



SPECT Flow Quantification and its Application for the Evaluation of Allograft Vasculopathy in Heart Transplant Recipients



Ricardo Andrés Nieves, MD; Syed Bukhari, MD; Joe Diez, CNMT; Kevin Hyanl, CNMT; Roy Sriwattanakomen, MD, Gavin Hickey, MD; Mary Keebler, MD; Prem Soman, MD PhD

University of Pittsburgh Medical Center Heart And Vascular Institute, University of Pittsburgh

INTRODUCTION

- Cardiac Allograft Vasculopathy (CAV) has become an increasingly important cause of morbidity and mortality in heart transplant recipients given improvement in long-term survival^{1,2}; however its diagnosis remains challenging⁴.
- CAV, is characterized by endothelial dysfunction, inflammation, and increased intimal thickening resulting in the development of proliferative fibrofatty plaques and degenerative foci³.
- PET derived Myocardial Blood Flow (MBF) and Myocardial Flow Reserve (MFR) on PET have been shown capable of detecting CAV and providing prognostic information⁵; however, PET is limited in its availability⁶.
- We explored SPECT derived MFR for the detection of CAV.

METHODOLOGY

- Heart transplant recipients referred for routine CAV monitoring vasodilator stress myocardial perfusion imaging (MPI) were selected for dynamic imaging on the DSPECT camera
- From 51 heart transplant recipients who completed the Flow Quantification protocol, 38 had available coronary angiogram results within our system for review and were included in this analysis.
- Patient positioning was accomplished with a hand-injected 1mCi Tc-99m sestamibi (MIBI) pre-scan.
- Vasodilator stress, and rest/ stress MIBI injection using an automated syringe pump, were performed with the patient under the camera:
- Data was acquired in list mode and processed on the Cedars-Sinai QCS/QPS platform
- Significant manual adjustments were routinely made to the blood pool and tissue ROI positions in each frame for input and myocardial activity curve derivation. A rate pressure product (RPP) correction was applied to each scan.
- Myocardial Flow Reserve (MFR) < 2.0 was considered abnormal.

OBJECTIVE OF STUDY

Cadium-Zinc-Telluride (CZT) cameras have made the assessment of MBF and MFR possible on the widely available SPECT imaging platform with substantial accuracy and correlation to other modalities including PET and coronary angiography⁷⁻¹⁰.

We posit that SPECT flow quantification can be applied to Sestamibi myocardial perfusion imaging for the more accurate identification of coronary allograft vasculopathy in heart transplant recipients.

AIMS

- (1) To determine the MFR value cut off value for heart transplant recipients with a known history of CAV via coronary angiogram,
- (2) To determine the relative sensitivities and specificities of Sestamibi myocardial perfusion imaging (MPI), Dobutamine stress echo (DSE), and SPECT flow quantification for the identification of CAV in our cohort.

RESULTS

| | Coronary Allograft Vasculopathy (n=8) | No Coronary Allograft Vasculopathy (n=30) |
|---|---------------------------------------|---|
| Age | 64.13 ± 6.97 | 61.13 ± 13.93 |
| Male Gender | 7 (87.5%) | 20 (66.7%) |
| Years from Transplant | 11.12 ± 5.93 | 10.66 ± 4.34 |
| Average Months Since Coronary Angiogram | 31.76 ± 26.67 | 45.43 ± 39.14 |
| Obesity | 1 (12.5%) | 10 (33.3%) |
| Smoking | | |
| Former | 2 (25%) | 9 (30%) |
| Current | 2 (25%) | 5 (16.6%) |
| Never | 4 (50%) | 16 (53.3%) |
| Hypertension | 7 (87.%) | 26 (86.6%) |
| Diabetes | 2 (25%) | 18 (60%) |
| Hyperlipidemia | 7 (87.5%) | 27 (90%) |
| Myocardial Perfusion Imaging Interpretation | | |
| Normal | 6 | 30 |
| Infarct | 1 | 1 |
| Ischemia | 1 | 0 |
| Dobutamine Stress Echo Interpretation | | |
| Negative | 4 | 23 |
| Positive | 1 | 1 |
| Non-diagnostic | 1 | 2 |
| Not available | 2 | 5 |

