Coronary artery disease screening and prognosis in incident dialysis patients

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Abstract

Background: Guidelines have recommended that physicians screen for coronary artery disease (CAD) at the initiation of dialysis. The purpose of this study was to examine the effects of CAD screening at the initiation of dialysis on prognosis after starting dialysis

Methods: This retrospective cohort study involved 224 consecutive incident dialysis patients without advanced cardiac disease. Pharmacological stress myocardial perfusion imaging (MPI) was performed to routinely screen incident dialysis patients within 3 months of starting dialysis therapy. The influence of MPI on prognosis after starting dialysis was explored by the propensity score adjustment method. The study outcome was defined as all-cause mortality and cardiac death.

Results: Of the 224 patients, 164 (73.2 %) underwent MPI screening at initiation of dialysis. During the median follow-up period of 5.5 years, 77 patients died, among whom 17 (22.1 %) cardiac deaths were observed. The patients who received MPI had a significantly higher survival rate for all-cause mortality and cardiac death compared with the patients without MPI (log-rank test, $p < 0.001$, $p = 0.021$, respectively). In multiple Cox regression analysis, MPI screening continued to have a statistically significant negative association with all-cause mortality after adjusting for confounding variables (hazard ratio 0.581, $p = 0.034$) and propensity score (hazard ratio 0.568, $p = 0.025$).

Conclusions: MPI CAD screening at dialysis initiation could improve prognosis after starting dialysis.

Keywords: Myocardial perfusion imaging, Propensity score, Initiation of dialysis, All-cause mortality, Cardiac death

Background

Although the underlying mechanism of the cardio-renal axis in patients with chronic kidney disease (CKD) has been determined in considerable detail over the past decade [1], cardiovascular disease is still a leading cause of death in maintenance dialysis patients worldwide [2, 3] and also in Japan [4]. The accelerated progression of atherosclerosis during the conservative phase of CKD, before starting dialysis therapy [5], is thought to be one of the causes of the high incidence of cardiovascular events in the dialysis phase [6, 7]. Therefore, it is well known that a high prevalence of atherosclerotic cardiovascular diseases is observed at the initiation of dialysis. For example, approximately 50 % of incident asymptomatic dialysis patients have been observed to suffer from advanced coronary artery disease (CAD) [8, 9] and show poor prognosis after starting dialysis [6, 10]. Based on this background, guidelines created by several organizations [11–13] have recommended that physicians screen for CAD at the initiation of dialysis in order to find it earlier and improve prognosis. However, it has not yet been established whether screening for CAD plays a crucial role in improving the prognosis for dialysis patients.

Pharmacological stress myocardial perfusion imaging (MPI), even in end-stage kidney disease (ESKD) patients, is one of the most frequently performed procedures for identifying patients with myocardial ischemia and CAD,

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and for stratifying the patients at high risk for poor prognosis [14]. Recently, the severity of abnormal MPI results has begun to have a great impact on the prediction of cardiac events in the conservative phase of advanced CKD patients without cardiovascular disease [15]. Therefore, MPI is becoming a useful screening procedure for patients at any stage of kidney disease as a non-invasive procedure that is not harmful to kidney function.

Our hypothesis for the present study was that screening for CAD at the initiation of dialysis by using MPI may lead to improved prognosis after starting dialysis. Therefore, this study examined the effect of MPI screening for CAD on the prognosis of incident dialysis patients.

