The prognostic value of regadenoson SPECT myocardial perfusion imaging in patients with end-stage renal disease

Rami Doukky, MD, MSc, FACC, FASNC,[a,b] Ibtihaj Fughhi, MD, MSc,[b] Tania Campagnoli, MD,[b] Marwan Wassouf, MD,[b] and Amjad Ali, MD[c]

[a] Division of Cardiology, John H. Stroger, Jr. Hospital of Cook County, Chicago, IL
[b] Division of Cardiology, Rush University Medical Center, Chicago, IL
[c] Department of Radiology and Nuclear Medicine, Rush University Medical Center, Chicago, IL

Received Aug 29, 2015; accepted Oct 1, 2015
doi:10.1007/s12350-015-0303-4

Background. **The prognostic value of regadenoson SPECT myocardial perfusion imaging (MPI) has not been specifically studied in patients with end-stage renal disease (ESRD).**

Methods and Results. **We prospectively followed ESRD patients enrolled in the ASSUAGE and ASSUAGE-CKD trials in which they received regadenoson-stress ^{99m}Tc-tetrofosmin SPECT-MPI. Images were semiquantitatively analyzed by an investigator blinded to clinical and outcome data. Patients were followed for cardiac death, myocardial infarction (MI), and coronary revascularization (CR). Revascularizations occurring >90 days post-MPI were considered ''late'' events. Survival analysis was performed using Cox regression models, adjusting for age, gender, diabetes, dyslipidemia, smoking, and known coronary artery disease. We analyzed 303 patients (mean age 54 years; 64% men), who were followed for 35 ± 10 months. Adjusting for clinical covariates, abnormal regadenoson-stress MPI (SSS ≥ 4) was associated with increased risk of the composite of cardiac death or MI (23.9% vs 14.4%; HR 1.88; CI 1.04-3.41; $P = .037$) and the composite of cardiac death, MI, or late CR (27.3% vs 16.7%; HR 1.80; CI 1.03-3.14; $P = .039$). Adjusting for clinical covariates, regadenoson-induced myocardial ischemia (SDS ≥ 2) was associated with increased rate of the composite endpoint of cardiac death, MI, or CR (33.3% vs 16.9%; HR 1.97; CI 1.19-3.27; $P = .008$).**

Conclusion. **Regadenoson-stress SPECT-MPI provides a significant prognostic value in patients with ESRD. ESRD patients with normal SPECT-MPI have relatively high adverse event rates. (J Nucl Cardiol 2017;24:112–8.)**

Key Words: Regadenoson • myocardial perfusion imaging (MPI) • end-stage renal disease (ESRD) • coronary artery disease • prognosis • outcome

Abbreviations

CAD	Coronary artery disease
CR	Coronary revascularization
ESRD	End-stage renal disease
LV	Left ventricular
MI	Myocardial infarction
MPI	Myocardial perfusion abnormality
SDS	Summed difference score
SPECT	Single-photon emission computed tomography
SSS	Summed stress score
TID	Transient ischemic dilation

Reprint requests: Rami Doukky, MD, MSc, Division of Cardiology, John H. Stroger, Jr. Hospital of Cook County, 1901 W. Harrison St., Suite # 3620, Chicago, IL 60612; *rami_doukky@rush.edu*

1071-3581/$34.00

See related editorial, pp. 119–121

BACKGROUND

Myocardial perfusion imaging (MPI) with single-photon emission computed tomography (SPECT) is a pivotal tool in the assessment and management of patients with known or suspected coronary artery disease (CAD).[1,2] In the U.S., more than 50% of all stress MPI studies are performed with pharmacologic stress agents.[3] Nearly 80% of pharmacologic SPECT-MPI studies are conducted with regadenoson, a selective A_{2A} adenosine-receptor agonist.[4] Regadenoson is partially metabolized by the kidneys (57%). Although regadenoson is not FDA approved for patients with ESRD, it is commonly used off-label with a good safety and tolerability profile.[5-8] The prognostic value of regadenoson-stress MPI is well established.[9-13] Bahtti et al demonstrated the prognostic value of regadenoson-stress in patients with chronic kidney disease, but their study included a limited number of patients with ESRD.[9] Hage et al established the prognostic value of regadenoson-stress MPI in all-comers, among whom 26% had ESRD.[11] To date, however, the prognostic value of regadenoson has not been specifically addressed in ESRD patients. This is important since patients with ESRD are at increased risk of adverse cardiac events,[9,11] and thus may benefit from additional risk stratification. On the other hand, if risk of adverse events in ESRD population is high despite normal MPI, the utility of MPI in clinical decision-making may be limited. Moreover, ESRD patients being evaluated for kidney transplantation often undergo vasodilator stress SPECT-MPI; the clinical utility of such testing is controversial.[8,14] In this study, we sought to investigate the prognostic utility of regadenoson-stress SPECT-MPI in ESRD patients.

