# Nuclear cardiology in the literature: A selection of recent, original research papers

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**Myocardial Microvascular Dysfunction in Rheumatoid Arthritis. Quantitation by 13N-Ammonia Positron Emission Tomography/Computed Tomography**

Isabelle Amigues, Cesare Russo, Jon T. Giles, Aylin Tugcu, Richard Weinberg, Sabahat Bokhari and Joan M. Bathon

New York, NY

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***Context:*** Patients with rheumatoid arthritis (RA) have a high prevalence of cardiovascular disease. Inflammation in RA could be associated with myocardial microvascular disease and in turn result in cardiac dysfunction.

***Methods and Results:*** In order to assess the prevalence of myocardial microvascular dysfunction in patients with RA, the authors prospectively performed rest/vasodilator stress N-13 ammonia positron emission tomography (PET) and echocardiography in 76 patients with RA, but no clinical cardiovascular disease. Data on non-RA controls was retrospectively collected from patients (asymptomatic, $n = 14$ and symptomatic, $n = 34$) who had undergone rest/vasodilator stress N-13 ammonia PET. Global myocardial blood flow was quantified at rest and during peak hyperemia, and myocardial flow reserve (MFR) was calculated as the ratio peak stress myocardial blood flow and resting myocardial blood flow. The authors observed that the mean MFR in RA patients was $2.9 \pm 0.8$, with 29% having reduced MFR ($< 2.5$). Male gender (β-coefficient, $p$ value: $-0.54$, 0.008) and higher interleukin-6 levels (β-coefficient, $p$ value: $-0.33$, 0.04) were significantly associated with lower MFR, while the use of tumor necrosis factor (TNF) inhibitors was associated with higher MFR (β-coefficient, $p$ value: 0.43, 0.02). Lower MFR was associated with higher left ventricle mass index and higher left ventricle volumes but not with ejection fraction or diastolic dysfunction. MFR was similar in RA and symptomatic controls ($2.9 \pm 0.8$ versus $2.55 \pm 0.6$; $p = 0.48$), while it was higher in the asymptomatic controls ($3.25 \pm 0.7$), though not statistically different. Results of this study indicate that microvascular dysfunction is present in a significant proportion of patient with RA and no clinical cardiovascular disease, and that MFR in RA patients was similar to symptomatic patients referred for a clinically indicated myocardial perfusion PET.

***Significance:*** The report of the high prevalence of microvascular dysfunction in RA is a novel finding. The association of microvascular dysfunction with inflammatory markers suggests a pathophysiologic mechanism of cardiac dysfunction in these patients. Whether microvascular dysfunction contributes to heart failure in RA patients needs to be further explored.

**Relative Apical Sparing of Myocardial Longitudinal Strain is Explained by Regional Differences in Total Amyloid Mass Rather Than the Proportion of Amyloid Deposits**

Paco E. Bravo, Kana Fujikura, Marie Foley Kijewski, Michael Jerosch-Herold, Sophia Jacob, Mohamed Samir El-Sady, William Sticka, Shipra Dubey, Anthony Belanger, Mi-Ae Park, Marcelo F. Di Carli, Raymond Y. Kwong, Rodney H. Falk and Sharmila Dorbala

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***Context:*** Relative apical sparing (RELAPS) of left ventricular (LV) longitudinal strain (LS) is being increasing used as a marker of cardiac amyloidosis (CA)

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on echocardiography. The pathophysiological mechanism of RELAPS is not well understood.

