

Chronic Kidney Disease and Health Status Outcomes Following Acute Myocardial Infarction

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Background—The association between chronic kidney disease (CKD) and health status outcomes after acute myocardial infarction (AMI) is unknown.

Methods and Results—Patients were enrolled between 2005 and 2008 in the Translational Research Investigating Underlying Disparities in Acute Myocardial Infarction Patients' Health Status (TRIUMPH) registry, a prospective multicenter observational study of AMI outcomes. The Seattle Angina Questionnaire and Short Form-12 were collected at baseline and at 1, 6, and 12 months following AMI. CKD was defined by an estimated glomerular filtration rate <60 mL/min, calculated during the AMI hospitalization. Linear repeated-measures models assessed the association between CKD and health status after AMI, accounting for the propensity to have follow-up health status measures. Of 3617 patients, 576 (16%) had CKD and 3041 (84%) did not have CKD. Patients with CKD were older and had more comorbidity. Patients with CKD were more likely to have multivessel coronary disease and less likely to undergo revascularization. Among AMI survivors, patients with and without CKD had similar health-related quality of life (adjusted difference of 0.24, 95% CI –1.46 to 1.95), angina frequency (adjusted difference of 1.27, 95% CI –0.05 to 2.58), and mental health (adjusted difference of –0.07, 95% CI –0.90 to 0.75). In contrast, patients with CKD had lower physical health (adjusted difference –1.61, 95% CI –2.49 to –0.74), which was not clinically significant, compared with patients without CKD.

Conclusions—Among AMI survivors, patients with CKD not only had more comorbidities but also, after adjusting for these patient differences, had similar health status compared with patients without CKD. Interventions aimed at improving health status after AMI should not focus on CKD status. (*J Am Heart Assoc.* 2016;5:e002772 doi: 10.1161/JAHA.115.002772)

Key Words: acute myocardial infarction • chronic kidney disease • health status • outcomes research • registry

Chronic kidney disease (CKD) is strongly associated with increased risk of morbidity and mortality in patients after acute myocardial infarction (AMI).^{1–3} Prior studies have demonstrated an association between declining renal function and increased risk of death from cardiovascular causes, recurrent AMI, congestive heart failure, and stroke. This association between renal dysfunction and adverse outcomes is graded and present even among patients with mild renal dysfunction; however, little is known regarding the impact of CKD on patient-centered outcomes such as health-related

quality of life (HRQL), symptom burden, and functional status. Following AMI, patients generally have a decline in health status. Nearly 15% of patients, for example, have a decline in physical function, and 20% have ongoing angina symptoms at 1 year after AMI regardless of CKD status.^{4,5} Furthermore, studies have demonstrated that CKD can negatively affect patient health status, and as CKD worsens, physical functioning, general health, and mental health also decline.^{6,7} Previous work with patients who had stable coronary artery disease and with those who underwent coronary artery bypass grafting showed that patients with CKD have lower physical functioning scores compared with those without CKD.^{8,9} Although 43% of patients have a decline in their health status from the time of their AMI to 1 year later,⁴ limited data have assessed whether CKD further accentuates this decline. Accordingly, using the Translational Research Investigating Underlying Disparities in Acute Myocardial Infarction Patients' Health Status (TRIUMPH) registry¹⁰ of 4340 AMI patients, we evaluated the association between CKD and health status outcomes of patients at 1 year after AMI. Specifically, we assessed the association between CKD with health status, including HRQL, and symptom burden using the Seattle Angina Questionnaire (SAQ). In addition, we

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assessed the association between CKD with physical and mental functioning using Short Form 12 (SF-12) at 1 year after AMI. We hope these data will improve our understanding of the impact of CKD on patient-centered outcomes following AMI. Insights into this relationship can help guide resources to improve the health status outcomes of patients with and without CKD in the year following AMI.

