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Chronic Kidney Disease and Risk of Presenting with Acute Myocardial Infarction versus Stable Exertional Angina in Adults with Coronary Heart Disease

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Abstract

Objective—To examine whether kidney dysfunction is associated with the type of clinical presentation of coronary heart disease (CHD).

Background—Reduced kidney function increases risk of developing CHD, but it is not known whether it also influences the acuity of clinical presentation, which has important prognostic implications.

Methods—We conducted a case-control study of subjects whose first clinical presentation of CHD was either acute myocardial infarction or stable exertional angina between October 2001-December 2003. Glomerular filtration rate (eGFR) before the incident event was estimated using calibrated serum creatinine and the abbreviated MDRD equation. Patient characteristics and use of medications were ascertained from self-report and health plan databases. We used multivariable logistic regression to examine the association of reduced eGFR and CHD presentation.

Results—We studied 803 adults with incident acute myocardial infarction and 419 adults with incident stable exertional angina who had a baseline eGFR ≤130 ml/min/1.73 m^2. Mean eGFR was lower among subjects with acute myocardial infarction compared with stable angina. Compared with eGFR 90–130 ml/min/1.73 m^2, we found a strong, graded independent association between reduced eGFR and presenting with acute myocardial infarction: adjusted odds ratio (OR) 1.36 (95% CI: 0.99 to 1.86) for eGFR 60–89 ml/min/1.73 m^2, OR 1.55 (0.92 to 2.62) for eGFR

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45–59 ml/min/1.73 m^2 and OR 3.82 (1.55 to 9.46) for eGFR <45 ml/min/1.73 m^2 (P<0.001 for trend).

Conclusion—eGFR less than 45 ml/min/1.73 m^2 is a strong, independent predictor of presenting with acute myocardial infarction versus stable angina as the initial manifestation of CHD.

Keywords

angina; myocardial infarction; renal failure; chronic kidney disease; risk factor

INTRODUCTION

Cardiovascular disease causes more than 50% of deaths in patients with chronic kidney disease (CKD) and end stage renal disease (ESRD).(1–2) CKD is an independent risk factor for both de novo and recurrent cardiovascular disease.(3–5) There is a graded-independent association between reduced estimated glomerular filtration rate (eGFR) and the risk of death, cardiovascular events and hospitalization.(6) Patients with CKD have a higher risk of dying from cardiovascular disease than developing ESRD.(7)

Coronary heart disease (CHD) is characterized by the development of atherosclerotic plaques— asymmetrical focal thickenings of the intima consisting of cells, connective tissue elements, lipids and debris. The development of these plaques is often manifested by stable angina symptoms. When the plaque ruptures, pro-thrombotic material in the center of the plaque is exposed to the blood. Myocardial infarction occurs when the ruptured plaque progresses to thrombosis, resulting in complete occlusion of the affected coronary artery with subsequent infarction of the downstream myocardial tissue. The constellation of symptoms associated with this sequence of events is an important identifier of CHD.

Patients with ESRD often have atypical presentations of CHD. Silent CHD (lack of angina symptoms) is often common in patients with ESRD.(8–9) One study found that 44% of a large cohort of asymptomatic hemodialysis patients had significant CHD.(10) Although there may be an association between silent CHD and ESRD, the clinical presentation of CHD in the much larger population of CKD patients has not been well defined.

CKD is frequently associated with hypertension, dyslipidemia and diabetes— all of which are major risk factors for endothelial dysfunction and atherosclerosis. Additionally, unique pathophysiologic mechanisms associated with CKD such as anemia, hyperphosphatemia, and inflammation may play important roles in the initiation of cardiovascular disease. The synergistic effect of these processes may accelerate coronary atherosclerosis in CKD patients and potentially affect the type of clinical presentation of CHD by altering the stability of coronary plaques and vascular function.