METHODS

The study population consisted of patients with ESRD enrolled in the ASSUAGE and ASSUAGE-CKD[15,16] trials who were followed prospectively until February 2015. The detailed methods and results of these trials were reported elsewhere.[15,16] Briefly, ASSUAGE and ASSUAGE-CKD were two double-blinded, placebo-controlled clinical trials in which patients referred for regadenoson-stress SPECT-MPI were randomized in a 1:1 ratio to receive an intervention of 75 mg of intravenous aminophylline or a matching placebo administered 90 s after radioisotope injection. The aim of these studies was to determine whether regimented aminophylline administration could attenuate the side effect profile of regadenoson. The studies demonstrated substantial reduction of gastrointestinal and other regadenoson-related side effects with aminophylline use. The ASSUAGE trial enrolled 248 patients (November 2010-February 2011), and the ASSUAGE-CKD trial enrolled 300 patients (June 2011-May 2012). The trials were identical in design and methods except that the ASSUAGE trial was open for all-comers regardless of kidney function, while the ASSUAGE-CKD trial included only patients with stages 4 and 5 chronic kidney disease, defined as glomerular filtration rate <30 mL/minutes/1.73 m^2 (Cockcroft-Gault formula), or dialysis therapy. Both studies were conducted at Rush University Medical Center (Chicago, IL), and ASSUAGE-CKD also recruited patients from the John H. Stroger, Jr Hospital of Cook County (Chicago, IL). The trials were approved by the Institutional Review Boards of the participating institutions and were registered on clinicaltrials.gov (NCT01250496; NCT01336140). All subjects signed informed and HIPAA consents. The outcome determination and analyses presented in this investigation was approved by the institutional review board of Rush University Medical Center [study # 13031912]. The detailed imaging and outcome determination methods were previously published.[17]

Patient Population and Clinical Data

From the pooled database of the ASSUAGE and ASSUAGE-CKD trials (n = 548), we identified patients with ESRD, defined as glomerular filtration rate <15 mL/minutes/1.73 m^2 or renal dialysis therapy. Subjects' baseline characteristics were tabulated before undergoing regadenoson-stress test. These included gender, indication, coronary risk factors, and known CAD which was defined as history of coronary revascularization (CR) or prior myocardial infarction (MI).

Stress MPI

Standard one-day rest/stress ^{99m}Tc-tetrofosmin SPECT-MPI protocol was implemented.[18,19] Patients received ^{99m}Tc-tetrofosmin intravenously at rest, followed by resting SPECT-MPI acquisition 30 minutes later. Afterward, patients underwent a pharmacologic stress test in which 0.4 mg of regadenoson was administered intravenously over 10 seconds and was followed, 30 seconds later, by the stress dose of ^{99m}Tc-tetrofosmin. Ninety seconds later, 75 mg of aminophylline or a matching placebo was administered intravenously. Patients then underwent stress SPECT-MPI acquisition 45 to 60 minutes later.

MPI Interpretation

The 4DM-SPECT software (INVIA; Ann Arbor, MI) was used for image processing and analysis. A semi-quantitative interpretation of MPI scans was performed by a single expert reader (AA) who was blinded to clinical and outcomes data. Using a 17-segment model, each myocardial segment was scored with a standard 5-point scale (0: normal; 1: equivocal; 2: moderate; 3: severe decrease in tracer uptake; 4: absence of detectable radiotracer activity). Summed stress (SSS) and summed rest scores (SRS) were obtained from the sum of the segmental scores of the stress and rest MPI scans, respectively. Summed difference scores (SDS) were calculated from the sum

of the difference scores derived from subtracting the segmental scores of the resting MPI from those of the stress MPI. Based on SSS, MPI studies were classified as normal (SSS $\leq$ 3), mildly abnormal (SSS = 4-8), and moderate to severely abnormal (SSS $\geq$ 9).[1] Based on SDS, ischemic burden on MPI scans was classified as no ischemia (SDS $\leq$ 1), mild ischemia (SDS = 2-4), and moderate to severe ischemia (SDS $\geq$ 5).[1] Furthermore, the quantitatively measured total and reversible defects size, as percentages of the myocardium, were tabulated.