Methods

The TRIUMPH registry is a national prospective multicenter registry created to investigate disparities in health status outcomes among AMI patients.¹⁰ TRIUMPH enrolled 4340 patients between April 2005 and December 2008 from 24 US medical centers. Eligible patients were aged ≥ 18 years, had elevated creatine kinase MB or troponin, and had symptoms suggestive of angina or electrocardiographic evidence of ischemia. Participants must have presented or transferred to an enrolling institution within the first 24 hours of symptom onset to be included in the study. The institutional review board at each institution approved the study, and participants gave informed consent. All patients underwent detailed interviews within 72 hours of initial presentation, and additional information was obtained through chart abstraction and laboratory studies. Follow-up was attempted for all survivors at 1, 6, and 12 months. It was performed by telephone contact from a single specialized center using health status measures and other psychosocial instruments.

Of the 4340 patients enrolled in the TRIUMPH registry, we excluded those who died during their index hospitalization, those without at least 1 assessment of health status outcomes ($n=703$), and those missing estimated glomerular filtration rate (eGFR) data ($n=20$), for a total of 3617 patients who were included in our primary analysis.

The eGFR was calculated using the Modification of Diet in Renal Disease (MDRD) equation and was based on the highest calculated eGFR recorded during the initial hospitalization. CKD was dichotomized to those with CKD and <60 mL/min/ 1.73m^2 and those without CKD and eGFR mL/min/ 1.73m^2 .

Detailed interviews, which included the disease-specific SAQ and the generic SF-12, were attempted with all survivors at baseline prior to hospital discharge and then at 1, 6, and 12 months following AMI hospital discharge. The SAQ and SF-12 surveys are validated and reliable measures of disease-specific and general health status, respectively.^{11–13}

The SAQ is a 19-item health status measure for patients with coronary artery disease. It assesses 5 domains: angina frequency, angina stability, physical limitation, quality of life, and treatment satisfaction. We used the quality of life and angina frequency domains in our analysis. Each domain is scored from 0 to 100, and scores are grouped into quartiles:

<25 (severe), 25 to 50 (moderate), 50 to 75 (mild), and 75 to 100 (minimal). Higher scores represent less impairment and better quality of life. A 5-point change in score is considered clinically significant.

The SF-12 is a 12-item survey of physical and mental functioning. A score of 50 is normalized to the mean health status of the US population, and every 10 points represents 1 SD from that mean. Score differences are related to the age-specific mean score, with higher scores indicating better health status.

Missing data were assumed to be missing at random and were imputed using a simple imputation model that contained all variables from the multivariable model.¹⁴ At least 1 study covariate was missing for 9.3% of patients, and >1 study covariate was missing for $<1\%$ of patients. The covariate with the most missing data was number of diseased vessels ($n=232$; 6.4%), followed by coronary angiography (not performed in 224 patients) and insurance status ($n=73$; 0.5%). All missing covariates that were used in the repeated-measures models were imputed.

The primary analysis included patients with an eGFR measurement available at baseline, a baseline health status assessment, and at least 1 follow-up assessment. Patient characteristics were compared for patients with and without CKD, using the Student *t* test for continuous variables and the chi-square or Fisher exact test for categorical variables. All health status data (SAQ and SF-12) available at 1, 6, and 12 months were included in the analyses. Linear repeated-measures models were used to assess the independent association between CKD and health status outcomes after AMI. The models were adjusted for site, baseline health status, age, sex, education, insurance status, and medical comorbidities. We also adjusted for left ventricular systolic dysfunction, number of diseased vessels, substance use, and discharge medications. In addition, we estimated the effect of CKD on mortality using a proportional hazards model adjusted for age, sex, race, and Global Registry of Acute Coronary Events (GRACE) score. In this analysis, we included all patients with an eGFR measurement, regardless of follow-up status. To address survival bias, specifically, incomplete follow-up among survivors, a multivariable logistic regression model was created to estimate the probability of having follow-up for each patient. The primary analysis described was then repeated, weighting each patient by the reciprocal value of their probability. This process “adjusted” the analyses to reflect the total population of patients, not just those with follow-up; for example, a patient with a predicted probability of follow-up of 0.5 would be given a weight of 2, which reflects the patient representing him- or herself plus 1 other similar patient who did not complete follow-up. This approach corrects for any complete-case biases associated with observed patient characteristics.

