HIGH RESOLUTION QUANTITATIVE SPIRAL CMR PERFUSION IMAGING DEMONSTRATES A REDUCED ENDOCARDIAL TO EPICARDIAL PERFUSION GRADIENT AND MYOCARDIAL FLOW RESERVE IN PATIENTS WITH MICROVASCULAR DISEASE

Michael Salerno[1,2], Yang Yang[3], Peter Shaw[4], Angela Taylor[4], Craig Meyer[3], Fred Epstein[3], and Christopher Kramer[4,5]

[1]Medicine, Cardiology, University of Virginia, Charlottesville, VA, United States, [2]Radiology, University of Virginia, Charlottesville, VA, United States, [3]Biomedical Engineering, University of Virginia, VA, United States, [4]Medicine, Cardiology, University of Virginia, VA, United States, [5]Radiology, University of Virginia, VA, United States

TARGET AUDIENCE: Clinicians and researchers interested in first-pass myocardial perfusion and microvascular disease.

INTRODUCTION:

It is increasingly recognized that patients that have chest pain without obstructive coronary artery disease (CAD) may have abnormal myocardial perfusion reserve (MPR) resulting from microvascular disease (MVD). An abnormal MPR as demonstrated by positron emission tomography (PET) is a significant predictor of cardiovascular death.[1] .The prevalence of MVD is increasing with the growing number of patients with obesity, diabetes, and metabolic syndrome. CMR perfusion imaging has recently detected transmural differences in the endocardial-to-epicardial perfusion ratio (EER) which was approximately 1.1 in segments without obstructive CAD and 0.4 in segments with ischemia and obstructive CAD.[2] High-resolution quantitative first-pass CMR provides the unique ability to quantify transmural differences in perfusion abnormalities which cannot be assessed with PET due to inadequate spatial resolution. We hypothesized that patients with anginal symptoms and non-obstructive CAD would have a reduction in global MPR, a reduction in EER, and transmural differences in MPR consistent with subendocardial ischemia.

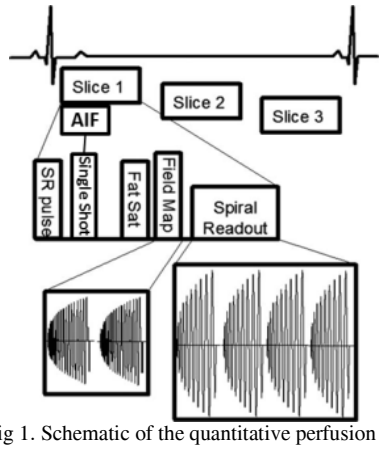

Fig 1. Schematic of the quantitative perfusion pulse sequence

METHODS: Seventeen patients with a high likelihood of MVD with symptoms of angina or shortness of breath without significant CAD at coronary angiography were recruited to undergo a vasodilator stress perfusion study on a 1.5T scanner (Siemens Avanto). Quantitative CMR perfusion imaging was performed using a dual-contrast high-resolution 2x accelerated spiral pulse sequence (fig. 1).[3] Sequence parameters included: 8 interleaves of variable density spirals with density from 0.75 to 0.2 Nyquist, 6.1ms readout per interleaf, TE 1.0 ms, TR 9ms, TI 80ms, FA 35°, FOV 320mm^2, in-plane resolution 1.48mm. Perfusion images were acquired at three short-axis slice positions during first pass using 0.075mmol/kg of Gd-DTPA. Quantification of perfusion was performed on a pixel-wise basis using Fermi-function deconvolution following image-alignment with non-rigid registration using ANTS (Advanced Normalization Tools)[4]. Results are expressed as mean±standard deviation. Two-tailed paired t-tests were used for comparisons with $p<0.05$ considered significant.

