Hemodialysis International 2013; **17**:568–575

Predictors of cardiovascular events in hemodialysis patients after stress myocardial perfusion imaging

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Abstract

Cardiovascular prognosis in patients under normal stress myocardial perfusion images (MPI) is generally excellent. However, this is not true for patients with chronic kidney disease (CKD) treated by hemodialysis. This study evaluated prognostic factors of adverse cardiovascular events in hemodialysis patients in whom stress MPI was performed. Pharmacological stress MPI was performed in 88 hemodialysis patients, and we retrospectively followed-up for 26 months. Cardiovascular events included cardiac death, nonfatal myocardial infarction, and unstable angina. Cardiovascular events occurred in 16 patients (18%). Univariate Cox regression analysis revealed that peripheral artery disease (PAD) and parameters of stress MPI were significant predictors of cardiovascular events. Multivariate Cox regression analysis revealed that only PAD (hazard ratio = 6.54; $P = 0.002$), and abnormal stress MPI (hazard ratio = 8.26; $P = 0.008$) were independent and significant predictors of cardiovascular events. Kaplan–Meier analysis showed better prognosis in patients with normal stress MPI than in patients with abnormal stress MPI ($P < 0.001$, log–rank test). However, in patients with normal stress MPI, cardiovascular events occurred in 10 of the 76 patients (13%). Among patients with normal stress MPI, Kaplan–Meier analysis showed that patients with no PAD had better prognosis than patients with PAD ($P = 0.001$, log–rank test). In hemodialysis patients, both PAD and stress MPI were powerful cardiovascular predictors. Normal stress MPI alone cannot guarantee good prognosis in terms of cardiovascular events. Consideration of PAD may improve the predictive value of stress MPI in some patients.

Keywords: cardiovascular events, peripheral artery disease, prognosis, thallium, hemodialysis

INTRODUCTION

Stress myocardial perfusion imaging (MPI) is a useful predictor of cardiovascular events such as cardiac mortality and acute coronary syndrome.[1–3] Normal stress MPI is usually associated with an excellent cardiovascular prognosis (<1% patients in one study annually experienced cardiovascular events after stress MPI returned normal results).[4] Large community-based studies have identified a relationship between chronic kidney disease (CKD) and

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Disclosure Statement of Financial Interest:
We do not have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this article.

DOI:10.1111/hdi.12045

adverse cardiovascular prognosis.[5–8] Poor cardiovascular prognosis is characteristic of CKD patients treated with hemodialysis. Some studies have shown that this is true even in patients with normal stress MPI (4–9% of hemodialysis patients per year experience cardiovascular events).[9,10] Another study reported that peripheral artery disease (PAD) is common in hemodialysis patients and is associated with increased risk of adverse cardiovascular prognosis.[11] This study investigated the prognostic factors of adverse cardiovascular events in hemodialysis patients in whom stress MPI was performed.

MATERIALS AND METHODS

Patients and study protocol

This study is a retrospective prognosis study for hemodialysis patients who underwent stress MPI. Thallium-201 stress MPI was performed in 100 consecutive continuous hemodialysis patients with suspected or prior coronary artery disease (CAD) from 2008 to 2010. Nine patients for whom no prognostic data after stress MPI could be obtained were excluded from the study. Of the remaining patients, a patient with summed difference score of >2 on stress MPI and requiring revascularization within 2 months of percutaneous coronary intervention to combat significant ischemia was excluded[12] Two patients with severe valvular disease were also excluded. Follow-up was performed in the remaining 88 patients. Of 88 patients, 27 patients (31%) had previous CAD, which included previous myocardial infarction (MI; $n = 8$, 9%). Fourteen of 88 (16%) patients had temporal chest oppression with no relationship of physical or mental stress. In the remaining 74 patients, 42 (48%) had shortness of breath during walking and 32 (36%) had temporal chest discomfort. All patients provided written informed consent to participate in this study, which was approved by the Committee on Human Investigation of the Toho University Ohashi Medical Center and performed in accordance with the ethical standards of the 1964 Declaration of Helsinki (as revised in Tokyo 2004) and subsequent revisions.

