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Arterial FDG Uptake in Rheumatoid Arthritis Correlates with Synovial Activity: A Human FDG-PET/CT Study

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To the Editor: Previous studies have demonstrated that patients with RA have increased risk of CVD. While a prior study has reported an increase in atherosclerotic plaque inflammation in RA patients (1), the relationship between joint inflammation and arterial inflammation has not been previously reported. Further, the contribution of RA to arterial inflammation, (after adjusting for CVD risk factors and statin use), remains unknown.

FDG-PET/CT is a well-established tool that has been used to quantitatively assess the burden of inflammation in atherosclerotic plaques(2), risk of future CVD events (3) and degree of disease activity in RA (4). In this study, we used FDG-PET/CT imaging to assess: 1) whether patients with RA have increased arterial FDG uptake, and 2) whether synovial activity correlates with arterial FDG uptake. The study population was identified from a database of individuals imaged for clinical purposes who were found to be free from cancer and CVD. First, 33 individuals with RA (RA Group) were identified based on a clinical diagnosis derived from the clinical records and then were matched (1:1) to individuals with neither RA nor CVD (Matched Controls) based on age (±6 years) and gender.

Measurement of FDG uptake in aorta and synovial tissues were performed as previously detailed. (2,4) Synovial activity was measured in glenohumeral, acromioclavicular, and

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acetabulofemoral joints and recorded as average of maximum SUVs (Figure 1D). Additionally, FDG uptake of subcutaneous adipose tissue (SAT) was measured as control tissue and coronary calcium scoring was performed for the entire patient population.

There were no statistically significant differences in age, gender, blood pressure, FRS, lipid profile or statin use between the RA group and Matched Controls. Arterial TBR was significantly higher in RA vs. Matched Controls (2.15±0.29 vs. 1.84±0.32; P=0.001; Figure 1A, C). This difference remained significant after adjusting for age, gender, hypertension, diabetes, smoking, dyslipidemia, BMI (β=0.273; P=0.001) and after adjusting for statin use, LDL and HDL (β=0.297; P=0.002).

The difference in arterial TBR remained consistent across subgroup analyses. In individuals with FRS<10, TBR was higher in subjects with RA (2.06±0.25 vs. 1.80±0.17; P=0.001). Likewise, arterial TBR remained significantly higher in RA group in individuals: 1) without coronary calcium (p=0.002), 2) with LDL <130 mg/dL (p=0.01), or 3) who were statin naive (p<0.001). Because a subset of the individuals were cancer survivors undergoing surveillance scanning, we evaluated the between-group differences after adjusting for prior cancer chemotherapy and radiotherapy, and observed a persistent increase in arterial TBR among those with RA (β=0.34, p<0.001).

Moreover, we observed a significant correlation between synovial and arterial FDG uptake (SUV) in patients with RA (R=0.42, P=0.015); but not in controls (R=0.28, P=0.11). This relationship remained significant after correcting for background venous activity (TBR) (R=0.55, P=0.001, Figure 1B). In contrast, there was no significant correlation between arterial vs. SAT FDG uptake (R=0.17; P=0.14). We did not observe a correlation between CRP levels and arterial (p=0.67) or synovial FDG uptake (p=0.42)

In this study, we demonstrated that patients with RA have significantly higher arterial FDG uptake compared to matched controls which remained significant after adjusting for atherosclerosis risk factors and statin therapy. Furthermore, we observed a significant correlation between synovial activity and arterial FDG uptake. Collectively, these findings suggest that patients with RA have elevated levels of arterial inflammation beyond that predicted by traditional risk factors; and that arterial inflammation may be related to the severity of RA disease activity (measured as synovial activity). Since arterial FDG uptake has been associated with the risk of subsequent CVD (at least in individuals without RA) (3), these findings add to the body of evidence linking RA disease activity with potentiated risk of CVD.

Abbreviations

CT	computed tomography
CVD	cardiovascular disease
FDG	^{18}F-fluorodeoxyglucose
FRS	Framingham Risk Score

PET	positron emission tomography
RA	rheumatoid arthritis
SUV	standardized uptake value
TBR	target-to-background ratio

References

1. Maki-Petaja KM, Elkhawad M, Cheriyan J, et al. Anti-tumor necrosis factor-alpha therapy reduces aortic inflammation and stiffness in patients with rheumatoid arthritis. Circulation 2012;126:2473–80. [PubMed: 23095282]
2. Tawakol A, Fayad ZA, Mogg R, et al. Intensification of Statin Therapy Results in a Rapid Reduction in Atherosclerotic Inflammation: Results of A Multi-Center FDG-PET/CT Feasibility Study. J Am Coll Cardiol 2013;62:909–17. [PubMed: 23727083]
3. Figueroa AL, Abdelbaky A, Truong QA, et al. Measurement of Arterial Activity on Routine FDG PET/CT Images Improves Prediction of Risk of Future CV Events. JACC Cardiovasc Imaging 2013;6:1250–9. [PubMed: 24269261]
4. Roivainen A, Hautaniemi S, Mottonen T, et al. Correlation of 18F-FDG PET/CT assessments with disease activity and markers of inflammation in patients with early rheumatoid arthritis following the initiation of combination therapy with triple oral antirheumatic drugs. Eur J Nucl Med Mol Imaging 2013;40:403–10. [PubMed: 23229747]

