Original Article

Korean J Transplant 2022;36:187-196
https://doi.org/10.4285/kjt.22.0029

KJT
KOREAN JOURNAL OF TRANSPLANTATION

pISSN 2671-8790
eISSN 2671-8804

Cardiac evaluation for end-stage kidney disease patients on the transplant waitlist: a single-center cohort study

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Background: Cardiac evaluation before deceased donor kidney transplant (DDKT) remains a matter of debate. Data on Asian countries and countries with prolonged waiting times are lacking. This study aimed to assess the outcomes of patients referred for DDKT after a cardiac evaluation at an Asian tertiary transplant center.
Methods: This single-center retrospective review analyzed patients who were referred for waitlist placement and underwent cardiac stress testing between January 2009 and December 2015. Patients with cardiac symptoms were excluded. The primary outcome was three-point major adverse cardiovascular events (MACE), a composite of non-fatal myocardial infarction, non-fatal stroke, and cardiovascular death.
Results: Of 468 patients referred for DDKT, 198 who underwent cardiac stress testing (myocardial perfusion studies in 159 patients and stress echocardiography in 39 patients) were analyzed. MACE occurred in 20.7% of the patients over a median follow-up of 4.6 years. Cardiac stress tests were positive for ischemia in 19.7% of the patients. Coronary angiography was performed in 63 patients, including 29 patients with diabetic kidney disease and negative cardiac stress tests. Significant coronary artery disease (CAD) was detected in 27 patients (42.8%), of whom 18 underwent revascularization. MACE was associated with significant CAD on coronary angiography in the multivariable analysis. Cardiac stress test results were not associated with MACE. Amongst diabetic patients who had negative cardiac stress tests, 37.9% had significant CAD on coronary angiography.
Conclusions: The cardiovascular disease burden is significant amongst DDKT waitlist candidates. Pretransplant cardiac screening may identify patients with significant CAD at higher risk of MACE.

Keywords: Kidney transplantation; Cardiovascular diseases; Echocardiography, Stress; Myocardial perfusion imaging; Coronary angiography

Received June 23, 2022
Revised August 20, 2022
Accepted August 29, 2022

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HIGHLIGHTS

- A cohort of 198 patients on the kidney transplant waitlist was followed for 4.6 years.
- Major adverse cardiovascular events developed in 20.7% of the patients during follow-up.
- Significant coronary artery disease on cardiac angiography was correlated with major adverse cardiovascular events.

INTRODUCTION

Cardiovascular disease is highly prevalent amongst patients with end-stage kidney disease (ESKD) and remains a leading cause of death amongst kidney transplant recipients [1,2]. Many transplant centers perform pretransplant cardiac screening for patients on the kidney transplant waitlist to detect asymptomatic coronary artery disease (CAD) with the goal of reducing peri-operative and posttransplant cardiovascular complications. Screening may also potentially identify candidates with unacceptably high cardiovascular risk and exclude them from the waitlist, thereby optimizing the allocation of the scarce deceased donor kidneys. Therefore, several guidelines have suggested considering non-invasive cardiac stress testing amongst kidney transplant candidates with significant cardiovascular risk factors [3,4].

However, there is growing disagreement over the utility of cardiovascular screening in kidney transplant candidates [5]. The sensitivity and specificity of non-invasive cardiac stress testing for angiographic CAD may be poorer amongst ESKD patients [3] and may not accurately predict future major adverse cardiovascular events (MACE) [6,7]. Moreover, false-positive results may lead to unnecessary invasive procedures, transplantation delays, or even exclusions from transplantation. Revascularization has also not been shown to improve outcomes in ESKD patients [8], who are also more likely to experience complications following revascularization [9]. Importantly, even patients with established ischemic heart disease have demonstrated better outcomes following transplantation compared to those who remained on dialysis [10], suggesting that exclusion from the waitlist based on CAD alone may not be justified.

Numerous studies have described the outcomes of patients following cardiac stress tests for ESKD patients on the transplant waitlist [11-13]. However, most studies were conducted in North America and Europe, and data from Asian centers are still lacking [14,15]. Given differences in disease epidemiology, cardiovascular risk factors and access to transplantation, the currently available data may not be applicable to Asian centers. Therefore, this study aimed to describe the cardiovascular outcomes of ESKD patients on the deceased donor kidney transplant (DDKT) waitlist at an Asian tertiary transplant center after cardiac evaluations.

