Acute kidney injury following coronary angiography is associated with a long-term decline in kidney function

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To determine whether acute kidney injury results in later long-term decline in kidney function we measured changes in kidney function over a 3-year period in adults undergoing coronary angiography who had serum creatinine measurements as part of their clinical care. Acute kidney injury was categorized by the magnitude of increase in serum creatinine (mild (50–99% or ⩾0.3 mg/dl) and moderate or severe (⩾100%)) within 7 days of coronary angiography. Compared to patients without acute kidney injury, the adjusted odds of a sustained decline in kidney function at 3 months following angiography increased more than 4-fold for patients with mild to more than 17-fold for those with moderate or severe acute kidney injury. Among those with an estimated glomerular filtration rate after angiography less than 90 ml/min per 1.73 m^2, the subsequent adjusted mean rate of decline in estimated glomerular filtration rate during long-term follow-up (all normalized to 1.73 m^2 per year) was 0.2 ml/min in patients without acute kidney injury, 0.8 ml/min following mild injury, and 2.8 ml/min following moderate to severe acute kidney injury. Thus, acute kidney injury following coronary angiography is associated with a sustained loss and a larger rate of future decline in kidney function.

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Acute kidney injury (AKI) following coronary angiography is often transient, with improvement in kidney function observed within days to weeks.[1–3] Although severe AKI that requires dialysis is a rare event in this setting,[4,5] even AKI of lesser severity has been consistently associated with adverse outcomes including death.[6,7] Patients with preexisting chronic kidney disease (CKD) constitute a high-risk group for AKI in the setting of radiocontrast administration.[2] Furthermore, CKD itself is associated with graded increases in risk of mortality with incremental reductions in glomerular filtration rate (GFR).[8–10] These observations suggest that the long-term effects of AKI on the development and progression of CKD are important to understand.

The long-term trajectory of kidney function following an episode of AKI remains unclear. The majority of what is currently known relates to the risk of developing end-stage renal disease (ESRD) requiring dialysis among survivors of severe AKI.[11–13] The effects of lesser degrees of AKI have not been characterized, nor have the long-term effects of AKI on kidney function based on the rate of decline in estimated GFR (eGFR) after hospital discharge. Furthermore, the effects of AKI on serial post-procedure measurements of kidney function have not been examined following coronary angiography specifically, an event which is particularly relevant given the high cardiovascular risk and use of this procedure in patients with or at risk for CKD. Identification of patients at high risk for progressive loss of kidney function after these procedures would provide important prognostic information to guide subsequent patient care.

The purpose of this study was to examine the association between AKI and long-term changes in kidney function following coronary angiography. We hypothesized that a graded association would exist between the severity of an AKI episode and loss of kidney function at 3 months after angiography. We also hypothesized that AKI would be an independent predictor of the subsequent rate of decline in GFR beyond 3 months following coronary angiography.

RESULTS

Cohort formation and characteristics

We identified 19,022 Alberta residents 18 years of age or older undergoing coronary angiography with ⩾1 outpatient serum creatinine measurement performed in both the pre- and greater than 3-month post-angiography time periods. We excluded 327 patients receiving renal replacement therapy before study entry, and 616 patients who underwent coronary artery bypass surgery within 7 days following angiography.

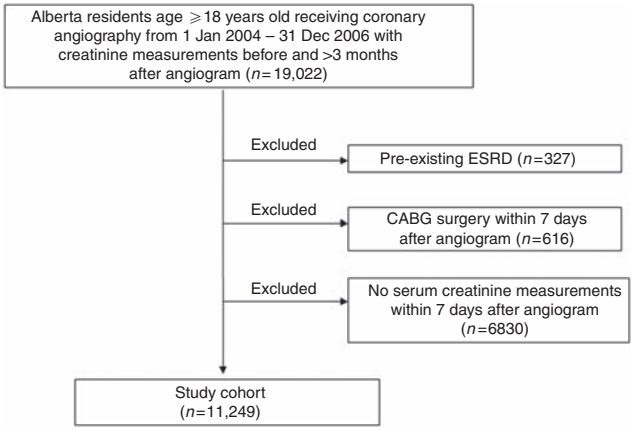

Figure 1 | Cohort formation.