The following patient data were collected during previous stress MPI: age, gender, medication use, and other coronary risk factors. Risk factors included cigarette smoking; history of hypertension (systolic blood pressure > 140 mmHg, diastolic blood pressure > 90 mmHg, and/or receiving antihypertensive therapy); diabetes (fasting blood glucose > 126 mg/dL, glycosylated hemoglobin > 6.1%, current treatment with insulin or oral antidiabetic agents, or patient history); hyperlipidemia (hypercholesterolemia [total cholesterol > 220 mg/dL], hypertriglyceridemia [serum triglyceride > 150 mg/dL], and/or current lipid lowering therapy); and history of CAD in first-degree relatives <60 years old. A pharmacological stress test comprising intravenous adenosine infusion was performed in all patients. In order to avoid artifact of stress MPI, meal and caffeine were restricted from previous night of stress MPI. Adenosine infusion and thallium-201 injection were administered in separate arms. An automatic infusion pump delivered adenosine (0.120 mg/kg/min) intravenously over 6 min. Pharmacological stress was adequate in all patients and significant side effects such as bradycardia and/or persistent dyspnea were not observed. During pharmacological stress test, persistent atrial fibrillation was observed in four patients. There was no patient who was observed left bundle branch block or ventricular tachycardia. Thallium-201 (111 MBq; FUJIFILM RI Pharma Co., Ltd, Tokyo, Japan) was injected into a peripheral vein approximately 3 min after initiation of adenosine infusion.

Myocardial perfusion single-photon emission computed tomography

All patients underwent stress MPI with thallium using a three-headed gamma camera (MS-3; Siemens, Chicago, IL, USA) equipped with a low-energy cardiofocal collimator and interfaced with a computer (ICON; Siemens). Stress single-photon emission computed tomography (SPECT) was performed 10 min after stress testing, and rest SPECT was performed 4 h after stress imaging. Ninety projections were obtained for 20 s each in four intervals of 360° and stored on 64 × 64 matrices. A 15% symmetrical energy window, centered on the 70-keV peak, was used. Tomographic reconstruction was performed using the standard filtered back-projection technique and a Butterworth filter with a cutoff frequency of 0.5 cycles/pixel and an order of 5. No correction was performed for attenuation or scatter.

SPECT images were reoriented along the short, horizontal, and vertical long axes for analysis. Presence of perfusion defects was determined by agreement between two experienced observers who were blinded to patient identity and clinical information. Defects were classified as reversible (including partially reversible) or fixed (irreversible). SPECT images were assessed in the following manner to determine the presence, location, and severity of any perfusion defect. Data of stress MPI were assessed by visual and semiquantitative of observers. We did not use certain software application. The left ventricle was divided into 17 segments, and each segment was assigned a score on the basis of agreement of at least two observers

using a 5-point scoring system (0 = normal, 1 = mildly reduced, 2 = moderately reduced, 3 = severely reduced, and 4 = uptake absent). The sum of the segment scores at stress (summed stress score [SSS]), scores at rest (summed rest score [SRS]), and the difference between the stress and rest scores (summed difference score [SDS]) were calculated. SSS ≤ 3 and SDS ≤ 1 were considered normal.[3,13,14]

Echocardiography and ankle–brachial index

The left ventricular ejection fraction was measured by M-mode echocardiography within 1 month of MPI. PAD was defined from prior medical history such as antiplatelet drugs and/or an ankle–brachial index of <0.9[15,16] and/or previous angioplasty of the peripheral arteries.

End-points and follow-up

Follow-up commenced after assessment of cardiac function and stress MPI. End-points included cardiac death, nonfatal MI, and Braunwald class III unstable angina requiring hospitalization. Cardiac death included sudden cardiac death, fatal MI, death due to heart failure, or death due to arrhythmia. Sudden cardiac death was defined as witnessed cardiac arrest, death within 1 hour of onset of acute symptoms, or unexpected death in patients considered well for the previous 24 hours. Braunwald class III unstable angina was defined as acute angina at rest within 48 hours of onset. These end-points were defined as cardiovascular events. Patients were followed regularly for a mean of 26 ± 13 months (range: 2–46 months). The prognosis of patients was followed-up from medical records, mailing or telephone interview. Outpatients are seen at least every 2 months by our institution.

