SUPPLEMENTARY APPENDIX

Supplemental 1. Imaging protocol and analysis

Imaging protocol

Myocardial perfusion reserve (MPR) was calculated on SPECT using a Discovery NM 530c camera (DNM, GE Healthcare). All stress tests were performed using dipyridamole infusion. Patients were told to abstain from caffeine-containing products for 12 hours before the test. Dipyridamole (0.56 mg/kg) was infused over 4 minutes and ^{99m}Tc-SestaMIBI was injected between 6 and 8 minutes following the beginning of dipyridamole infusion. Dipyridamole effect was reversed by systematic intravenous administration of aminophylline (50-100 mg). A six-minutes dynamic stress acquisition was started before ^{99m}Tc-SestaMIBI (3.7 MBq/Kg) manual injection over 30 sec. A conventional stress acquisition was performed 40 minutes after injection. Dynamic rest perfusion imaging started three hours following stress imaging. A 1-min background acquisition was performed prior to the injection of a three-fold higher dose of ^{99m}Tc-SestaMIBI than that used for stress imaging. A 6-min long dynamic rest acquisition was performed. Conventional rest perfusion imaging was performed 40 min following rest ^{99m}Tc-SestaMIBI injection. Stress and rest ^{99m}Tc-SestaMIBI injected doses were conditioned in a similar volume of 1.5 ml. Stress and rest LIST mode acquisitions were performed in the supine position while conventional stress and rest acquisitions were performed in both prone and supine positions.

Stress and rest conventional myocardial perfusion images were analyzed as previously described [1]. LIST mode data were reframed on a Xeleris station (v4.0; GE Healthcare) for myocardial flow and MPR quantification. The bolus phase was reframed in 12 frames of 5 sec each and the tissue phase was reframed in 2 frames of 120 sec each. Background acquisitions were performed prior to rest imaging in order to account for the residual activity from previous stress imaging. Quantification of MPR was performed using Corridor4DM software (INVIA Medical Imaging Solutions - Algorithm: GE 530c Tc-99m NetRet Leppo, v2015.0.2.66). The left ventricle surface and the location of the mitral valve plane were automatically estimated by

the program on summed frames from a portion of dynamic acquisition to extract time activity curves. Manual processing was performed when the surfaces were incorrectly identified due to poor orientation, suboptimal centering of the left ventricle or high extra-cardiac activity. The left ventricle blood time activity curves was sampled from a 3-dimensional region of interest placed on the mitral valve plane. Myocardial perfusion reserve (MPR) values were calculated from compartmental analysis of blood and tissue time activity curves [2].

Supplemental 2. Invasive coronary angiography and coronary functional assessment: protocol and analysis

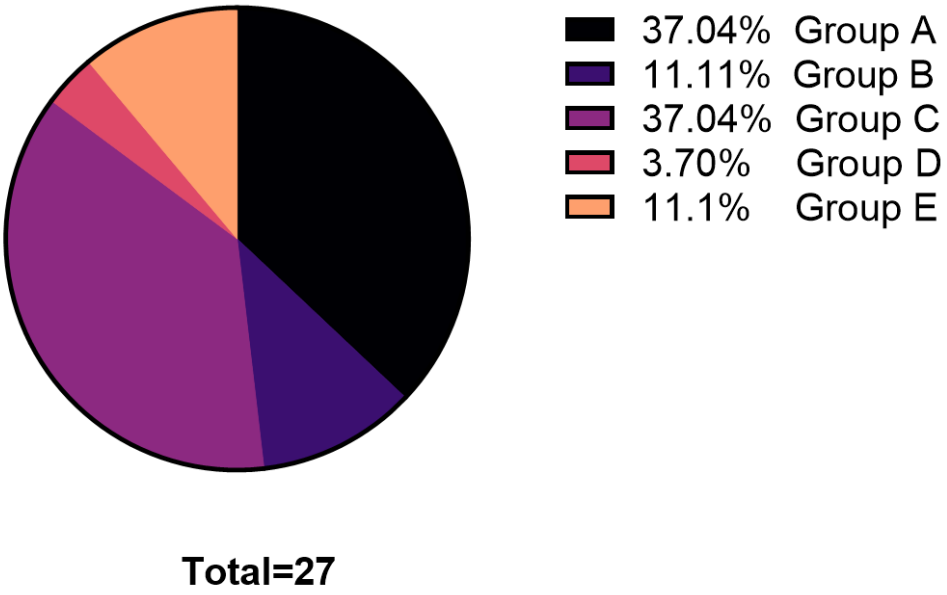
Invasive coronary angiography was performed using standard techniques using the Judkins technique and a radial approach with 6-French catheters (Philips Allura Xper FD10, Philips Healthcare). A coronary pressure wire (PressureWire X, Abbott, IL, USA) was introduced at maximal hyperemia induced by intravenous adenosine (140 µg/kg/min). The coronary pressure wire was flushed. Following calibration to zero pressure, the coronary pressure wire was equalized to the guide catheter pressure with the sensor positioned at the ostium of the coronary artery. The pressure sensor was then positioned at the distal segment of a target vessel, and intracoronary nitrate (100 or 200 mg) was administered before each measurement. Resting mean transit time was obtained in triplicate by rapid intracoronary manual administrations of a 3 mL bolus of saline at room temperature. Hyperemic mean aortic pressure, distal intracoronary pressure, and hyperemic mean transit time were measured in triplicate during sustained hyperemia.

