Detection and quantitation of right ventricular reversible perfusion defects by stress SPECT myocardial perfusion imaging: A proof-of-principle study

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Background. **In patients with right dominant coronary circulation, the right ventricular (RV) myocardium and the inferior region of the left ventricular (LV) myocardium share a common source of blood flow. We hypothesized that stress/rest SPECT myocardial perfusion imaging (MPI) could detect reversible perfusion defects in the RV in some patients with LV inferior wall perfusion abnormalities.**

Material and Methods. **We identified 2 groups of patients with LV inferior wall perfusion defects (with or without defects in other regions of LV myocardium) from our database. Patients in group 1 (n = 17) had reversible perfusion defects in the RV free wall by visual analysis, while patients in group 2 (n = 17) did not. The images were processed with filtered back projection and, separately, with iterative reconstruction. The images were then re-processed using an automated quantitative software that is specifically designed to include the RV in the region of interest.**

Results. **There were 76% men in group 1 and 94% in group 2 (P <0.05). The mean age was 65±20 in group 1 vs. 63±18 years in group 2 ($P < 0.05$). The stress type was exercise in 30% in group 1 and 35% in group 2, with the remaining patients studied with pharmacological stress testing (P = NS). The presence of RV reversible perfusion defects using filtered back projection was more evident in 13 patients (75%), while it was better seen with iterative reconstruction in 4 patients (25%). By automated analysis, the RV reversible perfusion defect size was 19 ± 14% of RV myocardium.**

Conclusion. **This proof-of-principle study demonstrates that reversible RV perfusion defects suggestive of ischemia can be detected by SPECT myocardial perfusion imaging in some**

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patients with LV inferior ischemia by visual analysis and can be quantitated by automated programs. Further studies on the diagnostic and prognostic relevance of assessing RV ischemia on SPECT MPI are needed. (J Nucl Cardiol 2019;26:266–71.)

Key Words: Right ventricle • ischemia • SPECT • myocardial perfusion • CAD

Abbreviations

HF	Heart failure
RV	Right ventricle/ventricular
ROI	Region of interest
LV	left ventricle/ventricular
LAD	Left anterior descending artery
LCX	Left circumflex coronary artery
RCA	Right coronary artery
SPECT	Single photon emission tomography
MPI	Myocardial perfusion imaging
MBF	myocardial blood flow
CAD	Coronary artery disease
CABG	Coronary artery bypass grafting
PCI	Percutaneous intervention

See related editorial, pp. 272–274

INTRODUCTION

The right ventricle (RV) is often not well visualized during SPECT myocardial perfusion imaging (MPI) regardless of the type of stress. This is likely due to lower myocardial blood flow (MBF) in the RV myocardium related to its lower muscle mass and its lower demand compared to the left ventricular (LV) myocardium. Further, due to the inherent limitations set by the resolution of SPECT MPI cameras, the partial volume effect will result in the RV appearing less bright than the LV.[1] The exception to this are patients with pulmonary hypertension, who often exhibit prominent RV uptake due to the hypertrophied RV myocardium.[2,3]

However, we have been intrigued by the fact that in many patients, the RV uptake is sufficiently visible on MPI (using technetium-labeled tracers) to allow interpretation of the perfusion pattern in patients with known or suspected coronary artery disease (CAD) but no pulmonary hypertension. The short-axis, and to a lesser extent the horizontal long-axis, projections are best to visualize the RV for this purpose.

Early studies using rest and exercise radionuclide ventriculography demonstrated (1) that RV ischemia/dysfunction occurs in patients with CAD and/or heart failure (HF) and (2) that it has important independent prognostic value, an observation that has been more recently reconfirmed using other imaging modalities.[4-9] The MBF to the RV myocardium is from the right coronary artery (RCA) in patients with right dominant coronary circulation. Therefore, it stands a good chance that patients with inferior LV ischemia are more likely to show RV ischemia, if that can be detected using SPECT imaging.[10-12]

In this proof-of-principle study, we used visual analysis, processing the images with filtered back projection as well as iterative reconstruction algorithms, and a specifically designed automated software to examine/quantify RV perfusion.

