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Prognostic Value of Demand Stress Real-Time Perfusion Imaging in Patients With Advanced Kidney Disease Undergoing Renal Transplantation

Cardiovascular disease accounts for 50% to 60% of all deaths in patients with end-stage renal disease (ESRD) (1). By adding myocardial perfusion (MP) imaging to wall motion (WM) analysis, real-time myocardial contrast echocardiography (RTMCE) increases the diagnostic sensitivity and prognostic value of the stress echocardiogram (2,3). However, its prognostic value in ESRD patients has not been defined. From the renal transplant database at the Nebraska Medical Center, patients with ESRD that underwent renal transplantation (RT) and stress RTMCE preoperatively between November 2008 and January 2014 were retrospectively identified (N = 487 patients). Patients' demographics, comorbidities, and transplantation data were retrospectively retrieved from the electronic medical records.

Patients undergoing treadmill stress RTMCE underwent a symptom-limited Bruce protocol. Patients undergoing dobutamine stress echocardiography received intravenous dobutamine infusion with increasing doses at 3-min intervals up to 50 μ/kg/min combined with atropine. The contrast agent was Definity (Lantheus Medical, North Billerica, Massachusetts) administered as a 3% intravenous continuous infusion. Both MP and WM were analyzed simultaneously during the replenishment phase of contrast following high mechanical index impulses using a 17-segment model (3,4). Any abnormal MP or WM response had to be confirmed by a second independent expert reviewer, blinded to angiographic or clinical outcome data. Fixed or inducible segments were considered abnormal. All patients had baseline biplane Simpson's measurements of ejection fraction, left atrial volume index, and diastolic function using current guidelines (4). Any subsequent angiograms were interpreted by an experienced interventional cardiologist, with 70% diameter stenosis in proximal or mid portions of the epicardial vessels or major branches considered significant. Patients were followed up for the primary outcome variable, event-free survival (EFS), defined as time from transplant to the incidence of myocardial infarction, heart failure hospitalization, or all-cause mortality. Kaplan-Meier method was used to estimate survival distributions and the log-rank tests were used to compare EFS distributions. Multivariate Cox regression models of EFS were

TABLE 1 Univariate Cox Model for Time From RT to Cardiac Events (n = 47 With MACE)

		Univariate			Multivariate		
	Total (N = 487)	HR	95% CI	p Value	HR	95% CI	p Value
Age, yrs	53.2 ± 12.1	1.02*	1.00–1.04	0.05	1.03*	1.00–1.06	0.023
Male	292 (60)	1.47	0.80–2.70	0.21			
CAD	101 (21)	3.4	2.00–5.90	<0.0001			
Diabetes mellitus	176 (36)	3.56	1.97–6.45	<0.0001	2.59	1.37–4.88	0.0033
Hypertension	456 (93)	1.25	0.30–5.15	0.76			
Hyperlipidemia	283 (58)	2.14	1.11–4.12	0.023			
Months between stress test and RT	11.2 ± 11.0	1.02†	1.00–1.04	0.054	1.02†	1.00–1.04	0.046
Abnormal stress test and no revascularization‡	43 (9)	2.92	1.48–5.75	0.0020	1.75	0.86–3.57	0.12
Abnormal stress test (inducible perfusion defect or WMA)	53 (11)	2.82	1.48–5.37	0.0016			
Abnormal stress test (inducible perfusion) ≥2 segments vs. <2 segments	42 (9)	2.63	1.30–5.31	0.0072			
Stress test/DD							
Abnormal stress/grade 0–1	40 (8)	2.43	1.15–5.17				
Abnormal stress/grade 2–3	13 (3)	5.10	1.78–14.6	0.0052			
Normal stress/grade 2–3	51 (10)	1.41	0.50–4.03				
Normal stress/grade 0–1	383 (79)	Ref.	—				

Values are mean ± SD or n (%). *1-year increase. †1-month increase. ‡Compared to normal or revascularized.

CAD = coronary artery disease; CI = confidence interval; DD = diastolic dysfunction; HR = hazard ratio; MACE = major adverse cardiovascular event; RT = renal transplantation; WMA = wall motion abnormal.

conducted adjusting for clinically relevant variables (p value <0.10 on univariate analysis). A C-statistic was used to compute the predictive power of abnormal WM and MP in predicting EFS. Statistical analyses were carried out with SAS Software version 9.3 (SAS Institute, Cary, North Carolina).

Patients were followed for a median of 39 months (range 4 to 112 months). Forty-seven (10%) patients experienced an event (death in 24, myocardial infarction in 8, and heart failure hospitalization in 15). Three-year EFS following a negative RTMCE was 98% (95% confidence interval: 96% to 99%). Revascularizations (coronary bypass grafting or percutaneous intervention) were performed in 10 patients with abnormal studies prior to transplantation. There was no difference in the number of abnormal MP or WM segments for those that underwent revascularization versus those that did not undergo revascularization ($p = 0.67$ for MP, $p = 0.26$ for WM).

Patients with abnormal stress MP and grade II/III diastolic dysfunction were at a 5-fold higher risk of an event (hazard ratio: 5.1; 95% confidence interval: 1.8 to 14.6). EFS in patients with inducible MP or WM abnormalities that were not revascularized was significantly worse ($p < 0.005$; C-index 0.93 for both WM and MP). The extent of the MP defect (<2 segments, ≥2 segments) was also predictive of events ($p = 0.02$), while this same cutoff for abnormal WM was not as predictive ($p = 0.06$). In the multivariate backward-selected model, only older age ($p = 0.023$) and diabetes mellitus ($p = 0.0033$) were associated with higher risk of a major adverse cardiovascular event, along with a longer time interval between stress RTMCE and RT (HR: 1.02 for each month increase; $p = 0.046$) (Table 1).

This study demonstrates that MP analysis with RTMCE during demand stress echocardiography is helpful in identifying higher-risk ESRD patients. Patients who are not revascularized after an abnormal study are at significant risk for complications, especially if concomitant grade II/III diastolic dysfunction exists. Because revascularization decision making was based on angiographic obstruction within the abnormal RTMCE territory, this would indicate that abnormal RTMCE in the absence of a significant angiographic abnormality identifies high-risk patients with microvascular disease. Although this study was a single-center study and RTMCE requires expertise, the current study emphasizes the importance of microvascular and WM abnormalities during demand stress in predicting cardiovascular outcomes following RT.

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Diminished Global Longitudinal Strain Predicts Late Allograft Failure in Pediatric Heart Transplant Recipients

Noninvasive measures to assess allograft status and prognosis in children post-heart transplantation (HT) have long been an area of investigation (1), yet robust markers of allograft dysfunction remain elusive. Recent adult guidelines recommend the serial evaluation of global longitudinal strain (GLS) in HT recipients to detect subclinical left allograft dysfunction (2). We hypothesized that abnormal GLS obtained by speckle-tracking echocardiography would predict late allograft failure in pediatric HT recipients.

We prospectively-recruited 104 pediatric HT patients to undergo speckle-tracking echocardiography prior to surveillance cardiac catheterization and endomyocardial biopsy. Standard 2-dimensional echocardiograms were performed using a GE Vivid