Prediction of long-term (> 10 year) cardiovascular outcomes in heart transplant recipients: Value of stress technetium-99m tetrofosmin myocardial perfusion imaging

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Background. **Myocardial perfusion imaging (MPI) using single-photon emission computed tomography (SPECT) is useful in the evaluation of cardiac allograft vasculopathy (CAV) in heart transplant (HTx) recipients. The current study evaluated the long-term prognostic value of stress SPECT MPI for predicting all-cause mortality and cardiac events in HTx recipients.**

Methods. **The study population consisted of 166 HTx recipients (mean age 54 ± 10 years, 84% male) who underwent exercise or dobutamine stress ^{99m}Tc-tetrofosmin SPECT MPI for the assessment of CAV. An abnormal SPECT MPI was defined as the presence of a fixed or a reversible perfusion defect. Endpoints were all-cause mortality, cardiac mortality, and non-fatal myocardial infarction (MI).**

Results. **MPI abnormalities were detected in 55 patients (33%), including fixed defects in 28 patients (17%), partially reversible in 17 patients (10%), and completely reversible defects in 10 patients (6%). During a median follow-up of 12.8 years (range 0-15, mean follow-up 9.5 years), 109 (66%) patients died (all-cause mortality), of which 67 (40%) were due to cardiac causes. A total of 5 (3%) patients experienced a non-fatal MI. HTx recipients with a normal stress ^{99m}Tc-tetrofosmin SPECT MPI had a significantly better prognosis as compared with those with an abnormal study, up to 5 years after the initial test. The presence of a reversible perfusion defect was a significant predictor of all-cause mortality, cardiac mortality, and major cardiac events, during the entire follow-up period.**

Conclusions. **Stress ^{99m}Tc-tetrofosmin SPECT MPI provides valuable prognostic information for the prediction of long-term outcome in HTx recipients. Patients with a normal stress ^{99m}Tc-tetrofosmin SPECT MPI have a significantly better prognosis as compared with those with an abnormal study, up to 5 years after initial testing. (J Nucl Cardiol 2019;26:845–52.)**

Key Words: Heart transplant recipients • cardiac allograft vasculopathy • long-term prognosis • stress SPECT MPI

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Abbreviations

CA	Coronary angiography
CAD	Coronary artery disease
CAV	Cardiac allograft vasculopathy
IVUS	Intravascular ultrasound
HTx	Heart transplantation
MBq	Megabecquerel
MI	Myocardial infarction
MPI	Myocardial perfusion imaging
SPECT	Single-photon emission computed tomography
^{99m}Tc	Technetium-99m

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INTRODUCTION

Heart transplantation (HTx) is the first choice in treatment of patients with end-stage heart failure. However, the long-term outcome is severely hampered by cardiac allograft vasculopathy (CAV), occurring up to 50% of the patients[1] and is associated with an increased risk of mortality.[2–4] As a result of denervation of the transplanted heart, angina symptoms resulting from CAV are usually absent and the first clinical sign of CAV can be heart failure, myocardial infarction, ventricular arrhythmias, or sudden death.[5] Serial coronary angiography (CA) and intravascular ultrasound (IVUS) are used for the evaluation of significant CAV.[6] However, these are invasive procedures with inherent risks. Among noninvasive modalities, myocardial perfusion imaging (MPI) using single-photon emission computed tomography (SPECT) is a useful clinical tool to evaluate CAV. Several studies have demonstrated that stress SPECT MPI has diagnostic and prognostic value in HTx recipients.[7–9] However, information regarding the value of stress SPECT MPI for the prediction of long-term cardiovascular outcomes in HTx recipients is limited.[10] Due to the relatively high prevalence and progression of CAV in these patients,[1] the long-term prognostic value of stress SPECT MPI may be impaired. This creates uncertainties in the clinical management of these patients. Accordingly, the aim of this study was to assess the long-term prognostic value of stress SPECT MPI for predicting all-cause mortality and cardiac events in HTx recipients.