Methods
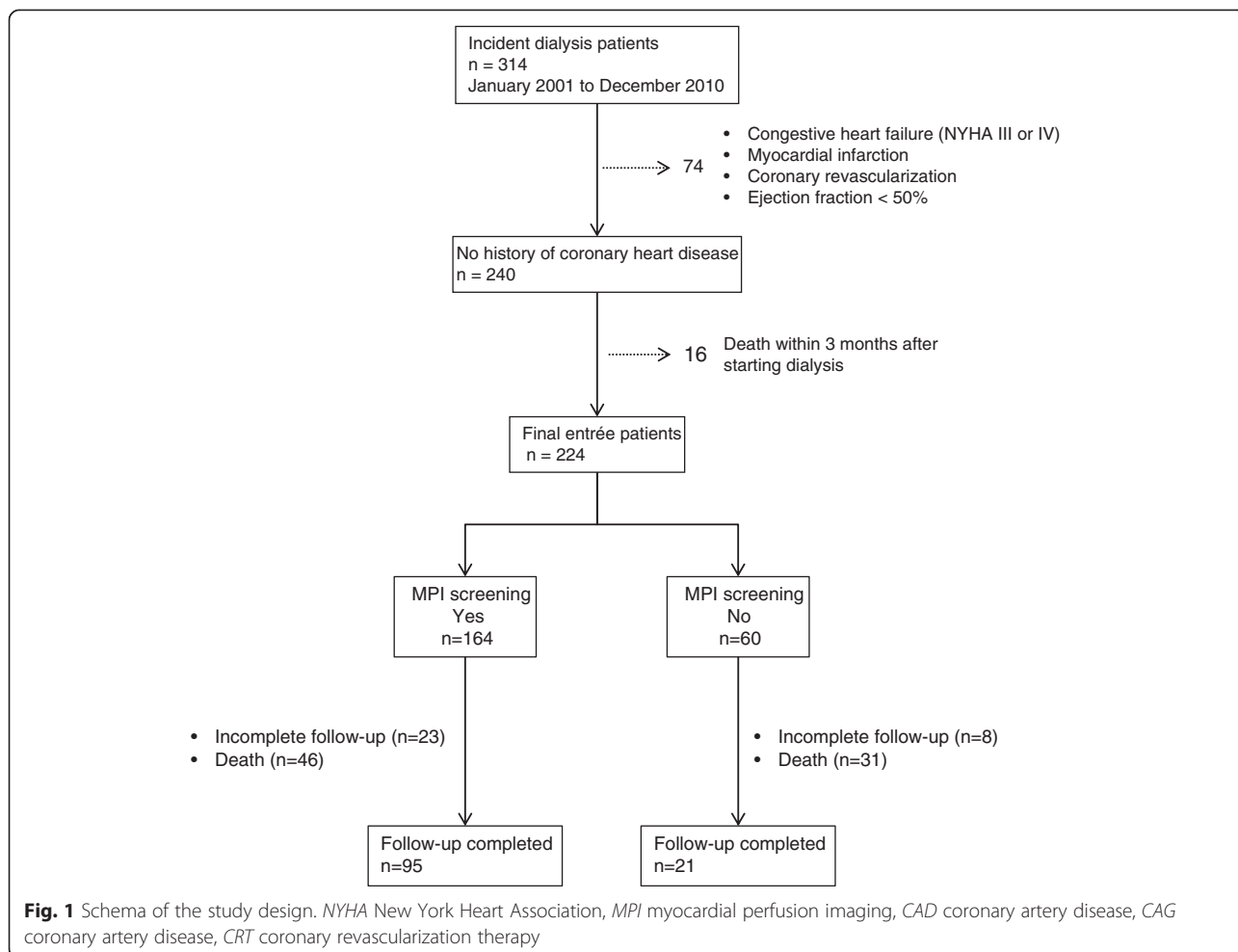### Study design and patients
This was a retrospective cohort study that involved 314 consecutive patients who started maintenance dialysis for ESKD at the Toho University Ohashi Medical Center between January 2001 and December 2010. In order to precisely evaluate the effect of MPI screening on prognosis, ESKD patients who already had cardiac disease before

starting dialysis were excluded. As shown in Fig. 1, 74 patients met the exclusion criteria as follows: (1) history of New York Heart Association (NYHA) level III or IV heart failure, (2) coronary heart disease such as myocardial infarction and/or coronary revascularization, or (3) left ventricular dysfunction defined as ejection fraction (EF) <50 % evaluated by echocardiography. Additionally, 16 patients who expired within 3 months of starting dialysis were excluded. The remaining 224 patients were enrolled into this study, among whom 164 underwent MPI as screening for CAD. The influence of MPI on prognosis after starting dialysis was explored by crude cohort analysis and by the propensity score adjustment method.

All patients provided informed consent to participate in the study, and the Ethics Committee for Clinical Research at Toho University Ohashi Medical Center approved the study protocol [Permission no. 13-52, 13-61]. This study adhered to the Declaration of Helsinki.

Data collection
Clinical information from all patients was recorded before the first hemodialysis (HD) session. All patients

Fig. 1 Schema of the study design. *NYHA* New York Heart Association, *MPI* myocardial perfusion imaging, *CAD* coronary artery disease, *CAG* coronary artery disease, *CRT* coronary revascularization therapy

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were initially interviewed to determine age, sex, type of primary renal disease, previous hospitalization, and history of hypertension and cardiac disease. We also collected information about the medications the patients were receiving after starting dialysis. Blood pressure was recorded from the supine position, and blood samples were withdrawn immediately before the first HD session. Serum calcium (Ca) concentrations were corrected by albumin levels as follows: corrected Ca (cCa) = measured Ca (mg/dL) + (4—measured albumin level (g/dL)). The estimated glomerular filtration rate (eGFR) was calculated using the Japanese equation as follows [16]: eGFR (mL/min/1.73 m^2) = $194 \times Cr^{-1.094} \times Age^{-0.287}$ (for women × 0.739). Body mass index (BMI) at optimal weight was calculated as weight (kg) divided by height (m) squared. All participants were assessed by echocardiography at optimum weight after a dialysis session or on an intermittent day of hemodialysis before discharge. Ejection fraction was measured as a marker of left ventricular (LV) dysfunction.