METHODS

We conducted this study in compliance with the principles of the Declaration of Helsinki. The study's protocol was reviewed by the SingHealth Centralized Institutional Review Board (CIRB Ref. 2019/2969). As this was a clinical audit of routine clinical care, where participants were not subjected to additional risks or burdens beyond usual clinical practice, ethics review and the requirement for informed consent were waived.

Study Design

This was a single-center, retrospective observational cohort study. All patients on dialysis referred for placement on the DDKT waitlist between 1 January 2009 and 31 December 2015 who had undergone pretransplant cardiac stress testing were included. Patients who had active cardiac symptoms (e.g., angina, exertional dyspnea) were excluded. Cardiac stress testing was performed for patients with cardiovascular risk factors such as advanced age (>50 years old), hypertension, dyslipidemia, smoking, family history of cardiovascular disease, and abnormal electrocardiography, as well as at the discretion of the treating physician. Patients could undergo either stress echocardiography or myocardial perfusion studies based on the physician's discretion and test availability. Patients with abnormal cardiac stress tests were referred to a cardiologist for further evaluation and coronary angiography.

Based on national transplant regulations, a coronary angiogram is required for all patients with ESKD due to diabetes mellitus prior to waitlist placement, regardless of the stress test results. An ejection fraction of <50%, history of CAD requiring revascularization (percutaneous coronary intervention [PCI] or coronary artery bypass grafting [CABG]), cardiac catheterization demonstrating function-

https://doi.org/10.4285/kjt.22.0029

ally significant major coronary artery stenosis (defined as ≥70%) or cerebrovascular accident are also listed as contraindications for waitlist placement. Patients were followed until one of the following occurred: MACE (cardiovascular death, acute myocardial infarction, or ischemic stroke), non-cardiovascular death, kidney transplant, or loss to follow-up.

Baseline Characteristics and Outcomes

Data were extracted from patients' electronic medical records. The baseline characteristics collected included the following: age, sex, ethnicity, cause of ESKD, dialysis vintage (time from the initiation of dialysis to the cardiac stress test), dialysis modality at the time of referral, hypertension, diabetes mellitus, dyslipidemia, smoking status, history of stroke, and history of CAD. Patients were then categorized by the results of stress testing and coronary angiography, if available. Significant CAD on coronary angiography was defined as >50% stenosis in the left main coronary artery or >70% stenosis in the major coronary arteries (i.e., left anterior descending artery, left circumflex artery, or right coronary artery). The primary outcome was the incidence of three-point MACE, a composite outcome of cardiovascular death, acute myocardial infarction, and ischemic stroke, calculated from the date of the stress test.

Statistical Analysis

Descriptive statistics were expressed as median with interquartile range (IQR) for continuous variables and frequencies (%) for categorical variables. The differences between categorical and continuous variables were assessed using the chi-square test and the Mann-Whitney U-test, respectively. Univariable and multivariable Cox proportional-hazards models were used to investigate the effect of variables on the risk of outcomes. A two-tailed P-value <0.05 was considered statistically significant, and 95% confidence intervals (CIs) were reported when appropriate. All missing values were handled by exclusion from relevant analysis without imputation. All statistical analyses were performed with IBM SPSS ver. 28.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Of the 468 patients referred for DDKT waitlist placement