Although it is well accepted that the CKD population has an increased burden of cardiovascular disease, it is not known if the high mortality from cardiovascular disease is due primarily to the high incidence of cardiovascular disease events or that CKD patients experience more severe types of events. To address this question, we examined whether CKD influenced the initial clinical presentation and clinical stability of CHD in a large community-based sample. We compared patients whose first presentation of CHD was acute myocardial infarction with patients with incident stable angina, as these symptoms are clinically and physiologically distinct on the spectrum of coronary atherosclerosis. We hypothesized that patients presenting with acute myocardial infarction are more likely to have CKD than those presenting with stable angina and that the association is related to the severity of pre-existing CKD.

METHODS

Study Sample

The source population included adults (age ≥20 years) who received medical care within Kaiser Permanente of Northern California, a large integrated healthcare delivery system providing comprehensive care to more than 3 million members in the San Francisco and greater Bay area. Previous studies have shown that the membership is representative of the local surrounding and statewide insured adult population, apart from slightly lower proportions of persons at the extremes of age and income level.(11) The ADVANCE (Atherosclerotic Disease, VAscular functioN, and genetiC Epidemiology) Study enrolled patients with either acute myocardial infarction or stable exertional angina as their first presentation of clinical CHD.(12) Institutional review boards of the collaborating institutions approved the study and informed consent was obtained in all participants.

We conducted a case-control study to examine the influence of reduced kidney function on the likelihood of presenting with either acute myocardial infarction or stable exertional angina as the first clinical expression of CHD.

Incident Acute Myocardial Infarction Cases

Recruitment of study subjects has been described in detail previously.(12) Briefly, we identified men aged 45 to 75 years old and women aged 55 to 75 years old who had acute myocardial infarction as their first presentation of clinical CHD between October 28, 2001 through December 31, 2003 by weekly searches of automated laboratory for elevated cardiac enzymes and hospital discharge databases for primary discharge diagnosis of myocardial infarction (ICD-9-CM code 410). We excluded subjects who had evidence in automated hospital discharge, ambulatory visit, pharmacy, and laboratory databases of previous diagnosed CHD, prior hospitalizations complicated by elevated serum troponin I levels, receiving chronic dialysis, prior organ or bone marrow transplant, lack of a primary care provider, death before study contact, serious cognitive impairment or uncontrolled psychiatric condition, or receiving prescriptions for nitroglycerin more than 14 days before index date. We also excluded patients who did not have a serum creatinine available before myocardial infarction. Subjects were screened by telephone interview to confirm the absence of prior diagnosed CHD, coronary revascularization, or ischemic symptoms more than 14 days before admission for acute myocardial infarction as well as any exclusion criteria not identified by health plan databases.

Incident Stable Exertional Angina Cases

We identified men and women aged 18 to 75 years old who had stable exertional angina as their first presentation of clinical CHD between October 28, 2001 through December 31, 2003 by weekly searches of automated ambulatory visit databases for new outpatient diagnoses of angina pectoris (ICD-9-CM 413.x). We applied the same exclusion criteria as for cases of myocardial infarction described above, except that we excluded patients who received prescriptions for nitroglycerin more than 6 months before index date. Subjects were similarly screened by telephone interview to confirm the absence of prior CHD and coronary revascularization as well as any exclusion criteria not identified by health plan databases. In addition, subjects had to report evidence of stable chest pain or chest pressure reproduced by the same level of physical exertion, lasting more than one minute and less than 15 minutes, and responded to rest or nitroglycerin. Subjects could only have had symptoms lasting six months or less before the outpatient angina diagnosis and could not have reported these symptoms to a health care provider before their index date.