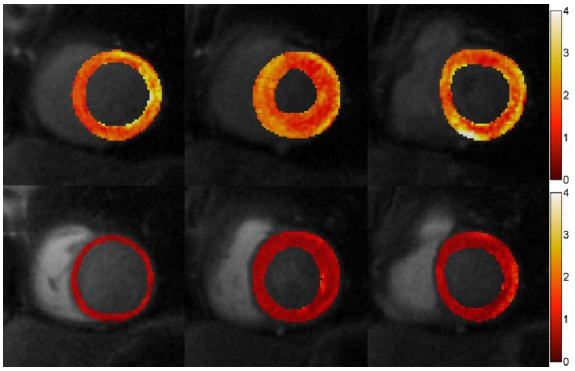

Fig 2. Quantitative (a) Stress and (b) Rest perfusion maps

RESULTS: Figure 2 shows absolute perfusion maps at stress (top) and rest (bottom) from one subject. Higher stress perfusion and greater perfusion reserve are evident in the epicardium as compared to the endocardium (fig 3). Across all subjects, the mean resting perfusion was 1.27±0.34 ml/g/min, the mean stress perfusion was 2.5±0.34 ml/g/min, and the MPR was 1.98±0.35. Stress EER was lower than rest EER (0.94 ±0.35 vs 1.04±0.08 $p<0.001$)(fig 4). While there was no difference in perfusion between the endocardium and epicardium at rest (1.31±0.38 vs1.24±0.32 $p=0.08$) there was a significant difference at stress (2.41±0.68 vs 2.56± 0.74 $p<0.001$). Furthermore, the MPR ratio from the endocardium to the epicardium differed between rest and stress ($p<0.001$) and was less than 1 at stress ($p<0.001$) but not at rest ($p=0.07$).

DISCUSSION: High resolution quantitative spiral perfusion imaging demonstrated a low MPR as well as a reduction in the ratio of endocardial to epicardial perfusion in patients with suspected MVD. Both the endocardial and epicardial microvasculature demonstrate autoregulation in response to changes in coronary perfusion.[5] In the absence of obstructive CAD stress endocardial blood flow typically exceeds epicardial blood flow by about 10% resulting in a stress EER of 1.1. However as the endocardium has a lower autoregulatory capacity, MPR is reduced in the endocardium before the epicardium.[5] Our finding of a stress EER<1 is consistent with impaired microvascular function in this patient population indicating worse exhaustion of vasodilatory capacity in the endocardial microvasculature as compared to the subepicardial microvasculature. The ability to detect transmural differences in perfusion and perfusion reserve is unique to CMR as PET has inadequate spatial resolution to resolve transmural differences in myocardial perfusion, and thus CMR is uniquely suited to study this disease entity.

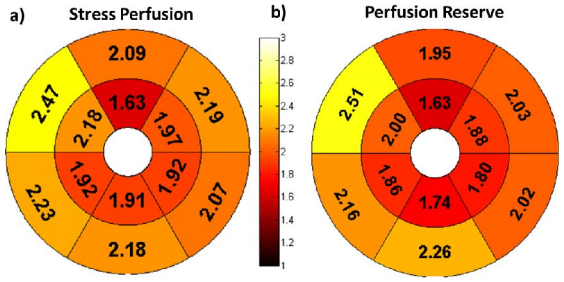

Fig 3: Epicardial (outer) and endocardial (inner) absolute stress perfusion (in ml/g/min) (a) and perfusion reserve (b) from the mid-slice of patient in figure 2 demonstrate a reduced EER

CONCLUSIONS: Patients with MVD and absence of significant epicardial coronary disease demonstrate reduced global MPR and EER ratios, suggesting that subendocardial ischemia due to impaired microvascular function may play an important role in this disease. High resolution CMR perfusion is unique in its ability to delineate transmural perfusion gradients and will be an important tool for studying MVD.

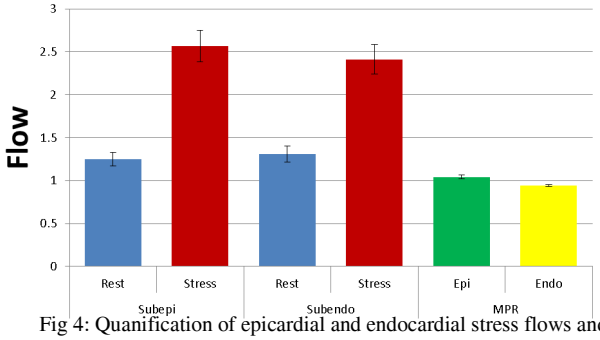

Fig 4: Quanification of epicardial and endocardial stress flows and MPR demonstrate a reduced EER at stress

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