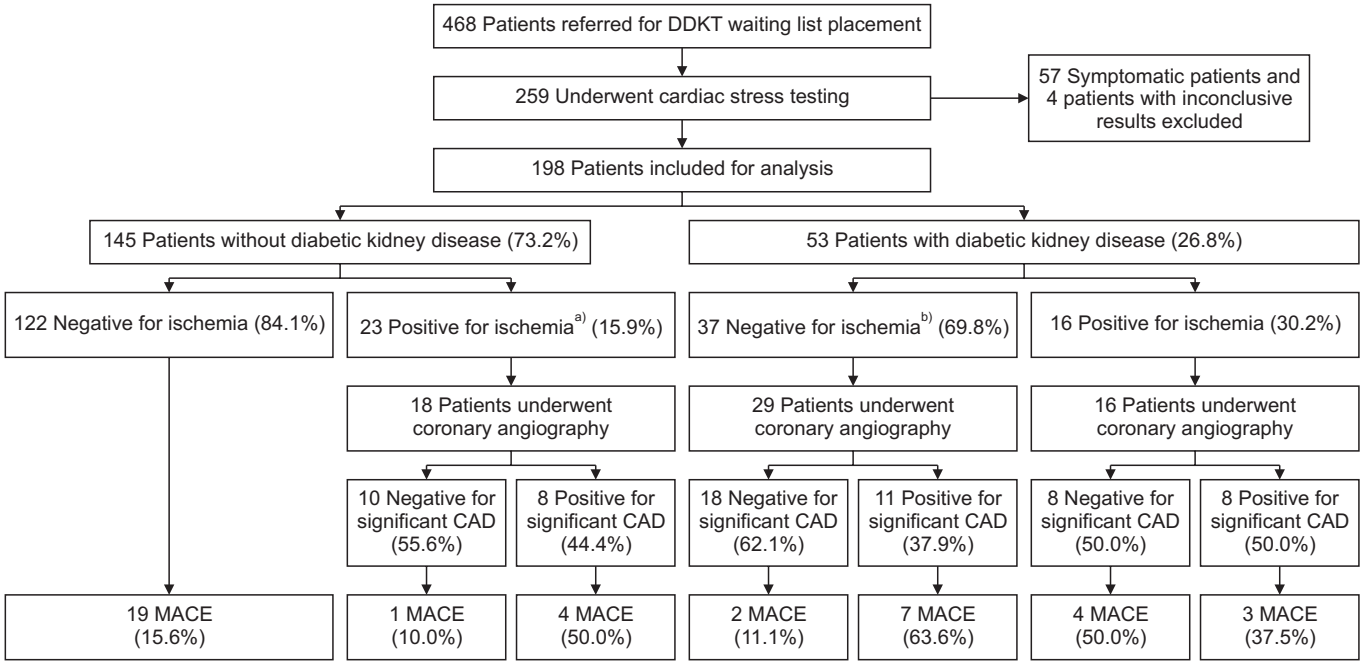

Fig. 1. Cardiovascular outcomes of patients who underwent cardiac stress testing after referral for deceased donor kidney transplant (DDKT) waitlist placement. CAD, coronary artery disease; MACE, major adverse cardiovascular events. [a]Five did not undergo coronary angiography, 0 MACE; [b]Eight did not undergo coronary angiography, 1 MACE.

between 2009 and 2015, 259 patients underwent cardiac stress tests. A total of 198 patients were included after excluding 57 patients with cardiac symptoms and four patients who had inconclusive results but had no further evaluation (Fig. 1). The baseline characteristics of the included patients are summarized in Table 1. The median age was 53 years (IQR, 46–59 years). The leading causes of ESKD were glomerulonephritis (54.5%) and diabetic kidney disease (26.8%). The median duration of dialysis was 3.5 years (IQR, 0.7–7.2 years) at the point of cardiac stress testing.

Stress echocardiography was performed for 39 patients (24 dobutamine and 15 exercise) and stress myocardial perfusion studies were performed for 159 patients (122 dipyridamole, 1 dobutamine, and 36 exercise). The cardiac stress tests were positive for ischemia in 39 (19.7%) patients. Patients who tested positive for ischemia on cardiac stress tests were more likely to be male and to have diabetes (Table 1). Sixty-three patients subsequently underwent coronary angiography, which demonstrated significant CAD in 27 patients (42.8%). Male and older patients were more likely to have significant CAD (Supplementary Table 1).

