Myocardial fatty acid imaging identifies a group of hemodialysis patients at high risk for cardiac death after coronary revascularization

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We prospectively evaluated if impaired myocardial fatty acid metabolism is involved in cardiac death after revascularization by percutaneous coronary artery intervention in dialysis patients. A cohort of hemodialysis patients was assessed by dual single-photon emission computed tomography using the radioiodinated fatty acid analogue BMIPP and radiolabeled thallium chloride. Tomography was done within one month before the first coronary intervention and at the last follow-up angiography at which neither restenosis nor *de novo* lesions were detected. Radiolabel uptake on tomography images was graded in segments and calculated as summed BMIPP or thallium scores. Among the 90 hemodialysis patients in the study, 19 died of cardiac events. Multivariate Cox hazard analysis found a significant association of cardiac death with the BMIPP summed scores at the last follow-up angiography. Kaplan–Meier analysis showed the cardiac death-free survival rates at 3 years of follow-up were significantly higher in patients with lower BMIPP summed scores. These results suggest that myocardial fatty acid imaging may be a useful test to identify high risk groups of cardiac death in hemodialysis patients.

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Percutaneous coronary artery intervention (PCI) as well as coronary artery bypass grafting is an established procedure for coronary revascularization in patients with end-stage renal disease (ESRD). Although the initial success of PCI was comparable between patients with and without ESRD, coronary restenosis or *de novo* coronary stenosis occur more frequently and survival rates are lower among patients with ESRD.[1–4] The study of Hemmelgarn *et al.*[5] found that the adjusted 8-year survival rates for PCI were significantly lower for a dialysis group (41.2%) than for a control group without renal dysfunction (80.4%). The reported 2-year all-cause survival rate is 48% for dialysis patients after PCI with stenting.[6] Although drug-eluting stents can reduce the rate of in-stent restenosis compared with bare-metal stents in patients without ESRD,[7,8] PCI with drug-eluting stents results in higher mortality rates among patients on dialysis compared with those who are not, despite a similar reduction in repeat revascularization.[9] Furthermore, the incidence of death or myocardial infarction (MI) does not differ between dialysis patients fitted with drug-eluting and bare-metal stents.[10] Other factors in addition to restenosis or repeat revascularization are involved in the lower survival rates of patients on dialysis who have undergone PCI. We recently showed that visualizing severely impaired myocardial fatty acid metabolism on images can help to identify patients at high risk of cardiac death among those on hemodialysis without coronary intervention or old MI.[11] The present study evaluates whether impaired myocardial fatty acid metabolism assessed by imaging can predict cardiac death after coronary revascularization by PCI among patients on hemodialysis.

RESULTS

After the last follow-up, coronary angiography (CAG) in which neither coronary restenosis nor *de novo* lesions were evident, the study participants routinely underwent echocardiography and dual single-photon emission computed tomography (SPECT) using the fatty acid analogue, iodine-123-β-methyl iodophenyl-pentadecanoic acid (BMIPP), and ^{201}thallium chloride (Tl) every 6 months. During follow-up,

8 of the 98 patients underwent additional PCI to treat unstable angina pectoris ($n=3$) or asymptomatic coronary artery disease identified as worsened BMIPP-Tl SPECT findings ($n=5$). Data from these eight patients were not included in the prognostic portion of the analysis, because the additional coronary revascularization would have affected the occurrence of cardiac death among them. Thus, the resulting study cohort comprised the remaining 90 ESRD patients undergoing maintenance hemodialysis for a mean of 105 ± 93 months (male/female: 64/26; mean age: 65 ± 9 years). The mean duration of follow-up after confirmation of coronary revascularization (last follow-up CAG) was 2.7 ± 1.4 years. The etiology of renal failure involved diabetes mellitus in 57.8% (52/90), chronic glomerular disease in 38.9% (35/90), polycystic kidney disease in 2.2% (2/318), and nephrosclerosis in 1.1% (1/90) of the patients.