METHOD AND RESULTS

We identified 34 patients with abnormal perfusion in the inferior wall of the LV myocardium who underwent SPECT MPI at the University of Alabama at Birmingham from March to December 2015. All patients underwent stress-rest gated SPECT MPI using previously described methods and in accordance with ASNC guidelines.[13-16] Briefly, all patients underwent same-day low-dose stress (10-15 mCi) followed by high-dose rest (30-35 mCi) imaging except for 1 patient who underwent a two-day high-dose stress and high-dose rest imaging protocol due to body habitus (body mass index of 38 kg/cm^2). Gated SPECT images were acquired 1 hour after tracer injection with a dual-head detector gamma camera with a low-energy, high-resolution collimator with a 64 × 64 matrix. The cameras operated in an elliptical 180° acquisition orbit with 32 projections and 30 seconds per projection. For image acquisition, a 15% energy window focused on the 140-keV gamma peak was utilized. Gating was performed with 8-16 frames/RR cycle. No attenuation correction was used. The data are presented as mean ± SD or numbers and percentages when applicable. Student *t* test was used for comparison between the 2 groups.

All 34 patients had a perfusion abnormality in the inferior wall of the LV with and without reversible, fixed or mixed perfusion defects in other vascular territories. Of these patients, one-half had RV reversible perfusion defects defined as perfusion abnormalities in the RV free wall on the stress images with either absent or less severe abnormality on the rest images by visual analysis (Group 1, n = 17, Figure 1 top panel), while the others did not (Group 2, n = 17, Figure 2 left panel).

The baseline characteristics and medication use for both groups are listed in Table 1. Most patients were men and had one or more coronary risk factors or known CAD. Regadenoson was used in 2/3 and treadmill exercise in 1/3 of the patients, while one patient

