http://www.kidney-international.org

see commentary on page 7

Location of acute coronary artery thromboses in patients with and without chronic kidney disease

David M. Charytan[1], Richard E. Kuntz[2], Michael Garshick[3], Susana Candia[3], M. Faisal Khan[4] and Laura Mauri[3]

[1]Renal Division and Clinical Biometrics, Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts, USA; [2]Genitourinary and Neurologic Division, Medtronic Incorporated, Minneapolis, Minnesota, USA; [3]Division of Cardiovascular Medicine and Clinical Biometrics, Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts, USA and [4]Department of Medicine, St. Elizabeth's Hospital, Boston, Massachusetts, USA

Patients with chronic kidney disease have high rates of myocardial infarction and death following an initial attack. Proximal location of coronary atherosclerotic lesions has been linked to the risk of acute myocardial infarction and to infarction-associated mortality. To examine if the spatial distribution of lesions differs in patients with and without chronic kidney disease, we used quantitative coronary angiography to measure this in patients with acute coronary thromboses who were having angiography following acute myocardial infarction. Multivariable linear regression was used to adjust for differences in baseline characteristics. Among 82 patients with stage 3 or higher chronic kidney disease, 55.6% of lesions were located within 30 mm and 87.7% were within 50 mm of the coronary ostia. This compared to 34.7 and 71.8%, respectively, among 299 patients without significant kidney disease. Chronic kidney disease was independently and significantly associated with a 7.0 mm decrease in the distance from the coronary ostia to the problem lesion. Our study suggests that a causal link between a more proximal culprit lesion location in patients with chronic kidney disease and their high mortality rates after myocardial infarct is possible and may have important implications for interventions to prevent infarction.

Kidney International (2009) **75,** 80–87; doi:10.1038/ki.2008.480; published online 24 September 2008

KEYWORDS: coronary artery disease; myocardial infarction; chronic kidney disease; atherosclerosis

Correspondence: *David M. Charytan, Renal Division and Clinical Biometrics, Brigham and Women's Hospital, 1620 Tremont Street, 3rd Floor, Boston, MA 02120, USA. E-mail: dcharytan@partners.org*

Preliminary results of this work were presented at the American Society of Nephrology Meetings in San Francisco, CA in November 2007.

Received 12 February 2008; revised 9 July 2008; accepted 24 July 2008; published online 24 September 2008

Individuals with chronic kidney disease (CKD) suffer from high rates of myocardial infarction (MI) and cardiovascular death[1] and suffer from high rates of death following MI[2] compared to individuals with normal renal function. Systemic factors such as inflammation and oxidative stress have been implicated in the etiology of this increased risk and have been the focus of numerous investigations,[3–5] but whether patients with CKD have a unique anatomic patters of atherosclerosis and plaque rupture remains undetermined.

In the general population, the location of MI has been measured. Coronary thromboses leading to MI are distributed in a nonuniform manner. They cluster within the proximal one-third of the coronary arteries, and the likelihood of clinically significant plaque rupture decreases by 13–30% for each 10 mm away from the coronary artery ostia.[6,7] Clinical outcomes following plaque rupture are also profoundly influenced by plaque location. In ST elevation MI, for example, the risk of death following acute plaque rupture is low when thromboses are distal, but doubles when thromboses occur proximally.[8–10]

These studies suggest that both the risk of MI and its clinical severity are closely linked to plaque location and vary inversely with distance away from the coronary artery ostium. Differences in the spatial distribution of culprit lesions for MI might partly explain CKD-related differences in both the risk of MI and the risk of death following MI. We sought to identify differences in MI location between patients with and without CKD.

RESULTS

Baseline characteristics

In total, 381 patients, 198 (52.0%) with ST elevation MI (STEMI) and 183 with non-ST elevation MI (NSTEMI) (48.0%) met the inclusion criteria and underwent quantitative angiographic analysis using standardized angiographic views of each coronary segment (Table 1). Mean estimated glomerular filtration rate (eGFR) was 80.0 ± 27.7 ml/min per 1.73 m^2, and 82 (21.5%) patients had an eGFR < 60 ml/min per 1.73 m^2. In all, there were 133 patients with normal renal function/class 1 CKD, 166 patients with class 2 CKD, and 69

Table 1 | Angiographic projections used in individual coronary artery segments

Segment	Projection
Left main artery	Anterior posterior caudal
Ramus intermedius	Left anterior oblique cranial
Right coronary artery	—
Proximal	Straight left anterior oblique
Mid	Straight left anterior oblique
Distal	Straight left anterior oblique
Posterior descending artery	Left anterior oblique cranial
Posterior lateral segment	Left anterior oblique cranial
Left anterior descending artery	—
Proximal	Right anterior oblique caudal
Mid	Right anterior oblique caudal
Distal	Right anterior oblique caudal
First diagonal	Left anterior oblique cranial
Second diagonal	Left anterior oblique cranial
Circumflex artery	—
Proximal	Right anterior oblique caudal
Mid	Right anterior oblique caudal
Distal	Right anterior oblique caudal
First obtuse marginal	Right anterior oblique caudal
Second obtuse marginal	Right anterior oblique caudal