Statistical analyses

Results are presented as mean ± standard deviation. The chi-squared test was used to compare differences in gender, underlying disease, and medical treatment between patients with and without cardiovascular events. Student's *t*-test was used for comparison in terms of age, body mass index, echocardiography parameters, and stress MPI. Non-parametric test was used for hemodialysis duration. Cox regression hazard analysis was performed to detect risk factors. Kaplan–Meier event-free curves were constructed, and the log–rank test was used to compare risk of cardiovascular events among patient groups. All analyses were performed using the Statistical Package for the Social Sciences (SPSS) statistical software (SPSS Inc., Chicago, IL, USA). $P < 0.05$ was considered significant.

RESULTS

Patient profile

Table 1 summarizes baseline patient characteristics. No significant differences were observed in age, gender, hypertension, diabetes, hyperlipidemia, smoking history, current smoking, familial history of CKD, cerebral artery disease, and previous CKD between patients with and without cardiovascular events. Frequency of PAD was significantly higher in patients with cardiovascular events than in those without. The ankle-brachial index tended to be lower in patients with cardiovascular events compared with those without, but this was not significantly different (0.89 vs. 1.03, $P = 0.06$). In patients with PAD, the rate of previous medical therapy and rate of previous angioplasty had no significant difference between patients with and without cardiovascular events.

The results of laboratory data and echocardiography, no significant differences were found between patients with and without cardiovascular events. The hemodialysis duration was significantly longer in patients with cardiovascular events than in those without. Values for all parameters of stress MPI (SSS, SRS, and SDS) were significantly higher in patients with cardiovascular events than in those without. With regard to medication, use of statins was significantly higher in patients with cardiovascular events than in those without.

Outcomes

During the mean follow-up period of 26 months, cardiovascular events occurred in 16 patients (cardiac death: $n = 8$, nonfatal MI: $n = 2$, Braunwald type III unstable angina: $n = 6$). Risk factors were assessed using univariate Cox regression hazard analysis (Table 2). PAD and parameters of stress MPI were significant predictors of cardiovascular events. Multivariate Cox regression analysis was used to assess the strength of risk among the patients with PAD and its association with the results of stress MPI. Only PAD (hazard ratio = 6.54; $P = 0.002$) and abnormal SSS of stress MPI (SSS > 3; HR = 8.26; $P = 0.008$) were independent and significant risk factors for cardiovascular events (Table 3). Abnormal SDS of stress MPI (SDS > 1) was not identified as an independent and significant risk factor for cardiovascular events. Figure 1 presents the Kaplan–Meier survival curves for freedom from cardiovas-