Table 1. Characteristics of patients who underwent cardiac stress testing after referral for deceased donor kidney transplant waitlist placement according to the presence of ischemia on the cardiac stress test

Characteristic	Total (n=198)	Ischemia (n=39)	No ischemia (n=159)	P-value
Age (yr)	53 (46–59)	53 (44–61)	52 (46–58)	0.71
Male	107 (54.0)	27 (69.2)	80 (50.3)	0.05
Ethnicity				0.82
Chinese	143 (72.2)	28 (71.8)	115 (72.3)	
Malay	45 (22.7)	10 (25.6)	35 (22.0)	
Indian	8 (4.0)	1 (2.6)	7 (4.4)	
Others	2 (1.0)	0	2 (1.3)	
Cause of ESKD				0.13
Glomerulonephritis	108 (54.5)	17 (43.6)	91 (57.2)	
Diabetes mellitus	53 (26.8)	16 (41.0)	37 (23.3)	
Hypertension	10 (5.1)	2 (5.1)	8 (5.0)	
ADPKD	9 (4.5)	0	9 (5.7)	
Others/unknown	18 (9.1)	4 (10.3)	14 (8.8)	
Dialysis modality				0.49
Hemodialysis	164 (82.8)	37 (87.2)	130 (81.8)	
Peritoneal dialysis	34 (17.2)	5 (12.8)	29 (18.2)	
Dialysis vintage (yr)	3.5 (0.7–7.2)	4.0 (0.6–6.5)	3.3 (0.7–7.8)	0.65
Hypertension	181 (91.4)	37 (94.9)	144 (90.6)	0.53
Diabetes mellitus	73 (36.9)	21 (53.8)	52 (32.7)	0.02
Dyslipidaemia	124 (62.6)	28 (71.8)	96 (60.4)	0.20
Current or past smoking	41 (22.8)	12 (32.4)	29 (20.3)	0.13
History of CAD	13 (6.6)	5 (12.8)	8 (5.0)	0.14
History of stroke	4 (2.0)	0	4 (2.5)	1.00
Ejection fraction <50%	34 (18.2)	11 (28.2)	23 (15.5)	0.10

Values are presented as median (interquartile range) or number (%).
ESKD, end-stage kidney disease; ADPKD, autosomal dominant polycystic kidney disease; CAD, coronary artery disease.

The outcomes of the included patients are summarized in Fig. 1. The primary endpoint, MACE, was observed in 41 (20.7%) patients over the median follow-up period of 4.6 years (IQR, 1.9–7.0 years). The observed MACE included 23 acute myocardial infarctions (56.1%), 13 strokes (31.7%), and 5 cardiovascular deaths (12.2%). Of the 36 patients who developed a non-fatal cardiovascular event, 18 (50.0%) subsequently died over a median period of 1.4 years (IQR, 0.2–3.3 years). During the follow-up period, 37 patients (18.7%) were transplanted, with 29 from deceased donors, six from living donors (one of whom was a retransplant) and two overseas kidney transplants. The median time from dialysis initiation (or return to dialysis for the re-transplant) to transplant was 7.4 years (IQR, 4.8–9.0 years). The median waiting time for a DDKT was 8.0 years (IQR, 6.6–9.0 years).

Amongst the 145 patients who did not have ESKD due to diabetes mellitus (Fig. 1), 24 (16.6%) developed MACE over a median follow-up period of 4.6 years (IQR, 1.7–6.9 years). Cardiac stress tests were positive for ischemia in 23 patients (15.9%). MACE developed in 5 (21.7%) patients with positive stress tests, compared with 19 (15.6%) of 122 patients with negative stress tests. Eighteen patients who tested positive for ischemia underwent coronary angiography. Five patients did not undergo coronary angiography, including two patients who refused, two at the discretion of the treating cardiologist, and one for unknown reasons. Significant CAD on coronary angiography was demonstrated in eight patients (44.4%), including three cases of single-vessel disease, three cases of dual-vessel disease, and two cases of triple-vessel disease. Six patients underwent revascularization (all PCI), while the remaining two patients did not undergo revascularization at the discretion of the treating cardiologist. MACE developed in four (50.0%) patients with significant CAD on angiography, compared with only one (10.0%) with a negative coronary angiogram.