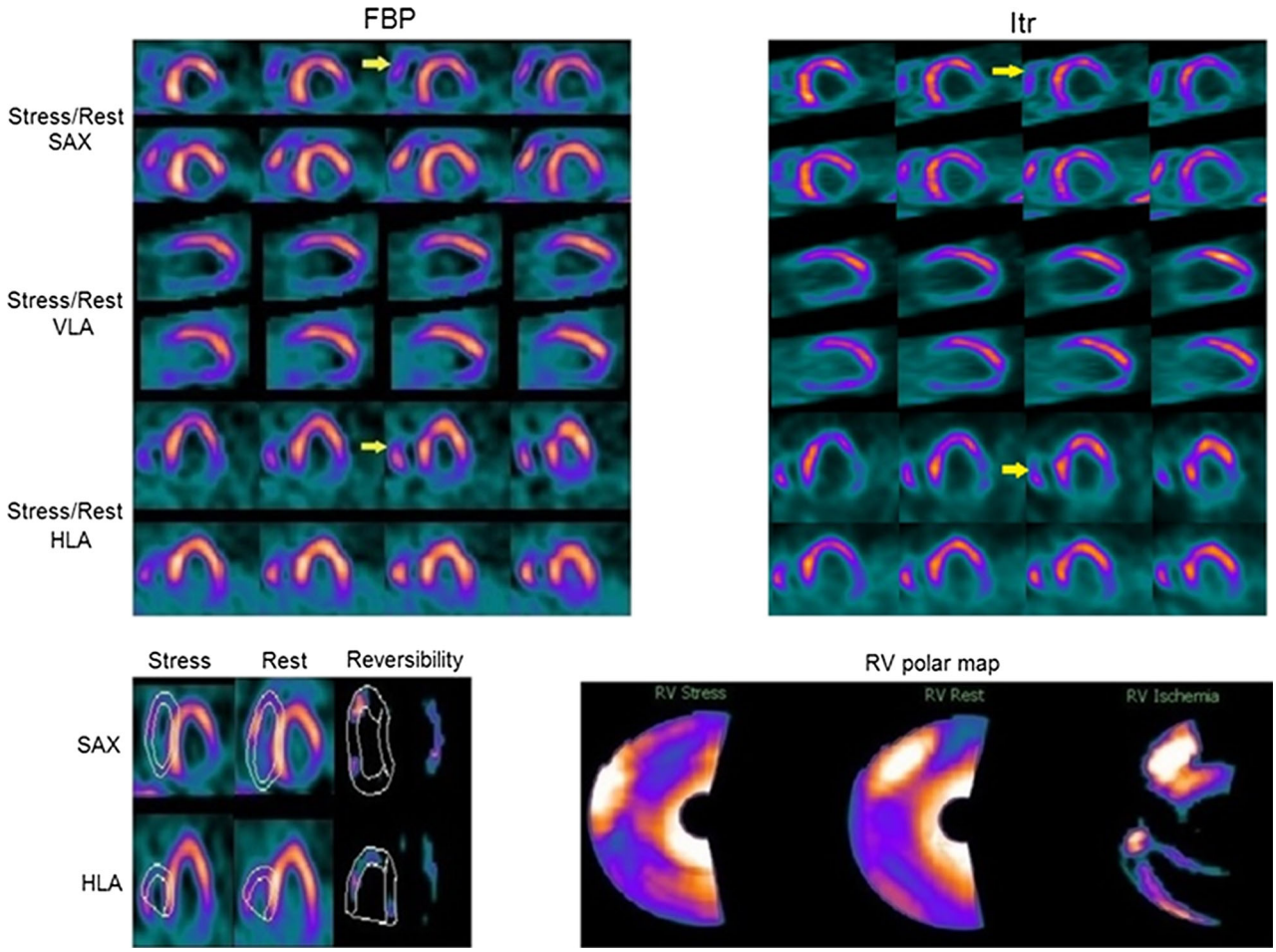

Figure 1. Stress/Rest SPECT Tc-99m sestamibi myocardial perfusion images (*top panel*) show abnormal perfusion pattern consistent with left circumflex and right coronary artery disease (partially reversible defect). There are also reversible perfusion defects involving the right ventricle seen in short-axis and horizontal long-axis projections which are more evident with FBP image processing (*top left*) and less evident though still seen with image iterative reconstruction (*top right*). The arrows point to 2 such slices though the abnormality is seen in multiple slices. Contouring of the RV free wall (*lower left*) in stress and rest studies for quantitative measurement of the RV myocardial perfusion. RV polar map (*lower right*) based on the quantitative analysis of the RV contouring image showing comparison of stress perfusion data to rest data producing the reversibility polar map that confirms a reversible perfusion defect involving 32% of the RV myocardium.

underwent dobutamine stress. The perfusion abnormality was reversible (with or without a fixed defect) in the majority of patients. The vascular distribution of LV perfusion abnormalities in both groups is shown in Table 1.

All images were processed twice, first using filtered back projection and then with iterative reconstruction. The images were then analyzed using a modified version of Cedars Sinai's QPS+QGS automatic quantification software, version 2013.1. The images produced by both the processing methods were reviewed to assess which approach is superior in visualizing RV reversible perfusion defects. Although RV reversible perfusion defects were visible by both the processing methods in all the patients in group 1, filtered back projection was subjectively felt to be superior to iterative reconstruction in 75% of the patients, while iterative reconstruction appeared superior in the remaining 25%. We were not able to appreciate any obvious differences in the patients who demonstrated superiority of one processing algorithm over the other. Most of the RV perfusion defects appeared partially reversible (Figure 1).

Finally, a specifically designed modification to a standard automated software program, not previously described or used, was used to quantify RV reversible perfusion defect size (Figure 1, bottom panel, and

