The Impact of Diabetes Mellitus on Territory-Specific Myocardial Flow Reserve in the Presence of Epicardial Coronary Disease

Kai Yi Wu[1,2], BHSc, Nicholas P. Timmerman[1,2], BHSc, Rachel McPhedran[2], BSc, Rob S. Beanlands[1,2], MD, Rob A. deKemp[1,2], PhD, Aun-Yeong Chong[1,2], MD, MRCP(UK), MBBS

[1]University of Ottawa Faculty of Medicine, [2]University of Ottawa Heart Institute, Ottawa ON, Canada

Background

Diabetes mellitus (DM) is associated with diffuse atherosclerosis and microvascular dysfunction which may impact measurement of flow and revascularization therapies.[1] The impact of diabetes-related microvascular dysfunction in the presence of epicardial disease is not well known. MFR is a measure of the capacity of the coronary vasculature to maximally increase blood flow, represented as a ratio of peak hyperemic (stress) to resting blood flow. It is blunted by epicardial stenoses and diffuse microcirculatory disease.[2] **We sought to determine if myocardial flow reserve (MFR) by positron emission tomography (PET) is reduced in patients with DM across the CAD spectrum.**

Methods

Patient Characteristics

- 252 consecutive patients (63.9 ± 10.6 years, 181 males, 101 DM) who had both 82Rb PET and invasive coronary angiography within 6 months between July 2012 and April 2016 were included.

Quantification of Atherosclerotic Burden:

- To account for the effect of multiple and diffuse epicardial lesions, vessel segments with stenoses >50% were assigned SYNTAX scores multiplied by the % stenosis, and summed to generate territory-specific SYNTAX-weighted Scores (SWS).

PET:

- 82Rb PET was used to measure each patient's left ventricular (LV) myocardial blood flow (MBF) and myocardial flow reserve (MFR) was calculated for each vessel territory (LAD, LCX, and RCA) by taking the ratio of MBF at stress divided by MBF at rest.
- A modified LAD MFR that excluded the apex (segment 17) was used to account for potential bias due to apical thinning.
- MFR for the whole left ventricle (global MFR) was obtained by averaging MFR in the 16 segments.

Statistical Analyses

- Univariate linear regression analysis was used to evaluate the strength of the relationship of potential predictors which included DM status, rate pressure product (RPP), LV ejection fraction (EF), sum stress score (SSS), ischemic ECG response, age, sex, BMI, angina status, smoking history, and the presence of hypertension, dyslipidemia, family history of CAD, and previous revascularization.
- Multiple linear regression was used to evaluate the relationship between vessel-specific MFR and vessel-specific SWS, along with significant predictors from the univariate analysis

Results

Table 1: Demographic and co-morbidity data accounting for diabetic and non-diabetic populations (n=252)

Description	DM (n=99)	No DM (n=153)
Age (years)	63.9±9.9	64.0±11.1
Body Mass Index (kg/m^2)†	33.5±6.9	29.2±5.6
Males	69 (69.7%)	112 (73.2%)
Smoker	68 (68.7%)	95 (62.1%)
Current	15 (15.2%)	26 (17.0%)
Former	53 (53.5%)	69 (45.1%)
Never	31 (31.3%)	58 (37.9%)
Hypertension	80 (80.8%)	122 (79.7%)
Dyslipidemia	85 (85.9%)	119 (77.8%)
First Degree Family History of CAD	55 (5.6%)	92 (60.1%)
Previous Revascularization	49 (49.5%)	69 (45.1%)
Ischemia on ECG	27 (27.3%)	37 (24.2%)
Medications		
ACE Inhibitor	70 (70.7%)	98 (4.1%)
ARBs	9 (9.1%)	9 (5.9%)
ASA	78 (78.8%)	120 (78.4%)
Beta Blocker	64 (64.6%)	85(55.6%)
Statin*	88 (88.9%)	120 (78.4%)

† p<0.05 as assessed by t-test
*p<0.05 as assessed by Chi-Squared test

Figure 1: Results from the univariate and multiple linear regression.