METHODS

Patient Selection

The study population consisted of 166 HTx recipients who underwent exercise ($n = 65$) or dobutamine ($n = 101$) stress SPECT MPI, more than 2 years after transplantation (mean of 7.4 ± 2.5 years after transplantation) at the Thoraxcenter, Rotterdam, The Netherlands between 1992 and 1998. At the time of this study, these nonselected HTx recipients underwent SPECT as a part of our standard protocol. The current study details the results of a long-term follow-up from a prior study at our center.[11] The reason for performing this repeat follow-up study was to assess the long-term (>10 year) prognostic value of stress SPECT MPI in HTx recipients. Follow-up was successful in all of the 166 patients. The Hospital Ethics Committee approved the study protocol. The study was conducted according to the Helsinki Declaration.[12] All patients consented to participation in this study. Before the stress test, a structured interview and clinical history were obtained, including assessment of cardiac risk factors. Hypertension was defined as a blood pressure of ≥140/90 mmHg or treatment with antihypertensive medication. Diabetes mellitus was defined as a fasting glucose level of ≥ 7.8 mmol/L or the need for insulin or oral hypoglycemic agents. Hypercholesterolemia was defined as a total cholesterol of ≥6.4 mmol/L or treatment with lipid-lowering medication.

Stress Test Protocol

The exercise or dobutamine stress test was performed as described previously.[11] At the time of this study dobutamine was the preferred stressor in our nuclear cardiology laboratory. Dobutamine was infused through an antecubital vein starting at a dose of 5 μg/kg/min, followed by 10 μg/kg/min at 3 minutes, increasing by 10 μg/kg/min every 3 minutes to a maximum of 40 μg/kg/min. Atropine was given to patients who could not achieve the 85% age-predicted heart rate at the maximal dobutamine dose. The test was discontinued if severe chest pain, ST-segment depression >2 mm, significant arrhythmia, hypertension (blood pressure ≥240/120 mmHg), systolic blood pressure decrease of >40 mmHg, or any intolerable side effect regarded as being due to dobutamine occurred during the test. Metoprolol (1 to 5 mg) was used intravenously to reverse the adverse effects of dobutamine/atropine. An ischemic electrocardiographic response was defined as ≥ 1 mm horizontal or downsloping ST-segment depression persisting 80 ms after the J point.

Symptom-limited upright bicycle ergometry test was performed with stepwise increments of 20 W each minute. Blood pressure and electrocardiographic recordings were performed as described for the dobutamine stress test.

SPECT MPI

The single-photon emission computed tomography protocol has been described previously.[11] An intravenous dose of 370 MBq of technetium-99m tetrofosmin (Myoview, Amersham, Buckinghamshire, United Kingdom) was administered approximately 1 minute before the termination of the dobutamine or the exercise stress test.[13] Acquisition of images began 1 hour after the stress test. For studies taken at rest, images were acquired 24 hour after the stress study,

1 hour after injection of 370 MBq of tetrofosmin. Image acquisition was performed with a triple-head gamma camera system (Picker Prism 3000 XP, Cleveland, Ohio). For each study, 6 oblique (short-axis) slices from the apex to the base and 3 sagittal (vertical long-axis) slices from the septum to the lateral wall were defined. Each of the 6 short-axis slices was divided into 8 equal segments. The interpretation of the scan was semiquantitatively performed by visual analysis assisted by circumferential profiles analysis. Stress and resting tomographic views were reviewed side by side by an experienced observer who was unaware of the patients' clinical data. A reversible perfusion defect was defined as a perfusion defect on a stress image that partially or completely resolved at rest in ≥2 contiguous segments or slices. A fixed perfusion defect was defined as a perfusion defect on stress images in ≥ 2 contiguous segments or slices that persisted on images taken at rest. An abnormal study was considered in the presence of a fixed and/or reversible perfusion defect. To assess the severity of perfusion abnormalities, the left ventricular myocardium was divided into 6 segments: anterior, inferior, septal anterior, septal posterior, posterolateral, and apical. Each of the 6 major left ventricular segments was scored using a 4-grade method (0 = normal, 1 = mildly reduced, 2 = moderately reduced, and 3 = severely reduced or absent uptake). The perfusion defect scores were derived by the summation of the score of the six myocardial segments at stress [summed stress score (SSS)]. The difference between the summation of the scores at rest and at stress was expressed as the summed difference score (SDS). These indices were expressed as the percent of the total myocardium (% myocardium) as described previously.[14]