Of the remainder, 11,249 (62.2%) had a serum creatinine measurement within 7 days following coronary angiography, and were included in the final cohort (Figure 1).

The mean age of the cohort was 63.6 years, 69.6% were men, and the mean eGFR before coronary angiography was 73.8 ml/min per 1.73 m^2. A total of 853 participants (7.6%) developed AKI following coronary angiography; 716 (6.4%) with mild AKI (increase in serum creatinine 50–99% or by ⩾0.3 mg/dl) and 137 (1.2%) with moderate or severe AKI (increase in serum creatinine ⩾100%). Patients who developed AKI were older, more likely to be women, with lower pre-angiography eGFR, proteinuria, and several comorbidities including diabetes mellitus, hypertension, and heart failure (Table 1).

Median follow-up from the date of coronary angiography was 2.5 years (interquartile range (IQR) 2.2, 2.8 years). The median number of serum creatinine measurements obtained between 7 days and 3 months after angiography was 6 (IQR 4, 9), whereas the median number of outpatient serum creatinine measurements obtained >3 months after angiography was 3 (IQR 2, 4), with a median interval between measurements of 7 months (IQR 1, 11 months). During follow-up beyond 3 months after coronary angiography, 638 participants (5.7%) died, whereas 46 (0.4%) initiated chronic renal replacement therapy.

Table 1 | Characteristics of patients undergoing coronary angiography, according to AKI status

	No AKI (*n*=10,396)	Mild AKI (*n*=716)	Moderate or severe AKI (*n*=137)	*P*-value[a]
Age, years, mean (s.d.)	63.3 (12.2)	68.3 (11.8)	66.8 (12.0)	<0.0001
Sex, male, no. (%)	7263 (69.9)	490 (68.4)	79 (57.7)	0.007
Pre-angiography eGFR, ml/min per 1.73 m^2, mean (s.d.)	74.0 (19.8)	62.4 (24.3)	61.8 (26.2)	<0.0001
Pre-angiography eGFR, categories, no. (%)				
⩾90 ml/min per 1.73 m^2	1897 (18.2)	84 (11.7)	16 (11.7)	<0.001
60–89 ml/min per 1.73 m^2	6195 (59.6)	280 (39.1)	49 (35.8)	
30–59 ml/min per 1.73 m^2	2196 (21.1)	315 (44.0)	59 (43.1)	
<30 ml/min per 1.73 m^2	108 (1.0)	37 (5.2)	13 (9.5)	
Proteinuria, no. (%)				
Absent	6779 (65.2)	424 (59.2)	71 (51.8)	<0.001
Microalbuminuria	1225 (11.8)	161 (22.5)	50 (36.5)	
Proteinuria	40 (3.8)	11 (1.5)	1 (0.7)	
Unmeasured	2352 (22.6)	120 (16.8)	15 (10.9)	
Comorbidities, no. (%)				
Diabetes mellitus	2730 (26.3)	265 (37.0)	62 (45.2)	<0.001
Hypertension	7024 (67.6)	537 (75.0)	93 (67.9)	<0.001
Hyperlipidemia	8098 (77.9)	538 (75.1)	90 (65.7)	0.001
Heart failure	1450 (13.9)	224 (31.3)	60 (43.8)	<0.001
Cerebrovascular disease	751 (7.2)	83 (11.2)	25 (18.2)	<0.001
Peripheral vascular disease	786 (7.6)	84 (11.7)	20 (14.6)	<0.001
Chronic pulmonary disease	1709 (16.4)	190 (26.5)	29 (21.1)	<0.001
Liver disease	141 (1.4)	14 (2.0)	5 (3.6)	0.014
Malignancy	451 (4.3)	41 (5.7)	8 (5.8)	0.16
Current smoker	3030 (29.1)	166 (23.2)	25 (18.2)	<0.001
Procedures following diagnostic angiogram, no. (%)				
Percutaneous coronary intervention	5356 (51.5)	329 (45.9)	50 (36.5)	<0.001
Coronary artery bypass surgery	1335 (12.8)	112 (15.6)	21 (15.3)	0.072

Abbreviations: AKI, acute kidney injury; s.d., standard deviation.
[a]ANOVA or χ^2-test.