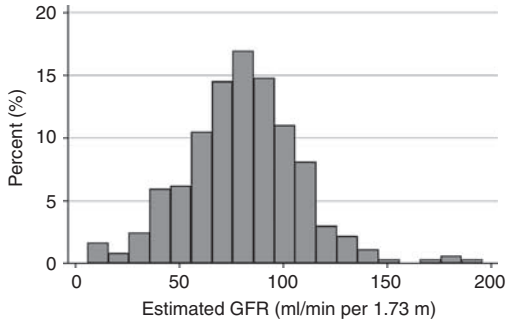

Figure 1 | Distribution of estimated glomerular filtration rate in the study population. CKD was defined as estimated GFR <60 ml/min per 1.72 m^2. Using this definition 82 of the population of 381 (21.5%) had CKD.

patients with class 3 CKD. Of 13 patients with class 4/5 CKD, 3 were on chronic dialysis. Distribution of eGFR is shown in Figure 1.

Individuals with stage 3 or higher CKD were older (72.5 years vs 60.7 years) more likely to be women (52.2 vs 27.4%), and they were more likely to have diabetes (41.5 vs 22.4%), dyslipidemia (72.0 vs 55.2%), or a prior history of MI (31.7 vs 14.7%). STEMI was less common in individuals with stage 3 or higher CKD (30.5 vs 58.9%) and left main artery infarct location was more common (6.1 vs 1.0%). Other MI characteristics did not differ by CKD class. Patient characteristics are summarized in Table 2.

Overall lesion characteristics

Median distance to lesion (DTL) for the entire cohort was 35.3 mm. Lesions were more frequently located in the left anterior descending (LAD) or diagonal vessels ($N=140$) and the right coronary (RCA; $N=145$) than in other vessels. Left main ($N=8$) and ramus intermedius vessels ($N=5$) were infrequent sites of acute thrombosis. Thromboses in the RCA were more distal than lesions in other coronary arteries ($P<0.001$) whereas left main lesions were significantly more proximal ($P<0.002$). Distribution of lesions according to vessel and CKD status is shown in Table 3.

Lesion location

On univariate analysis (Table 4), male patients ($\beta=8.18$, $P<0.001$), patients with STEMI ($\beta=8.58$, $P<0.001$), and patients with an RCA infarct ($\beta=11.78$, $P<0.001$) had more distal lesions. Patients with diabetes ($\beta=-5.78$, $P<0.001$), stage 3 or higher CKD ($\beta=-10.21$, $P<0.001$), left main infarct or LAD infarcts had more proximal lesions. Lesion location was not associated with peak CK or ejection fraction, but patients with congestive heart failure did have more proximal lesions ($\beta=-7.11$, $P=0.05$) than patients without heart failure. Overall DTL was closely related to the stage of CKD with lower distances observed in more advanced stages of CKD (P for trend <0.001). Mean (s.d.) DTL was 43.3 (25.1) in patients with no CKD/class 1 CKD, 41.3 (24.0) in class 2 CKD, 32.5 (24.0) in class 3 CKD, and 29.7 (15.6) in class 4/5 CKD.

When the major vessels were examined individually (vessel analysis), patients with stage 3 or higher CKD had more proximal lesions in the left circumflex (LCX; 19.6 vs 27.6, $P=0.06$) and the RCA (34.5 vs 50.2, $P=0.02$), but not in the LAD (19.4 mm vs 21.5, $P=0.43$). In patients with CKD, 55.6% of lesions were located within 30 mm and 87.7% were located within 50 mm of the coronary ostia (left main analysis). Conversely, in patients without stage 3 or higher CKD, only 34.7% of lesions were located within 30 mm and only 71.8% were located within 50 mm of the coronary ostia. Unadjusted associations of CKD with lesion location are shown in Figures 2 and 3.

Chronic kidney disease remained a significant predictor of DTL after adjustment for age, sex, race, diabetes, hypertension, smoking, hyperlipidemia, infarct vessel, and family history of coronary artery disease (Table 5). Stage 3 or higher CKD was independently associated with a 7.0 mm more proximal MI location (95% confidence interval (CI): 13.39–0.61, $P=0.03$) compared to patients without CKD. Conversely RCA lesions and male sex were associated with adjusted increases of 10.54 mm (95% CI: 5.14–15.94, $P<0.001$) and 7.31 mm (95% CI: 2.05–12.58, $P=0.01$), respectively. The association of CKD with DTL was similar in diabetics vs nondiabetics (P for interaction 0.18), STEMI vs NSTEMI (P for interaction 0.23) and men vs women (P for interaction 0.30). The adjusted association of CKD with DTL was not significantly different in patients with LAD infarcts compared to those with infarcts in other vessels (P for interaction 0.18).

Secondary analyses using the stages of CKD in place of the binary definition of CKD revealed a trend toward shorter DTL in patients with more advanced stages of CKD. Results were qualitatively similar regardless of the serum creatinine used to estimate eGFR (Table 6).