Patient Follow-Up

Follow-up data were obtained in 2011. The patient's survival status was determined by contacting the municipal civil registry. For those patients who were still alive, follow-up was obtained by contacting the patients, the patient's general practitioner or by reviewing hospital records. The date of the last review or consultation was used to calculate the follow-up time. Endpoints were all-cause mortality, cardiac mortality, and non-fatal myocardial infarction (MI). Causes of death were obtained from the Central Bureau of Statistics Netherlands (www.cbs.nl). Cardiac mortality was defined as death caused by acute myocardial infarction, significant cardiac arrhythmias, or refractory congestive heart failure. Sudden death occurring without another explanation was included as cardiac mortality. Major cardiac events were defined as cardiac mortality and non-fatal MI.

Statistical Analysis

All statistical analyses were performed using SPSS, version 21.0 (Chicago, IL, USA). Continuous data were expressed as mean value ± SD and compared using the Student's t test. Categorical data were expressed in numbers and percentages and compared using the Chi-squared test. The probability of survival was calculated using the Kaplan–Meier method. Survival curves were compared using the log-rank test. To investigate whether SPECT MPI has additional prognostic value in predicting long-term prognosis, the Cox proportional-hazards regression model was used. To determine the perishable date of SPECT MPI in HTx recipients, the Kaplan–Meier method and multivariable analysis were repeated at 1, 2, 3, and so on years of follow-up. The risk of a variable was expressed as a hazard ratio (HR) with a corresponding 95% confidence interval (CI). The incremental value of SPECT MPI over the clinical variables in the prediction of the endpoints of interest was performed according to 4 models. In Model 1, the presence of an abnormal SPECT MPI was entered. In Model 2, the presence of a reversible or fixed defect was entered. In Model 3, the variable entered was SDS and in Model 4, the variable entered was SSS. The predictive value of each model was expressed using the Chi-squared statistic.

RESULTS

Clinical Characteristics

The baseline characteristics of the 166 patients are presented in Table 1. Mean age was 54 ± 10 years and 84% of the patients were male. SPECT MPI findings were normal in 111 patients (67%). Myocardial perfusion abnormalities were fixed in 28 patients (17%), partially reversible in 17 patients (10%), and completely reversible defects in 10 patients (6%). During the stress test, there was a significant increase in heart rate (93 ± 13 to 140 ± 17 beats per minute, $P < .001$) and systolic blood pressure (146 ± 18 to 166 ± 30 mmHg, $P < .001$). Two patients developed atypical and 1 patient developed typical chest pain during the stress test. A total of 117 patients (70%) reached the target heart rate (85% of the age-predicted maximal exercise heart rate). Minor side effects of dobutamine administration included nausea in 3 patients (3%), flushing in 4 patients (4%), headache in 5 patients (5%), and chills in 3 patients (3%). Non-sustained ventricular tachycardia during exercise stress testing was observed in 1 patient.

Patient Outcomes

During a median follow-up time of 12.8 years (range 0-15 mean follow-up 9.5 years), 109 (66%) patients died (all-cause mortality), of which 67 (40%) were due to cardiac causes. A total of 5 (3%) patients experienced a non-fatal myocardial infarction. Kaplan–Meier survival curves for all-cause mortality, cardiac mortality and major cardiac events are presented in Figures 1, 2, and 3, respectively. The survival curves showed a significantly better long-term survival of HTx recipients with a normal SPECT MPI compared to patients with an abnormal SPECT MPI (annualized all-cause mortality rate: 9% vs 15% at 3 years, 8% vs 11% at 6 years and 6% vs 9% at 9 years, overall $P = .011$, Figure 1). To determine up to what time point during follow-up the stress SPECT MPI holds its prognostic value, the log-rank test was performed at subsequent follow-up durations (Figures 1, 2, 3). This analysis demonstrated that HTx recipients with a normal stress SPECT MPI had a significantly better prognosis as compared with those with an abnormal stress SPECT MPI, up to 5 years after the test is performed for all-cause mortality. The ''warranty period'' of stress SPECT MPI in HTx recipients for the prediction of all-cause mortality was approximately 5 years. According to cardiac mortality and major cardiac events, patients with a normal stress SPECT MPI had a significantly better prognosis as compared with patients with an abnormal stress SPECT MPI, up to 2 years and 1 year after testing, respectively.