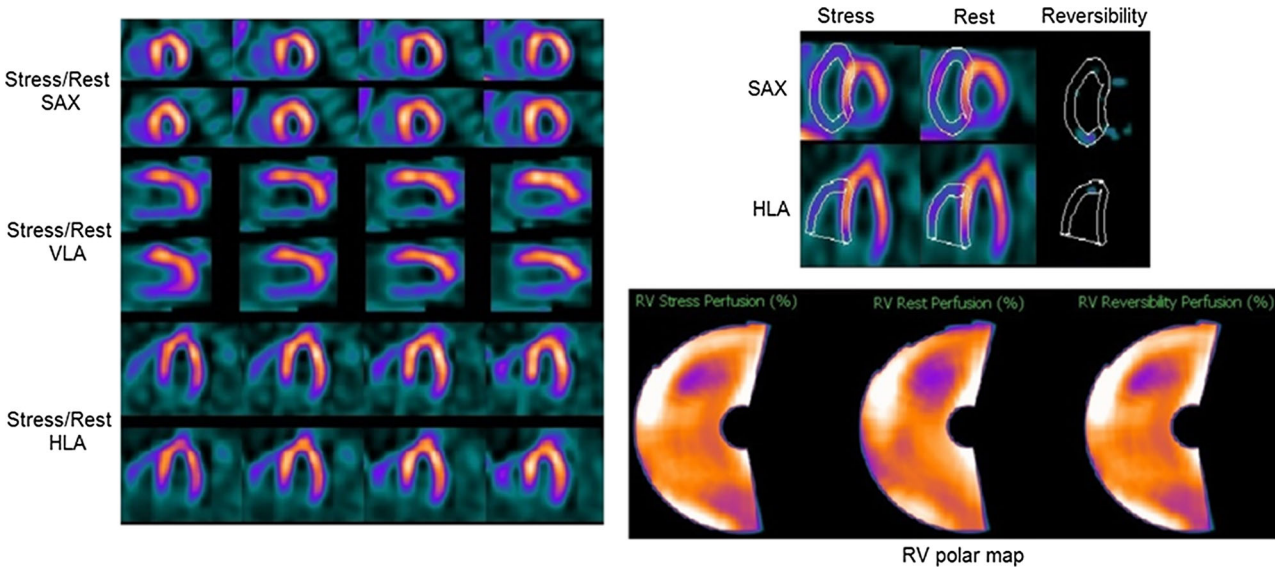

Figure 2. Stress/Rest SPECT Tc-99m sestamibi myocardial perfusion images (*left image*) show abnormal perfusion pattern consistent with right coronary artery disease (partially reversible defect) with RV free wall well visualized with no detectable perfusion defect. Contouring of the RV free wall (*top right*) and RV polar map (*lower right*) of the stress and rest studies for quantitative analysis and comparison of the RV myocardial perfusion between the two studies producing a reversibility polar map that confirms the visual assessment; normal RV myocardial perfusion.

Figure 2, right panel). This software segments the RV myocardium by combining the previously segmented LV septum, which is taken as a starting point, with the free wall myocardium, which is segmented using a version of the LV segmentation algorithm[17] modified to account for RV geometry and count distributions. Reversible perfusion defect size is then computed by comparing stress and rest RV myocardial perfusion using a similarly modified version of a registration-based LV quantitation algorithm.[18] Since the stress and rest images were acquired with different doses and at different times, an optimized normalization factor was used in the registration algorithm. Also, to avoid the influence of perfusion defects on registration, a 2-pass method was used as previously described for the LV[18] By automated analysis, the size of the RV reversible perfusion defects was 19% ± 14% of RV myocardium (range 5%-33%).

DISCUSSION

This proof-of-principle study shows that at least in some patients with CAD and inferior LV perfusion abnormality, a perfusion pattern suggestive of RV ischemia could be seen using technetium-labeled tracers and standard Anger gamma camera and software and quantitated using a novel software program. This is likely better than using thallium and may be improved further by means of newer cameras that utilize CZT detectors and advanced software processing algorithms including attenuation correction.[16,19-21]

The RV reversible perfusion defect pattern described in our report is different from that described by Williams and Schneider who observed increased RV:LV activity during exercise/rest dual isotope imaging and attributed it to severe CAD, particularly high-grade left main with less severe proximal right CAD.[10]

The prevalence of RV ischemia by MPI and its implications on prognosis were not addressed in this report and will need to be addressed in larger studies. Also, we did not have data from coronary angiography in our patients to correlate perfusion with anatomy. It is not clear whether RV ischemia could occur without inferior LV ischemia, but certainly disease location in the RCA proximal or distal to the RV and the acute marginal branches would suggest that it is possible.[11,12] Whether isolated RV ischemia detected by MPI in the absence of inferior LV ischemia impacts prognosis should be evaluated in a larger study that recruits patients with multiple LV perfusion patterns and follows them over time for outcomes.

