing that these patients had more severe coronary anatomy (Table 2).

The median follow-up time after cardiac catheterization was 3.7 years for the reference patient group, 1.9 years for patients with nondialysis kidney disease, and 2.1 years for dialysis patients. The risk-adjusted survival curves for the reference patient group, nondialysis kidney disease patient group, and dialysis patient group are shown in the Figure. Treatment with CABG was associated with the best adjusted survival rates and no revascularization with the worst for each of the 3 categories of kidney function. The adjusted 8-year survival rates in the reference patient group associated with CABG, PCI, and no revascularization were 85.5%, 80.4%, and 72.3%, respectively (Figure, A). For patients with nondialysis kidney disease, the adjusted 8-year survival rates were 45.9% with CABG, 32.7% with PCI, and 29.7% with no revascularization (Figure, B). For patients on dialysis, the adjusted 8-year survival rates were 44.8% with CABG, 41.2% with PCI, and 30.4% with no revascularization (Figure, C).

A summary of 8-year unadjusted and adjusted survival rates for CABG and PCI, with their associated adjusted survival differences and hazard ratios relative to no revascularization, are provided in Table 3. CABG was associated with a survival advantage compared with no revascularization for all 3 categories of kidney function, with nondialysis kidney disease patients experiencing the greatest survival advantage for CABG compared with no revascularization, at 16.2%.

PCI was not associated with as positive a survival advantage as CABG, particularly for patients with nondialysis kidney disease (Table 3; Figure, B). In both the reference patient group and the dialysis patient group, PCI was associated with a statistically significant lower risk of death than no revascularization. However, nondialysis kidney disease patients experienced a similar outcome regardless of whether they were treated with PCI or no revascularization (adjusted hazard ratio 0.91; 95% CI 0.69 to 1.19). When we additionally controlled for the propensity to be selected for CABG or PCI, the adjusted hazard ratios changed little (Table 3). Compared with PCI, CABG was associated with a statistically significant lower risk of death in both the reference and
TABLE 1. Baseline Characteristics by Treatment Group and Category of Kidney Function

<table>
<thead>
<tr>
<th>Clinical Variable</th>
<th>CABG</th>
<th>PCI</th>
<th>No Revascularization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=10 728), %</td>
<td>Disease (n=219), %</td>
<td>Disease (n=153), %</td>
</tr>
<tr>
<td>Male</td>
<td>79.3</td>
<td>82.2</td>
<td>72.6</td>
</tr>
<tr>
<td>Age ≥65 yr</td>
<td>53.6</td>
<td>69.4</td>
<td>48.4</td>
</tr>
<tr>
<td>Diabetes</td>
<td>23.1</td>
<td>42.1</td>
<td>50.3</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>9.5</td>
<td>24.2</td>
<td>27.5</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>7.5</td>
<td>20.6</td>
<td>19.0</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>14.1</td>
<td>58.0</td>
<td>45.8</td>
</tr>
<tr>
<td>Hypertension</td>
<td>58.1</td>
<td>74.4</td>
<td>86.3</td>
</tr>
<tr>
<td>Known hyperlipidemia</td>
<td>56.3</td>
<td>50.2</td>
<td>51.6</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>10.2</td>
<td>23.3</td>
<td>21.6</td>
</tr>
<tr>
<td>GI or liver disease</td>
<td>3.7</td>
<td>12.3</td>
<td>10.5</td>
</tr>
<tr>
<td>Neoplastic disease</td>
<td>3.3</td>
<td>6.9</td>
<td>6.5</td>
</tr>
<tr>
<td>Prior myocardial infarction†</td>
<td>51.9</td>
<td>69.0</td>
<td>49.7</td>
</tr>
<tr>
<td>Prior thrombolytic therapy†</td>
<td>6.5</td>
<td>5.5</td>
<td>5.9</td>
</tr>
<tr>
<td>Prior CABG†</td>
<td>8.1</td>
<td>8.7</td>
<td>4.6</td>
</tr>
<tr>
<td>Prior PCI†</td>
<td>10.6</td>
<td>11.0</td>
<td>7.8</td>
</tr>
</tbody>
</table>