Table 1 Patient characteristics

	Overall ($n = 88$)	Events+ ($n = 16$)	Events − ($n = 72$)	P-value
Age (years)	69 ± 11	72 ± 10	68 ± 11	n.s.
Male	60 (68%)	11 (69%)	49 (68%)	n.s.
Hypertension	80 (91%)	14 (88%)	66 (92%)	n.s.
Diabetes	49 (56%)	10 (63%)	39 (54%)	n.s.
Hyperlipidemia	33 (38%)	8 (50%)	25 (35%)	n.s.
Smoking history	47 (53%)	8 (50%)	39 (54%)	n.s.
Current smoking	8 (9%)	2 (13%)	6 (8%)	n.s.
Familial history of CAD	8 (9%)	2 (13%)	6 (8%)	n.s.
Cerebral vascular disease	22 (25%)	6 (38%)	16 (22%)	n.s.
PAD	24 (27%)	10 (63%)	14 (19%)	0.001
Ankle-brachial index	1.00 ± 0.23	0.89 ± 0.22	1.03 ± 0.23	n.s.
Previous medical therapy of PAD patients	22 (92%)	8 (80%)	14 (100%)	n.s.
Previous angioplasty of PAD patients	11 (46%)	5 (50%)	6 (43%)	n.s.
Previous CAD	27 (31%)	7 (44%)	20 (28%)	n.s.
Laboratory data				
Hemoglobin	10.4 ± 1.7	10.4 ± 1.4	10.5 ± 1.7	n.s.
Albumin	3.8 ± 0.5	3.7 ± 0.7	3.8 ± 0.4	n.s.
HbA1c	5.7 ± 1.1	5.7 ± 1.2	5.7 ± 1.1	n.s.
LDL-cholesterol	93 ± 31	83 ± 29	96 ± 32	n.s.
HDL-cholesterol	46 ± 13	42 ± 11	48 ± 14	n.s.
Calcium	8.7 ± 1.0	9.2 ± 1.3	8.6 ± 0.9	n.s.
Phosphate	5.4 ± 1.5	4.9 ± 2.0	5.5 ± 1.4	n.s.
Calcium × phosphate	46 ± 13	44 ± 16	46 ± 12	n.s.
Echocardiography				
LVDd	46 ± 6.9	47 ± 8.2	46 ± 6.6	n.s.
LVDs	31 ± 7.1	32 ± 9.2	31 ± 6.6	n.s.
LVEF	64 ± 12	60 ± 16	65 ± 11	n.s.
Duration of hemodialysis (months)	35 ± 42	52 ± 50	31 ± 40	0.049
Stress myocardial perfusion images				
SSS	1.6 ± 3.2	4.2 ± 6.2	1.0 ± 1.6	<0.001
SRS	0.9 ± 2.2	2.6 ± 4.4	0.5 ± 1.2	0.001
SDS	0.7 ± 1.9	1.6 ± 3.5	0.5 ± 1.2	0.027
Follow-up period (months)	26 ± 13	13 ± 9.2	29 ± 12	<0.001
Medication				
Aspirin	33 (38%)	8 (50%)	25 (35%)	n.s.
ACE-I/ARB	56 (64%)	11 (69%)	45 (63%)	n.s.
Beta-blocker	23 (26%)	7 (44%)	16 (22%)	n.s.
Diuretics	39 (44%)	6 (38%)	33 (46%)	n.s.
Insulin	18 (20%)	4 (25%)	14 (19%)	n.s.
Statins	24 (27%)	8 (50%)	16 (22%)	0.033

ACE-I = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor blocker; CAD = coronary artery disease; HDL = high-density lipoprotein; LDL = low-density lipoprotein; LVDd = left ventricular diastolic diameter; LVDs = left ventricular systolic diameter; LVEF = left ventricular ejection fraction; n.s. = not significant; PAD = peripheral artery disease; SDS = summed difference score; SRS = summed rest score; SSS = summed stress score.

cular events in patients with scores between SSS ≤ 3 and SSS > 3. The prognosis of cardiovascular events was significantly better in patients with SSS ≤ 3 than in patients with SSS > 3 ($P < 0.001$, log–rank test). Cardiovascular prognosis among patients with normal stress MPI (SSS ≤ 3) was also assessed. As shown in the Kaplan–Meier survival curves for freedom from cardiovascular events (Figure 2), the prognosis was significantly better in patients without PAD than in patients with PAD ($P = 0.001$, log–rank test). Of eight patients who were

Table 2 Results of univariate Cox regression analysis

	Hazard ratio	95% CI	*P*-value
Male	1.01	0.35–2.91	n.s.
Age	1.04	0.99–1.10	n.s.
Previous CAD	1.81	0.67–4.85	n.s.
Cerebral vascular disease	1.87	0.68–5.15	n.s.
PAD	5.56	2.01–15.4	<0.001
Hypertension	0.76	0.17–3.36	n.s.
Diabetes	1.39	0.50–3.82	n.s.
Hyperlipidemia	1.68	0.63–4.46	n.s.
Smoking history	0.89	0.34–2.38	n.s.
Current smoking	1.61	0.37–7.09	n.s.
Familial history of coronary artery disease	1.42	0.32–6.25	n.s.
Laboratory data			
Hemoglobin	0.93	0.70–1.25	n.s.
Albumin	0.76	0.24–2.36	n.s.
LDL-cholesterol	0.99	0.97–1.01	n.s.
HDL-cholesterol	0.97	0.92–1.01	n.s.
Calcium	1.76	0.99–3.11	n.s.
Phosphate	0.81	0.54–1.20	n.s.
Calcium × phosphate	0.99	0.95–1.04	n.s.
Echocardiography			
LVDd	1.03	0.95–1.11	n.s.
LVDs	1.03	0.96–1.12	n.s.
LVEF	0.96	0.92–1.00	n.s.
Duration of hemodialysis	1.01	1.00–1.02	n.s.
Stress myocardial perfusion images			
SSS	1.20	1.10–1.31	<0.001
SRS	1.23	1.10–1.37	<0.001
SDS	1.29	1.08–1.53	0.005

