Prognostic Value of Albuminuria on Cardiovascular Outcomes After Elective Percutaneous Coronary Intervention

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Albuminuria is the most widely evaluated marker of kidney damage. Many previous studies have demonstrated an association between the presence of albuminuria and increased cardiovascular events. However, there are limited data regarding the impact of albuminuria in patients requiring coronary revascularization. This study investigated whether the urinary albumin excretion rate could predict cardiovascular events in such a population. We enrolled 698 consecutive patients who underwent elective percutaneous coronary intervention. The baseline urinary albumin-to-creatinine ratio (ACR; mg/gCr) was measured and patients were divided into those with normoalbuminuria (ACR <30 mg/gCr), microalbuminuria (ACR 30 to 300 mg/gCr), or macroalbuminuria (ACR >300 mg/gCr). We collected data on the incidences of cardiac death and/or nonfatal myocardial infarction. We identified 389, 230, and 79 patients with normoalbuminuria, microalbuminuria, and macroalbuminuria, respectively. During follow-up (median: 1,564 days), 41 events occurred. The event-free survival rate was 89% in patients with macroalbuminuria, 92% in those with microalbuminuria, and 97% in those with normoalbuminuria, respectively (log-rank test $p = 0.002$). After adjustment for conventional risk factors, Cox analysis revealed hazard ratios for cardiac death and/or nonfatal myocardial infarction were 2.56 (95% CI 1.23 to 5.32, $p = 0.01$) in those with microalbuminuria and 4.02 (95% CI 1.59 to 10.12, $p = 0.003$) in those with macroalbuminuria compared with those with normoalbuminuria. In conclusion, an elevated urinary albumin excretion rate independently predicted adverse cardiovascular outcomes, with a gradual risk increase that progressed from microalbuminuria to macroalbuminuria in patients undergoing elective percutaneous coronary intervention. **(Am J Cardiol 2016;117:714−719)**

Albuminuria is the most widely evaluated marker of renal damage. Many previous studies[1−5] have demonstrated associations between albuminuria and advanced atherosclerosis and their cardiovascular outcomes. The Kidney Disease Improving Global Outcomes guidelines indicate that both estimated glomerular filtration rate (eGFR), which is a commonly used marker of renal dysfunction, and albuminuria are important when predicting mortality and cardiovascular outcomes.[6−7] We previously demonstrated the association between albuminuria and the incidence of periprocedural myocardial injury after elective percutaneous coronary intervention (PCI).[8] However, there are limited data regarding the impact of albuminuria on cardiovascular outcome in patients who require coronary revascularization. The aim of this study was to determine whether albuminuria could be a useful marker to detect those subjects at higher risk after elective PCI.

Methods

This observational study consisted of 698 consecutive non-dialysis−dependent patients successfully undergoing elective PCI to de novo lesion in Chubu Rosai Hospital, Nagoya, Japan from January 2008 to December 2012. We excluded patients who were lost to follow-up (4 patients). The ethics committee of Chubu Rosai Hospital approved the study, and all patients provided written informed consent.

According to the Kidney Disease Improving Global Outcomes 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease,[7] the patients were classified into 3 groups on the basis of their albumin level: normoalbuminuria (albumin-to-creatinine ratio [ACR] <30 mg/gCr), microalbuminuria (ACR 30 to 300 mg/gCr), and macroalbuminuria (ACR >300 mg/gCr). Spot urinary albumin and creatinine were measured by immunonephelometry and enzymatic methods, respectively. The urinary ACR (mg/gCr) was calculated at baseline. Serum eGFR was calculated using the Modification of Diet

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See page 718 for disclosure information.

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Table 1
Baseline characteristics