Table 1. Patient Characteristics

	CKD, n=576	No CKD, n=3041	P Value
Age, y	67.2±11.7	57.8±11.5	<0.001
Race			0.197
White	396 (68.8)	2137 (70.3)	
Black	149 (25.9)	699 (23.0)	
Other	31 (5.4)	205 (6.7)	
Male	297 (51.6)	2121 (69.7)	<0.001
High school education	424 (74.1)	2464 (81.4)	<0.001
Noncardiac history			
Hypertension	500 (86.8)	1884 (62.0)	<0.001
Diabetes mellitus	297 (51.6)	775 (25.5)	<0.001
Diabetes type			0.123
Type I	23 (8.3)	41 (5.6)	
Type II	254 (91.7)	686 (94.4)	
Dyslipidemia	336 (58.3)	1462 (48.1)	<0.001
Peripheral vascular disease	56 (9.7)	119 (3.9)	<0.001
Cerebrovascular accident	52 (9.0)	120 (3.9)	<0.001
Cancer	56 (9.7)	206 (6.8)	0.012
Chronic lung disease	65 (11.3)	195 (6.4)	<0.001
Sleep apnea	21 (3.6)	85 (2.8)	0.267
Depression on medication	49 (8.5)	228 (7.5)	0.404
Alcohol abuse	39 (6.8)	314 (10.3)	0.008
Alcohol use in past year			<0.001
Never	347 (60.3)	1217 (40.2)	
Monthly or less	130 (22.6)	791 (26.1)	
2–4 times a month	50 (8.7)	538 (17.8)	
4–5 times a week	25 (4.3)	253 (8.4)	
≥6 times a week	23 (4.0)	229 (7.6)	
Illicit drug use	9 (1.6)	107 (3.5)	0.015
Smoking status			<0.001
Current (<30 days)	118 (20.5)	1260 (41.8)	
Former (>30 days)	244 (42.4)	952 (31.6)	
Never (or <100 total)	213 (37.0)	805 (26.7)	
Cardiac history			
Chronic heart failure	103 (17.9)	164 (5.4)	<0.001
Prior coronary artery bypass grafting	137 (23.8)	272 (8.9)	<0.001
Prior myocardial infarction	152 (26.4)	577 (19.0)	<0.018
Prior percutaneous coronary intervention	134 (23.3)	577 (19.0)	0.018
Presentation			<0.001
ST-segment elevation myocardial infarction	160 (27.8)	1435 (47.2)	
Non-ST-segment elevation myocardial infarction	416 (72.2)	1606 (52.8)	

Continued

Table 1. Continued

	CKD, n=576	No CKD, n=3041	P Value
Diseased vessels			<0.001
0	37 (7.8)	244 (8.4)	
1	144 (30.2)	1288 (44.3)	
2	128 (26.8)	765 (26.3)	
3	168 (35.2)	611 (21.0)	
Left ventricular systolic function			<0.001
Normal	324 (56.3)	1938 (63.8)	
Mild	118 (20.5)	588 (19.4)	
Moderate	68 (11.8)	325 (10.7)	
Severe	65 (11.8)	186 (6.1)	
Revascularization	347 (60.2)	2386 (78.5)	<0.001
GRACE mortality risk score	124.5±27.6	95.5±27.1	<0.001
Heart rate, initial, bpm	85.0±24.1	81.3±21.5	<0.001
Systolic blood pressure, initial, mm Hg	146.2±32.6	142.7±29.8	0.009
Hemoglobin, initial, g/L	126±21.0	143±19.0	<0.001
Troponin maximum level, µg/L	24.9±82.9	29.9±70.6	0.132
Creatinine, initial, µmol/L	203±176	88±27	<0.001
Creatinine, final, µmol/L	194±150	88±18	<0.001

Data are shown as number (percentage) or mean±SD. CKD indicates chronic kidney disease; GRACE, Global Registry of Acute Coronary Events.