Measurement of Kidney Function

Kidney function was assessed using glomerular filtration rate (eGFR) estimated using the four-variable abbreviated Modification of Diet in Renal Disease (MDRD) Study equation (*GFR, ml/min/1.73m^2 =186 x (serum creatinine, mg/dl)$^{-1.154}$ x (age)$^{-0.203}$ x 0.742 (if female) x 1.212 (if Black)*) based on the outpatient serum creatinine test result found in health plan laboratory databases closest to but before the index date.(13) As previously described, serum creatinine values were calibrated to the core laboratory used to generate the MDRD estimating equation.(6) Based on prior work demonstrating an important eGFR threshold of 45 ml/min/1.73 m^2 for risk of adverse outcomes,(6) and the recently published updated Kidney Disease: Improving Global Outcomes (KDIGO) guidelines (14) we used the following classification system to define chronic kidney disease:: 90 to 130, 60 to 89, 45–59, and less than 45 ml/min/1.73 m^2. Patients on maintenance dialysis were identified from a longitudinal, comprehensive health plan end-stage renal disease registry.(6)

Covariates

Age at index date was based on self-report and confirmed in health plan databases. Subjects also provided self-reported information on gender and race/ethnic group marital status, employment status, annual household income, parental and sibling history of CHD, personal medical history of prior stroke, prior peripheral arterial disease, diabetes mellitus, and hypertension. Self-reported information on smoking status at index date (current, former, or never) as well as alcohol drinking pattern and intensity of leisure-time activity during the 12 months prior to study visit date were obtained. The most recent outpatient systolic and diastolic blood pressure values before index date were obtained from ambulatory visit databases, which have been shown to reliably reflect chronic blood pressure levels in our database.(15) Body mass index (kg/m^2) was measured at the study visit using standard procedures. We used automated health plan pharmacy databases to identify receipt of selected cardiac medications during the 160 days before index date. This time period was chosen to identify medications prescribed for chronic conditions which are generally given as a 90-to-100 day supply. We identified recent use of HMG-CoA reductase inhibitors (statins), niacin/nicotinic acid derivatives, fibrates, bile acid binding resins, beta-adrenergic antagonists, calcium channel antagonists, alpha adrenergic antagonists, angiotensin-converting enzyme (ACE) inhibitors, and angiotensin receptor blockers (ARBs), diuretics, and among women, hormone replacement therapy (estrogen ± progestins). We searched health plan laboratory databases for evidence of testing for total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoproprotein (HDL) cholesterol, and triglyceride levels before index date. LDL cholesterol values were routinely calculated using the Friedewald equation.(16) Among tested patients, we examined the most recent value for each lipoprotein component before index date.

Statistical Approach

All analyses were performed using SAS statistical software version 9.1 (Cary, N.C.). Differences between subjects with incident acute myocardial infarction or stable exertional angina were compared using Student's t test for continuous variables and chi-squared test for categorical variables. We performed a series of multivariable logistic regression models to examine the association between level of prior kidney function and the odds of presenting with acute myocardial infarction versus stable angina after adjustment for potential confounders. Variables included in models were based on variables that were significantly different between cases and controls on bivariate analyses or have previously been shown to be associated either with kidney function or acute myocardial infarction. Variables were grouped into four categories: (1) sociodemographic, family history and lifestyle characteristics; (2) comorbidities; (3) blood pressure, anthropometry, and lipoprotein levels; and (4) prior cardiovascular medication use. A series of nested models were conducted that

additionally adjusted for each category of covariates. For models including systolic and diastolic blood pressure, LDL cholesterol, or HDL cholesterol categories, patients were assigned to the "missing" category if the data were unavailable. Model fit for the final models were assessed using Hosmer-Lemeshow goodness-of-fit methods.(17)

RESULTS

Distribution of Kidney Function and Baseline Characteristics

We prospectively enrolled 930 adults with incident enzyme-positive acute myocardial infarction and 451 adults with incident stable exertional angina. We excluded 127 patients with acute myocardial infarction and 32 patients with stable exertional angina who had a prior eGFR >130 ml/min/1.73 m^2 or no available serum creatinine data. This left a final analytic sample of 803 patients with incident acute myocardial infarction and 419 patients with incident stable exertional angina and who had a prior eGFR ≤130 ml/min/1.73 m^2 (Table 1). Median time between the event date and pre-event baseline serum creatinine measurement was 157 (interquartile range: 31 to 440) days. There were no significant differences in mean age and race or ethnic group, but there were more women among subjects with angina. Mean eGFR was lower among subjects with acute myocardial infarction compared with stable angina, with a higher proportion of subjects with eGFR less than 45 ml/min/1.73 m^2.