***Methods and Results:*** To determine whether regional differences in markers of amyloid burden explain the occurrence of RELAPS, the authors prospectively studied 32 patients (62 ± 7 years; 50% males) with light-chain CA. All subjects underwent two-dimensional echocardiography for LS estimation and 18F-florbetapir PET for quantification of LV florbetapir retention index (RI). Additionally, a subset of patients ($n = 22$) also underwent estimation of extracellular volume fraction [ECV] by cardiac magnetic resonance (CMR). Extracellular LV mass (LV mass x ECV) and total florbetapir binding (extracellular LV mass x florbetapir RI) were also calculated. All parameters were measured globally and regionally (base, mid, and apex). The authors found a significant base-mid-apex gradient in LS (− 7.4 ± 3.2% vs − 8.6 ± 4.0% vs − 20.8 ± 6.6%; $p < 0.0001$), maximal LV wall thickness (15.7 ± 1.9 cm vs 15.4 ± 2.9 cm vs 10.1 ± 2.4 cm; $p < 0.0001$), and LV mass (74.8 ± 21.2 g vs 60.8 ± 17.3 g vs 23.4 ± 6.2 g; $p < 0.0001$). On the contrary, florbetapir RI (0.089 ± 0.03 μmol/min/g vs 0.097 ± 0.03 μmol/min/g vs 0.085 ± 0.03 μmol/min/g; $p = 0.45$) and ECV (0.53 ± 0.08 vs 0.49 ± 0.08 vs 0.49 ± 0.07; $p = 0.15$) did not show any significant base-to-apex gradient in the tissue concentration or proportion of amyloid infiltration. However, markers of total amyloid load, such as total florbetapir binding (3.4 ± 1.7 μmol/min vs 2.8 ± 1.5 μmol/min vs 0.93 ± 0.49 μmol/min; $p < 0.0001$) and extracellular LV mass (40.0 ± 15.6 g vs 30.2 ± 10.9 g vs 11.6 ± 3.9 g; $p < 0.0001$), showed a significant base-to-apex gradient. Results of this multimodality imaging study suggest that regional differences in LS on echocardiography are likely due to the distribution of total amyloid mass, than by the proportion of amyloid deposits.

***Significance:*** This important investigation provides a mechanistic basis for RELAPS, and, confirms that RELAPS is related to the total amyloid mass and not to the proportion of amyloid infiltration. There is a greater amyloid mass in the basal and mid segments when compared to the apical segments, resulting in reduced deformation in the basal and mid segments, and producing the characteristic RELAPS pattern of LS on echocardiography.

### FDG Atrial Uptake is Associated with an Increased Prevalence of Stroke in Patients with Atrial Fibrillation

Mathieu Sinigaglia, Besma Mahida, Eve Piekarski, Renata Chequer, Nidaa Mikail, Khadija Benali1, Fabien Hyafil, Dominique Le Guludec, François Rouzet

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***Context:*** Inflammatory and fibrotic changes in the atria have been reported among patients with atrial fibrillation (AF). Relationship between atrial inflammation and the occurrence of cardioembolic events among patients with AF is not known.

***Methods and Results:*** To determine the relationship between atrial inflammation in AF and occurrence of cardioembolic events, the authors performed a case–control study of patients who had undergone a [$^{18}$F]fluorodeoxyglucose-positron emission tomography/computed tomography ($^{18}$F-FDG-PET/CT) for assessment of cardiac inflammation or infection. All PET studies included in this evaluation were performed after a high-fat low-carbohydrate diet and a prolonged fast. A total of 128 patients were retrospectively studied—64 patients with AF (cases) and 64 age, gender matched controls without AF. Visual (0 = no uptake and 1 = uptake superior to mediastinum) and quantitative FDG uptake in the atria and the atrial appendages was determined. The authors noted that diffuse right atrial uptake was present in one-third of patients with AF and only two patients in the control group (3%). FDG uptake intensity of both atria was significantly associated with the presence of AF. The occurrence of stroke was strongly associated with detectable right atrial uptake in multivariate analysis (OR, 95% CI right atrium—14.3, 4.4-46.5), with an odds ratio superior to that of other known risk factors. These results indicate significant atrial FDG uptake among patients with AF, which is associated with the occurrence of cardioembolic events.

***Significance:*** This is a novel retrospective analysis showing the increased atrial FDG uptake among patient with AF, and the association between atrial uptake and occurrence of stroke. The relationship between right atrial, and not left atrial, FGD uptake with the occurrence of stroke is particularly intriguing. However, since the study patients were originally imaged for other inflammatory and infectious indications, it cannot be ascertained with certainty that atrial FDG uptake is a result of AF or underlying cardiac conditions (e.g. sarcoidosis). A confirmative evaluation among patients with AF and without other inflammatory conditions is thus warranted.

## Disclosure

*The author has nothing to disclose.*