Table 2 | Sustained loss of kidney function at 3 months following coronary angiography

	No AKI	Mild AKI	Moderate or severe AKI
No. of patients	10,396	716	137
No. serum creatinine measurements per patient, median (IQR)	6 (3, 9)	8 (5, 14)	7 (4, 17)
Decline in kidney function[a]			
No. (%)	613 (5.9)	202 (28.2)	81 (59.1)
Crude odds ratio (95% CI)	1 (reference)	6.30 (5.25–7.56)	23.20 (16.34–32.94)
Adjusted odds ratio (95% CI)[b]	1 (reference)	4.74 (3.92–5.74)	17.31 (12.03–24.90)

Abbreviations: AKI, acute kidney injury; CI, confidence interval.
[a]Loss of kidney function=serum creatinine >50% or 0.3 mg/dl above pre-angiography concentration on all measurements obtained 7 days to 3 months following angiogram.
[b]Final model adjusted for age, sex, pre-angiography eGFR, proteinuria, comorbidities (diabetes mellitus, hypertension, heart failure, cerebrovascular disease, chronic pulmonary disease), revascularization following coronary angiogram (percutaneous coronary intervention or coronary artery bypass surgery).

Loss of kidney function at 3 months following coronary angiography

The proportion of patients with a sustained loss of kidney function (serum creatinine concentration >50% or 0.3 mg/dl above pre-angiography concentration >3 months following the procedure) increased with greater severity of AKI, occurring in 5.9% of patients without AKI, 28.2% of patients with mild AKI, and 59.1% among patients with moderate or severe AKI (Table 2). In the final model adjusted for age, sex, pre-angiography eGFR, proteinuria, comorbidities, and revascularization procedures, compared with patients without AKI, the odds of a decline in kidney function by 3 months increased more than 4-fold for subjects with mild AKI Stage (odds ratio (OR) 4.74, 95% confidence interval (CI) 3.92–5.74), and more than 17-fold for those with moderate or severe AKI (OR 17.31, 95% CI 12.03–24.90).

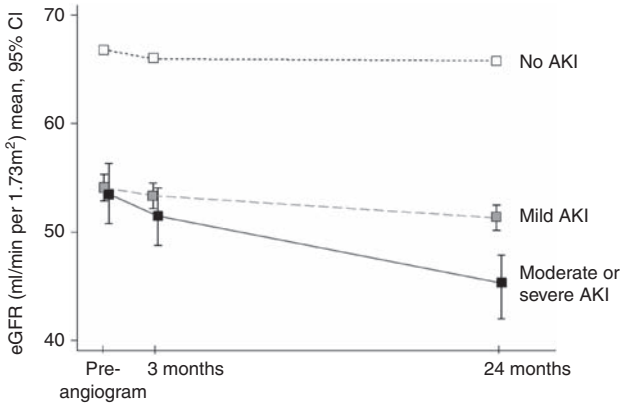

Figure 2 | Kidney function following coronary angiography among patients with post-angiography estimated glomerular filtration rate (eGFR) <90 ml/min per 1.73 m², according to acute kidney injury status.