This feasibility study also suggests that automated quantification of perfusion defect size is possible, even though the geometric shape of the RV is difficult to model and ascertainment of the location of the pulmonic valve is not always straightforward. The automated software may help in more reproducible reading and

Table 1. Baseline characteristics stratified by the presence or absence of right ventricular ischemia

Characteristics	Group 1 "RV reversible perfusion defects" (N = 17)	Group 2 "No RV reversible perfusion defects" (N = 17)
Age	65 ± 20	63 ± 18
Men	13 (76%)	16 (94%)
Weight (kg)	97 ± 30	106 ± 40
BMI (kg/m^2)	30 ± 10	31 ± 10
Hypertension	16 (94%)	15 (88%)
Diabetes mellitus	5 (30%)	6 (35%)
Hyperlipidemia	14 (82%)	17 (100%)
Coronary artery disease	17 (100%)	17 (100%)
Prior myocardial infarction	4 (24%)	4 (24%)
Prior PCI	9 (53%)	12 (70%)
Prior CABG	7 (41%)	7 (41%)
Recent coronary angiogram	10 (59%)	13 (75%)
Stress type: Regadenoson	11 (65%)	11 (65%)
Exercise	5 (30%)	6 (35%)
Dobutamine	1 (5%)	0
Perfusion abnormality: RCA only	6 (35%)	13 (76%)
RCA + LCX	7 (41%)	2 (12%)
RCA + LAD	3 (18%)	1 (6%)
3-VD	1 (6%)	1 (6%)
LV-EF	46% ± 25%	51% ± 26%
Perfusion defect type: Ischemia	5 (30%)	7 (41%)
Scar	4 (24%)	4 (24%)
Ischemia + scar	8 (46%)	6 (35%)
Medications		
Aspirin	11 (65%)	15 (90%)
Clopidogrel	6 (35%)	10 (59%)
Beta-Blockers	11 (65%)	8 (46%)
ACE-I/ARB	11 (65%)	7 (41%)
Calcium Channel Blockers	5 (30%)	1 (5%)
Statins	11 (65%)	13 (76%)
Diuretics	9 (53%)	4 (24%)

RV, right ventricular; *BMI*, body mass index; *PCI*, percutaneous intervention; *CABG*, coronary artery bypass grafting; *RCA*, right coronary artery; *LCX*, left circumflex coronary artery; *LAD*, left anterior descending coronary artery; *3-VD*, 3-vessel disease; *ACE-I*, Angiotensin converting enzyme inhibitor; *ARB*, Angiotensin receptor blocker

avoid misinterpretation due to differences in geometry and scaling of the 2 sets of the images. Analogously to the LV, it should also be possible to develop normal limit databases for automated quantification of RV perfusion and function. Similar to LV,[22,23] automated analysis of perfusion pattern should provide improved accuracy and reproducibility compared to visual analysis. In our report, we processed images using filtered back projection and iterative reconstruction and noted the superiority of filtered back projection for visualization of RV reversible perfusion defects in most but not all cases. It should be noted that this constituted a subjective evaluation that may differ from reader to reader (see Fig. 1 as typical example). Further, we stress that RV reversible perfusion defects were visible by using both processing algorithms in all patients. Although future studies may determine if processing may impact the visualization of RV perfusion, we suggest that the quantitative evaluation of the RV perfusion pattern, similar to the LV, should depend on automated softwares. In our cohort, the automated quantitation of the RV perfusion defect size was not significantly dependent on the processing method used (19 ± 4 by filtered back projection and 18 ± 14 by iterative reconstruction), further highlighting the subjectivity of the visual assessment.

It is possible that RV infarction may have contributed to the RV perfusion defect seen in some of our patients. Another possibility is that the perfusion pattern in the RV is artefactual due to the partial volume effect, the higher dose of radionuclide tracer in the rest study, and possible slight misalignment between images.[1,16] We doubt if these factors accounted for perfusion pattern seen in the majority of our patients, but it is not possible to refute or prove this. Another contributing factor could be attenuation artifact due to body habitus since the majority of our patients were overweight. We have not used attenuation correction in this study and it is not possible to speculate on the effect of attenuation correction on RV from our study.

This study shows that RV ischemia can occur in some patients with CAD and may be detected by current imaging systems and software. It is likely that newer detectors will perform even better in this regards. More studies are needed to confirm these findings and explore their implications on patient care.

NEW KNOWLEDGE GAINED

RV reversible perfusion defects suggestive of ischemia can be detected using SPECT MPI and quantitated using a novel automated software.

Disclosure

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