Of the 53 patients with ESKD due to diabetes mellitus (Fig. 1), 17 (32.1%) developed MACE over a median fol-

https://doi.org/10.4285/kjt.22.0029

low-up period of 5.5 years (IQR, 2.4–7.9 years). Cardiac stress tests were positive for ischemia in 16 patients (30.2%). MACE developed in seven (43.8%) patients with positive stress tests, compared with 10 (27.0%) of 37 patients with negative stress tests. All 16 patients who tested positive for ischemia underwent coronary angiography. Coronary angiography demonstrated significant CAD in eight patients (50.0%) including three cases of single-vessel disease, two cases of dual-vessel disease and three cases of triple-vessel disease. Four patients underwent revascularization (two PCI and two CABG), while the remaining four patients refused revascularization. Of the 37 patients who tested negative for ischemia on the cardiac stress test, 29 underwent coronary angiography. Eight patients who tested negative for ischemia did not undergo coronary angiography, including six patients who refused and two who developed other contraindications for waiting list placement. Coronary angiography demonstrated significant CAD in 11 patients (37.9%) including five cases of single-vessel disease, one case of dual-vessel disease, and cases of triple-vessel disease. Seven patients underwent revascularization (five PCI and two CABG), while the remaining four patients did not undergo revascularization at the discretion of the treating cardiologist.

In the analysis of the entire cohort (Table 2, Fig. 2), ischemia on the cardiac stress test was not associated with MACE (30.8% vs. 18.2%, P=0.12). More patients with significant CAD on coronary angiography than those without significant CAD developed MACE (51.9% vs. 19.4%, P=0.01). Other factors associated with MACE (Table 3) were older age, previous or current history of smoking, diabetes mellitus, and revascularization. In the multivariable analysis (Table 4), only significant CAD on coronary angiography remained associated with MACE (adjusted hazard ratio, 2.81; 95% CI, 1.02–7.70; P=0.05). Subgroup analyses were not performed due to the limited sample size.

Forty-five patients with ESKD due to diabetes mellitus underwent both a cardiac stress test and a coronary angiogram. Of the 27 patients who tested negative for ischemia, 11 (37.9%) had significant CAD on coronary angiography. Forty-three patients underwent both a myocardial perfusion study and a coronary angiogram. The sensitivity of the myocardial perfusion study for significant CAD

Table 2. Development of MACE based on cardiac stress tests and coronary angiograms

Variable	MACE	No MACE	P-value
Cardiac stress test			0.12
Ischemia	12 (30.8)	27 (69.2)	
No Ischemia	29 (18.2)	130 (81.8)	
Coronary angiography			0.01
Significant CAD	14 (51.9)	13 (48.1)	
No significant CAD	7 (19.4)	29 (80.6)	

Values are presented as number (%).
MACE, major adverse cardiovascular events; CAD, coronary artery disease.