From the post-stress ECG-gated MPI, the quantitatively measured left ventricular (LV) ejection fraction, LV end-diastolic volume, and LV mass were recorded. Transient ischemic dilation (TID) ratios were tabulated from the ungated SPECT-MPI images.[20,21]

Endpoints

Patients were prospectively followed for cardiac death, MI, and CR. Death events were determined using chart review or social security death index. Cardiac death was defined as one caused by fatal MI, arrhythmias, or heart failure. Cause of death was ascertained from chart review or death certificates. Events of non-fatal MI and CR were determined via chart review by an adjudicator blinded to MPI data. Late CR was defined as one performed >90 days after stress MPI, thus representing events not directly triggered by MPI findings, a common assumption in nuclear cardiology literature.[11,17] The primary endpoint was a composite of cardiac death or MI based on MPI abnormality (SSS). The secondary endpoints included 1) the composite endpoint of cardiac death, MI, or late CR, based on MPI abnormality (SSS) and 2) the composite endpoint of cardiac death, MI, or CR, based on ischemic burden (SDS). Since CRs (early and late) are heavily determined by ischemic burden, and in order to encompass all ischemia-driven events, we chose a composite endpoint of cardiac death, MI, and CR when analyzing the impact of ischemic burden (SDS) on outcome. Study composite endpoints were selected a priori to provide the study maximum statistical power.

Statistical Analysis

Continuous data were expressed as means ± standard deviations. Categorical data were presented as frequencies and percentages. Kaplan–Meier curves and the log-rank test were used to compare cumulative event rates according to severity of perfusion abnormalities. Univariate and multivariate Cox regression models were used to determine the risk associated with abnormal MPI, myocardial ischemia, TID, and LV ejection fraction. Clinical covariates adjusted for were age, gender, diabetes, dyslipidemia, tobacco use, and known CAD. We did not adjust for hypertension since nearly all subjects had hypertension. Risk was expressed as hazard ratio (HR) with 95% confidence interval (CI). Survival analyses treated the date of MPI as ''time 0.'' Follow-up time was defined by a qualifying event, last event-free encounter, non-cardiac death, or a maximum follow-up period of 46 months, whichever occurred first. We also explored possible interactions between aminophylline use in the original trials and SDS as predictors of the study endpoints. In order to ascertain that the predictive value of regadenoson-stress MPI is consistent irrespective of other imaging parameters, we tested for interactions between MPI findings and ejection fraction ($\geq$50% vs <50%), LV end-diastolic volume index, and LV mass index.

The incremental prognostic value of regadenoson-stress MPI was determined using stepwise logistic regression models. In these models, we first introduced clinical covariates (age, gender, diabetes, dyslipidemia, tobacco use, and known CAD) and subsequently added MPI finding (abnormal MPI or myocardial ischemia). Based on the increment in the global Chi-square value of each model (likelihood ratio test) and the corresponding P value, we determined the significance of the incremental predictive value of regadenoson-stress MPI.

All tests were 2-tailed, and a P value <.05 was considered statistically significant. All statistical analyses were performed with SPSS version 22 software package (IBM, Inc., Armonk, NY).

RESULTS

There were a total of 303 patients with ESRD enrolled in the ASSUAGE and ASSUAGE-CKD trials. The baseline clinical and imaging characteristics are detailed in Table 1. Notably, their mean age was 54 ± 13 years, 64% were men, and 56% had diabetes mellitus. The vast majority of studies (96%) were performed in the context of kidney transplant evaluation. Among those subjects, 29% had abnormal MPI, and 30% had myocardial ischemia.

During mean follow-up of 35 ± 10 months, 52 (17.2%) subjects had cardiac death or MI, 60 (19.8%) had cardiac death, MI, or late CR, and 66 (21.8%) had cardiac death, MI, or CR (Table 2). As illustrated in Figure 1, severity of MPI abnormality was associated with a stepwise increase in the rates of the composite of cardiac death or MI and the composite of cardiac death, MI, or late CR (Figure 1). Among patients with normal MPI, the annualized adverse event rates were 4.9% per year for cardiac death or MI and 5.7% per year for cardiac death, MI, or late CR. Myocardial ischemia of any severity was associated with increased risk of the composite endpoint of cardiac death, MI, or CR (Figure 1). The study is underpowered to detect differences in the individual study endpoints; however, with the exception of late CR, abnormal MPI findings were generally associated with increased risk of individual study endpoints (Table 2). The quantitative defect size on post-stress images, measured as a percentage of the myocardium affected, was associated with increased risk of the composite of cardiac death or MI (HR 1.02 per 1% increment; CI 1.001-1.04; P = .035) and the composite of cardiac death, MI, or late CR (1.02 per 1% increment; HR 1.003-1.039; P = .019). Reversible defect size was associated with increased risk of the