Predictors of Long-Term Outcome

Univariable and multivariable predictors of all-cause mortality are summarized in Table 2. Based on the maximum length of prognostic value at Kaplan–Meier analysis, the univariable and multivariable predictors are shown at a follow-up duration of 5 years. Univariable predictors of all-cause mortality were age, gender, and an abnormal SPECT MPI (Table 2). The presence of a reversible perfusion defect and SDS were univariable predictors of cardiac mortality and an abnormal SPECT MPI, the presence of a reversible perfusion defect and SDS were univariable predictors of major cardiac events.

Multivariable analyses were performed to determine the maximum length of the prognostic value, or the 'warranty period,' of SPECT MPI. An abnormal SPECT MPI and the presence of a reversible defect provided incremental prognostic information for the prediction all-cause mortality up to a follow-up duration of 5 years (Table 2). An abnormal SPECT MPI provided incremental prognostic information for the prediction of cardiac mortality up to a follow-up duration of 2 years. The presence of a reversible defect was a significant predictor of cardiac mortality during the entire follow-up. For the prediction of major cardiac events, an abnormal SPECT MPI was a significant predictor up to 2 years of follow-up. The presence of a reversible defect was a significant predictor of major cardiac events during the entire follow-up duration.

Table 1. Clinical characteristics ($n = 166$)

Age (years)	54 ± 10
BMI (kg/m^2)	26.4 ± 4.5
Male gender	140 (84%)
Hypertension	117 (71%)
Diabetes mellitus	18 (11%)
Smoking	24 (15%)
Hypercholesterolemia	70 (42%)
Beta blocker use	23 (14%)
Target heart rate reached[a]	117 (70%)

Data are presented as mean ± SD or numbers (percentages)
BMI, body mass index
[a]Target heart rate reached is defined as 85% of the maximal predicted heart rate

DISCUSSION

The present study evaluated the long-term prognostic value of SPECT MPI in HTx recipients, examining the incremental prognostic value of SPECT MPI over clinical and stress test variables. The results show that stress SPECT MPI provides useful prognostic information for the prediction of cardiovascular outcomes in HTx recipients. HTx recipients with a normal stress SPECT MPI have a significantly better prognosis as compared to patients with an abnormal stress SPECT MPI, up to 5-years after initial testing. After that period, the risk of adverse events does not significantly differ in patients with both normal and abnormal SPECT MPI. So, the warranty period of stress SPECT MPI in HTx

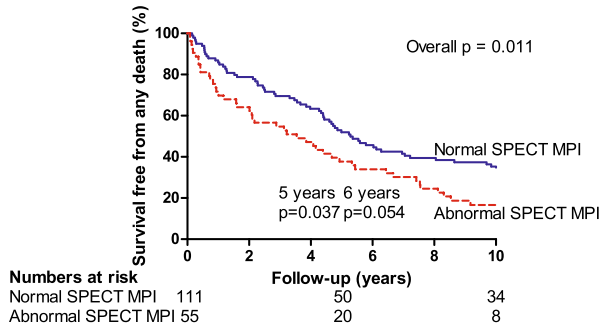

Figure 1. Kaplan–Meier event-free survival for all-cause mortality in HTx recipients with normal and abnormal SPECT MPI.

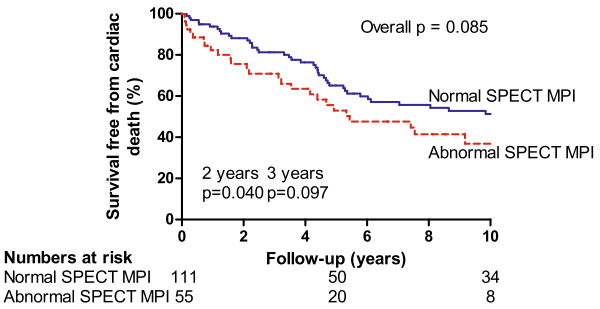

Figure 2. Kaplan–Meier event-free survival for cardiac mortality in HTx recipients with normal and abnormal SPECT MPI.