Long-term decline in kidney function following coronary angiography

Among the 10,418 (92.6%) patients with a post-angiography eGFR <90 ml/min per 1.73 m² more than 3 months following angiography, those who had developed AKI had lower eGFR at 3 months, as well as further decline in eGFR during subsequent long-term follow-up (Figure 2). The unadjusted mean annual rate of decline in eGFR during long-term follow-up was 0.1 (95% CI −0.1 to 0.2) ml/min per 1.73 m² per year among patients without AKI, 1.0 (95% CI 0.4–1.5) ml/min per 1.73 m² per year among patients with mild AKI, and 3.1 (95% CI 2.0–4.2) ml/min per 1.73 m² per year among patients with moderate or severe AKI. After adjustment for age, sex, proteinuria, and comorbidities, the adjusted rate of decline in eGFR was 0.2 (95% CI −0.4 to 0.8) ml/min per 1.73 m² per year in patients without AKI, 0.8 (95% CI 0.1–1.6) ml/min per 1.73 m² per year in those who had developed mild AKI, and 2.8 (95% CI 1.7–4.1) ml/min per 1.73 m² per year in patients who had experienced moderate to severe AKI (*P*-trend <0.001). The odds of rapid progression of kidney disease during the long-term follow-up period also increased in a graded manner with increasing severity of AKI (Table 3). The test for interaction between AKI and post-angiogram eGFR was nonsignificant (*P*-interaction 0.24) suggesting that AKI was associated with similar risks of subsequent rapid progression of kidney disease regardless of the eGFR at the start of long-term follow-up.

Comparison of pre- and post-angiography rates of decline in kidney function

There were 5,478 (59.2%) patients who also had estimates of GFR available spanning >1 year before angiography with which to estimate the pre-angiography rate of decline in kidney function. The annual rate of decline in eGFR was similar for the pre- and the post-angiography time periods for patients without AKI or with mild AKI. For patients who experienced moderate or severe AKI, there was a statistically significant increase in the rate of decline in kidney function following the episode of AKI by 1.8 (95% CI 0.6–3.0) ml/min per 1.73 m² per year, compared with the pre-angiography rate.

Sensitivity analyses

Sensitivity analyses were conducted to explore the impact of the number and frequency of serum creatinine measurements on results. For the analysis of kidney function at 3 months, we restricted the cohort to patients who had ⩾2 creatinine measurements obtained between 7 days and 3 months

Table 3 | Long-term changes in kidney function beyond 3 months following coronary angiography among patients with post-angiography eGFR <90 ml/min per 1.73 m^2 (*n*=10,418), according to AKI status

	No AKI	Mild AKI	Moderate or severe AKI
No. of patients	9539	742	137
eGFR 3 months post-angiography, ml/min per 1.73 m^2 (95% CI)	66.0 (65.7–66.3)	53.4 (50.1–52.7)	51.5 (48.8–54.1)
Follow-up duration, months, median (IQR)	21.8 (13.0, 30.8)	20.4 (12.8, 30.1)	22.5 (13.4, 30.4)
No. serum creatinine measurements per patient, median (IQR)	3 (1, 5)	4 (2, 8)	4 (2, 10)
Rate of decline in eGFR (ml/min per 1.73 m^2/year)			
Crude mean (95% CI)	0.1 (−0.1–0.2)	1.0 (0.4–1.5)	3.1 (2.0–4.2)
Adjusted mean (95% CI)[a]	0.2 (−0.4–0.8)	0.8 (0.1–1.6)	2.8 (1.7–4.1)
Rapid progression of kidney disease			
Decline in eGFR >4 ml/min per 1.73 m^2 per year, no. (%)	333 (3.4)	58 (7.8)	22 (16.0)
Initiated chronic renal replacement therapy, no (%)	21 (0.2)	18 (2.4)	8 (5.8)
Composite outcome[b]			
Crude odds ratio (95% CI)	1 (reference)	2.81 (2.15–3.67)	6.52 (4.22–10.07)
Adjusted odds ratio (95% CI)[c]	1 (reference)	1.60 (1.19–2.14)	3.12 (1.95–4.99)

Abbreviations: AKI, acute kidney injury; eGFR, estimated glomerular filtration rate; IQR, interquartile range.
[a]Final model adjusted for age, sex, and comorbidities (diabetes mellitus, hypertension, proteinuria, and heart failure).
[b]Composite outcome=decline in eGFR >4 ml/min per 1.73 m^2 per year or initiation of chronic renal replacement therapy.
[c]Final model adjusted for age, sex, baseline eGFR, proteinuria, comorbidities (diabetes mellitus, hypertension, heart failure, cerebrovascular disease, peripheral vascular disease, chronic pulmonary disease, liver disease, malignancy, and current smoking).

following angiography, which produced similar findings to our primary analysis. For the analysis of long-term progression of kidney function beyond 3 months following angiography, we stratified the cohort according to the number of serum creatinine measurements during the follow-up period ($\leqslant$ 2, 3, or $\geqslant$4 measurements). Although the subsequent rate of decline in eGFR increased with greater number of serum creatinine measurements across all categories of AKI, the relative increases in rate of decline in eGFR, and odds of rapid progression with mild and moderate or severe AKI were comparable across all strata to those observed in the primary analyses.