MPI as a screening method for coronary artery disease

From January 2001, ESKD patients at our hospital have been routinely screened for CAD within 3 months of starting HD therapy, regardless of any suspicion for ischemic heart disease (IHD). Pharmacological stress MPI by using thallium-201 was performed for screening in 164 of the 224 ESKD study patients. Clinically significant CAD was defined when myocardial perfusion defects were reversible in patients examined by pharmacological stress thallium-201 MPI.

Follow-up

The outcome of this study was defined as all-cause mortality and cardiac death. Cardiac death was defined as death from heart failure, myocardial infarction, or sudden death. Information about death was obtained from a questionnaire survey sent to the maintenance hemodialysis facilities or the hospital medical records. The cohort was followed until the end of 2012.

Statistical analysis

Data are summarized as number, prevalence, arithmetic mean ± standard deviation, or median (interquartile range), as appropriate. Comparisons of prevalence and values between groups were performed by Student's t test and the χ^2 test. In the prospective analysis, the Kaplan-Meier method was used with the log-rank test. Prognostic variables were examined by Cox proportional hazard models, and hazard ratios and 95 % confidence intervals are reported. p values <0.05 were considered significant. To adjust for differences in baseline characteristics between the two patient groups (with and without screening MPI), a propensity score analysis was performed using multivariate logistic regression modeling, including all baseline covariates such as age, sex, diabetes, BMI, systolic blood pressure (SBP), LV EF, albumin, hemoglobin (Hb), total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), eGFR, cCa, phosphate (P), intact-parathyroid hormone (iPTH), c-reactive protein (CRP), and usage of three medications: renin angiotensin aldosterone system inhibitor (RAS-I), beta blocker (BB), and statin. The score was then incorporated into a Cox proportional hazards model as a covariate. All statistical analyses were performed using SPSS for Windows version 20 (IBM, Tokyo, Japan).

Results

Baseline characteristics

Of the 224 study patients, 164 (73.2 %) patients underwent MPI screening at the initiation of dialysis (Table 1). Significantly higher incidence of diabetes, higher diastolic pressure, and higher creatinine concentration (lower eGFR) were observed in the MPI screening group compared with the non-MPI group. Although the MPI group had a younger age, more males, higher SBP, lower Hb, higher HDL-C, lower cCa, and higher P than the non-MPI group, no statistically significant differences were found. Among the 164 patients who underwent the screening, 27 patients (16.5 %) showed abnormal MPI. The usage of three medications (statin, RAS-I, and BB) did not differ significantly between the two groups.

Follow-up

The median follow-up period was 5.5 years. During the follow-up period, 77 patients died, including 17 cardiac deaths (22.1 %), as shown in Table 2. A total of 31 patients were lost to follow-up, and two patients received renal transplantation and were censored at the time of the last observation, which was the operation day for renal transplantation (Fig. 1). At the end of the follow-up period on December 31, 2012, a total of 114 patients were alive on maintenance hemodialysis and had completed follow-up.

As shown in Fig. 2a, the Kaplan-Meier curves indicated that the patients with MPI screening had a significantly higher survival rate than the patients who did not undergo MPI screening (log-rank test, $p < 0.001$). The cumulative survival rates at 5 years after starting dialysis with and without MPI were 74.9 and 49.1 %, respectively. Regarding cardiac death in Fig. 2b, the cardiac death event-free 5-year survival rate was 94.8 % in patients with the screening and 86.6 % in patients without the screening (log-rank test, $p = 0.021$). After adjusting by propensity score, the Kaplan-Meier curves still showed higher survival in patients with MPI than in those without MPI (dotted line in Fig. 2a, b).