Characteristics	Albuminuria			p-value
	normo (n = 389)	micro (n = 230)	macro (n = 79)	
Age (years)	68 ± 11	72 ± 9	71 ± 9	<0.001
Male	286 (74%)	152 (66%)	45 (57%)	0.007
Body mass index (kg/m^2)	24.1 ± 3.7	23.7 ± 3.5	23.9 ± 3.7	0.4
C-reactive protein (mg/dl)	0.11 (0.05 − 0.30)	0.14 (0.06 − 0.47)	0.21 (0.07 − 0.55)	0.2
Serum creatinine (mg/dl)	0.8 ± 0.2	0.9 ± 0.4	1.3 ± 0.8	<0.001
Estimated glomerular filtration rate (ml/min/1.73m^2)	68 ± 16	63 ± 22	50 ± 21	<0.001
Estimated glomerular filtration rate <60 ml/min/1.73m^2	91 (23%)	95 (41%)	54 (68%)	<0.001
Albumin creatinine ratio (mg/gCr)	10 (6 − 17)	82 (52 − 138)	707 (485− 1240)	<0.001
Ejection fraction (%)	67 ± 11	67 ± 13	67± 12	0.8
Diabetes mellitus	178 (46%)	150 (65%)	68 (86%)	<0.001
Hypertension	337 (87%)	208 (90%)	77 (98%)	0.01
Dyslipidemia	329 (85%)	201 (87%)	71 (90%)	0.4
Current smoker	132 (34%)	66 (29%)	17 (22%)	0.07
Previous myocardial infarction	99 (25%)	63 (27%)	18 (23%)	0.7
Multiple vessel coronary disease	170 (44%)	111 (48%)	42 (53%)	0.2
Previous percutaneous coronary intervention	115 (30%)	62 (27%)	24 (30%)	0.7
Previous coronary artery bypass grafting	26 (7%)	20 (9%)	7 (9%)	0.6
Medications				
Aspirin,	385 (99%)	230 (100%)	77 (98%)	0.1
Thienopyridine derivatives	369 (95%)	222 (97%)	73 (92%)	0.3
Statins	353 (91%)	204 (89%)	68 (86%)	0.4
Calcium channel blocker	142 (37%)	108 (47%)	40 (51%)	0.009
β-blockers	170 (44%)	89 (39%)	37 (47%)	0.3
Angiotensin converting enzyme inhibitor or angiotensin-II receptor blocker	230 (59%)	151 (66%)	62 (79%)	0.003

Normally distributed continuous values are expressed as the mean ± SD. Nonnormally distributed continuous values are expressed as the median (interquartile range). Categorical values are expressed as a number (percentage).

in Renal Disease equations modified with the Japanese coefficient.[9]

Baseline angiography was evaluated by an independent investigator who was not involved in the procedures and was blinded to the outcomes. A computerized quantitative analysis system (QCA-CMS system, version 6.0.39.0; Medis, Leiden, the Netherlands) was used with the guide catheter for calibration. The operators in charge, who were blinded to the ACR levels, determined the method and device for PCI according to angiography and conventional intravascular ultrasound findings.

Follow-up data were obtained through admission and outpatient medical records or by telephone interview. The primary end point of this study was the incidence of cardiac death and/or nonfatal myocardial infarction. The secondary end points were total major adverse cardiac events (MACEs) defined as the composite of cardiac death, nonfatal myocardial infarction, and any revascularization including target lesion revascularization and new lesion revascularization. Events at the time of the index interventional procedure and during the index hospitalization were not assessed. For multiple occurrences of events, the time to the first event was used as the time when the total MACE was detected. We also assessed the incidence of target lesion revascularization and new lesion revascularization as secondary end points, respectively.

Myocardial infarction was defined as the development of signs and/or symptoms of ischemia accompanied by the elevation of creatine kinase-MB or troponin T levels at least twofold higher than normal or new significant Q waves in 2 or more contiguous leads. The target lesion was defined as the area covered by the stents plus 5-mm margins proximal and distal to the edge of the stent. Any revascularization was driven by clinical findings such as the presence of ischemic symptoms, a positive functional ischemia assessment, or an ischemic electrocardiogram change. The events were assessed by investigators blinded to the clinical data.

All normally or nonnormally distributed continuous values are expressed as the mean ± SD and median (interquartile range), respectively. Categorical variables are expressed as a number (proportion). We compared normally distributed continuous variables using analysis of variance and nonnormally distributed variables (ACR, C-reactive protein) with the Kruskal−Wallis test, whereas categorical variables were compared using the Fisher's exact test or chi-squared test. Event-free survival rate was analyzed using Kaplan−Meier estimation with a log-rank test. The Cox proportional hazards model was used to estimate the contribution of ACR to the prediction of cardiovascular events during follow-up. We considered age, men, body mass index, ejection fraction, and conventional coronary risk factors (current smoker, eGFR <60 ml/min/1.73 m^2, diabetes mellitus, hypertension, and dyslipidemia) as candidate variables for inclusion in the