Abbreviations as shown in Table 1.
CI = confidence interval.

observed nonfatal cardiovascular events such as nonfatal MI and unstable angina, cardiac death was observed in five patients after a mean period of 10 months after primary cardiovascular events.

DISCUSSION

This prognostic study identified SSS of stress MPI and PAD as an independent predictor of cardiovascular events

Table 3 Results of multivariate Cox regression analysis

	Hazard ratio	95% CI	*P*-value
PAD	6.54	2.01–21.3	0.002
SSS > 3	8.26	1.73–38.5	0.008
SDS > 1	4.46	0.73–26.8	n.s.

Abbreviations as shown in Table 1.
CI = confidence interval.

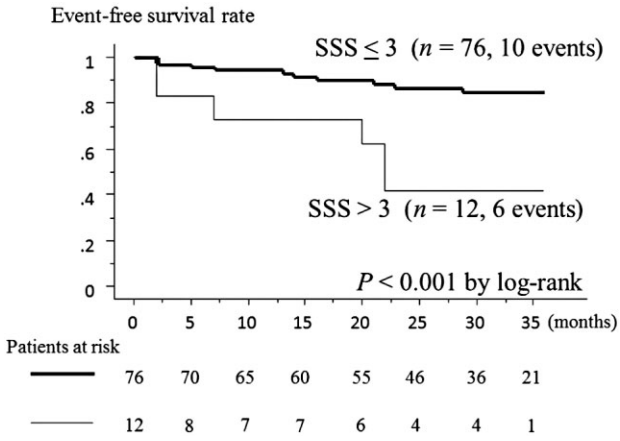

Figure 1 Kaplan–Meier survival curves for absence of cardiovascular events in patients with summed stress score (SSS) between <3 and >3. The prognosis of cardiovascular events was significantly better in patients with SSS ≤ 3 than in patients with SSS > 3.

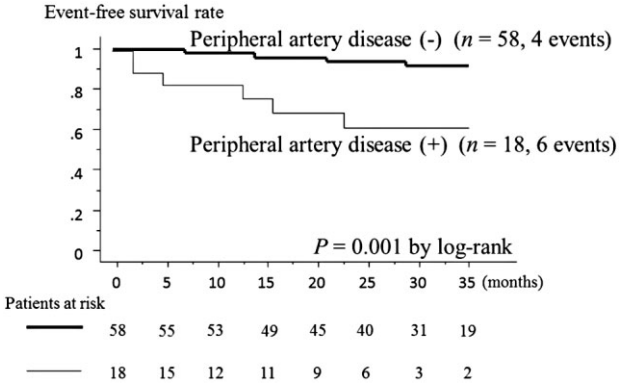

Figure 2 Kaplan–Meier survival curves for freedom from cardiovascular events in patients with normal stress myocardial perfusion images (summed stress score ≤ 3). The prognosis of cardiovascular events was significantly better in patients without peripheral artery disease (PAD) than in patients with PAD.

in hemodialysis patients. The prognosis of cardiovascular events in hemodialysis patients was poor even for those with normal stress MPI, as reported in previous studies.[9,10] Therefore, aggressive medical management for prevention of cardiovascular events is necessary in hemodialysis patients. Although these patients share many of the same cardiovascular risk factors as in the general population, they also face additional risk factors, including anemia and abnormal calcium/phosphorus metabolism. These factors promote increased vascular calcification and reduced oxygen-carrying capacity, thereby increasing the cardiovascular risk.[17] In this study, serum calcium level, phosphate level, and calcium × phosphate were not predictors for cardiovascular events. We could not assess the relationship of bone chemistry abnormalities and influences of cardiovascular outcome. In addition, hemodialysis patients require artificial water volume control and potassium/sodium balance control, which may also increase the risk of cardiovascular events.