DISCUSSION

In this large cohort undergoing coronary angiography, a loss of kidney function at 3 months following coronary angiography was common after AKI. Among patients with an eGFR <90 ml/min per 1.73 m^2 following angiography, the long-term risk of further progressive loss of kidney function also increased with greater severity of AKI. Furthermore, patients with moderate or severe AKI experienced acceleration in the rate of eGFR decline following an episode of AKI compared with their pre-angiography rate of progression. These results show that patients who develop AKI following coronary angiography are at increased risk for progressive long-term loss of kidney function following angiography.

Although the short-term adverse effects of AKI during hospitalization are well recognized,[7,14,15] the long-term effects of AKI on renal outcomes have been unclear because comparisons to patients without AKI have been lacking, the confounding effects of preexisting CKD have not been controlled for, or identification of progression of kidney disease has been based solely on receipt of treatment for ESRD.[16,17] Elderly patients hospitalized with diagnosis codes for AKI superimposed on CKD[11] as well as patients with increases in creatinine following hospitalization with myocardial infarction have been shown to be at increased risk for enrollment in ESRD programs in the United States.[18] Severe AKI leading to dialysis during hospitalization has recently been shown to be associated with an increased risk for chronic renal replacement therapy in later life,[12,13] whereas patients with diagnosis codes for acute tubular necrosis or dialysis-requiring AKI have also been reported to be at risk for earlier identification of stage 4 or 5 CKD.[19,20]

This analysis expands upon the findings of previous studies by identifying both AKI and subsequent changes in kidney function using serial measurements of serum creatinine and eGFR. This is a significant advantage given the limitations in sensitivity and specificity when using administrative codes to define AKI and CKD in isolation or combination.[21–23] Furthermore, the use of pre- and post-angiography estimates of GFR allowed for the confounding effects of preexisting CKD (and its severity) to be accounted for in these analyses.[16]

A number of mechanisms may explain the associations between AKI and progressive loss of kidney dysfunction following coronary angiography. First, the association may be due to numerous comorbidities (that is, hypertension, diabetes mellitus, proteinuria, or later stages of CKD) in patients who develop AKI. However, the magnitude of the associations that remained after statistical adjustment suggests that confounding by these characteristics is unlikely to explain our findings. Second, patients who develop AKI may be more likely to have a serum creatinine measurement obtained during follow-up, thus introducing potential for ascertainment bias. However, we observed similar results when analyses were stratified by the number of serum creatinine measurements performed during

follow-up, suggesting that the clinical decisions that lead to the measurement of serum creatinine do not explain our findings. Third, patients who develop AKI may be susceptible to other processes that lead to progressive kidney disease following angiography such as atheroemboli.[24] Alternatively, the long-term decline in eGFR following AKI may be due to persisting renal damage after an episode of acute tubular injury. Animal studies suggest that chronic changes to the renal microvasculature may result from acute ischemic renal injury.[25,26] Our observations that kidney function was less likely to recover to pre-angiography levels, and further declined at a faster rate following an episode of AKI, are in keeping with this hypothesis.