Table 1. Baseline clinical and imaging characteristics

Variable	Mean ± SD/N (%)
N	303
Socio-demographics	
Age (years)	54 ± 13
Male gender	194 (64)
African American	172 (57)
Aminophylline arm	156 (51)
Kidney transplant evaluation	290 (96)
Dialysis	289 (95)
Hemodialysis	267 (88)
Peritoneal dialysis	22 (7)
Duration of dialysis (months)	43 ± 42
Comorbidities	
Body mass index (kg/m^2)	30 ± 7
Hypertension	288 (95)
Diabetes mellitus	170 (56)
Dyslipidemia	176 (58)
Coronary artery disease	64 (21)
Smoking	44 (15)
SPECT-MPI	
Post-stress LVEF, %	63 ± 14
LVEDVi (ml/m^2)	68 ± 30
LVMi (g/m^2)	80 ± 21
Transient ischemic dilation	1.0 ± 0.14
Summed stress score	3.7 ± 6.0
Summed rest score	3.2 ± 5.3
Summed difference score	1.6 ± 3.0
Abnormal MPI (SSS $\geq$ 4)	88 (29%)
Ischemia (SDS $\geq$ 2)	90 (30%)
Stress defect size (%)*	6.3 ± 11.4
Reversible defect size (%)*	2.4 ± 6.7

SD standard deviation, *SPECT* single-photon emission tomography, *MPI* myocardial perfusion imaging, *LVEF* left ventricular ejection fraction, *LVEDVi* left ventricular end-diastolic volume index, *LVMi* left ventricular mass index
* Quantitatively measured as percentage of the myocardium

composite of cardiac death, MI, or CR (HR 1.03 per 1% increment; HR 1.003-1.06; $P = .031$).

As illustrated in Figure 2 and Table 2, abnormal regadenoson SPECT-MPI (SSS $\geq$ 4) was associated with increased risk of cardiac death or MI (HR, 1.88; CI, 1.04-3.41; $P = .037$) and the composite of cardiac death, MI, and late CR (HR 1.80; CI 1.03-3.14; $P = .039$), after adjusting for age, gender, diabetes mellitus, dyslipidemia, tobacco use, and known CAD. Moreover, regadenoson-induced myocardial ischemia (SDS $\geq$ 2) was associated with increased risk of the composite of cardiac death, MI, and CR (HR 1.97; CI 1.19-3.27; $P = .008$), after adjusting for the aforementioned clinical covariates. There was no interaction between aminophylline use following regadenoson (according to the ASSUAGE protocol) and SDS as a determinant of any of the study endpoints (all P values $\geq$.115), adjusting for the aforementioned clinical covariates.

Abnormal regadenoson SPECT-MPI added incremental prognostic value for the composite of cardiac death or MI (Chi-square increase = 3.94; $P = .047$) and the composite of cardiac death, MI, or late CR (Chi-square increase = 3.99; $P = .046$). Similarly, regadenoson-induced myocardial ischemia added incremental prognostic value for the composite of cardiac death, MI, or CR (Chi-square increase = 6.76; $P = .009$).

Post-stress LV ejection fraction <50% was associated with increased risk of the composite endpoint of cardiac death or MI (HR 2.21; CI 1.11-4.39; $P = .024$), after adjusting for abnormal MPI finding (SSS $\geq$ 4). Furthermore, there were no significant interactions between MPI findings (abnormal MPI or myocardial ischemia) and ejection fraction ($\geq$50% vs <50%), LV end-diastolic volume index, and LV mass index as a determinant of any of the study outcomes (all P values $\geq$.281). In other words, the predictive value of abnormal MPI and myocardial ischemia was consistent, irrespective of ancillary imaging parameters.

Among the 258 patients with normal LV systolic function, there was a trend toward increased risk of cardiac death or MI with increasing TID ratio (HR 1.22 per 0.1 increment in TID; CI 0.97-1.53; $P = .087$). This association was weaker once we adjusted for SSS ($P = .150$) or SDS ($P = .142$). TID ratio in the top quartile (>1.09) was associated with an insignificant increase in the risk of the composite endpoint of cardiac death or MI (HR 1.51; CI 0.83-2.76; $P = .176$).