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Table 1 Baseline characteristics of incident dialysis patients with and without MPI screening

	MPI screening		
	Yes	No	p
	n = 164	n = 60	
Age (years)	64 ± 12	66 ± 17	0.350
Male (%)	67	55	0.097
BMI (kg/m^2)	22 ± 3	22 ± 3	0.170
Diabetes (%)	55	37	0.016
SBP (mmHg)	154 ± 23	147 ± 30	0.069
DBP (mmHg)	78 ± 16	72 ± 11	0.014
Ejection fraction (%)	67 ± 9	66 ± 9	0.403
Albumin (g/dL)	3.3 ± 0.5	3.3 ± 0.5	0.525
Hemoglobin (g/dL)	8.1 ± 1.5	8.4 ± 1.6	0.260
Total cholesterol (mg/dL)	175 ± 53	177 ± 55	0.828
Triglyceride (mg/dL)	123 ± 72	132 ± 61	0.378
HDL-C (mg/dL)	50 ± 17	46 ± 15	0.172
Creatinin (mg/dL)	9.8 ± 3.5	8.6 ± 3.9	0.037
eGFR (mL/min/1.73 m^2)	5.0 ± 1.7	5.8 ± 2.3	0.007
cCa (mg/dL)	8.0 ± 1.0	8.2 ± 0.9	0.107
P (mg/dL)	6.2 ± 1.7	5.8 ± 1.6	0.082
iPTH (pg/mL)	338 ± 315	302 ± 170	0.396
CRP (mg/dL) (IQR)	0.1	0.15	0.154
Statin (%)	18	19	0.953
RAS inhibitor (%)	66	53	0.071
Beta blocker (%)	23	17	0.321
Coronary artery disease (%)	27 (16.5)		
CRT (%)	9 (5.5)		

BMI body mass index, *CRP* c-reactive protein, *CRT* coronary revascularization therapy, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *eGFR* estimated glomerular filtration rate, *HDL-C* high-density lipoprotein cholesterol, *RAS* renin angiotensin system

Figure 3 depicts the survival curves in three patient groups: 27 patients with CAD, 137 patients without CAD, and 60 patients without screening. Interestingly, the 5-year survival rate was the same for patients with and without CAD (74.9 vs. 74.9 %). After 5 years, the survival curve of patients with CAD steeply decreased and became close to the same level as the patients without the screening at 10 years (26.7 vs. 27.4 %) (Fig. 3a). Similar findings were confirmed in the survival curves for cardiac death (Fig. 3b).

Coronary angiography and revascularization

Coronary angiography was performed within 180 days in 9 (33.3 %) of 27 with abnormal MPI findings. Seven of nine with coronary angiography had significant CAD that was treated with coronary revascularization therapy (CRT) (one coronary artery bypass surgery and six percutaneous transluminal coronary angioplasty).

Cox proportional hazards model for the factors associated with death

In the univariate Cox proportional hazards model, age, SBP, serum albumin, Hb, creatinine, eGFR, cCa, CRP, usage of RAS-I, and MPI screening showed significant positive or negative associations with death (Table 3). CRT did not show any significant association with death (Table 3). In the multiple Cox regression analysis, MPI screening was significantly associated with all-cause mortality after adjusting for age, SBP, albumin, hemoglobin, eGFR, calcium, CRP, and usage of RAS-I (Table 4). Furthermore, a significant association with all-cause mortality was observed for MPI screening after adjusting the propensity score (Table 4).

Age, triglyceride, creatinine, eGFR, corrected Ca, CRP, and MPI screening showed significant positive or negative associations with cardiac death in the univariate Cox proportional hazards model. CRT did not show any significant association with cardiac death. In multiple Cox regression analysis, MPI screening was negatively associated with cardiac death after adjusting for age, eGFR and, CRP (Table 4). Furthermore, a negative association with cardiac death was observed for MPI screening after adjusting the propensity score (Table 4). However, neither of these negative associations was statistically significant.
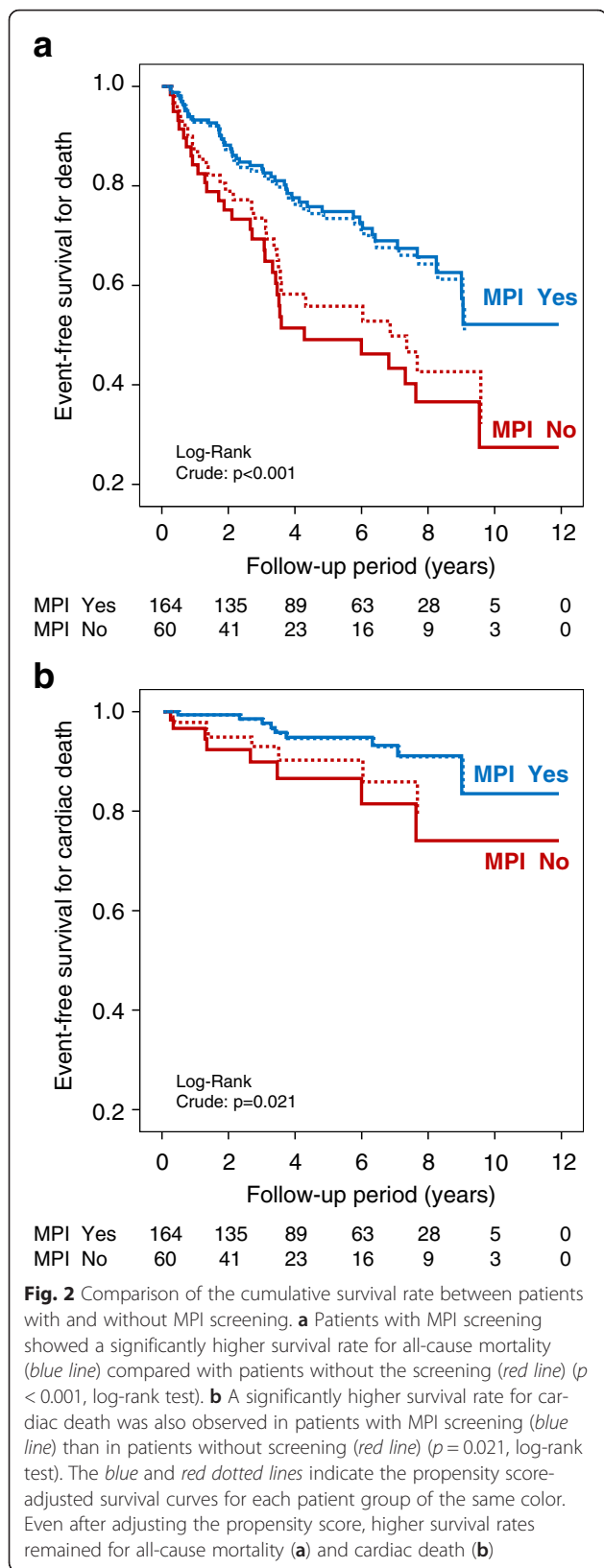
Discussion