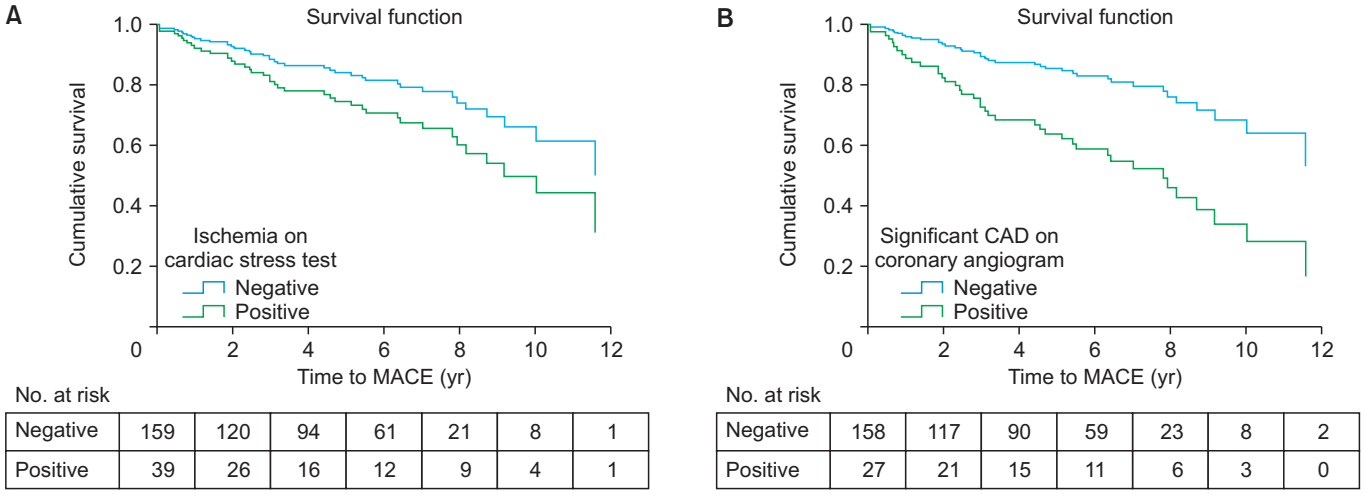

Fig. 2. Kaplan-Meier survival curves for major adverse cardiac events of patients who underwent cardiac stress testing after referral for deceased donor kidney transplant waitlist placement, comparing (A) positive versus negative for ischemia, (B) positive versus negative for significant coronary artery disease. MACE, major adverse cardiovascular events; CAD, coronary artery disease.

Table 3. Characteristics of patients who underwent cardiac stress testing after referral for deceased donor kidney transplant waitlist placement according to the occurrence or non-occurrence major adverse cardiac events

Characteristic	MACE (n=41)	No MACE (n=157)	P-value
Age (yr)	55 (49–60)	52 (44–59)	0.04
Male	25 (61.0)	82 (52.2)	0.38
Ethnicity			0.56
Chinese	28 (68.3)	115 (73.2)	
Malay	10 (24.4)	35 (22.3)	
Indian	3 (7.3)	5 (3.2)	
Others	0	2 (1.3)	
Cause of ESKD			0.20
Glomerulonephritis	18 (43.9)	90 (57.3)	
Diabetes mellitus	17 (41.5)	36 (22.9)	
Hypertension	2 (4.9)	8 (5.1)	
ADPKD	1 (2.4)	8 (5.1)	
Others/unknown	3 (7.3)	15 (9.6)	
Dialysis modality			1.00
Hemodialysis	34 (82.9)	130 (82.8)	
Peritoneal dialysis	7 (17.1)	27 (17.2)	
Dialysis vintage (yr)	1.5 (0.4–6.2)	3.9 (0.8–7.6)	0.13
Hypertension	38 (92.7)	143 (91.1)	1.00
Diabetes mellitus	22 (53.7)	51 (32.5)	0.02
Dyslipidemia	29 (70.7)	95 (60.5)	0.28
Current or past smoking	13 (36.1)	28 (19.4)	0.05
History of CAD	4 (9.8)	9 (5.7)	0.48
History of stroke	1 (2.4)	3 (1.9)	1.00
Ejection fraction <50%	8 (23.5)	26 (17.7)	0.82
Ischemia on the cardiac stress test	12 (29.3)	27 (17.2)	0.12
Significant CAD on coronary angiography	14 (34.1)	13 (8.3)	<0.001
Underwent revascularization	8 (19.5)	9 (5.7)	0.01

Values are presented as median (interquartile range) or number (%).
MACE, major adverse cardiovascular events; ESKD, end-stage kidney disease; ADPKD, autosomal dominant polycystic kidney disease; CAD, coronary artery disease.

was 42.1%, while the specificity was 66.7%. The myocardial perfusion study results were not associated with the presence of significant CAD on coronary angiography (P=0.75). Only two patients underwent both stress echocardiography and coronary angiography, and an analysis was not performed.

DISCUSSION

Over a median follow-up of almost 5 years, 20.7% of our cohort developed MACE, including 2.5% who developed cardiovascular death. Amongst those who suffered non-fatal events, 50% passed away within a median duration of less than 1.5 years. Of the patients who underwent cardiac stress testing, 19.7% tested positive for ischemia, out of whom 41.0% were found to have significant CAD on coronary angiography. Amongst the patients with diabetic kidney disease and negative cardiac stress tests, 37.9% had significant CAD. Amongst the patients with significant CAD on coronary angiography, 51.9% developed MACE during follow-up, compared to 19.4% for those without significant CAD. Only significant CAD on coronary angiography remained associated with the development of MACE in the multivariable analysis.