Cardiac death and baseline characteristics

Of the 90 participants, 19 (21.1%) died of cardiac events (acute MI, $n=3$; congestive heart failure, $n=2$; cardiac sudden death, $n=14$) during a mean follow-up period of 2.7 ± 1.4 years. After the onset of acute MI, all three patients had undergone emergency CAG and direct PCI, but cardiac death resulted within 24 h after PCI. The mean values of patients who died of cardiac events revealed that they were older, and that the ratio of female gender, the mean BMIPP summed score, and BMIPP-Tl mismatch score at the last follow-up CAG were higher, whereas the ratio of a history of alcohol consumption and diastolic blood pressure before dialysis were lower than in those who did not die in this manner (Tables 1 and 2). We found no difference between patients with and without cardiac death in terms of mean values of dialysis duration, body mass index, systolic blood pressure before dialysis, cardiothoracic ratio, left ventricular (LV) ejection fraction, LV mass index, blood hemoglobin concentration, serum concentrations of albumin, total cholesterol, high-density lipoprotein-cholesterol, triglyceride, calcium, inorganic phosphorus, intact parathyroid hormone, high-sensitivity C-reactive protein or hemoglobin A1c, and ratios of diabetes mellitus, smoking habit, or prescribed medications such as calcium channel blockers, angiotensin-I-converting enzyme inhibitors, angiotensin II type-1 receptor blockers, α_1-blockers, β-blockers, nitrates, antiplatelet drugs, anticoagulants, and statins. We found no difference between patients with and without cardiac death in terms of mean number of repeat PCI, use of rotablator, and the incidences of multivessel, right coronary artery, left circumflex artery, and *de novo* coronary lesions and restenosis, whereas the incidence of left anterior descending artery lesions tended

Table 2 | SPECT findings of hemodialysis patients with or without cardiac death after coronary revascularization

	Cardiac death (+) (n=19)	Cardiac death (−) (n=71)	P-values
Before first PCI			
BMIPP summed score	19.3 ± 8.0	21.2 ± 10.1	0.455
Tl summed score	7.6 ± 6.2	7.6 ± 7.2	0.989
BMIPP-Tl mismatch score	11.7 ± 4.4	13.6 ± 7.2	0.272
At last follow-up CAG			
BMIPP summed score	25.2 ± 7.4**	14.6 ± 6.1**	<0.0001
Tl summed score	4.8 ± 4.3*	4.9 ± 4.6**	0.915
BMIPP-Tl mismatch score	20.4 ± 5.0**	9.7 ± 5.1**	<0.0001

BMIPP, iodine-123-β-methyl iodophenyl-pentadecanoic acid; CAG, coronary angiography; PCI, percutaneous coronary artery intervention; SPECT, single-photon emission computed tomography; Tl, ^{201}thallium chloride.
*$P<0.05$, **$P<0.01$ compared with values before first PCI using paired *t*-test.

Table 1 | Clinical characteristics of hemodialysis patients with or without cardiac death after coronary revascularization

	Cardiac death (+) (n=19)	Cardiac death (−) (n=71)	P-values
Age (years)	69.9 ± 7.6	63.9 ± 9.1	0.010
Female gender	9/19 (47.4%)	54/71 (23.9%)	0.046
Dialysis duration (months)	104.9 ± 97.6	105.5 ± 92.2	0.983
Smoking habit	8/19 (42.1%)	32/1 (43.7%)	0.820
Alcohol consumption	3/19 (15.8%)	31/71 (43.7%)	0.026
Diabetes mellitus	13/19 (68.4%)	39/71 (54.9%)	0.296
Systolic blood pressure before dialysis (mm Hg)	146 ± 17	146 ± 14	0.899
Diastolic blood pressure before dialysis (mm Hg)	369 ± 12	74 ± 11	0.042
Left ventricular ejection fraction (%)	360.3 ± 14.3	59.7 ± 13.8	0.866
Left ventricular mass index (g/m^2)	151.2 ± 60.1	168.8 ± 91.3	0.431
PCI			
Number of repeat PCI	2.2 ± 1.5	32.8 ± 2.1	0.290
Use of rotablator	10/19 (52.6%)	39/71 (54.9%)	0.860
Multivessel lesions	11/19 (57.9%)	47/71 (66.2%)	0.507
Right coronary artery lesion	11/19 (57.9%)	41/71 (57.8%)	0.991
Left anterior descending artery lesion	9/19 (47.4%)	50/71 (70.4%)	0.061
Left circumflex artery lesion	14/19 (73.7%)	48/71 (67.6%)	0.616
Restenosis	11/19 (57.9%)	32 /71 (45.1%)	0.326
De novo coronary stenosis (>50%)	5/19 (26.3%)	31/71 (43.7%)	0.174

CRP, C-reactive protein; HDL, high-density lipoprotein; PCI, percutaneous coronary intervention.
Smoking habit defined as >10 cigarettes per week; alcohol consumption defined as >20 g of alcohol per week.