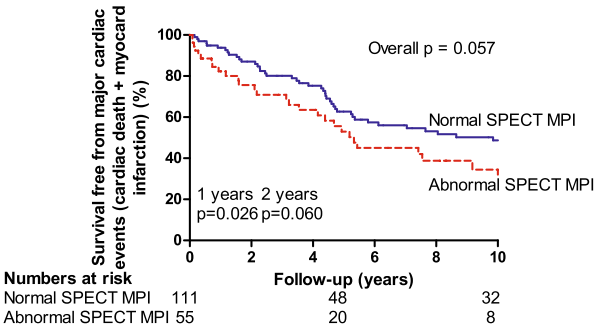

Figure 3. Kaplan–Meier event-free survival for major cardiac events in HTx recipients with normal and abnormal SPECT MPI.

recipients is approximately 5 years. As the multivariable analysis showed, the presence of a reversible perfusion defect was a significant predictor of all-cause mortality and cardiac events during the entire follow-up.

SPECT MPI using either exercise or pharmacological stress is a commonly used noninvasive technique for the evaluation of known or suspected CAD. The prognostic value of dobutamine stress SPECT MPI has been firmly established in non-transplant patients.[15–17] However, there are scarce data regarding the utility of stress SPECT MPI for the prediction of long-term outcome in HTx recipients.[10] This creates uncertainties in the prognostic stratification in these patients. Previous studies have reported the short- and medium-term outcome of SPECT MPI in HTx recipients.[10,11,18–20] Bacal et al.[18] studied 39 patients (mean age was 48 ± 13 years) after orthotopic HTx who underwent thallium SPECT MPI for the detection of CAV. In this small number of patients, thallium SPECT MPI was not a significant predictor of outcomes during the 4-year follow-up period. Hacker et al.[8] followed 77 HTx recipients with a mean age of 53 ± 11 years (80% males) who underwent dobutamine stress technetium SPECT MPI. Cardiac events (revascularization, heart failure, death and/or MI) occurred in 32% of the patients with an abnormal SPECT MPI during a mean follow-up duration of 22 months. The authors concluded that dobutamine stress SPECT MPI identified patients at risk for future cardiac events. A normal SPECT MPI was associated with a negative predictive value of 98% for cardiac events. Wu et al.[20] investigated the value of dobutamine thallium SPECT to detect CAV and to predict clinical events in 47 HTx recipients. Mean age was 51.6 ± 11.7 years (79% males). During a mean follow-up period of 40 months, a total of 6 patients died, of whom 4 patients due to cardiac causes. Only large reversible perfusion defects on stress SPECT MPI were associated with a significant risk of cardiac mortality ($P = .002$). In 110 HTx recipients, Manrique et al.[19] investigated the diagnostic and prognostic value of thallium and technetium SPECT MPI. Mean age was 53 ± 13 years (85% males). During a mean follow-up period of 4.8 years, a stress perfusion defect > 3 segments was an independent predictor of cardiac mortality. SPECT MPI identified patients with a high risk of poor outcome. As the authors noted, a normal SPECT MPI might alleviate the need for coronary angiography. More recently, Wenning et al.[10] studied 104 HTx recipients (mean age 50.7 ± 12.2 years and 85% were male) who underwent ^{99m}Tc-tetrofosmin SPECT. During a mean follow-up of 9.4 years, no difference was observed according to all-cause mortality between patients with homogeneous perfusion (defined as < 10% decreased tracer uptake of the myocardial segments) and inhomogeneous perfusion (defined as decreased tracer uptake of > 20% of the myocardial segments).