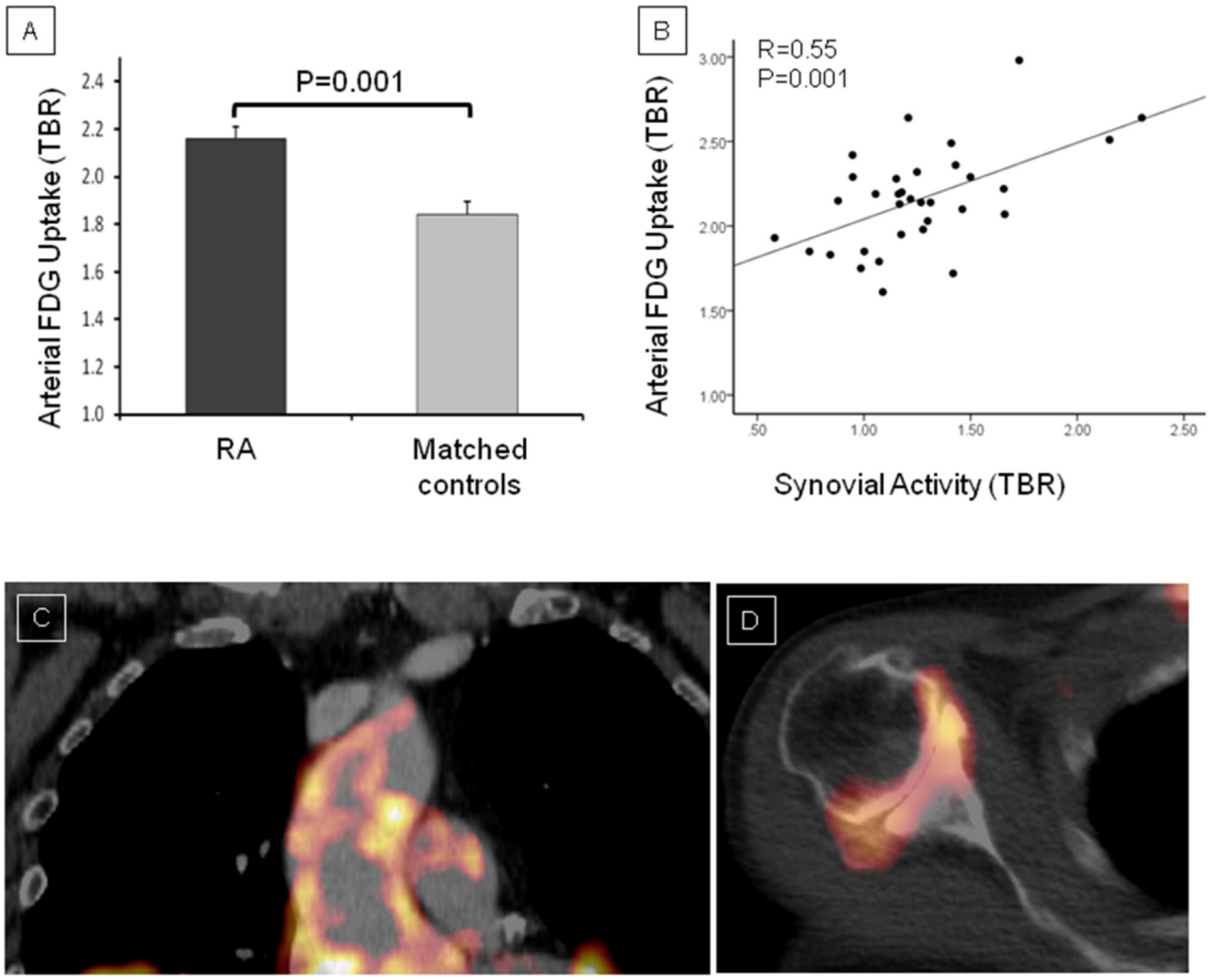

Figure 1.

Aortic TBR was significantly higher in patients with RA vs. Matched Controls. (A) A significant correlation was observed between synovial FDG uptake (a marker of RA disease activity) and arterial TBR in patients with RA. (B) Higher FDG uptake in the wall of ascending aorta in an individual with RA. (C) High synovial activity (FDG uptake) in a patient with RA in the right shoulder (D).