DISCUSSION

This is the first study to specifically investigate the prognostic value of regadenoson SPECT-MPI in patients with ESRD. We established that abnormal regadenoson SPECT-MPI in patients with ESRD is associated with approximately twice the risk of composite cardiac specific endpoints, independent of clinical covariates. Furthermore, we illustrated a stepwise increase in the risk of adverse cardiac events, commensurate with the severity of perfusion abnormality. Additionally, regadenoson SPECT-MPI added incremental prognostic value above and beyond traditional risk factors. The prognostic value of regadenoson-stress MPI was consistent irrespective of LV ejection fraction, LV end-diastolic volume, and LV mass. This study underlines the fact that ESRD patients with normal MPI are at relatively high risk of adverse cardiac events and may benefit from

Table 2. Impact of MPI finding on cardiovascular outcomes in patients with ESRD

	Crude event rates			Unadjusted risk		Adjusted risk†	
Outcomes	**Total N (%)**	**Abnormal MPI* N (%)**	**Normal MPI N (%)**	**Hazard ratio (95% CI)**	***P* value**	**Hazard Ratio (95% CI)**	***P* value**
All-cause death	48 (15.8)	20 (22.7)	28 (13.0)	1.89 (1.06-3.35)	.030	1.65 (0.89-3.06)	.112
CD	20 (6.6)	9 (10.2)	11 (5.1)	2.16 (0.89-5.21)	.087	2.57 (0.97-6.82)	.058
MI	36 (11.9)	15 (17.0)	21 (9.8)	2.10 (1.08-4.07)	.029	1.91 (0.95-3.85)	.071
Late CR	18 (5.9)	4 (4.5)	14 (6.5)	0.79 (0.26-2.41)	.684	0.76 (0.23-2.47)	.643
CR	27 (8.9)	12 (13.3)	15 (7.0)	2.13 (1.00-4.55)	.051	1.90 (0.87-4.18)	.108
CD, MI	52 (17.2)	21 (23.9)	31 (14.4)	1.97 (1.13-3.44)	.016	1.88 (1.04-3.41)	.037
CD, MI, Late CR	60 (19.8)	24 (27.3)	36 (16.7)	1.94 (1.16-3.25)	.012	1.80 (1.03-3.14)	.039
CD, MI, CR	66 (21.8)	30 (33.3)	36 (16.9)	2.24 (1.38-3.63)	.001	1.97 (1.19-3.27)	.008

Hazard ratios, 95% CI, and *P* values were derived from Cox proportional hazard models
MPI SPECT myocardial perfusion imaging, *ESRD* end-stage renal disease, *CD* cardiac death, *CI* confidence interval, *MI* myocardial infarction, *CR* coronary revascularization, *Late CR* coronary revascularization occurring >90 days after stress myocardial perfusion imaging study
* Abnormal MPI defined as SSS ≥ 4 for all endpoints except for CR and CD, MI, CR where it is defined as SDS ≥ 2
† Adjustment was made for age, gender, diabetes mellitus, dyslipidemia, tobacco use, and known coronary artery disease

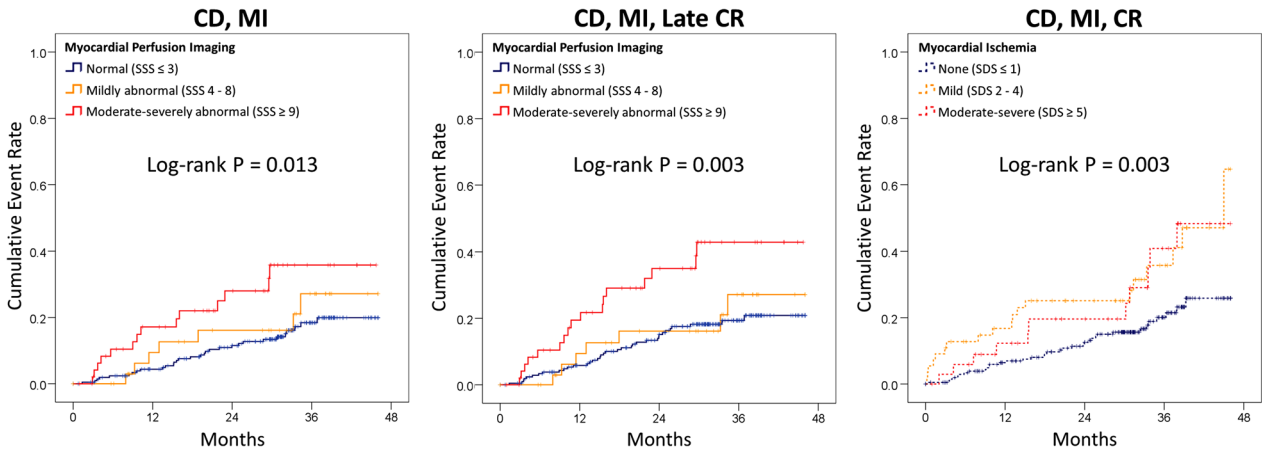

Figure 1. Impact of regadenoson-induced perfusion abnormalities on cardiac outcomes. The figure depicts Kaplan–Meier survival plots for cumulative event rates. *SPECT* single-photon emission computed tomography, *MPI* myocardial perfusion imaging, *ESRD* end-stage renal disease, *CD* cardiac death, *MI* myocardial infarction, *CR* coronary revascularization, *Late CR* coronary revascularization occurring >90 days post-MPI.

additional risk stratification. These findings were derived from high-quality prospective data.