Similar to previous studies, our study demonstrated a significant cardiovascular disease burden in potential kidney transplant recipients, with a sizeable proportion developing MACE on follow-up. In a previous systematic review, the pooled rates of MACE for cohorts who underwent myocardial perfusion studies or dobutamine stress echocardiography were 9.7% and 11.1%, respectively, while the pooled rates of cardiovascular death were 7.8% and 6.4%, respectively, with a high degree of heterogeneity amongst the included studies [16]. Differences in study designs, the prevalence of pre-existing cardiovascular

Table 4. Cox regression analysis of factors associated with major adverse cardiovascular events

Variable	Univariable model			Multivariable model		
	HR	95% CI	P-value	Adjusted HR	95% CI	P-value
Age, per year	1.04	1.01–1.08	0.02	1.03	1.00–1.07	0.09
Diabetes mellitus	1.69	0.91–3.13	0.10	1.32	0.61–2.83	0.48
Current or past smoking	1.99	1.01–3.93	0.05	1.43	0.70–3.04	0.36
Significant CAD on coronary angiography	2.93	1.53–5.60	0.001	2.81	1.02–7.70	0.05
Underwent revascularization	2.24	1.03–4.89	0.04	0.78	0.25–2.41	0.69

HR, hazard ratio; CI, confidence interval; CAD, coronary artery disease.

https://doi.org/10.4285/kjt.22.0029

disease and cardiovascular risk factors, screening protocols, treatment regimens, and the duration of follow-up likely contribute to differences in MACE and cardiovascular death rates. In our cohort, the MACE rates may have been higher despite a lower prevalence of pre-existing cardiovascular disease at baseline, due to a higher proportion of patients with diabetes mellitus and a longer follow-up duration. Regardless, given the significant cardiovascular burden amongst potential kidney transplant candidates, it remains important to identify high-risk candidates to optimize risk, provide risk counselling to potential recipients and donors where appropriate, and improve the allocation of scarce donor kidneys.

Our study suggests that significant CAD detected on coronary angiography in asymptomatic ESKD patients during the pretransplant evaluation may be associated with poorer cardiovascular outcomes. Moreover, the association remained significant after adjustment for cardiovascular risk factors, such as age, history of smoking and diabetes mellitus, and revascularization. Previous studies and a systematic review have also demonstrated that CAD detected on pretransplant cardiac screening can be associated with poorer cardiovascular outcomes both before and after kidney transplantation [16,17]. At the same time, our results also highlight that MACE in the absence of CAD on coronary angiogram can be substantial. Microvascular ischemia, volume overload, and arrhythmias, likely attributable to ESKD and diabetes mellitus, may contribute to the adverse cardiovascular outcomes in these patients [1].

Conversely, our study did not demonstrate an association between the results of cardiac stress tests and cardiovascular outcomes. Numerous studies have attempted to investigate the prognostic value of cardiac stress tests, with mixed results [16]. However, it may be difficult to ascertain the prognostic value of cardiac stress tests given the effect of potential confounders, including differences in pre-existing risk factors and the effects of treatment after the cardiac stress test, such as revascularization and more aggressive risk factor control. The accuracy of cardiac stress tests in predicting angiographic CAD amongst ESKD patients may be suboptimal [18,19].

In our study, patients with diabetic kidney disease underwent coronary angiography prior to waitlist placement, regardless of the stress test results, due to the requirements of the national transplant regulations. An analysis of this subgroup demonstrated the suboptimal performance of cardiac stress tests in detecting significant angiographic CAD. One proposed mechanism to explain the limited accuracy of cardiac stress tests is that ESKD patients may be more likely to exhibit "balanced" ischemia due to multivessel disease, which causes myocardial perfusion studies to be misleadingly normal [20]. It is also known that some stenoses that appear angiographically significant may not have a functional effect on blood flow, resulting in a normal stress test. As also shown in our diabetic subgroup, patients with ischemia on the cardiac stress test may have poorer outcomes, even if they tested negative for significant CAD on coronary angiography, and coronary microvascular ischemia may contribute to this pattern [21]. Therefore, it is important for clinicians to interpret the results of cardiac stress testing in ESKD patients with caution and to consider confirmatory coronary angiography, particularly for high-risk patients.