There are limitations to our study resulting from its observational nature and the use of serum creatinine and eGFR to determine kidney function. First, because this study was conducted retrospectively, participant selection was limited to patients who had pre- and post-angiography serum creatinine measurements including measurements within 7 days of coronary angiography as part of their clinical care. Although many outpatients were thus excluded because of the inability to ascertain AKI, these patients had few risk factors for AKI and showed a low rate of CKD progression during follow-up (decline in eGFR 0.1 ml/min per 1.73 m^2 per year). Therefore exclusion of these patients from the study and restriction of the control group to those with creatinine measurements are unlikely to have impacted our findings. Second, episodes of AKI and their severity may have been misclassified due to our dependence on existing creatinine measurements captured following coronary angiography. However, our approach to identification of AKI is most vulnerable to missing episodes of mild AKI or underestimating the severity of AKI in those who developed it. If such misclassification occurred, we anticipate this would have underestimated the risk of renal outcomes following moderate or severe AKI. Finally, measurement of long-term study outcomes required that patients survive beyond 3 months to obtain repeated measures of kidney function. Loss of patients due to death, ESRD, or loss to clinical follow-up may thus have influenced results. However, because patients with more rapid decline in kidney function are more likely to experience death or ESRD,[27,28] our estimates of the rate of progression are likely conservative.[29]

The associations between AKI and progressive kidney dysfunction have potentially important implications for clinical management of patients following coronary angiography, given the availability of strategies that may slow the progression of CKD.[30,31] Our findings suggest a need for clinical follow-up and further research evaluating strategies to reduce progression of kidney disease in patients developing AKI following angiographic procedures.

In conclusion, patients with AKI are at increased risk of sustaining a loss of kidney function following coronary angiography, and further decline in kidney function during long-term follow-up. Patients who develop AKI following coronary angiography should be considered at increased risk for progressive kidney disease and its associated complications. Further research should focus on the effects of interventions to slow the progression of CKD in survivors of radiocontrast-associated AKI.

MATERIALS AND METHODS

Study population

The study cohort was derived from the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH), a prospective data collection initiative that captures detailed clinical information on all patients undergoing coronary angiography in Alberta, Canada at the time of their procedure.[32] Coronary angiography was performed using nonionic iodinated radiocontrast agents with the choice of low- or iso-osmolar radiocontrast agents and use of *N*-acetylcysteine and intravenous fluid made at the discretion of treating physicians.

The cohort consisted of all Alberta residents, $\geqslant$18 years of age, undergoing coronary angiography from 1 January 2004 to 31 December 2006 in Alberta. To be eligible for inclusion, participants required at least one serum creatinine measurement obtained from an outpatient laboratory in each of two time periods relative to the coronary angiogram: within a 6-month period preceding the coronary angiogram; and $>$3 months following the angiogram (Supplementary Figure S1). Patients with a renal transplant or who were receiving dialysis before coronary angiography were excluded based on linkage with the Northern and Southern Alberta Renal Program registries[33] or by physician billing claims (*Canadian Classification of Procedures* codes 13.99A, 13.99B, 13.99C, 13.99D, and 13.99O).[34] Patients undergoing coronary artery bypass surgery within 7 days of coronary angiography were excluded to minimize causes of AKI other than those related to angiography. The cohort entry date for each patient was the date of the first coronary angiogram performed during the study period.

Measurement of exposure

All serum creatinine measurements performed in Alberta outpatient facilities, or inpatient facilities that perform coronary angiography, were obtained from the Alberta Kidney Disease Network repository of laboratory data.[35] AKI was defined based on the change in serum creatinine concentration from the last pre-angiogram level to the peak level observed within 7 days following the coronary angiogram. We defined mild AKI as an increase in serum creatinine of 50–99% or by $\geqslant$0.3 mg/dl, and moderate or severe AKI as an increase in serum creatinine $\geqslant$100%.[36] Patients with no creatinine measurements within 7 days after angiography with which to ascertain AKI were excluded.

Measurement of kidney function

The four-variable Modification of Diet in Renal Disease Study equation[37] was used to estimate eGFR before coronary angiography and after 3 months following angiography (Supplementary Figure S1). Although data on race were not available, misclassification of eGFR was expected to be minimal as $<$1% of the Alberta population is black.[35] During the study period several Alberta laboratories switched from nonstandardized creatinine assays to isotope dilution mass spectroscopy-calibrated serum creatinine assays;[38] we used the non-isotope dilution mass spectroscopy traceable Modification of Diet in Renal Disease study equation as well as the isotope dilution mass spectroscopy-traceable Modification of Diet in Renal Disease study equation to determine eGFR as

appropriate based on the laboratory and date of creatinine measurement.[39] To reduce interlaboratory variation in eGFR, we standardized creatinine measurements across provincial laboratories to an isotope dilution mass spectroscopy reference standard, and a laboratory-specific correction factor was applied as previously described.[35]