Table 1: Baseline characteristics for the patients included in this retrospective analysis

| | Myocardial Perfusion Imaging (MPI) | Dobutamine Stress Echo (DSE) | Myocardial Flow Reserve (MFR) |
|-------------|------------------------------------|------------------------------|-------------------------------|
| Sensitivity | 25% | 20% | 25% |
| Specificity | 97% | 97% | 93% |
| PPV | 67% | 50% | 50% |
| NPV | 83% | 85% | 93% |

Table 2: Relative sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for the imaging modalities utilized in this study. The above table assumes an MFR cutoff of 2.0 as normal

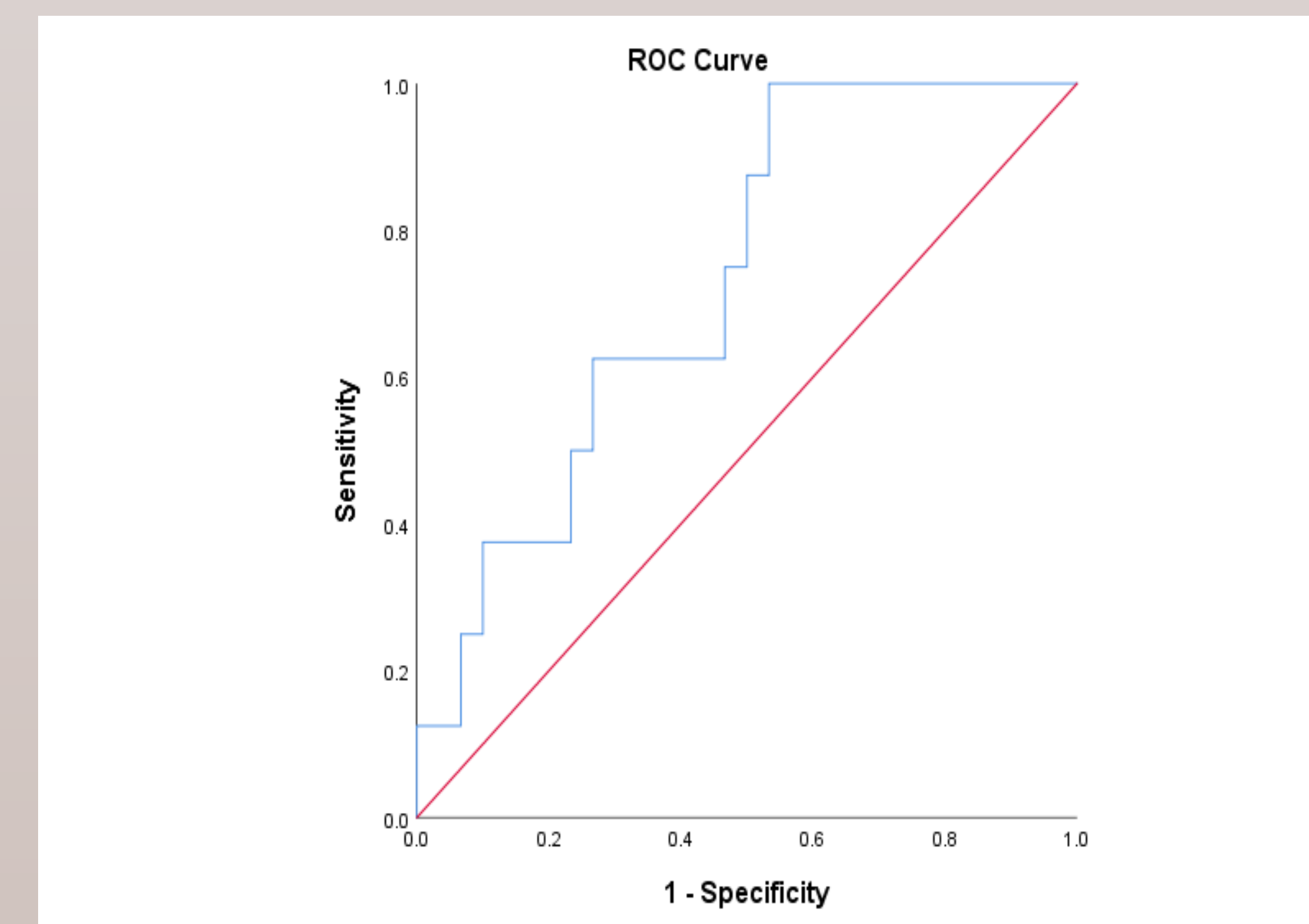


Figure 1: ROC Curve of MFR for prediction of CAV. The optimal MFR cutoff was noted at 2.5 rather than the conventionally held value of 2.0