The reciprocal value of the propensity score was obtained so that those who were the most similar to patients without follow-up were weighted more heavily. This weight was then accounted for in the main analysis. Sensitivity analyses also assessed the association between more severe stages of CKD (stage 4 and 5) and health status outcomes. All tests for statistical significance were 2-tailed and were evaluated at a significance level of 0.05. All analyses were conducted with SAS 9.3 (SAS Institute).

Results

Of 3617 patients included in the study, 3041 (84%) did not have CKD (eGFR ≥60 mL/min), 459 (13%) had stage 3 CKD (eGFR 30–59 mL/min), 72 (2%) had stage 4 CKD (eGFR 15–29 mL/min), and 45 (1%) had stage 5 CKD (eGFR <15 mL/min or dialysis). Patients with CKD (stages 3–5) were older (aged 67.2 versus 57.8 years, $P<0.001$), were less likely to be male (52% versus 70% female, $P<0.001$), and had more comorbidities, including history of myocardial infarction, percutaneous coronary intervention, and coronary artery bypass grafting. Patients with CKD were less likely to smoke tobacco, use illicit drugs, or use alcohol. During hospitalization, patients with CKD were more likely to have 3-vessel coronary disease on coronary angiography and left ventricular

systolic dysfunction and were less likely to undergo revascularization (Table 1).

Patients with CKD were also more likely to experience in-hospital adverse events compared with patients without CKD, including cerebrovascular accident (1.4% versus 0.3%), renal failure (10.1% versus 1.6%), or need for dialysis (2.3% versus 0.1%) (Table 2).

At discharge, patients with CKD were less likely to receive guideline-recommended therapies such as aspirin, statins, and angiotensin-converting enzyme inhibitors (Table 3), despite having more severe coronary disease, higher GRACE mortality risk scores, and decreased rates of revascularization. Adjusted survival at 1 year was lower for patients

Table 2. Adverse In-Hospital Events

Adverse Hospital Events	CKD, n=576	No CKD, n=3041	P Value
Renal failure	58 (10.1)	48 (1.6)	<0.001
Dialysis	13 (2.3)	3 (0.1)	<0.001
Cardiogenic shock	15 (2.6)	86 (2.8)	0.765
Cerebrovascular accident	8 (1.4)	10 (0.3)	0.004
Pacemaker	35 (6.1)	132 (4.3)	0.069

Variables are categorical, compared using the chi-square or Fisher exact test. Data are shown as number (percentage). CKD indicates chronic kidney disease.

Table 3. Percentage of Patients Receiving Medications at Hospital Discharge

Treatment	CKD n=576	No CKD n=3041	P Value
Beta-blocker	517 (89.8)	2773 (91.2)	0.272
Angiotensin-converting enzyme inhibitor	301 (52.3)	2144 (70.5)	<0.001
Statin	486 (84.4)	2710 (89.1)	0.001
Nitrate	138 (24.0)	264 (8.7)	<0.001
Aspirin	524 (91.0)	2902 (95.4)	<0.001
Diuretic	233 (40.5)	714 (23.5)	<0.001
Antidepressant	84 (14.6)	363 (11.9)	0.077

Variables are categorical, compared using the chi-square or Fisher exact test. Data are shown as number (percentage). CKD indicates chronic kidney disease.

with CKD than for those without CKD (hazard ratio 2.14, 95% CI 1.73–2.65).