No significant differences were observed for annual household income or marital status between groups (Table 1). Subjects presenting with acute myocardial infarction were more likely to be current or former cigarette smokers and report minimal or light prior physical leisure-time activity compared with angina subjects, but there was no significant difference in self-reported prior alcohol use between groups. Subjects with acute myocardial infarction were more likely than those with angina to have self-reported hypertension, but there were no other differences in prevalent non-coronary cardiovascular disease or diabetes mellitus. Subjects with acute myocardial infarction were less likely than those with angina to report a parental or sibling history of CHD.

As previously noted,(12) recent statin and beta-blocker use were higher in subjects with acute myocardial infarction compared with stable angina, but there were no other significant differences in other medication use (Table 1). Diastolic, but not systolic, blood pressure was more likely to be higher among subjects with acute myocardial infarction, but there were no significant differences in the distribution of body mass index between groups. Among tested patients, LDL cholesterol levels were on average 5 mg/dL higher and HDL cholesterol 2 mg/dl lower in subjects with acute myocardial infarction versus stable angina.

Level of estimated glomerular filtration rate and CHD presentation

Compared with eGFR 90–130 ml/min/1.73 m^2, the unadjusted odds of presenting with acute myocardial infarction versus stable exertional angina was only significantly higher for eGFR below 45 ml/min/1.73 m^2: odds ratio (OR) 1.25 (95% CI: 0.96 to 1.63) for eGFR 60–89 ml/min/1.73 m^2, OR 1.27 (95% CI: 0.82 to 1.97), and OR 2.58 (95% CI: 1.16 to 5.75).

After adjustment for differences in sociodemographic, family history and lifestyle factor, we found that eGFR <45 ml/min/1.73 m^2 was associated with 2.8-fold increased odds of acute myocardial infarction versus stable exertional angina when compared with eGFR 90–130 ml/min/1.73 m^2, but no statistically significant increased odds for eGFR 60–89 ml/min/1.73 m^2 or 45–59 ml/min/1.73 m^2 (Table 2). Further adjustment for comorbidities, systolic blood pressure, odds ratios. However, after additional adjustment for prior use of relevant cardiovascular medications, we found a stronger, graded association between reduced eGFR and presenting with acute myocardial infarction versus stable angina: compared with eGFR

90–130 ml/min/1.73 m^2, the adjusted odds increased from 1.36 for eGFR 60–89 ml/min/1.73 m^2 to 3.82 for eGFR below 45 ml/min/1.73 m^2 (P<0.001 for trend) (Table 2). The Hosmer-Lemeshow goodness-of-fit test for the final model showed a P=0.10.

DISCUSSION

The purpose of our study was to evaluate the impact of CKD on the clinical stability and the initial clinical presentation of CHD (acute myocardial infarction versus stable exertional angina). We chose patients who presented with stable exertional angina as a control group to isolate risk factors for clinical instability of CHD rather than underlying coronary atherosclerosis. Our results suggest that the risk of presenting with acute myocardial infarction (compared with stable exertional angina) is greater in patients with CKD, particularly below eGFR of 45 ml/min/1.73m^2. The odds ratio of this association increased by nearly threefold after adjustment for sociodemographic and lifestyle characteristics, traditional cardiovascular risk factors and pre-event use of a wide range of relevant medications (Table 2). These results suggest that there may be alternative mechanisms related to CKD that promote plaque instability and subsequent myocardial infarction.

