Disproving the obesity paradox-not

Salvatore Carbone¹ and Carl J. Lavie^{2*}

¹VCU Pauley Heart Center, Department of Internal Medicine, Virginia Commonwealth University, 1200 E Broad Street, Room 520, Richmond, VA 23298, USA; and ²John Ochsner Heart and Vascular Institute, Ochsner Clinical School, The University of Queensland School of Medicine, 1514 Jefferson Highway, New Orleans, LA 70121-2483, USA

Online publish-ahead-of-print 9 September 2018

This commentary refers to ‘The impact of confounding on the associations of different adiposity measures with the incidence of cardiovascular disease: a cohort study of 296 535 adults of white European descent’, by Iliodromiti et al., on page 1514.

We read with great interest the article from Iliodromiti et al.¹ The investigators performed a very large prospective study in almost 300 000 white European subjects, showing a positive association between increased body mass index (BMI), measures of adiposity and body fat distribution, and risk of cardiovascular diseases (CVD). Moreover, the increased risk of CVD typically reported in underweight subjects (BMI < 18.5 kg/m²) mostly disappeared after statistical adjustment for pre-existing comorbidities. The authors also concluded that this study may confute the ‘obesity paradox’, in which obese subjects portend to a better prognosis compared with the leaner counterparts.

Having a clear definition of the ‘obesity paradox’ in mind is important to avoid confusion related to the increased risk of CVD in those with greater adiposity, yet without established CVD. For instance, the ‘obesity paradox’ is exceptionally relevant in heart failure (HF). Increased adiposity clearly increases HF risk, however, when obesity and HF coexist, greater body weight, to a certain degree, is associated with a more favourable prognosis.² Such paradoxical relationship between obesity and HF, or other CVD, is a clear example of the ‘obesity paradox’.

Similar to prior reports,³ the authors have shown that a BMI between 22 and 23 kg/m² was associated with the lowest risk for CVD.¹ However, the study did not assess the role of BMI and body composition compartments on prognosis (i.e. mortality) after CVDs were diagnosed. Such analysis is necessary to determine whether an ‘obesity paradox’ exists, or whether prior studies, including meta-analysis and systematic reviews, which performed adjustments for a number of variables suggesting a protective effects of obesity, particularly in HF,⁴ but also other CVD, could be disproven.

The role of obesity in determining prognosis has been also challenged by the confounding factor of cardiorespiratory fitness (CRF) levels. Even in the setting of coronary heart disease or HF, obesity is protective only in those patients with low CRF, while in those with greater CRF the obesity paradox may not be as pronounced,⁵ suggesting that the focus of therapeutics should be targeting improvements in CRF, rather than obesity alone (i.e. weight loss) to finally

improve prognosis. Of note, CRF was not measured in the study by Iliodromiti et al.¹

We would like to emphasize that while studies reporting an ‘obesity paradox’ suggest a protective role of obesity, the obese patients could have prevented the development of that CVD (i.e. HF) if they did not accumulate excess body fat in the first place and/or maintained a good level of CRF during the course of their life. Avoiding weight gain and obesity should still remain a cornerstone for the prevention of CVD and metabolic diseases.

In conclusion, we believe that the study added an important piece to the field of obesity and CVD, also in light of the elegant use of body composition measures (i.e. fat mass) and distribution (i.e. waist circumference). However, more studies investigating the effects of obesity and increased adiposity in patients with an established CVD are needed, but this study in no way refutes the obesity paradox.

Funding

This work was supported by a Mentored Clinical & Population Research Award [16MCPRP31100003 to S.C.] from the American Heart Association.

Conflict of interest: none declared.

References

1. Iliodromiti S, Celis-Morales CA, Lyall DM, Anderson J, Gray SR, Mackay DF, Nelson SM, Welsh P, Pell JP, Gill JMR, Sattar N. The impact of confounding on the associations of different adiposity measures with the incidence of cardiovascular disease: a cohort study of 296 535 adults of white European descent. *Eur Heart J* 2018;**39**:1514–1520.
2. Carbone S, Lavie CJ, Arena R. Obesity and heart failure: focus on the obesity paradox. *Mayo Clin Proc* 2017;**92**:266–279.
3. Berrington de Gonzalez A, Hartge P, Cerhan JR, Flint AJ, Hannan L, MacInnis RJ, Moore SC, Tobias GS, Anton-Culver H, Freeman LB, Beeson WL, Clipp SL, English DR, Folsom AR, Freedman DM, Giles G, Hakansson N, Henderson KD, Hoffman-Bolton J, Hoppin JA, Koenig KL, Lee I-M, Linet MS, Park Y, Pocobelli G, Schatzkin A, Sesso HD, Weiderpass E, Willcox BJ, Wolk A, Zeleniuch-Jacquotte A, Willett WC, Thun MJ. Body-mass index and mortality among 1.46 million white adults. *N Engl J Med* 2010;**363**:2211–2219.
4. Padwal R, McAlister FA, McMurray JJV, Rich M, Pocock S, Swedberg K, Maggioni A, Gamble G, Ariti C, Earle N, Cowie MR, Rich M, Pocock S, Swedberg K, Maggioni A, Gamble G, Ariti C, Earle N, Whalley G, Poppe KK, Doughty RN, Bayes-Genis A; Meta-analysis Global Group in Chronic Heart Failure (MAGGIC). The obesity paradox in heart failure patients with preserved versus reduced ejection fraction: a meta-analysis of individual patient data. *Int J Obes (Lond)* 2014;**38**:1110–1114.
5. Lavie CJ, Cahalin LP, Chase P, Myers J, Bensimhon D, Peberdy MA, Ashley E, West E, Forman DE, Guazzi M, Arena R. Impact of cardiorespiratory fitness on the obesity paradox in patients with heart failure. *Mayo Clin Proc* 2013;**88**:251–258.

* Corresponding author. Tel: +1 504 842 1281, Fax: +1 504 842 5875, Email: clavie@ochsner.org email

Published on behalf of the European Society of Cardiology. All rights reserved. © The Author(s) 2018. For permissions, please email: journals.permissions@oup.com.