Some have argued against pretransplant screening for CAD in asymptomatic kidney transplant candidates given the suboptimal accuracy and prognostic value of cardiac stress tests in potential kidney transplant recipients [5]. Moreover, a previous randomized controlled trial and systematic review did not demonstrate an improvement in outcomes for patients with advanced chronic kidney disease with abnormal cardiac stress tests who underwent coronary angiography and revascularization compared to optimal medical therapy [8,22]. This is potentially because a significant proportion of ESKD patients experience adverse cardiovascular outcomes secondary to mechanisms other than CAD, such as arrhythmias from electrolyte abnormalities and volume overload [1]. Furthermore, patients with kidney disease have a higher risk of complications during coronary angiography, such as acute kidney injury or cholesterol embolism [23].

However, other studies have suggested that cardiac stress test results can predict outcomes in patients at lower risk of CAD and help avoid unnecessary coronary angiography [13]. The lack of benefit for revascularization may also be related to the poor accuracy of cardiac stress tests in detecting obstructive CAD. This can occur when the potential beneficial impact of revascularization becomes diluted if a significant proportion of patients undergoing coronary angiography for abnormal cardiac stress tests do not actually require revascularization [8]. Improved screening strategies with better patient selection and the use of alternative screening modalities, such as coronary computed tomography (CT) angiography and positron emission tomography/CT myocardial perfusion imaging may be useful, but more studies are needed to

determine the optimal screening strategy [24,25].

Additionally, most current studies have a short duration of follow-up. Given that the prognostic performance of pretransplant cardiac screening and benefits of revascularization may be better demonstrated in studies with a longer duration of follow-up [8,16], current studies may not be adequate, especially for countries with prolonged waiting times. It has also been suggested that patients with severe ischemia on cardiac stress tests may still benefit from revascularization [8]. Importantly, the optimized control of cardiovascular risk factors in a clinical trial may be difficult to replicate in real-world settings [26]. Therefore, there may still be value in coronary angiography screening and subsequent revascularization for selected potential transplant candidates. Interest has also recently emerged in the use of fractional flow reserve to guide revascularization, although more studies are needed to evaluate its utility [27].

Although our study did not demonstrate associations of age, diabetes mellitus, and history of smoking with future cardiovascular events in the multivariable analysis, these traditional risk factors likely remain important during the cardiovascular risk assessment and management of ESKD patients. Previous studies have shown that these factors not only confer a risk of cardiovascular complications in ESKD patients, but may also be more prevalent amongst ESKD patients than in the general population [28,29].

Given its retrospective and single-center nature, the current study is subject to confounding and its generalizability may be limited. Data on certain interventions (e.g., blood pressure control) and other cardiovascular risk factors (e.g., mineral bone disease) were not available. Additionally, myocardial perfusion studies and stress echocardiography were analyzed together despite possible differences in test performance [11]. We were not able to perform a subgroup analysis based on the type of stress test due to the limited sample size. However, a recent meta-analysis did not demonstrate the superiority of one modality over another for predicting all-cause mortality, cardiovascular mortality, and MACE [16]. Our protocol also did not include alternative screening modalities such as CT coronary angiography. Despite these limitations, the present study is one of the few studies done in Asia with a longer duration of follow-up. Of the 52 studies included in a previous systematic review, only two studies had a median follow-up duration of 4 years or longer and only one study was performed in Asia [16].

In summary, there was a high cardiovascular burden amongst ESKD patients on waitlist, leading to poor pre- and posttransplant outcomes. Therefore, it remains important to identify high-risk individuals to optimize pretransplant risk and allocation of scarce donor kidneys. While the performance of cardiac stress tests and the optimal screening strategy may be unclear, pretransplant cardiac screening may help identify patients with significant CAD, which can predict poorer outcomes amongst ESKD patients on the kidney transplant waitlist. Further studies are required to determine the optimal cardiovascular screening strategy for potential kidney transplant recipients [30].

ACKNOWLEDGMENTS

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Additional Contributions

The authors would like to thank the staff at SingHealth

https://doi.org/10.4285/kjt.22.0029

Duke-NUS Transplant Centre for their assistance.

Supplementary Materials

Supplementary materials can be found via https://doi.org/10.4285/kjt.22.0029.

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https://doi.org/10.4285/kjt.22.0029