In this study, although hemodialysis duration varied widely (1–156 months), duration of hemodialysis was significantly longer in patients with cardiovascular events than in patients without cardiovascular events. And in univariate Cox regression analysis, hemodialysis duration was not a significant, but had a tendency of cardiovascular risk factor (hazard ratio = 1.01, $P = 0.05$). Moreover, we assessed the relationship between hemodialysis duration and previous CAD or abnormality of stress MPI. The hemodialysis duration was significantly longer in patients with previous CAD than without previous CAD (55 ± 47 vs. 26 ± 37 months, $P = 0.003$) and in patients with abnormal stress MPI than in patients with normal stress MPI (62 ± 52 vs. 31 ± 39 months, $P = 0.016$). It might suggest that long hemodialysis duration could be a risk factor for CAD.

Previous studies have suggested PAD as a risk factor for cardiovascular disease.[15,16] In this study, among hemodialysis patients with normal stress MPI, the prognosis was significantly better in patients without PAD than in patients with PAD. In patients without PAD with normal stress MPI, the prognosis of cardiovascular events may be relatively good (4 events in 58 patients, only 1 event in the first year).

Statins are established as secondary prevention for cardiovascular disease and cardiovascular events were significantly more frequent in statin users compared with those not taking a statin. In this study, SSS of stress MPI was significantly higher in statins users than no statins users (2.2 vs. 1.3, $P = 0.004$). Higher frequency of statin use in these patients might be due to the fact that they were in highest risk such as abnormal stress MPI and/or history of CAD.

Electrocardiogram (ECG)-gated SPECT was performed in only 37 patients. This technique is not performed regularly at our institution. Only five cardiovascular events were observed in the patients in this study. Exact left ventricular systolic function and systolic and diastolic volumes could not be investigated in this study. The rate of cardiovascular event was not significantly different between patients with ECG-gated SPECT and patients without. Among patients who underwent electrocardiogram-gated SPECT, in Cox regression hazard analysis, parameters of stress MPI including left ventricular ejection fraction (both stress and rest phases) could not be significant predictors for cardiovascular events. It might be due to very small number of patients and cardiovascular events. However, only PAD could be a predictor for cardiovascular events (hazard ratio = 6.06, $P = 0.048$). Moreover, transient ischemic dilatation, which indicates severe myocardial ischemia and poor cardiovascular prognosis, was also not assessed, at least in patients with normal stress MPI, because no patient was suspected of transient ischemic dilatation based on a visual impression.

This was a retrospective study, which is an important limitation. The baseline clinical data such as form of symptoms and/or past history might not partially exact. All patients underwent ankle-brachial index. However, not all patients underwent blood laboratory testing (77 of 88 [88%]), and 82 of 88 (93%) patients underwent echocardiography. The periods between stress MPI and laboratory data, examination of ankle-brachial index or

echocardiography were various, but all of these examinations underwent within 3 months before and after stress MPI. We could not deny a probability that several cardiovascular events might be missed because of lack of follow-up. The sample of hemodialysis patients with cardiovascular events was small in this study, and the analysis was conducted over a relatively short follow-up period. In addition, only 16 cardiovascular events were observed in this study. The prognosis of each of these cardiovascular events, such as cardiac mortality and nonfatal MI was not individually assessed. Despite these limitations, we believe the findings of this study provided valuable insight into the usefulness of PAD and stress MPI as powerful cardiovascular predictors in hemodialysis patients.

CONCLUSION

In hemodialysis patients, both PAD and stress MPI were powerful predictors of cardiovascular events. Normal stress MPI itself does not guarantee a good cardiovascular prognosis in these patients. However, a relatively good prognosis may be expected in patients with normal stress MPI with no PAD.

ACKNOWLEDGMENTS

We thank Chihiro Hamazaki and Takeharu Ando for their technical assistance with stress myocardial perfusion imaging. We also thank Professor Eiichi Kouda for his helpful comments.

Manuscript received December 2012; revised March 2013.