S**upplemental 3. Baseline characteristics of RA patients who declined coronary angiography and studied population.**

	Coronary angiography declined N=6	MPR<2 N=37	P value
Demographic			
Mean (SD) age, y	64.5 (8.0)	66.7 (10.3)	N.S
Gender, female n (%)	4 (66.7)	26 (70.2)	N.S
RA characteristics			
RF and/or ACPA, n (%)	6 (100.0)	30 (81.1)	N.S
Median (ICQ) disease duration, months	162.0 (225.0)	120.0 (186.0)	N.S
Median (ICQ) DAS28-CRP, units	4.6 (2.0)	3.4 (2.2)	N.S
Median (ICQ) CRP, mg/L	3.2 (6.2)	2.8 (9.6)	N.S
Median ESR (ICQ), mm/h	6.5 (15.0)	8.0 (14.0)	N.S
Cardiovascular risk factor			
Median (ICQ) BMI, kg/m2	26.5 (8.0)	26.5 (5.1)	N.S
Current smoker, n (%)	1 (16.7)	8 (21.6)	N.S
Hypertension, n (%)	3 (50)	17 (45.9)	N.S
Diabetes Mellitus, n (%)	1 (16.7)	5 (13.5)	N.S
Dyslipidaemia, n (%)	0 (0.0)	9 (24.3)	N.S
Cardiovascular familial history, n (%)	1 (16.7)	6 (8.7)	N.S
Symptoms			
Dyspnoea NYHA>1, n (%)	1 (16.7)	9 (24.3)	N.S
Atypical chest pain, n (%)	1 (16.7)	3 (8.0)	N.S
Current treatment (yes vs no)			
TNF inhibitors, n (%)	1 (16.7)	11 (29.7)	N.S
Methotrexate, n (%)	2 (33.3)	18 (48.6)	N.S
Prednisone, n (%)	1 (16.7)	10 (27.0)	N.S

ACPA, anti- citrullinated protein/peptide antibody; BMI, Body mass index; CRP, C-reactive protein; DAS, disease activity score; ECG, electrocardiogram; ESR, erythrocyte sedimentation rate; ICQ, interquartile; MPR, myocardial perfusion reserve; NYHA, New York Heart Association; RA, rheumatoid arthritis; RF, rheumatoid factor; SD, standard deviation; TNF, tumour necrosis factor
Absence of coronary dysfunction: MPR<2, or ≥2 and normal coronary angiography
N/A: not appropriate as the outcome measure was not included in the multivariate analysis
N.S: non-significant

Supplemental 4. Proportion of functional or structural coronary dysfunction on coronary angiography



Group A : CFR≥2, IMR≥25 (n=10); Group B : CFR ≥2, IMR<25 (n=3); Group C : CFR<2, IMR≥25 (n=10); Group D : CFR<2, PTDVG>15 mmHg (n=1); Group E : CFR not available, PTDVG>15 mmHg (n=3)

Supplemental 5. Predictors of microvascular or macrovascular dysfunction according to coronary angiography

	Coronary microvascular dysfunction N=17	Coronary macrovascular dysfunction N=7	P value
Demographic			
Mean (SD) age, y	68.5 (10.4)	69.9 (12.9)	N.S
Gender, female n (%)	12 (70.6)	4 (57.1)	N.S
RA characteristics			
RF or ACPA, n (%)	13 (76.5)	6 (85.3)	N.S
Median (ICQ) disease duration, months	72.0 (150.0)	120.0 (264.0)	N.S
Mean (SD) DAS28-CRP, units	3.0 (1.3)	3.8 (1.5)	N.S
Median (ICQ) CRP, mg/L	3.2 (14.0)	6.6 (12.4)	NS
Median (ICQ) ESR, mm/h	8.0 (12.0)	19.5 (44.7)	N.S
Cardiovascular risk factor			
Median (ICQ) BMI, kg/m2	**28.6 (4.0)**	**24.6 (3.6)**	**<0.01**
Current smoker, n (%)	4 (23.5)	2 (28.6)	N.S
Hypertension, n (%)	7 (41.2)	5 (71.4)	N.S
Diabetes Mellitus, n (%)	2 (11.2)	1 (14.7)	N.S
Dyslipidaemia, n (%)	5 (29.4)	1 (14.3)	N.S
Cardiac Heredity, n (%)	4 (23.5)	1 (14.3)	N.S
Current treatment (yes vs no)			
TNF inhibitors, n (%)	7 (41.2)	2 (28.6)	N.S
Methotrexate, n (%)	9 (52.9)	4 (57.1)	N.S
Prednisone, n (%)	4 (23.5)	3 (42.8)	N.S
ECG			
ECG abnormality, n (%)	8 (47.0)	6 (85.7)	N.S
Repolarisation abnormality, n (%)	5 (29.6)	4 (57.1)	N.S

ACPA, anti- citrullinated protein/peptide antibody; BMI, Body mass index; CRP, C-reactive protein; DAS, disease activity score; ECG, electrocardiogram; ESR, erythrocyte sedimentation rate; ICQ, interquartile; NYHA, New York Heart Association; RA, rheumatoid arthritis; RF, rheumatoid factor; SD, standard deviation; TNF, tumour necrosis factor
N.S: non-significant

Results were presented as number of patients and percentages for categorical data and analysed using Chi-square test, Fisher's exact test as appropriate.

1 Djaileb L, Dubois B, de Leiris N, *et al.* Prospective diagnostic performance of semiconductor SPECT myocardial perfusion imaging: wall thickening analysis reduces the need for an additional prone acquisition. *Eur J Nucl Med Mol Imaging* 2019;**46**:2042–50. doi:10.1007/s00259-019-04415-3

2 Agostini D, Roule V, Nganoa C, *et al.* First validation of myocardial flow reserve assessed by dynamic 99mTc-sestamibi CZT-SPECT camera: head to head comparison with 15O-water PET and fractional flow reserve in patients with suspected coronary artery disease. The WATERDAY study. *Eur J Nucl Med Mol Imaging* 2018;**45**:1079–90. doi:10.1007/s00259-018-3958-7