The present study differs from these previous studies for several reasons. First, these previous studies used thallium-201,[18,20] ^{99m}Tc-tetrofosmin,[10] ^{99m}Tc-sestamibi[8] or both thallium-201 and ^{99m}Tc-sestamibi[19] as radionuclide tracers. The current study evaluated SPECT MPI in HTx recipients using ^{99m}Tc-tetrofosmin as a tracer, which is currently the most commonly used tracer along with ^{99m}Tc-sestamibi.[21] Second, some of these previous studies [8,19,20] concluded that SPECT MPI provides prognostic information for the prediction of cardiac events in HTx recipients, whereas other studies found no significant prognostic information.[10,18] The latter studies[10,18] had a relatively longer follow-up period (9.4 and 4 years, respectively). All these previous studies have not investigated the warranty period of stress SPECT MPI in HTx recipients. The current study found that the warranty period of stress SPECT MPI in HTx recipients is approximately 5 years. Third, the range of follow-up duration in these previous studies varies between 22 months and 9.4 years. In a previous study of our center, [11] the same population was studied with a median follow-up of 2.5 years. The current study evaluated the long-term outcome (> 10 years) after

Table 2. Univariable and multivariable predictors of all-cause mortality at 5-year follow-up

		Multivariable					
Parameter	**Univariable**	**Clinical variables**	**Clinical and stress variables**	**Model 1**	**Model 2**	**Model 3**	**Model 4**
Age[a]	**1.03 (1.01–1.06)**	**1.04 (0.101–1.06)**	**1.04 (1.01–1.06)**	**1.03 (1.01–1.06)**	**1.03 (1.01–1.06)**	**1.04 (1.02–1.07)**	**1.04 (1.01–1.07)**
Gender	**2.60 (1.20–5.66)**	2.10 (0.94–4.69)	2.13 (0.96–4.76)	2.05 (0.92–4.56)	2.15 (0.97–4.79)	2.06 (0.92–4.64)	1.96 (0.87–4.41)
Diabetes	0.80 (0.39–1.66)	0.64 (0.30–1.35)	0.66 (0.31–1.39)	0.61 (0.29–1.30)	0.61 (2.8–1.29)	0.63 (0.29–1.34)	0.61 (0.29–1.31)
Hypertension	1.14 (0.70–1.85)	1.13 (0.67–1.91)	1.10 (0.65–1.87)	1.24 (0.72–2.14)	1.24 (0.73–2.10)	1.07 (0.61–1.85)	1.08 (0.62–1.89)
Smoking	1.41 (0.79–2.52)	1.54 (0.85–2.79)	1.59 (0.87–2.90)	1.59 (0.87–2.92)	1.52 (0.83–2.79)	1.84 (0.97–3.46)	1.86 (0.98–3.51)
Hypercholesterolemia	0.92 (0.59–1.44)	0.78 (0.49–1.27)	0.77 (0.48–1.25)	0.71 (0.43–1.16)	0.77 (0.47–1.25)	0.80 (0.49–1.31)	0.75 (0.45–1.24)
ST-segment changes	1.26 (0.69–2.28)	-	1.25 (0.67–2.34)	1.20 (0.64–2.26)	1.20 (0.64–2.25)	1.18 (0.62–2.25)	1.24 (0.66–2.34)
Abnormal SPECT MPI	**1.59 (1.02–2.49)**	-	-	**1.61 (1.01–2.56)**	-	-	-
Reversible defect	1.66 (0.96–2.87)	-	-	-	**1.87 (1.03–3.38)**	-	-
Fixed defect alone	1.28 (0.75–2.19)	-	-	-	1.39 (0.78–2.47)	-	-
SDS[b]	1.11 (0.93–1.33)	-	-	-	-	1.15 (0.93–1.41)	-
SSS[b]	1.05 (0.97–1.14)	-	-	-	-	-	1.06 (0.95–1.18)
Total Chi-square	-	16.1	16.5	20.6	20.7	19.3	19.1

Values are expressed as Cox proportional hazard ratio with 95% confidence interval. Bold values are significant
SPECT MPI, single-photon emission computed tomography myocardial perfusion imaging; *SDS*, summed difference score; *SSS*, summed stress score; -, variable excluded
[a]Per unit increment
[b]Per 5.6% of the total myocardium increment

SPECT MPI in HTx recipients and extends the conclusions drawn from these previous studies. The results show that SPECT MPI has a limited predictive value of adverse outcome in these patients. HTx recipients with a normal stress SPECT MPI have a relatively favorable outcome compared to patients with an abnormal stress SPECT MPI up to 5 years after the test. This is in line with previous studies indicating that a warranty period exists after a normal SPECT MPI.[22] CAV apparently is a chronic progressive disease in HTx recipients that may alter the risk status of the patients over time.