The prognostic value of regadenoson-stress SPECT-MPI in the general patient population is well established.[13] Using propensity score-matching technique, Iqbal et al demonstrated similar 2-year outcome of patients with normal regadenoson MPI to those with normal adenosine MPI.[10] Moreover, Farzaneh-Far et al demonstrated that SSS and SDS derived from regadenoson-stress SPECT-MPI have similar prognostic significance as those derived from adenosine stress study.[12] Bhatti et al demonstrated that renal function is a powerful risk predictor in patients undergoing regadenoson SPECT-MPI and established that regadenoson SPECT-MPI provides robust prognostication across the entire spectrum of renal function.[9] However, their study included a limited number of patients with ESRD. Moreover, in 1400 patients, of whom 26% had ESRD, Hage et al demonstrated that regadenoson SPECT-MPI provides powerful prognostic information that can aid in clinical decision-making.[11] These authors also demonstrated

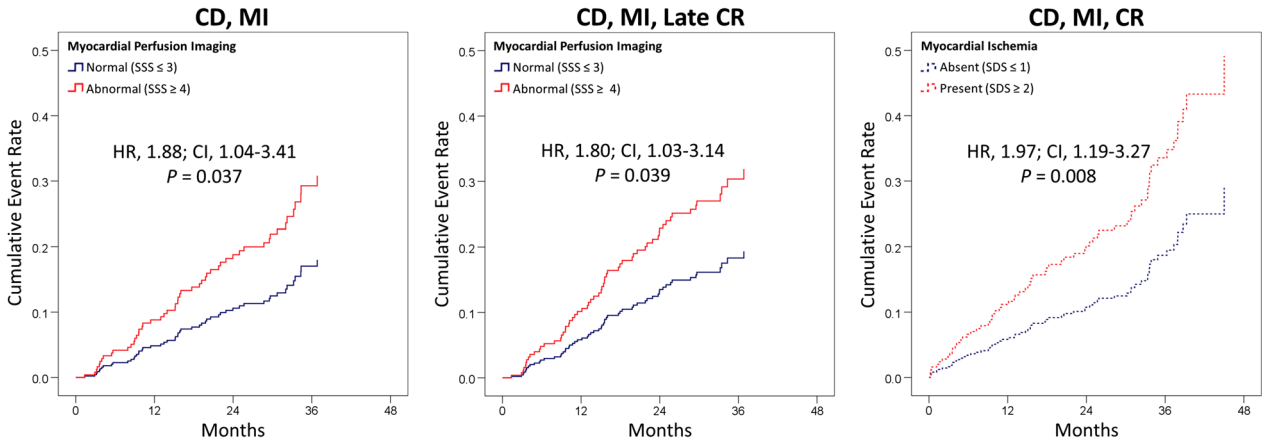

Figure 2. Impact of regadenoson-induced perfusion abnormalities on cardiac outcomes adjusted for clinical covariates. The figure depicts Cox proportional hazards survival plots adjusted for age, gender, diabetes, dyslipidemia, smoking, and history of coronary artery disease. *SPECT* single-photon emission computed tomography, *MPI* myocardial perfusion imaging, *ESRD* end-stage renal disease, *CD* cardiac death, *MI* myocardial infarction, *CR* coronary revascularization, *Late CR* coronary revascularization occurring >90 days post-MPI, *HR* hazard ratio, *CI* 95% confidence interval.

that ESRD is a strong and independent predictor of adverse cardiac events, and perfusion defect size on MPI was a predictor of adverse cardiac events, independent of ESRD status and other clinical covariates. Nonetheless, the study did not specifically address the prognostic value of MPI in ESRD patients. On the other hand, among ESRD patients undergoing transplant evaluation, Venkataraman et al demonstrated significant incremental prognostic value of dipyridamole-stress SPECT-MPI, above and beyond invasive coronary angiography data.[22] Our investigation established the prognostic value of regadenoson SPECT-MPI in ESRD patients, the majority of whom received testing as part of kidney transplant evaluation. Notably, abnormal MPI and regadenoson-induced myocardial ischemia were associated with nearly twice the risk of major adverse cardiac events. This is a slight deviation from other reports in which abnormal MPI has been associated with several-fold increase in risk.[2,11] Two important features about this population may help explain this observation: first, these are predominantly ESRD patients without ischemic symptoms who are undergoing CAD surveillance as part of kidney transplant evaluation, and second, due to ESRD, all patients are at increased risk irrespective of MPI finding.[9,11] Both factors may have degraded the discriminative capacity of regadenoson SPECT-MPI.