Coronary atherosclerosis is a spectrum of disease, ranging from clinically stable plaques to vulnerable plaques susceptible to rupture and thrombosis. The initial expression of CHD is largely dependent on the stability of these atherosclerotic plaques. The severity and stability of the initial presentation of CHD significantly impacts clinical management and long-term cardiovascular outcomes. Certain populations have unique manifestations of CHD. Our study suggests that patients with CKD may have distinct risk factors for plaque vulnerability.

To our knowledge, no other studies have evaluated the impact of CKD on the clinical stability and presentation of CHD. CKD has been a well-described risk factor for atherosclerosis and CHD, with cardiovascular disease causing the greatest mortality in the CKD population.(6) A key understudied question has been whether high cardiovascular disease morbidity and mortality in this unique population is a result of both more frequent cardiovascular events(6) as well as more severe events. Our results support the hypothesis that patients with CKD appear to have greater likelihood of more clinically unstable and severe disease. Our results also suggest that clinical efforts should be targeted to identify this high risk population before incident symptoms of atherosclerosis occur and that we should aim to develop effective interventions and strategies to shift the expression of CHD from acute myocardial infarction to more stable presentations in patients with CKD.

Several mechanisms can be postulated to possibly explain the association between reduced eGFR and greater risk for acute myocardial infarction. In addition to the high prevalence of “traditional” risk factors, such as hypertension, hyperlipidemia and diabetes, CKD patients often have unique pathophysiologic mechanisms that may play important roles in the initiation and acceleration of cardiovascular disease. It is possible that these CKD-related mechanisms may also promote plaque vulnerability to rupture and thrombosis. For example, it appears that atherosclerotic plaque morphology in ESRD is accompanied by marked sub-intimal calcification and medial thickening as a result of hypertrophy and hyperplasia of vascular smooth muscle cells, causing arterial stiffness which may affect plaque formation. Elevated pulse pressure may be a reflection of this arterial stiffness and has been an indicator of increased risk of cardiovascular events and mortality for patients on hemodialysis.(18–19) Also, anemia in patients with kidney disease has been strongly associated with increased cardiovascular and all-cause mortality in patients with CKD and ESRD and may increase plaque instability.(20–21) Additionally, CKD-related metabolic derangements have been associated with increased cardiovascular mortality; for example

hyperphosphatemia may contribute to arterial calcification, although the exact pathogenesis is not known.(22–25) Inflammation has also been shown to be closely related to cardiovascular death in the CKD and ESRD population.(26–27) Models have shown that various inflammatory markers are elevated in CKD and may enhance production of free radicals that increase atherosclerosis. Inflammation may also alter plasma protein composition and endothelial structure to promote vascular disease.(28) The synergistic effect of these novel processes may accelerate coronary atherosclerosis in CKD patients and potentially affect the type of clinical presentation of CHD by altering the stability of coronary plaques and vascular function.

Our study had several strengths. Our study population was a large and diverse sample of well-characterized community-based patients. We were able to capture incident clinical CHD by symptoms and diagnostic tests such as cardiac enzymes and electrocardiograms, with careful phenotyping of the clinical presentation of CHD. We also had calibrated outpatient serum creatinine measurements available before the index cardiac event. Our study had several limitations as well. The exact mechanism of the association between CKD and clinically unstable CHD cannot be delineated from our study. For example, information on circulating inflammatory or pro-thrombotic factors was unavailable prior to the index event. The timing of the last outpatient creatinine measurement varied in the study population, and use of a single measurement could have led to some misclassification in eGFR level even though we relied on outpatient, non-emergency department serum creatinine measurements that likely reflected steady-state renal function. Data on urinary protein excretion were unavailable. We also could not determine the use of pre-event aspirin in our study population as it was not available in our health plan databases because it is routinely used as an over-the-counter medication. Patients with acute myocardial infarction or stable angina who died before attempted contact were not enrolled which may contribute to spectrum bias. There may be other residual confounders for which we were unable to identify and adjust for. While we found no evidence of poor model fit, the Hosmer-Lemeshow goodness-of-fit test has limited power to detect poor fit in certain circumstances. Finally, we conducted our study among health plan members within a large integrated health care delivery system in Northern California, so our findings may not be completely generalizable to other health care settings or to uninsured patients.