Main findings of this study

Several studies have observed a high prevalence of CAD at the initiation of dialysis [8, 9], with severe CAD having a large influence on poor prognosis after starting dialysis [10]. Therefore, international [11, 12] and Japanese [13] guidelines have recommended that physicians screen patients for coronary heart disease at the

Table 2 Causes of death in the present study

	Total	MPI screening	
		Yes	No
		n = 164	n = 60
All cause of death	77		
Cardiac disease	17	9	8
Infectious disease	22	12	10
Malignant disease	14	8	6
Cerebrovascular disease	7	6	1
Other	14	10	4
Unknown	3	1	2
Cardiac cause death	17		
Heart failure	5	1	4
Myocardial infarction	4	3	1
Sudden death	8	5	3

MPI myocardial perfusion imaging

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Fig. 2 Comparison of the cumulative survival rate between patients with and without MPI screening. **a** Patients with MPI screening showed a significantly higher survival rate for all-cause mortality (*blue line*) compared with patients without the screening (*red line*) (*p* < 0.001, log-rank test). **b** A significantly higher survival rate for cardiac death was also observed in patients with MPI screening (*blue line*) than in patients without screening (*red line*) (*p* = 0.021, log-rank test). The *blue* and *red dotted lines* indicate the propensity score-adjusted survival curves for each patient group of the same color. Even after adjusting the propensity score, higher survival rates remained for all-cause mortality (**a**) and cardiac death (**b**)

initiation of dialysis in order to improve their prognosis. However, to date, no evidence has been obtained to prove the effect of screening on prognosis in dialysis patients. The present study demonstrated that MPI screening for CAD at the initiation of dialysis may lead to improved prognosis in incident dialysis patients without cardiac disease. An approximately 50 % risk reduction for death produced by the screening was confirmed by using crude cohort analysis, and also by using propensity score adjustment analysis. Our findings may serve as evidence to support the international guidelines [11, 12].

Effect of CAD screening on mortality

Several previous studies have shown the effect of screening on prognosis in the field of cardiovascular disease. Thompson et al. reported the elegant results of their randomized controlled study, in which ultrasound screening for abdominal aortic aneurysm (AAA) resulted in a reduction in all-cause mortality and was beneficial for AAA-related mortality in a population-based sample of men aged 65–74 years [17]. A relative 42 % risk reduction for AAA-related death and 3 % risk reduction in all-cause mortality were confirmed in the screening group compared with the non-screening group. Similarly, Lindholt et al. conducted a randomized single-center mass screening trial for AAA [18]. Screening reduced the number of emergency operations by 68 % and lowered the mortality of AAA by 73 % over a 10-year period in the screening group compared with the control group. Although these reports demonstrate the benefit of screening for AAA in the asymptomatic general population, which is different from the aim of the present study, it is not surprising that the same beneficial findings are confirmed by screening for CAD even in ESKD patients without cardiac disease.