It is remarkable that patients with ESRD and normal MPI experienced a relatively high rate of cardiac death or MI (4.9% per year). Therefore, ESRD patients with normal vasodilator stress MPI can benefit from additional risk stratification derived from ancillary electrocardiographic or MPI findings, such as ischemic ST-segment changes, heart rate response, mechanical dyssynchrony indices by phase analysis, and perhaps TID.[17,21,23-27] In a recent study, our group demonstrated that blunted heart rate response to regadenoson-stress (<28% increase from baseline) is associated with increased risk of all-cause death in patients with ESRD, irrespective of MPI findings.[17] Notably, among patients with normal MPI (SSS $\leq$ 3), blunted heart rate response to regadenoson-stress was associated with significant increase in the risk of all-cause death compared to patients with adequate response (7.5% vs 1.7% annually, HR 4.20; CI 1.70-10.37; $P = .001$).[17] Thus, heart rate response could be a valuable adjunct to MPI findings to identify truly low-risk ESRD patients. Moreover, in the present investigation, we found a trend for an association between TID and the composite of cardiac death or MI. This is worthy of additional investigation as TID may provide additional prognostic information, particularly among patients with normal MPI.[21]

Strengths and Limitations

The data were generated prospectively from patients enrolled in two randomized clinical trials with rigorously tabulated clinical and imaging data. However, this is a single-center study with relatively small number of events. Furthermore, the majority of the study subjects were ''healthier'' ESRD patients, being considered for kidney transplantation; this may limit the applicability of the findings to ESRD population at large.

NEW KNOWLEDGE GAINED

Abnormal regadenoson-stress MPI in patients with ESRD provides independent and incremental prognostic value beyond traditional risk factors and CAD status.

CONCLUSION

Regadenoson-stress SPECT-MPI provides a significant prognostic value among patients with ESRD. ESRD patients with normal regadenoson-stress SPECT-MPI have relatively high event rates and may benefit from additional risk stratification.

Disclosure

Rami Doukky serves on the Advisory Board for Astellas Pharma and receives research funding from Astellas Pharma. Other authors have no conflicts to report.