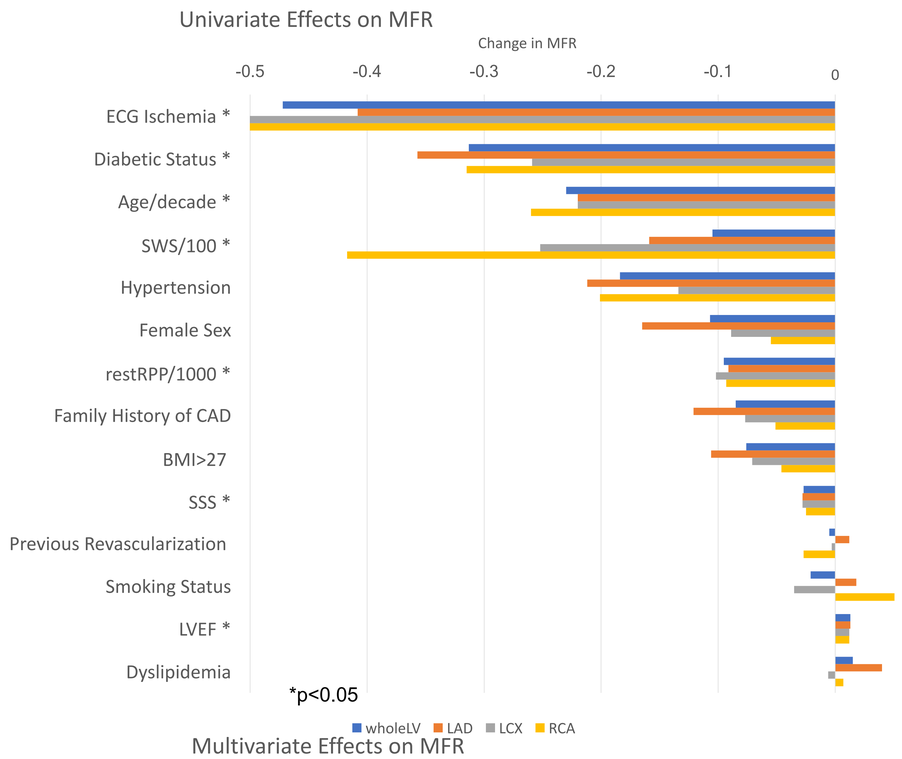


Figure 2: An example of invasive angiography data in a patient with DM with the corresponding 17-segment model polar map from 82Rb PET. The similar MFR for all three vascular territories with different degrees of vascular stenosis suggest the preferential effect of microvascular dysfunction on different vessels.

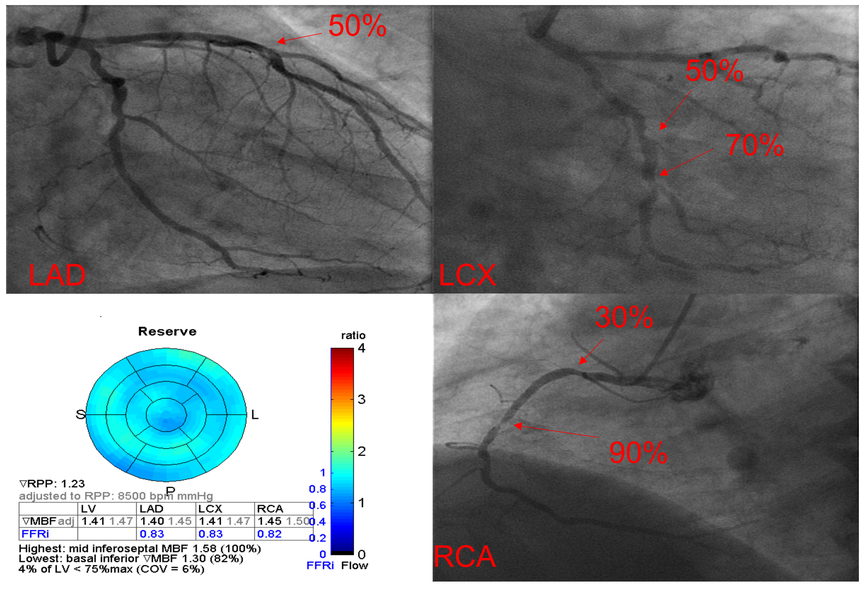
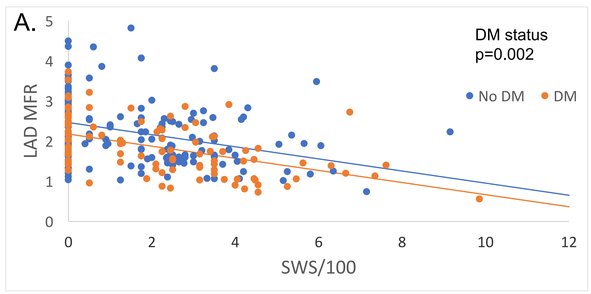
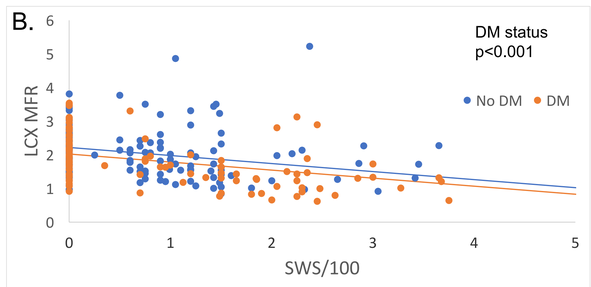
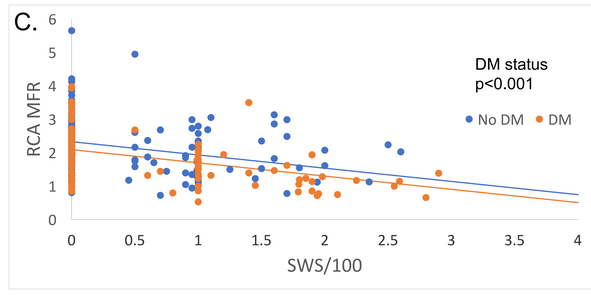


Figure 3: Scatterplots of MFR vs. SWS. Data is separated into patients with DM (orange) and patients without DM (blue) **A.** LAD MRF vs. LAD SWS **B.** LCX MFR vs. LCX SWS **C.** RCA MFR vs. RCA SWS. The regression lines from the bivariate regression with DM and SWS are shown to illustrate the effect of DM on MFR.







Conclusions

- DM is associated with a reduction in MFR independent of other risk factors and epicardial CAD, and therefore should be considered in the clinical interpretation of PET perfusion.
- Epicardial disease underestimates the degree of flow impairment in DM.
- This may impact flow directed revascularization whereby flow measurements may indicate severe disease not appreciated by anatomy.

References

1. Laakso M. Heart in diabetes: a microvascular disease. Diabetes care. 2011 May 1;34(Supplement 2):S145-9.
2. Murthy VL, Naya M, Foster CR, Hainer J, Gaber M, Di Carli G, Blankstein R, Dorbala S, Sitek A, Pencina MJ, Di Carli MF. Improved Cardiac Risk Assessment With Noninvasive Measures of Coronary Flow ReserveClinical Perspective. Circulation. 2011 Nov 15;124(20):2215-24.

Presenter contact information: Kai Yi Wu, BHSc
kwu095@uottawa.ca