RESULTS

- Of the 38 patients included in this analysis, 8 carried a diagnosis of CAV
- Global Myocardial Flow Reserve (MFR):
 - MFR was noted to be significantly higher in patients without a history of CAV as compared to those with a history of CAV (2.86 ± .674 v 2.3±.377 , p = .009).
- Peak Stress Flow (PSF) & Rest Flow (RF)
 - PSF values were noted to be higher in patients with a history of CAV, but without statistical significance (2.1 v 2.04, p = .202).
 - RF values were higher in patients with CAV as compared to those without (0.92 v 0.74, p = .021).
- Using a conventional cutoff value of 2.0 as a normal MFR value, Flow quantification yielded a sensitivity of 25% for the process of CAV
- An MFR cutoff value of 2.5, instead of the conventionally held 2.0, yields a sensitivity of 62.5%, false positive rate of 30% and specificity of 70%

CONCLUSION

- Myocardial flow quantification with dynamic SPECT is feasible in heart transplant recipients.
- SPECT derived MFR is lower in patients with CAV compared to those without and seems to be partly driven by higher rest flows.
- SPECT derived MFR may be helpful in the non-invasive evaluation of cardiac transplant patients.
- The optimal diagnostic cutoff for MFR may be different from the non-transplant population.
- Additional studies are needed in order to determine the prognostic value of SPECT flow quantification in patients with a history of CAV.

REFERENCES

¹ Mehra MR, et al. International Society for Heart and Lung Transplantation working formulation of a standardized nomenclature for cardiac allograft vasculopathy—2010. *J Heart Lung Transplant* 2010;29:717–27. ² Stehlik J, et al. The Registry of the International Society for Heart and Lung Transplantation: twenty seventh official adult heart transplant report—2010. *J Heart Lung Transplant* 2010;29:1089–103. ³ Rahmani M, et al. Allograft vasculopathy versus atherosclerosis. *Circ Res* 2006;99:801–15. ⁴ Aranda JM Jr, Hill J. Cardiac transplant vasculopathy. *Chest* 2000;118: 1792–800. ⁵ Miller RJH, et al. Comparative Prognostic and Diagnostic Value of Myocardial Blood Flow and Myocardial Flow Reserve After Cardiac Transplantation. *J Nucl Med* 2020; 61:249–255. ⁶ Driessen RS, Rajmakers PG, Stuijzand WJ, and Knaapen P. Myocardial perfusion imaging with PET. *Int J Cardiovasc Imaging*. 2017; 33(7): 1021–1031. ⁷ Agostini D, et al. First validation of myocardial flow reserve assessed by dynamic 99mTc-sestamibi CZT-SPECT camera: head to head comparison with 150-water PET and fractional flow reserve in patients with suspected coronary artery disease. The WATERDAY study. *Eur J Nucl Med Mol Imaging* 2018; 45, 1079–1090. ⁸ de Souza ACDAH, et al. Quantification of myocardial flow reserve using a gamma camera with solid-state cadmium-zinc-telluride detectors: Relation to angiographic coronary artery disease. *J Nucl Cardiol*. 2019;10.1007/s12350-019-01775-z. ⁹ Nkoulou R, et al. Absolute myocardial blood flow and flow reserve assessed by gated SPECT with cadmium-zinc-telluride detectors using 99mTc-Tetrofosmin: head-to-head comparison with 13N-ammonia PET. *J Nucl Med*. 2016;57:1887–92. ¹⁰ Wells RG, et al. Optimization of SPECT measurement of myocardial blood flow with corrections for attenuation, motion, and blood-binding compared to PET. *J Nucl Med* 2017;58:2013-9.

DISCLOSURES

Prem Soman: Grant funding to the institution Astellas Pharma & Advisory Board: Alnylam Pharma. Ricardo Nieves: no personal disclosures