



## Editorial

# Leptin in hand osteoarthritis: Potential biomarker or spurious association?☆



## Leptina en osteoartritis de mano: ¿Potencial biomarcador o asociación espuria?

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There are more of us and we live longer. As our life expectancy increases, so does the prevalence of chronic and degenerative diseases, such as osteoarthritis. Similarly, the epidemic of obesity and related diseases is growing globally every day. Over the next decades we will continue to observe the already recognized change in the health profile of most countries, with a large disease burden led by chronic non-communicable diseases, such as osteoarticular diseases, neoplasms, dementia and neurodegenerative diseases, as well as chronic pulmonary and cardiovascular pathologies.<sup>1</sup>

Many osteoarticular diseases share common risk factors with other chronic non-communicable health conditions, such as obesity or sedentary lifestyles. Finding connections between such diseases of increasing prevalence could reveal common pathogenic mechanisms and possible targets and therapeutic interventions of high clinical impact. In osteoarthritis, for example, obesity has been identified as a major risk factor. It has been suspected, however, that excess weight may trigger or accelerate osteoarthritis beyond the likely mechanical effects, through local and systemic inflammatory mechanisms related to adipose tissue from a wide variety of cytokines, chemokines and adipokines.<sup>2</sup>

It is precisely in hand osteoarthritis, a disease in which it is difficult to ascertain the connection between obesity/arthritis exclusively due to biomechanical effects, that the search

for pathogenic inflammatory mechanisms related to adipose tissue and its regulatory mechanisms has been insisted on. Within this complex endocrine regulatory system, leptin stands out.<sup>3</sup> In the paper by Morales et al. published in this issue of the journal, the authors provide additional evidence of the likely relationship between regulatory hormones such as leptin with osteoarthritis of the hand. These results are consistent with those recently reported by Kroon et al.<sup>4</sup> in a similarly cross-sectional study involving 6408 participants, 12% of whom had hand osteoarthritis, in which serum leptin levels were associated with both knee and hand osteoarthritis.

It is appropriate however, to take into account the design of these and other published papers that seek to clarify this interesting connection. Such an association cannot be simply attributed to a causal relationship exclusively based on biological plausibility or on the extent of the association. It is necessary to consider first the influence of chance, to anticipate and correct biases, in addition to trying to eliminate any potential confounding factors, such as reverse causality when it is impossible to ascertain that the presumed cause occurred before the consequence (it may be that patients with hands osteoarthritis also have osteoarthritis of the hips and knees, and this has led to sedentarism, overweight and altered levels of leptin, and not the other way around).<sup>5</sup>

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The sum total of all the information collected and future related work, together with the rigorous analysis of its biases and possible confounding factors, would help to clarify whether the association between leptin and hand arthrosis is real or spurious, whether it is not mediated by confounding factors and, finally, whether it is a casual epiphenomenon or actually determines an element of causality. It would be really wonderful to be able to demonstrate that leptin triggers the onset or the progression of this disease and to be able to design curative or disease modifying drugs for this terrible condition,<sup>3</sup> replicating the great achievements that rheumatology has witnessed with other diseases. Although leptin is not a direct causal element or a therapeutic target, it could still be a useful biomarker offering diagnostic, prognostic, predictive, monitoring or therapeutic response information, among other things. Rigorous research in this field should be promoted with collaborative efforts and prospective, multicenter designs.

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### Disclosures

No conflicts of interest to disclose.

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