Indication for coronary angiography
- Stable angina: 34.5%
- Myocardial infarction: 25.7%
- Unstable angina: 30.8%
- Other: 8.1%

GI indicates gastrointestinal.
*P calculated by χ² tests.
†At any point in the past.

nondialysis kidney disease groups, with adjusted hazard ratios (95% CIs) of 0.69 (0.63 to 0.75) and 0.75 (0.56 to 0.99), respectively, whereas the dialysis kidney disease group experienced a nonsignificant lower risk of death (adjusted hazard ratio 0.89, 95% CI 0.59 to 1.32).

In these analyses, we used time of catheterization as a common "time zero" across treatment groups. For the PCI group, this reflects the treatment time, given a median waiting time of only 1 day, but the CABG median waiting time was longer, at 48 days. To assess the impact of including this waiting time, we performed a sensitivity

TABLE 2. Prevalence of Cardiac Catheterization Results by Treatment Group and Category of Kidney Function

<table>
<thead>
<tr>
<th>Clinical Variable</th>
<th>CABG</th>
<th>PCI</th>
<th>No Revascularization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=10 728), %</td>
<td>Disease (n=219), %</td>
<td>Disease (n=153), %</td>
</tr>
<tr>
<td>Coronary anatomy†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimal disease</td>
<td>1.4</td>
<td>0.9</td>
<td>2.0</td>
</tr>
<tr>
<td>1- or 2-VD</td>
<td>6.2</td>
<td>2.7</td>
<td>10.5</td>
</tr>
<tr>
<td>2-VD and prox LAD</td>
<td>12.2</td>
<td>8.7</td>
<td>11.1</td>
</tr>
<tr>
<td>3-VD</td>
<td>28.8</td>
<td>32.9</td>
<td>26.8</td>
</tr>
<tr>
<td>3-VD and prox LAD</td>
<td>27.8</td>
<td>27.4</td>
<td>29.4</td>
</tr>
<tr>
<td>Left main</td>
<td>23.5</td>
<td>27.4</td>
<td>20.3</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;50%</td>
<td>56.8</td>
<td>26.9</td>
<td>45.8</td>
</tr>
<tr>
<td>35% to 50%</td>
<td>27.3</td>
<td>22.4</td>
<td>22.9</td>
</tr>
<tr>
<td>&lt;35%</td>
<td>7.0</td>
<td>14.6</td>
<td>9.2</td>
</tr>
<tr>
<td>Ventriculogram not done</td>
<td>3.6</td>
<td>28.8</td>
<td>18.3</td>
</tr>
<tr>
<td>Missing</td>
<td>5.2</td>
<td>7.3</td>
<td>3.9</td>
</tr>
</tbody>
</table>

VD indicates vessel disease; LAD, left anterior descending coronary artery.
*P calculated by χ² tests.
†Minimal disease defined as a lesion with <50% stenosis.
analysis using the date of CABG or PCI as time zero. This sensitivity analysis yielded almost identical results to the analysis that used time of catheterization as time zero.

Discussion

The value of aggressive coronary artery revascularization compared with no revascularization in improving outcomes for patients with kidney disease is unknown. In the present study, we have shown that revascularization with CABG was associated with a lower risk of death than no revascularization for all categories of kidney function. Revascularization with PCI was also associated with a lower risk of death than no revascularization in reference patients and dialysis patient group (B), adjusted for age, gender, clinical risk factors, and severity of coronary artery disease. revasc indicates revascularization.

Survival curves for reference patient group (A), nondialysis kidney disease patient group (B), and dialysis patient group (C), adjusted for age, gender, clinical risk factors, and severity of coronary artery disease. revasc indicates revascularization.

revascularization and outcome has been demonstrated, the observed associations may or may not be causal. Although randomized controlled trials are the best means of confirming causation, large observational studies such as this can also be informative.