Among patients surviving the index AMI hospitalization, there were no significant adjusted differences in angina frequency, HRQL, or mental health between baseline and 1 year for patients with and without CKD (Table 4). For patients with and without CKD, HRQL scores at baseline (63.6 versus 63.7, respectively) and 1 year (81.8 versus 81.7, respectively) were not statistically different (with an adjusted difference of 0.24 at 1 year, 95% CI –1.46 to 1.95). Angina frequency scores for patients with and without CKD were significantly different at baseline (84.1 versus 86.7, respectively) and 1 year (91.4 versus 93.1, respectively) but were not statistically significant after adjustment at 1 year (adjusted difference of 1.27, 95% CI –0.05 to 2.58). Mental component scores for patients with and without CKD at baseline (50.3 versus 49.9, respectively) and 1 year (52.7 versus 51.9, respectively) were not statistically different (adjusted difference of –0.07, 95% CI –0.90 to 0.75).

In contrast, physical component scores were significantly lower among patients with CKD compared with patients without CKD at baseline (37.2 versus 43.7, respectively) and 1 year (38.4 versus 44.4, respectively). Physical component scores remained significantly lower among patients with CKD

after risk adjustment (adjusted difference of –1.61, 95% CI –2.49 to –0.74) (Table 4). The findings were similar in models adjusting for the propensity for follow-up to account for survival bias. There was no significant difference in HRQL (difference 0.35, $P=0.69$), angina frequency (difference 1.33, $P=0.05$), and mental component score (difference –0.04, $P=0.92$). Physical functioning scores were significantly different (difference –1.6, $P=0.0004$) between patients with and without CKD.

In sensitivity analyses, there were no significant differences in quality of life, angina burden, or mental component score between those with more severe CKD (stages 4–5) and those with CKD stages 1 to 3. As in the primary analysis, there was a similar decrease in physical component scores for those with severe CKD (stages 4–5) compared with CKD stages 1 to 3 (adjusted difference, –2.3, $P=0.009$).

Discussion

To our knowledge, this study is the first to examine the association of CKD with health status outcomes in patients after AMI. In our study, CKD was present among 1 in 6 patients during AMI hospitalization. Furthermore, patients with CKD represent a high-risk cohort with higher rates of comorbidities and risk of death in the year following AMI. Among AMI survivors, patients with CKD had HRQL, symptom burden, and mental functioning similar to patients without CKD. Although there was an association between patients with CKD and lower physical functioning, this difference (–1.6) was not clinically significant.

Previous work showed a negative effect of CKD on physical functioning in cardiovascular patients.^{4,9} In contrast, our study demonstrated that physical functioning was similar among patients with and without CKD; however, the average physical functioning scores (37–44) at 1 year were much lower in this group of patients after AMI compared with other CKD populations. Patients with CKD undergoing coronary artery bypass grafting, for example, had physical functioning

Table 4. Adjusted and Unadjusted Health Status Outcomes at 1 Year Using Linear Repeated-Measures Models

Outcome	Baseline Score		1-Year Score [†]		Difference (95% CI)	
	CKD	No CKD	CKD	No CKD	Unadjusted*	Adjusted
SAQ, quality of life (score)	63.6	63.7	81.8	81.7	1.89 (0.26–3.53)	0.24 (–1.46 to 1.95)
SAQ, angina frequency (score)	84.1	86.7	91.4	93.1	0.65 (–0.58 to 1.88)	1.27 (–0.05 to 2.58)
SF-12, physical component (score)	37.2	43.7	38.4	44.4	–2.81 (–3.65 to –1.97)	–1.61 (–2.49 to –0.74)
SF-12, mental component (score)	50.3	49.9	52.7	51.9	0.77 (0.00–1.55)	–0.07 (–0.90 to 0.75)

CKD indicates chronic kidney disease; SAQ, Seattle Angina Questionnaire; SF-12, Short Form 12.

*Adjusted for baseline and site only.