REFERENCES

1 Hachamovitch R, Hayes SW, Friedman JD, Cohen I, Berman DS. Stress myocardial perfusion single-photon emission computed tomography is clinically effective and cost effective in risk stratification of patients with a high likelihood of coronary artery disease (CAD) but no known CAD. *J Am Coll Cardiol*. 2004; **43**:200–208.

2 Hachamovitch R, Berman DS, Kiat H, et al. Exercise myocardial perfusion SPECT in patients without known coronary artery disease: Incremental prognostic value and use in risk stratification. *Circulation*. 1996; **93**:905–914.

3 Hachamovitch R, Berman DS, Shaw LJ, et al. Incremental prognostic value of myocardial perfusion single photon emission computed tomography for the prediction of cardiac death: Differential stratification for risk of cardiac death and myocardial infarction. *Circulation*. 1998; **97**:535–543.

4 Shaw LJ, Hendel R, Borges-Neto S, et al. Myoview Multicenter Registry. Prognostic value of normal exercise and adenosine 99 mTc-tetrofosmin SPECT imaging: Results from the multicenter registry of 4,728 patients. *J Nucl Med*. 2003; **44**:134–009.

5 Meisinger C, Döring A, Löwel H, KORA Study Group. Chronic kidney disease and risk of incident myocardial infarction and all-cause and cardiovascular disease mortality in middle-aged men and women from the general population. *Eur Heart J*. 2006; **27**:1245–1250.

6 Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med*. 2004; **351**:1296–1305.

7 Manjunath G, Tighiouart H, Ibrahim H, et al. Level of kidney function as a risk factor for atherosclerotic cardiovascular outcomes in the community. *J Am Coll Cardiol*. 2003; **41**:47–55.

8 Weiner DE, Tighiouart H, Amin MG, et al. Chronic kidney disease as a risk factor for cardiovascular disease and all-cause mortality: A pooled analysis of community-based studies. *J Am Soc Nephrol*. 2004; **15**:1307–1315.

9 Hase H, Joki N, Ishikawa H, et al. Prognostic value of stress myocardial perfusion imaging using adenosine triphosphate at the beginning of haemodialysis treatment in patients with end-stage renal disease. *Nephrol Dial Transplant*. 2004; **19**:1161–1167.

10 Caglar M, Mahmoudian B, Aytemir K, et al. Value of 99 mTc-methoxyisobutylisonitrile (99 mTc-MIBI) gated SPECT for the detection of silent myocardial ischemia in hemodialysis patients: Clinical variables associated with abnormal test results. *Nucl Med Commun*. 2006; **27**:61–69.

11 Rajagopalan S, Dellegrottaglie S, Furniss AL, et al. Peripheral arterial disease in patients with end-stage renal disease: Observations from the Dialysis Outcomes and Practice Patterns Study (DOPPS). *Circulation*. 2006; **114**:1914–1922.

12 Sharir T, Germano G, Kavanagh PB, et al. Incremental prognostic value of post-stress left ventricular ejection fraction and volume by gated myocardial perfusion single photon emission computed tomography. *Circulation*. 1999; **100**:1035–1042.

13 Ladenheim ML, Pollock BH, Rozanski A, et al. Extent and severity of myocardial hypoperfusion as predictors of prognosis in patients with suspected coronary artery disease. *J Am Coll Cardiol*. 1986; **7**:464–471.

14 Berman DS, Abidov A, Kang X, et al. Prognostic validation of a 17-segment score derived from a 20-segment score for myocardial perfusion SPECT interpretation. *J Nucl Cardiol*. 2004; **11**:414–423.

15 Newman AB, Shemanski L, Manolio TA, et al. The Cardiovascular Health Study Group. Ankle-arm index as a

predictor of cardiovascular disease and mortality in the Cardiovascular Health Study. *Arterioscler Thromb Vasc Biol*. 1999; **19**:538–545.
16 Resnick HE, Lindsay RS, McDermott MM, et al. Relationship of high and low ankle brachial index to all-cause and cardiovascular disease mortality: The Strong Heart Study. *Circulation*. 2004; **109**:733–739.
17 Sarnak MJ. Cardiovascular complications in chronic kidney disease. *Am J Kidney Dis*. 2003; **41**:11–17.