Response to ‘Adipokines, inflammation, insulin resistance, and carotid atherosclerosis in patients with rheumatoid arthritis’

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In a recent report in Arthritis Research & Therapy, Kang and colleagues [1] assessed a series of patients with rheumatoid arthritis (RA) to establish whether adipokines could be a link between inflammation, insulin resistance, and atherosclerosis in RA.

We have noticed that Kang and colleagues did not pay attention to our former studies on the same issue. In this regard, in the last decade, we conducted a series of studies on insulin resistance and adipokines in a cohort of Spanish patients with long-standing RA, undergoing anti-tumor necrosis factor-alpha (anti-TNF-α) infliximab therapy because of severe disease, refractory to conventional disease-modifying anti-rheumatic drugs [2-6].

Kang and colleagues described that resistin was associated with erythrocyte sedimentation rate (ESR) \(r = 0.322, P < 0.001\), C-reactive protein (CRP) \(r = 0.209, P = 0.004\), and increased disease duration \(r = 0.176, P = 0.014\) [1]. Although adipokines have been demonstrated to exert a key role in the interface between obesity, inflammation, insulin resistance, and atherosclerosis in the general population of RA patients and serum leptin levels \(r = -0.369, P < 0.001\) [1]. In our series of RA patients with active disease despite anti-TNF-α therapy, we observed that high-grade inflammation was independently and negatively correlated with circulating adiponectin concentrations [4]. CRP levels correlated with circulating adiponectin concentrations (partial \(r = -0.370, P = 0.04\), independently of age and gender [4].

In contrast, low adiponectin levels clustered with metabolic syndrome features that contribute to atherogenesis in RA [4]. Adiponectin concentrations correlated with triglycerides/high-density lipoprotein (HDL) cholesterol ratios \(r = 0.396, P = 0.03\), total cholesterol/HDL cholesterol ratios \(r = 0.444, P = 0.01\), and high fasting plasma glucose levels \(r = 0.366, P = 0.04\), independently of CRP levels and the body mass index [4]. These results also suggest an implication of adiponectin in the development of cardiovascular disease in RA.

In the series by Kang and colleagues, leptin was associated with homoeostasis model assessment-estimated insulin resistance \(r = -0.369, P < 0.001\) [1]. In our series of RA patients with active disease despite anti-TNF-α therapy, there was a positive correlation between body mass index of RA patients and serum leptin levels \(r = 0.665, P < 0.001\) [5]. Also, a significant correlation of leptin with biomarkers of endothelial activation (vascular cell adhesion molecule-1; \(r = 0.349, P = 0.04\)) was observed [5]. However, no significant correlations between leptin levels and disease duration, ESR and CRP levels, disease activity score using 28 joint counts, lipids, insulin sensitivity, resistin, adiponectin, or the cumulative prednisone dose at the time of the study were found [5]. Therefore, in Western patients with severe and active RA, leptin levels seem to be related to adiposity [5]. However, in our series, circulating visfatin levels were unrelated to disease activity, adiposity, or metabolic syndrome [6].

Although adipokines have been demonstrated to exert a key role in the interface between obesity, inflammation, insulin resistance, and atherosclerosis in the general
population, we agree with Kang and colleagues that information on their potential contribution is still limited in RA. In this regard, in Western individuals with RA, adipokines have not been demonstrated to represent a significant risk factor for indirect measures of organic arterial wall atherosclerotic damage, as assessed by carotid intima-media thickness in our cohort of long-standing active RA patients undergoing infliximab treatment [7], or by coronary artery calcification evaluation, as shown in recent work by Rho and colleagues [8].

Abbreviations
anti-TNF-α: Anti-tumor necrosis factor-alpha; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; HDL: High-density lipoprotein; RA: Rheumatoid arthritis.

Competing interests
The authors declare that they have no competing interests.

Authors’ contributions
MAG-G made substantial contributions to conception and design of the manuscript, helped to draft the manuscript, and has given final approval of the version to be published. RL-M, CG-J, and JL helped in the design of the manuscript, helped to draft the manuscript, and has given final approval of the manuscript. All authors have read and approved the final manuscript.

Acknowledgments
The studies on rheumatoid arthritis by the MAG-G group were supported by ‘Instituto de Salud Carlos III’ grants PI06/0024, P509/00748, and PI12/00060 (Spain). This work was also partially supported by RETIC Programs RD08/0075 (RIER) and RD12/009/0013 from the ‘Instituto de Salud Carlos III’ (ISCIII) (Spain). RL-M is a recipient of a Sara Borrell postdoctoral fellowship from the Instituto Carlos III de Salud at the Spanish Ministry of Health (Spain).

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Published: 10 Feb 2014

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Cite this article as: Gonzalez-Gay et al.: Response to ‘Adipokines, inflammation, insulin resistance, and carotid atherosclerosis in patients with rheumatoid arthritis’. Arthritis Research & Therapy 2014, 16:401