Conversely, several reports have demonstrated that screening for disease had no beneficial effects on mortality. In a randomized controlled trial [19], ultrasound screening for AAA was found to be not effective in men aged 65–83 years and did not reduce overall death rates. Another study [20] showed that echocardiographic screening for structural and valvular heart disease in the general population provided no benefit for mortality or for the risk of myocardial infarction or stroke. The reasons for the contrary outcomes between those studies remain unclear; however, some potential underlying reasons might exist. The prevalence of an implicit target disease for screening in a study cohort would be an important factor affecting the outcome for screening success. If the prevalence of a target cardiovascular disease is very low in a study cohort, there is a high possibility that the screening will not show any beneficial effect if the study cohort is not enough large. Indeed the clinical guideline in American college of physicians has not

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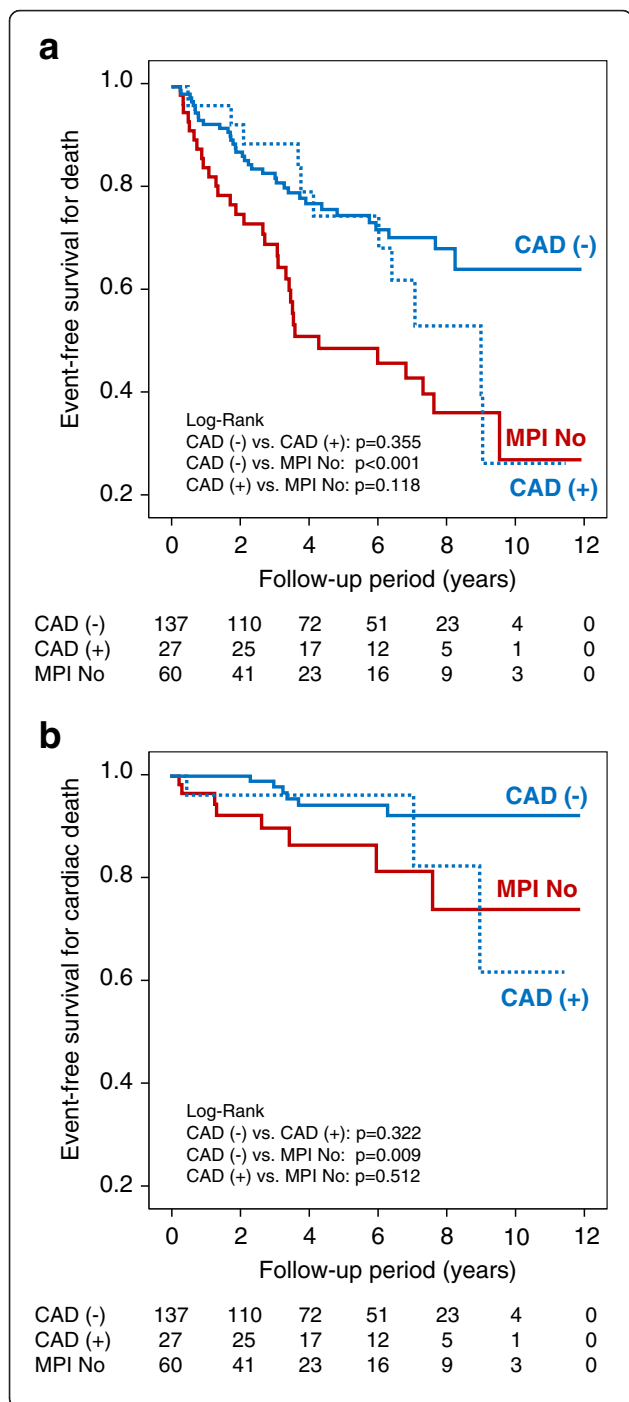
Fig. 3 Comparison of the cumulative survival rate between three patient groups: with CAD, without CAD, and without MPI screening. **a** Patients without CAD by MPI screening showed a significantly higher survival rate for all-cause mortality (*blue line*) compared with patients without screening (*red line*) ($p < 0.001$, log-rank test). The survival curve for the patients with CAD (*dotted blue line*) depicts almost the same pattern as the patients without CAD (*blue line*) until the sixth year of the follow-up period; then, the curve steeply drops to the level of the patients without screening (*red line*) at 10 years. **b** A significantly higher survival rate for cardiac death was also observed in patients without CAD by MPI screening (*blue line*) than in patients without screening (*red line*) ($p = 0.009$, log-rank test). Similar to the curves for all-cause mortality, the survival curve for the patients with CAD (*dotted blue line*) shows almost the same pattern as the patients without CAD (*blue line*) until the sixth year of the follow-up period; then, the curve steeply drops to below the level of the patients without screening (*red line*) at 10 years