Measurement of covariates

Age, sex, comorbidities, and information on coronary revascularization procedures (percutaneous coronary intervention and coronary artery bypass surgery) were determined from the APPROACH database. Pre-angiography eGFR was estimated using the last available outpatient creatinine measurements performed within 6 months before coronary angiography. Post-angiography eGFR was calculated using the first available outpatient creatinine measurement performed >3 months after angiography. Provincial laboratory data were used to obtain all outpatient urine protein results collected before angiography.[35] Urine protein was categorized as absent, microalbuminuria, or macroalbuminuria/proteinuria as previously described.[40] Classification was based on the most recent pre-angiography urine specimen for patients with two measurements, and based on the median result when $\geqslant 3$ measurements were available.

Measurement of outcomes

Participants were followed until death (identified from Alberta Vital Statistics Registry), the date of registration for chronic dialysis or renal transplantation (identified from the Northern or Southern Alberta Renal Program databases), or the study end date (31 December 2007). We considered a sustained loss of kidney function to be present after coronary angiography when the lowest serum creatinine concentration obtained between 7 days and 3 months after angiography was more than 50% or 0.3 mg/dl greater than the last pre-angiography measurement[41,42] The subsequent decline in kidney function occurring beyond 3 months following angiography was assessed for patients with a post-angiography eGFR <90 ml/min per 1.73 m^2 (captured >3 months following the angiogram) and was based upon the annual rate of decline in eGFR during the remaining follow-up period.[43] To address the effect that AKI may have on acceleration of progression of kidney function, we compared the rate of decline in eGFR in periods before and after coronary angiography in the subgroup of these patients who also had eGFR measurements that spanned a minimum of 1 year during the pre-angiography time period.[16] Rapid progression of kidney disease, defined as a rate of decline in eGFR >4 ml/min per 1.73 m^2 per year (ref. 28) or the initiation or chronic renal replacement therapy (dialysis or renal transplant) during the follow-up period beyond 3 months after coronary angiography, was also identified.

Statistical analysis

Differences in baseline characteristics according to AKI status were compared using analysis of variance or χ^2-tests as appropriate. Logistic regression models including terms for covariates in Table 1 were fit to determine the association between AKI and decline in kidney function at 3 months. For patients with post-angiography eGFR <90 ml/min per 1.73 m^2, further progression of kidney dysfunction according to the annual rate of decline in eGFR in ml/min per 1.73 m^2 was determined using mixed-effect models with random intercepts and random slopes. These models estimate the rate of change in eGFR as a linear function over time, taking into account the varying number and spacing of measurements of eGFR as well as the variable follow-up for each subject, and avoid high variability in estimates for patients with short follow-up.[44,45] All outpatient eGFR measurements obtained more than 3 months after coronary angiography until death, initiation of renal replacement therapy, or the study end-date were included in these models that were adjusted for age, sex, proteinuria, and comorbidities. In a subgroup analysis, the mixed-effect model was expanded to include pre-angiography estimates of eGFR, incorporating a fixed effect to assess differences in the annual rate of change in eGFR in the pre- and post-angiography time periods. Logistic regression models were used to determine the association between AKI and the risk of rapid progression occurring >3 months after angiography in patients with post-angiography eGFR <90 ml/min per 1.73 m^2. Stepwise elimination and backward selection were used to select variables for inclusion in the final logistic regression and mixed-effect models. The normal distribution of random effects for the mixed-effect model and linearity of the logit for logistic regression models were tested using graphical approaches. All statistical analyses were conducted using STATA (version 10.0; STATA Corp., College Station, TX). The conjoint health research ethics board of the University of Calgary approved the study.

DISCLOSURE

All the authors declared no competing interests.

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SUPPLEMENTARY MATERIAL

Figure S1. Overview of study design.
Supplementary material is linked to the online version of the paper at http://www.nature.com/ki

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