In the annually published report of the International Society for Heart and Lung Transplantation (ISHLT), the median survival of HTx recipients between 1982 and 2013 was 11 years.[23] Due to advanced immunosuppressive therapy and prevention and treatment of opportunistic infections survival of patients after HTx has improved.[23,24] The median survival in the present study was 12.8 years. Patients in the current study were enrolled form 1992. So, according to the median survival, the present findings are comparable with this ISHLT report.

Due to denervation of the allograft and incomplete reinnervation, angina pectoris is usually lacking in HTx recipients. First clinical signs of CAV in HTx recipients include heart failure, silent MI, and sudden death.[25] As a consequence, screening for early detection of CAV is required. Therefore, in most centers, HTx recipients undergo an annual or biannual coronary angiography during the first 5 years following cardiac transplantation to search for asymptomatic CAV.[26] However, many HTx recipients with clinical cardiac events do not have significant disease on coronary angiography.[27] Moreover, invasive coronary angiography has inherent risks. As a result, there is a continuing need for noninvasive techniques to evaluate CAV. The results of the current study show that dobutamine stress SPECT MPI is useful in risk stratifying HTx recipients up to 5 years after testing.

The ISHLT guidelines for the care of HTx recipients[28] state that SPECT MPI may be useful for diagnosing CAV in HTx recipients unable to undergo invasive evaluation. The sensitivity of dobutamine SPECT MPI has been reported to be 90% and a specificity of 60% in this patient cohort. The negative predictive value of the test was found to be 79%.[13] During the first 5 years after transplantation annual coronary angiography is recommended. In patients with kidney disease, dobutamine stress echocardiography (DSE) represents an alternative. After 5 years following transplantation, DSE is recommended annually in low-risk patients (defined as normal coronary angiography at 5 years). For patients with poor echocardiographic quality dobutamine stress SPECT MPI is a feasible alternative.[28] There are indications that assessment of myocardial blood flow using positron emission tomography (PET) as an alternative technique is an indicator of CAV in patients after heart transplantation.[29] The present findings support the frequent monitoring of HTx recipients and the role of noninvasive dobutamine stress SPECT MPI in order to avoid coronary angiography when possible. In our center, we conduct in the first and fourth year after HTx a coronary angiogram, followed by yearly SPECT MPI from the sixth year after HTx. CAG was performed after the fourth year if the annual perfusion scintigraphy was positive, or when ischemia was suspected due to cardiac markers or clinical, electrocardiographic or echocardiographic criteria.

This study has some limitations. First, at time of SPECT MPI gated SPECT was not routinely performed. Functional data derived from gated SPECT provide additional information. As a result, left ventricular ejection fraction (LVEF) was not available. Information about LVEF could have improved the analysis of the current study. Second, no attenuation or scatter correction was used for SPECT MPI. Application of attenuation or scatter correction may have further improved the accuracy of this technique. Third, CAV is a major complication associated with higher mortality in HTx recipients.[3] In the present study, angiographic data to examine CAV were not evaluated. However, the endpoints used in this study are cardiac events related to CAV.

In conclusion, stress ^{99m}Tc-tetrofosmin SPECT MPI provides valuable prognostic information for the prediction of outcome in HTx recipients. Patients with a normal stress ^{99m}Tc-tetrofosmin SPECT MPI have a significantly better prognosis as compared with those with an abnormal study, up to 5 years after initial testing.

NEW KNOWLEDGE GAINED

Stress SPECT MPI provides useful prognostic information for the prediction of cardiovascular outcomes in HTx recipients. HTx recipients with a normal stress ^{99m}Tc-tetrofosmin SPECT MPI have a significantly better prognosis as compared with those with an abnormal study, up to 5 years after initial testing.

Disclosure

The authors declare that they have no conflicts of interest to disclose.

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