recommended screening for cardiac disease in asymptomatic, low-risk adults with resting or stress electrocardiography, stress echocardiography, or stress myocardial perfusion imaging [21]. The accuracy of a screening test would also play an important role in the study outcome. A lack of sufficient sensitivity and specificity to capture a target disease would crucially influence the results. It is well known that a high prevalence (40–50 %) of underlying CAD is observed in asymptomatic ESKD patients [8, 9, 22]. Even in ESKD patients, the accuracy of the pharmacological stress MPI for detecting CAD is reported to be sufficiently high, with a sensitivity of 80 % and specificity of 73 % observed in 42 chronic dialysis patients [23] and a sensitivity of 86 % and specificity of 79 % in 80 type I diabetes ESKD patients [24]. Also, the event rate after screening influences the study outcome. Young et al. assessed whether routine screening for CAD by MPI affects cardiac outcomes in asymptomatic type 2 diabetic patients [25]. These investigators concluded that cardiac event rates were not significantly reduced by MPI screening over a follow-up period of 4.8 years due at least in part to a low cardiac event rate of 2.9 %. In the present study, during the median follow-up period of 5.5 years, the cardiac death rate was 22.1 %, which is seven times higher than that in the Young study. This is also one of the reasons for the beneficial effect of screening. Therefore, although we used a small sample of ESKD patients in a single-center study, we believe that the findings of the present study provide valuable data.

Greater beneficial effect for all-cause mortality than for cardiac death

In general, a greater beneficial effect is expected for cardiac death than for all-cause mortality by MPI screening. In the present study, MPI screening had a negative impact on cardiac death; however, this did not reach a statistically significant level in multivariate Cox proportional hazards

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Table 3 Cox proportional hazards model for identifying the factors associated with all-cause mortality and cardiac death

	All cause of death			Cardiac cause death		
	HR	95 % CI	*p* value	HR	95 % CI	*p* value
Age (per year)	1.053	1.032–1.074	<0.001	1.056	1.012–1.102	0.012
Male	1.568	0.956–2.573	0.075	0.912	0.347–2.400	0.852
BMI (kg/m^2)	0.940	0.873–1.014	0.108	1.010	0.870–1.174	0.893
Diabetes (yes)	1.119	0.715–1.751	0.624	0.889	0.343–2.309	0.810
SBP (mmHg)	0.991	0.982–1.000	0.040	0.995	0.977–1.013	0.559
DBP (mmHg)	0.987	0.970–1.004	0.121	0.988	0.954–1.024	0.517
Ejection fraction (%)	0.989	0.965–1.013	0.355	0.957	0.914–1.002	0.063
Albumin (g/dL)	0.503	0.307–0.823	0.006	0.613	0.209–1.792	0.371
Hemoglobin (g/dL)	1.171	1.006–1.363	0.042	1.305	0.946–1.802	0.105
Total cholesterol (mg/dL)	1.001	0.997–1.006	0.613	1.006	0.998–1.014	0.156
Triglyceride (mg/dL)	1.001	0.997–1.004	0.701	1.004	1.000–1.009	0.046
HDL-C (mg/dL)	0.995	0.980–1.010	0.508	0.979	0.944–1.017	0.275
Creatinin (mg/dL)	0.818	0.745–0.899	<0.001	0.725	0.577–0.913	0.006
eGFR (mL/min/1.73 m^2)	1.292	1.166–1.431	<0.001	1.332	1.074–1.650	0.009
cCa (mg/dL)	1.303	1.027–1.654	0.030	1.932	1.112–3.359	0.020
P (mg/dL)	0.867	0.744–1.010	0.067	0.783	0.560–1.094	0.152
iPTH (pg/mL)	0.999	0.998–1.000	0.155	0.999	0.996–1.001	0.389
CRP (mg/dL)	1.29	1.055–1.578	0.013	1.497	1.049–2.138	0.026
Statin (%)	1.273	0.710–2.282	0.418	1.272	0.363–4.466	0.707
RAS inhibitor (%)	0.522	0.333–0.820	0.005	0.502	0.193–1.307	0.158
Beta blocker (%)	1.083	0.630–1.861	0.773	1.559	0.546–4.448	0.407
MPI screening	0.449	0.284–0.708	0.001	0.342	0.131–0.887	0.027
Coronary artery disease	1.376	0.698–2.716	0.357	1.999	0.494–8.091	0.332
CRT	1.102	0.274–4.439	0.891	2.673	0.167–42.794	0.487

BMI body mass index, *CRP* c-reactive protein, *CRT* coronary revascularization therapy, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *eGFR* estimated glomerular filtration rate, *HDL-C* high-density lipoprotein cholesterol, *RAS* renin angiotensin system

analysis. Few cardiac death events during the follow-up period may lead to insufficient statistical power for analysis. However, a possible explanation can be raised for this issue. The first possible explanation is that the patients with MPI screening may be a special sub-cohort who pays more attention to their own health, compared to the patients without the screening. Although it is a matter of speculation, screening for CAD at the initiation of dialysis could be a trigger to alert patients to be vigilant regarding their overall health. This would be a reason why the screening might exert a more beneficial effect on improving prognosis for all-cause mortality than for cardiac death.