References

1. Doukky R, Hayes K, Frogge N, Balakrishnan G, Dontaraju VS, Rangel MO, et al. Impact of appropriate use on the prognostic value of single-photon emission computed tomography myocardial perfusion imaging. Circulation. 2013;128:1634–43.
2. Doukky R, Frogge N, Balakrishnan G, Hayes K, Collado FM, Rangel MO, et al. The prognostic value of cardiac SPECT performed at the primary care physician's office. J Nucl Cardiol. 2013;20:519–28.
3. AMR/Arlington Medical Resources Inc. Myocardial Study Market Guide, Jan-Jun 2012; 2012.
4. Astellas Pharma US. Lexiscan; 2015.
5. Doukky R, Rangel MO, Wassouf M, Dick R, Alqaid A, Morales Demori R. The safety and tolerability of regadenoson in patients with end-stage renal disease: the first prospective evaluation. J Nucl Cardiol. 2013;20:205–13.
6. Aljaroudi W, Hermann D, Hage F, Heo J, Iskandrian AE. Safety of regadenoson in patients with end-stage renal disease. Am J Cardiol. 2010;105:133–5.
7. Rangel MO, Morales Demori R, Voll ST, Wassouf M, Dick R, Doukky R. Severe chronic kidney disease as a predictor of benefit from aminophylline administration in patients undergoing regadenoson stress myocardial perfusion imaging: A substudy of the ASSUAGE and ASSUAGE-CKD trials. J Nucl Cardiol. 2015;22:1008–18.
8. Parikh K, Appis A, Doukky R. Cardiac imaging for the assessment of patients being evaluated for kidney or liver transplantation. J Nucl Cardiol. 2015;22:282–96.
9. Bhatti S, Hakeem A, Dhanalakota S, Palani G, Husain Z, Jacobsen G, et al. Prognostic value of regadenoson myocardial single-photon emission computed tomography in patients with different degrees of renal dysfunction. Eur Heart J Cardiovasc Imaging. 2014;15:933–40.
10. Iqbal FM, Hage FG, Ahmed A, Dean PJ, Raslan S, Heo J, et al. Comparison of the prognostic value of normal regadenoson with normal adenosine myocardial perfusion imaging with propensity score matching. JACC Cardiovasc Imaging. 2012;5:1014–21.
11. Hage FG, Ghimire G, Lester D, McKay J, Bleich S, El-Hajj S, et al. The prognostic value of regadenoson myocardial perfusion imaging. J Nucl Cardiol. 2015. doi:10.1007/s12350-014-0050-y.
12. Farzaneh-Far A, Shaw LK, Dunning A, Oldan JD, O'Connor CM, Borges-Neto S. Comparison of the prognostic value of regadenoson and adenosine myocardial perfusion imaging. J Nucl Cardiol. 2015;22:600–7.
13. Doukky R. The prognostic value of regadenoson stress: Has the case been made? J Nucl Cardiol. 2015;22:608–10.
14. Lentine KL, Costa SP, Weir MR, Robb JF, Fleisher LA, Kasiske BL, et al. Cardiac disease evaluation and management among kidney and liver transplantation candidates: a scientific statement from the American Heart Association and the American College of Cardiology Foundation. J Am Coll Cardiol. 2012;60:434–80.
15. Doukky R, MoralesDemori R, Jain S, Kiriakos R, Mwansa V, Calvin JE. Attenuation of the side effect profile of regadenoson: A randomized double-blinded placebo-controlled study with aminophylline in patients undergoing myocardial perfusion imaging. ''The ASSUAGE trial''. J Nucl Cardiol. 2012;19:448–57.
16. Doukky R, Rangel MO, Dick R, Wassouf M, Alqaid A, Margeta B. Attenuation of the side effect profile of regadenoson: a randomized double-blind placebo-controlled study with aminophylline in patients undergoing myocardial perfusion imaging and have severe chronic kidney disease—the ASSUAGE-CKD trial. Int J Cardiovasc Imaging. 2013;29:1029–37.
17. AlJaroudi W, Campagnoli T, Fughhi I, Wassouf M, Ali A, Doukky R. Prognostic value of heart rate response during regadenoson stress myocardial perfusion imaging in patients with end stage renal disease. J Nucl Cardiol. 2015. doi:10.1007/s12350-015-0234-0.
18. Henzlova MJ, Cerqueira MD, Hansen CL, Taillefer R, Yao SS. ASNC imaging guidelines for nuclear cardiology procedures: Stress protocols and tracers. J Nucl Cardiol. 2009;16:331–44.
19. Ballany W, Mansour K, MoralesDemori R, Al-Amoodi M, Doukky R. The impact of regimented aminophylline use on extracardiac radioisotope activity in patients undergoing regadenoson stress SPECT myocardial perfusion imaging: A substudy of the ASSUAGE trial. J Nucl Cardiol. 2014;21:496–502.
20. Golzar Y, Olusanya A, Pe N, Dua SG, Golzar J, Gidea C, et al. The significance of automatically measured transient ischemic dilation in identifying severe and extensive coronary artery disease in regadenoson, single-isotope technetium-99 m myocardial perfusion SPECT. J Nucl Cardiol. 2015;22:526–34.
21. Doukky R, Frogge N, Bayissa YA, Balakrishnan G, Skelton JM, Confer K, et al. The prognostic value of transient ischemic dilatation with otherwise normal SPECT myocardial perfusion imaging: A cautionary note in patients with diabetes and coronary artery disease. J Nucl Cardiol. 2013;20:774–84.
22. Venkataraman R, Hage FG, Dorfman T, Heo J, Aqel RA, de Mattos AM, et al. Role of myocardial perfusion imaging in patients with end-stage renal disease undergoing coronary angiography. Am J Cardiol. 2008;102:1451–6.
23. Doukky R, Olusanya A, Vashistha R, Saini A, Fughhi I, Mansour K, et al. Diagnostic and prognostic significance of ischemic electrocardiographic changes with regadenoson-stress myocardial perfusion imaging. J Nucl Cardiol. 2015;22:700–13.
24. Aggarwal H, AlJaroudi WA, Mehta S, Mannon R, Heo J, Iskandrian AE, et al. The prognostic value of left ventricular mechanical dyssynchrony using gated myocardial perfusion imaging in patients with end-stage renal disease. J Nucl Cardiol. 2014;21:739–46.
25. AlJaroudi W, Aggarwal H, Venkataraman R, Heo J, Iskandrian AE, Hage FG. Impact of left ventricular dyssynchrony by phase analysis on cardiovascular outcomes in patients with end-stage renal disease. J Nucl Cardiol. 2010;17:1058–64.
26. Aljaroudi W, Koneru J, Iqbal F, Aggarwal H, Heo J, Iskandrian AE. Left ventricular mechanical dyssynchrony by phase analysis of gated single photon emission computed tomography in end-stage renal disease. Am J Cardiol. 2010;106:1042–7.
27. Poulin MF, Alexander S, Doukky R. Prognostic implications of stress modality on mortality risk and cause of death in patients undergoing office-based SPECT myocardial perfusion imaging. J Nucl Cardiol. 2015. doi:10.1007/s12350-014-0064-5.