

The Adipokine Hypothesis: Does it Play a Major or Minor Role in HFpEF?

Luís Beck-da-Silva^{1,2}  and Flávio D. Fuchs^{1,2} 

Hospital de Clínicas de Porto Alegre (HCPA),¹ Porto Alegre, RS – Brazil

Universidade Federal do Rio Grande do Sul (UFRGS),² Porto Alegre, RS – Brazil

We read with great interest the paper “The Adipokine Hypothesis of Heart Failure With a Preserved Ejection Fraction”.¹

The adipokine hypothesis explores biological mechanisms beyond the well-known risk factors for heart failure with preserved ejection fraction (HFpEF). The article presents a well-supported hypothesis based on data from bench research, animal studies, preclinical findings, and epidemiological evidence. The biological plausibility of the hypothesis is sound. However, certain considerations merit further discussion regarding the interpretation of HFpEF risk factors.

The manuscript somewhat underestimates the established role of hypertension in the development of HFpEF. It proposes a link between obesity – a major risk factor for HFpEF – and the pro-inflammatory effects of adipokines. However, hypertension has been recognized as an independent risk factor for HFpEF pathogenesis. In the Women’s Health Initiative cohort, 40.9% of the population-attributable risk for incident HFpEF was due to high blood pressure, compared with 25.8% for obesity.²

The mechanisms by which hypertension leads to HFpEF are likely independent of inflammatory pathways and are primarily related to concentric ventricular hypertrophy, diastolic dysfunction, and atrial remodeling, along with elevated natriuretic peptides.³ The beneficial effects of incretins in reducing cardiovascular disease in individuals with excess adiposity appear to be mediated by their blood-pressure-lowering effect, which results from weight loss.⁴

Not all patients with HFpEF are obese. A significant proportion of elderly, hypertensive, non-obese patients – particularly women – develop HFpEF. Geographic analyses reveal that North American patients with HFpEF tend to have a higher body mass index compared with counterparts from other continents.⁵ Therefore, the relevance of the adipokine

hypothesis may vary across populations, potentially having greater applicability in North American cohorts.

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Study Association

This study is not associated with any thesis or dissertation work.

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This article does not contain any studies with human participants or animals performed by any of the authors.

Use of Artificial Intelligence

The authors did not use any artificial intelligence tools in the development of this work.

Availability of Research Data

The underlying content of the research text is contained within the manuscript.

Keywords

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Mailing Address: Luís Beck da Silva •

Serviço de Cardiologia - Hospital de Clínicas de Porto Alegre - Ramiro Barcelos, 2350. Postal Code 90035-903, 2 andar, Porto Alegre, RS – Brazil
E-mail: lbneto@hcpa.edu.br

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