The second possible explanation may relate to the results of our previous study [26]. In that study, we analyzed the survival rates for major adverse cardiac events in incident dialysis patients without CAD and found that even in patients without significant CAD, cardiac events occurred after 1 year of starting dialysis. We have proposed to administer a second screening for CAD at least 2 years after starting dialysis, even if no significant CAD was confirmed at the initiation of dialysis. It is

Table 4 Freedom from events of MPI

	Crude			Propensity score adjusted		
	HR	95 % CI	*p* value	HR	95 % CI	*p* value
All cause of death	0.581[a]	0.352–0.959[a]	0.034[a]	0.568	0.347–0.932	0.025
Cardiac death	0.419[b]	0.157–1.118[b]	0.082[b]	0.491	0.175–1.377	0.177

CRP c-reactive protein, *SBP* systolic blood pressure, *eGFR* estimated glomerular filtration rate, *RAS* renin angiotensin system
[a]Adjusted by age, SBP, albumin, hemoglobin, eGFR, calcium, CRP, and RAS inhibitor
[b]Adjusted by age, eGFR, and CRP, *MPI* myocardial perfusion imaging

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conceivable that a higher number of physician visits may be made by patients who underwent a first screening compared with the patients without screening; consequently, the mortality rate may decrease in the patients who undergo screening for CAD.

The third possible explanation is attempts to lower the rate of cardiac death. Twenty-seven patients among the 164 (16.4 %) who received screening suffered from CAD in the present study. Physicians may pay more attention and add intensive treatment to those patients to improve prognosis. In fact, it was found that the 5-year survival rate of the 27 ESKD patients with CAD was 74.9 %, which is not inferior to the 5-year survival rate of 74.9 % in the 137 ESKD patients without CAD. The 1-year survival rate showed a large difference (26.7 vs. 64.5 %) between patients with and without CAD. On the other hand, in the 60 ESKD patients without the screening, approximately 10 patients (about 16.5 %) were calculated to have suffered from CAD if the same prevalence in the 164 ESKD patients with the screening had occurred. Failure to pay attention and insufficient management in those 10 patients may have played a role, at least in part, in poor prognosis for all-cause mortality. However, the possible advantages of screening on prognosis could not be fully explained based only on the difference in management of CAD.

The fourth possible explanation of greater benefit for all-cause mortality than for cardiac death is the potential for selection bias. The design of our study was an observational cohort study, not a randomized prospective study. It cannot be denied that relatively low-risk patients were selected and underwent the screening by chance. In order to minimize the selection bias, according to the analytical technique used in the present study, we calculated the propensity score by using all background factors to adjust for differences in baseline characteristics. As shown in Table 4, an approximately 50 % risk reduction for death engendered by the screening appeared even after adjusting the propensity score. Therefore, it is more plausible that screening at the initiation of dialysis could lead to a better prognosis for incident dialysis than ever before.

The timing of screening in CKD patients

To improve the prognosis of hemodialysis patients, the best goal we should reach is to start dialysis without any cardiovascular complication. Therefore, we think that the screening should be performed in earlier predialytic phase of CKD such as CKD 3 or 4. The initiation of HD as timing for screening may be too late. This would be a reason why the beneficial effect of MPI screening at the initiation of dialysis on cardiac mortality in this study showed marginal.

Limitations

The present study had some limitations. In order to accurately evaluate the effects of screening on prognosis, a prospective randomized controlled study is the gold standard. However, based on the recommendations of international guidelines [11, 12], it is impossible to plan a study in which the patients are randomly divided according to whether screening is performing. We felt constrained to use the propensity score adjustment method to prove our hypothesis. Another limitation was that this was a single-center observational study with a relatively small number of patients. A larger-scale study should be conducted in the future.

Conclusions

Screening for CAD at the initiation of dialysis could lead to better prognosis after starting dialysis. This finding is considered to be in line with the recommendation of international guidelines [11, 12]. A larger-scale randomized controlled study is needed to confirm this finding.

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