In conclusion, reduced eGFR was associated with a greater likelihood of presenting with acute myocardial infarction versus stable exertional angina among patients with new-onset symptoms of CHD. Our study suggests that patients with kidney dysfunction are at substantially higher risk for severe, clinically unstable CHD that are not explained by known clinical cardiovascular risk factors and other major confounders. Our results support the need to focus our efforts towards early identification of this high-risk population and the development of effective targeted cardio-preventive interventions to reduce the risk of irreversible cardiovascular complications.

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ABBREVIATIONS LIST

ACE	angiotensin converting enzyme
ARBs	angiotensin receptor blockers
CHD	coronary heart disease
CKD	chronic kidney disease
eGFR	estimated glomerular filtration rate
ESRD	end-stage renal disease
HDL	high-density lipoprotein
LDL	low-density lipoprotein
MDRD	Modification of Diet in Renal Disease

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Table 1

Baseline characteristics of adults with acute myocardial infarction or stable exertional angina as the first presentation of coronary heart disease.

Characteristic	Acute Myocardial Infarction (N=803)	Stable Exertional Angina (N=419)	P Value
Prior estimated glomerular filtration rate, ml/min/1.73 m^2			
Mean (SD)	78.2 (18.7)	81.2 (17.9)	0.006
Median (interquartile range)	78.0 (66.0–90.0)	80.0 (70.0–92.0)	0.006
Category of prior estimated glomerular filtration rate, (ml/min/1.73 m^2), %			0.07
90–130	26.5	31.7	
60–89	59.5	57.0	
45–59	9.8	9.3	
<45	4.1	1.9	
Mean (SD) age, yr	62.5 (8.4)	62.1 (8.4)	0.35
Women, %	23.8	33.7	<0.001
Race/ethnicity, %			0.68
White European/Middle Eastern	67.8	69.5	
African American	4.6	3.3	
Hispanic/Latino	9.6	11.0	
South Asian	2.1	1.2	
Asian/Pacific Islander	5.4	5.0	
Native American	0.0	0.0	
Non-Hispanic admixed	10.6	10.0	
Annual household income, %			0.28
< $25,000	13.2	11.5	
$25,000 to $49,999	25.0	25.1	
$50,000 to $99,999	39.3	35.4	
≥ $100,000	15.6	19.6	
Refused to answer	7.0	8.4	
Marital status, %			0.46
Married/Domestic Partner	72.6	76.4	
Divorced/Separated	14.3	12.5	
Widowed	8.2	6.3	
Never Married	5.0	4.8	
Cigarette smoking, %			0.01
Current	9.7	6.7	
Former	55.5	50.6	
Never	34.8	42.7	
Alcohol use in prior 12 months, %	67.7	73.3	0.04
Leisure-time Activity in past 12 mos., %			<0.001
Minimal	34.0	30.0	
Light	20.8	12.7	

