Impaired Myocardial Flow Reserve on ^{82}Rubidium Positron Emission Computed Tomography in Patients with Systemic Sclerosis

Attila Feher, Nabil E. Boutagy, Evangelos K. Oikonomou, Stephanie Thorn, Yi-Hwa Liu, Edward J. Miller, Albert J. Sinusas and Monique Hinchcliff

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Slide 1: Coronary Microvascular Disease in RP
The coronary microcirculation represents small intramural vessels with an intraluminal diameter of <500μm. In the absence of epicardial coronary artery disease, myocardial flow reserve (MFR) is an indirect measure of coronary microvascular function. The MFR is calculated as a ratio of myocardial blood flow during pharmacological stress compared to rest myocardial blood flow. The normal MFR greatly depends on age and gender, however, it is well accepted that a MFR <2.0 is low enough to result in ischemia, and a MFR <1.5 is associated with poor outcomes. To date, no studies have investigated the relationship between Raynaud phenomenon (RP) and coronary microvascular disease by positron emission tomography (PET) MFR assessment, which is the gold standard for the assessment for coronary microvascular disease (CMVD). We hypothesized that secondary RP may be associated with reduced PET MFR.

Slide 2: Methods
In order to investigate this, we conducted a retrospective cohort study where we identified 49 patients with a diagnosis of RP who underwent ^{82}Rubidium PET/CT myocardial perfusion imaging at Yale New Haven Hospital. We compared these patients to two sets of controls: 14 healthy controls without any co-existing medical conditions and a matched control group of 49 patients without RP or any autoimmune disease who were matched for age, gender, BMI, smoking, and cardiovascular comorbidities. All of the patients and the controls underwent Dynamic PET myocardial perfusion imaging.

Slide 3: PET myocardial blood flow quantification
Here you can see two representative sets of images for a patient who has RP and SSc, on the left, and a control patient without RP or autoimmune disease, on the right. On the top rows you can see representative short axis slices and long axis slices with stress at the top and rest at the bottom. These are representative slices of the myocardium. Here you can see that there are no big perfusion defects, so the radiotracer uptake is homogeneous. This is true for both the patient with RP and SSc and for the patient without RP. If you record the blood pool and the myocardial radiotracer uptake over time and you apply kinetic modeling you can estimate myocardial blood flow. Here you can see that the stress myocardial blood flow is reduced in the patient with RP and SSc, with normal rest myocardial blood flow resulting in reduced MFR. Again, with severely reduced being <1.5. At the same time, the patient without RP had normal stress myocardial blood flow, normal rest myocardial blood flow, and normal MFR.

Slide 4: Patient demographics
Here on this table, you can see that the matching process worked quite well. Patients were comparable to controls with regards to age, gender, body mass index (BMI) and co-morbidities.

Slide 5: Results – correlations with MFR

The time since RP diagnosis correlated inversely with myocardial flow reserve. However, there was no correlation between sedimentation rate or C-reactive protein levels with myocardial flow reserve.

Slide 6: Results – MBF quantification
As for the main results of our findings, you can see that for stress myocardial blood flow, patients with SSc and RP, as indicated by red, had significantly reduced stress myocardial blood flow when compared to healthy participants. At the same time, they had significantly increased rest myocardial blood flow when compared to the matched control patients. This, according to this formula, resulted in a reduced MFR in patients with SSc and RP when compared to both the healthy participants and the matched control patients. At the same time, if you look at the light blue bar, the patients with primary RP had very similar stress myocardial blood flow, rest myocardial blood flow, and MFR values when compared to both healthy participants and matched control patients.

Slide 7: Results – univariate predictors of low MFR (<2.0)
We also did univariate analysis to identify predictors of low MFR, and with this we found SSc and prior revascularization to be associated with low MFR, meaning MFR <2.0.

Slide 8: Results – multivariate predictors of low MFR
In this multivariate analysis, only SSc was an independent predictor for reduced MFR.

Slide 9:
In conclusion, our results indicate that in patients with secondary RP, SSc was associated with reduced global PET MFR when compared to both healthy participants and patients without RP and autoimmune disease who were similar in age, gender, BMI, and co-morbidities. Therefore, SSc may be an independent predictor of reduced MFR. At the same time, patients with primary RP had MFR values that were comparable with healthy participants and matched patient controls. Larger prospective studies are needed to validate these findings and to find out whether MFR has any prognostic value in patients with RP.