[†]Average scores at 1 year.

scores of 56 to 64 for those with CKD versus 73 for those without CKD.⁹ In addition, in patients with stable coronary artery disease, physical functioning scores ranged from 54 to 63 for patients with CKD versus 66 to 67 for patients without CKD.⁸ This suggests that the experience of AMI may have a significant impact on the physical functioning of patients, independent of the presence of CKD. Although past studies showed that worsening CKD is associated with worsened physical functioning, general health, and limited activities of daily living, our study did not have the power to detect differences across CKD stages.^{7,15}

Our results add to the growing literature on health status outcomes in those with CKD. Despite a large body of research demonstrating negative outcomes in cardiovascular patients with CKD, including mortality, in-hospital complications, and sudden death, we found that patients with CKD surviving their index AMI could achieve good quality of life with low symptom burden. This was demonstrated in our cohort with high HRQL on the SAQ (scores >80) and angina frequency (scores >90). There are several potential explanations for these findings. First, patients with lower physical functioning and CKD may not exert themselves as much as patients without CKD and consequently may not expend enough physical exertion to elicit anginal symptoms. Furthermore, patients with CKD may have lower expectations of their quality of life, and thus the discrepancy between actual and desired quality of life may not be as great compared with patients without CKD. If this were true, then we would also assume that patients with longstanding CKD would report different health status from those recently diagnosed. In addition, because patients with CKD had high prescription rates of nitrate medications, which have been shown to improve HRQL and decrease angina symptoms,¹⁶ this may have contributed to their improved health status. Notably, we found that patients with CKD also had fewer discharge medications of aspirin, statins, and angiotensin-converting enzyme inhibitors, although their benefits for these patients are well established. Previous data have also shown that guideline-recommended therapy is underused in CKD patients, likely contributing to these patients' increased morbidity and mortality.^{17,18} Why CKD patients are treated less often than their healthier counterparts is not well understood. More studies are needed to investigate the treatment paradox for patients with CKD. Regardless of the potential explanations, these findings suggest that clinicians should treat patients with CKD similarly to patients without CKD because they can achieve similar health status outcomes.

Several limitations must be considered in interpreting our results. First, patients who died during the index hospitalization (n=24) or prior to the 1-month health status assessment (n=53) were not included in our analysis;

therefore, our cohort represents healthier patients with CKD who survived >1 month following AMI hospitalization. The overall unadjusted Kaplan–Meier mortality rate was 17.4% for those with CKD and 4.7% for those without CKD. Despite this, our findings are likely still generalizable to the large majority of patients with CKD who survived up to 1 year following AMI hospitalization. Second, not all patients completed all follow-up questionnaires at 6 and 12 months; however, a large number of patients completed the follow-up questionnaires at 6 months (n=2797) and 1 year (n=2748) and represent the largest cohort to date describing health status outcomes of patients with and without CKD. In addition, to address survivor bias and lack of follow-up in patients, inverse propensity treatment-weighted analysis was performed, and the findings were consistent with our primary results. Third, the estimate of eGFR in our study was based on the highest measurement of serum creatinine during the index hospitalization and may not have represented true steady-state kidney function of patients in an acute setting. This may have led to some misclassification of CKD status. Nevertheless, measured serum creatinine levels at baseline and at discharge were similar, suggesting only a small variation in eGFR in both cohorts. Furthermore, we thought that taking the highest eGFR measurement would help minimize confounding from those who had acute kidney injury on admission. The MDRD equation is the most widely used method of calculating eGFR; however, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation has been validated recently and may provide more accurate assessment of eGFR.¹⁹ Nevertheless, after analyzing our data using the CKD-EPI equation for eGFR, we found no clinically significant differences in our outcome measures. Finally, as with any observational study, we cannot exclude the potential for unmeasured confounding and do not imply causality with our findings.

In conclusion, we found that patients with CKD have similar HRQL, angina frequency, and mental functioning compared with patients without CKD. Although patients with CKD had statistically significantly lower physical component scores than patients without CKD, this finding was not clinically significant. Overall, our findings suggest that health status outcomes after AMI are similar in patients with and without CKD. Resources aimed at improving health status outcomes in patients after AMI should focus on all patients, regardless of CKD status.

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Disclosures

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