Previous studies have also suggested a survival benefit for CABG in dialysis patients. The present study had the added advantage over other studies of being able to adjust for severity of cardiac disease and left ventricular function. The reduced survival for dialysis patients treated with PCI compared with CABG may be related to an increased risk of restenosis. Despite the reduced survival for dialysis patients treated with PCI compared with CABG, the results of the present study nonetheless suggest a survival advantage for PCI over no revascularization.

We also found a lower risk of death for CABG over both PCI and no revascularization for patients with nondialysis kidney disease (serum creatinine >2.3 mg/dL). These results are in contrast to those reported by Szczech et al., in which CABG was not associated with better survival among patients with a creatinine >2.5 mg/dL (hazard ratio 0.86, 95% CI 0.56 to 1.33). This discrepancy may be explained by their shorter duration of follow-up (3 years). To the best of our knowledge, only 1 other study of patients with nondialysis kidney disease has included a nonrevascularized group. Similar to the present results, CABG was associated with a survival benefit across all levels of kidney function, whereas PCI failed to offer a significant benefit among patients with severe (creatinine clearance <30 mL/min) kidney disease.

The lack of an improvement in survival for PCI among nondialysis kidney disease patients is less likely to be explained by atherosclerotic risk factors and accelerated atherogenesis, because dialysis patients would also be so exposed, and yet a benefit of PCI over no revascularization was apparent in the dialysis group. A possible mechanism for the poor survival after PCI among nondialysis kidney disease patients is their increased risk of acute renal failure, an event associated with a greater risk of adverse outcomes after coronary intervention. The potential for increased complications after PCI, but not after CABG, in patients with kidney disease has been described. Another explanation may be higher rates of incomplete revascularization. Completeness of revascularization, as defined by the Duke jeopardy score, has been shown to vary by level of kidney function in a previous study from the APPROACH database, with complete revascularization obtained in 67.6% of reference patients, 64.3% of dialysis kidney disease patients, and only 42.4% of nondialysis kidney disease patients. Although speculative, incomplete revascularization in patients with nondialysis kidney disease may be related to conservative use of dye during angiography.

Survival after revascularization for dialysis kidney disease patients was better in the present study than previously reported in the United States. A possible explanation for this finding is that unlike previous studies that included only patients hospitalized after revascularization, the APPROACH database includes both inpatients and outpatients after catheterization, thus including patients with less urgent indications for catheterization. A second explanation may be that...
there are differences in outcomes between healthcare systems, a possibility supported by recent research showing better survival in dialysis patients in Canada than in the United States.\(^{31}\)

Given the observational nature of the present study, it has important limitations. First, selection bias is likely in that healthier patients may have been chosen for surgical interventions. Nevertheless, multivariate analysis and propensity adjustment were used to mitigate the impact of selection bias. A selection process and possible bias are also likely in the decision to pursue a cardiac catheterization. Second, the dichotomy of creatinine into values greater or less than 2.3 mg/dL (200 \(\mu\)mol/L) in the definition of nondialysis kidney disease limits an assessment of risk for various levels of kidney function. Third, the inception point for the cohort was cardiac catheterization. These patients are a subset of all patients with CVD and do not reflect the outcomes of all patients with CVD. Fourth, information on medication use during follow-up was not available, which prevented us from characterizing the medical treatment provided to the nonvascularized group. Finally, we were unable to track patients who may have left the province. This, however, is unlikely to have a major influence given the stability of the population, with a general trend in Alberta for increased inward rather than outward migration. In addition, we limited our study to residents of Alberta, and it would be rather atypical for a patient to move out of the province during a cardiac evaluation.

To summarize, we found a survival advantage for CABG compared with no revascularization for patients with all categories of kidney function. PCI was also associated with a survival advantage over no revascularization except in patients with non–dialysis-dependent kidney disease. These results indicate that the presence of kidney disease or dependence on dialysis treatment should not be a deterrent to revascularization, particularly with CABG. A better understanding of the factors associated with poor outcomes after PCI in patients with non–dialysis-dependent kidney disease may lead to improved management strategies for such patients.

Appendix

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Edmonton
S. Archer, M.M. Graham, W. Hui (Chair), A. Koshal, C.M. Norris, and R.T. Tsuyuki.

Calgary

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