Characteristic	Acute Myocardial Infarction (N=803)	Stable Exertional Angina (N=419)	P Value
Moderate	32.5	39.8	
Heavy	12.8	17.5	
Medical history, %			
Stroke/transient ischemic attack	10.0	11.2	0.51
Peripheral arterial disease	10.5	8.8	0.35
Diabetes mellitus	29.0	24.6	0.10
Diagnosed hypertension	83.4	76.1	0.002
Parental history of coronary heart disease, %	46.8	57.5	<0.001
Sibling history of coronary heart disease, %	21.2	27.2	0.02
Medication use within 160 days before event, %			
Statin	21.9	41.3	<0.001
Niacin	0.9	0.7	0.77
Cholestyramine	0.4	0.7	0.42
Colestipol	0.1	0.5	0.24
Colesevelam	0.0	0.0	N/A
Gemfibrozil	1.6	2.6	0.23
Fenofibrate	0.1	0.7	0.09
Beta blockers	21.1	48.4	<0.001
Calcium channel blockers	14.7	10.3	0.03
Alpha blockers	2.2	1.2	0.20
ACE inhibitors*	22.7	27.0	0.10
Angiotensin receptor blockers	3.2	3.8	0.60
Diuretics	21.5	24.6	0.23
Hormone replacement therapy	31.9 (of 191 women)	36.9 (of 141 women)	0.35
Blood pressure at most recent outpatient visit before index date			
Systolic (mmHg), %	(N=714)	(N=389)	0.05
≤120	16.5	22.9	
121–129	12.8	15.7	
130–139	27.9	23.9	
140–159	31.4	26.5	
160–179	9.1	9.3	
>180	2.4	1.8	
Diastolic (mmHg), %	(N=714)	(N=390)	<0.001
≤80	55.5	67.2	
81–84	16.8	10.5	
85–89	11.6	7.7	
90–99	11.8	11.3	
100–109	3.6	1.0	
≥110	0.7	2.3	
Mean (SD) body mass index (kg/m^2)	29.3 (5.5)	29.0 (4.8)	0.31
Category of body mass index (kg/m^2), %			0.74

Characteristic	Acute Myocardial Infarction (N=803)	Stable Exertional Angina (N=419)	P Value
<25	20.2	19.7	
25–29	42.6	44.8	
≥30	37.2	35.5	
Prior lipoprotein testing and results			
Total Cholesterol			
Tested, %	95.3	97.6	0.05
Mean (SD), mg/dL	221.6 (39.5)	217.8 (41.3)	0.13
Low-density lipoprotein cholesterol			
Tested, %	82.2	91.0	<0.001
Mean (SD), mg/dL	137.0 (34.3)	131.7 (35.4)	0.02
High density lipoprotein cholesterol			
Tested, %	91.8	96.4	0.002
Mean (SD), mg/dL	45.1(12.5)	47.1 (13.1)	0.01
Triglycerides			
Tested, %	82.9	91.4	<0.001
Mean (SD), mg/dL	195.0 (115.6)	198.9 (126.7)	0.62

* ACE= angiotensin converting enzyme

Table 2

Multivariable association between level of renal function and the risk of presentation of coronary heart disease as acute myocardial infarction versus stable exertional angina.

eGFR,* ml/min/1.73m^2	**Adjusted Odds Ratio (95% Confidence Interval)**				
	Model 1 (eGFR only)	Model 2 (Model 1 + age, gender, race/ethnicity, family history of coronary heart disease, cigarette smoking history, physical activity level)	Model 3 (Model 2 + prior stroke or peripheral arterial disease, diabetes mellitus, hypertension)	Model 4 (Model 3 + systolic blood pressure, body mass index, prior low-density lipoprotein and high-density lipoprotein cholesterol level)	Model 5 (Model 4 + prior use of statins, β-blockers, calcium channel blockers, ACE† inhibitors, ARBs,‡ diuretics
90 to 130	Referent	Referent	Referent	Referent	Referent
60 to 89	1.25 (0.96–1.63)	1.30 (0.98–1.73)	1.33 (1.00–1.78)	1.31 (0.98–1.80)	1.36 (1.00–1.86)
45 to 59	1.27 (0.81–1.97)	1.38 (0.86–2.21)	1.34 (0.84–2.16)	1.34 (0.82–2.19)	1.55 (0.91–2.62)
<45	2.58 (1.16–5.75)	2.77 (1.21–6.34)	2.64 (1.15–6.10)	2.71 (1.16–6.34)	3.82 (1.55–9.46)

*eGFR= estimated glomerular filtration rate

†ACE = angiotensin-converting enzyme

‡ARB = angiotensin II-receptor blockers