

# Adverse right ventricular remodelling, function, and stress responses in obesity: insights from cardiovascular magnetic resonance

Andrew J.M. Lewis <sup>1\*</sup>, Ines Abdesselam<sup>1</sup>, Jennifer J. Rayner<sup>1</sup>, James Byrne<sup>2</sup>, Barry A. Borlaug<sup>3</sup>, Stefan Neubauer<sup>1</sup>, and Oliver J. Rider<sup>1</sup>

<sup>1</sup>University of Oxford Centre for Clinical Magnetic Resonance Research, Radcliffe Department of Medicine, University of Oxford, Headley Way, Oxford OX3 9DU, UK;

<sup>2</sup>University Hospital Southampton NHS Foundation Trust, Tremona Rd, Southampton SO16 6YD UK; and <sup>3</sup>Department of Cardiovascular Medicine, Mayo Clinic and Foundation, 200 First St SW, Rochester, MN 55905, USA

Received 15 April 2021; editorial decision 15 August 2021; accepted 16 August 2021; online publish-ahead-of-print 28 August 2021

## Aims

We aimed to determine the effect of increasing body weight upon right ventricular (RV) volumes, energetics, systolic function, and stress responses using cardiovascular magnetic resonance (CMR).

## Methods and results

We first determined the effects of World Health Organization class III obesity [body mass index (BMI)  $> 40 \text{ kg/m}^2$ ,  $n = 54$ ] vs. healthy weight (BMI  $< 25 \text{ kg/m}^2$ ,  $n = 49$ ) upon RV volumes, energetics and systolic function using CMR. In less severe obesity (BMI  $35 \pm 5 \text{ kg/m}^2$ ,  $n = 18$ ) and healthy weight controls (BMI  $21 \pm 1 \text{ kg/m}^2$ ,  $n = 9$ ), we next performed CMR before and during dobutamine to evaluate RV stress response. A subgroup undergoing bariatric surgery ( $n = 37$ ) were rescanned at median 1 year to determine the effects of weight loss. When compared with healthy weight, class III obesity was associated with adverse RV remodelling (17% RV end-diastolic volume increase,  $P < 0.0001$ ), impaired cardiac energetics (19% phosphocreatine to adenosine triphosphate ratio reduction,  $P < 0.001$ ), and reduction in RV ejection fraction (by 3%,  $P = 0.01$ ), which was related to impaired energetics ( $R = 0.3$ ,  $P = 0.04$ ). Participants with less severe obesity had impaired RV diastolic filling at rest and blunted RV systolic and diastolic responses to dobutamine compared with healthy weight. Surgical weight loss ( $34 \pm 15 \text{ kg}$  weight loss) was associated with improvement in RV end-diastolic volume (by 8%,  $P = 0.006$ ) and systolic function (by 2%,  $P = 0.03$ ).

## Conclusion

Increasing body weight is associated with significant alterations in RV volumes, energetic, systolic function, and stress responses. Adverse RV modelling is mitigated with weight loss. Randomized trials are needed to determine whether intentional weight loss improves symptoms and outcomes in patients with obesity and heart failure.

## Keywords

obesity • magnetic resonance • remodelling

## Introduction

Obesity is associated with impaired exercise tolerance<sup>1</sup> and a two-fold increased risk of developing heart failure,<sup>2</sup> leading to declines in quality of life and life expectancy.<sup>3</sup> The mechanisms by which obesity leads to impaired exercise tolerance<sup>4</sup> and an increased risk of heart failure are incompletely understood but are of interest,<sup>5</sup> especially as

obesity is, in principle, a risk factor which could be modified via weight loss.

The mechanisms linking obesity to the development of heart failure are incompletely understood but are likely to include adverse haemodynamic conditions due to an increased circulating volume,<sup>6</sup> a dysregulated inflammatory state and impaired left ventricular (LV) energy supply<sup>7</sup> linked to altered substrate metabolism.<sup>8</sup> LV

\* Corresponding author. Tel: +44 1865234580. E-mail: [andrew.lewis@cardiov.ox.ac.uk](mailto:andrew.lewis@cardiov.ox.ac.uk)

© The Author(s) 2021. Published by Oxford University Press on behalf of the European Society of Cardiology.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact [journals.permissions@oup.com](mailto:journals.permissions@oup.com)

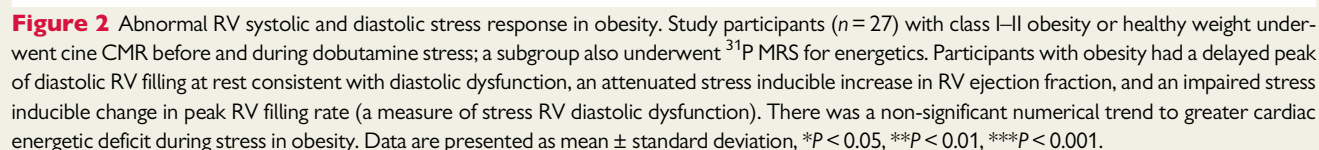






Participants of healthy weight had a  $19 \pm 3\%$  absolute increase in RV ejection fraction during dobutamine stress, which was significantly attenuated to a  $12 \pm 8\%$  absolute increase in obesity ( $P = 0.004$ , Figure 2). This finding is consistent with impaired RV systolic contractile response to dobutamine. The stress inducible change in peak RV filling rate was also significantly reduced (from  $2.1 \pm 1$  mL/s to  $0.5 \pm 1$  mL/s,





	Healthy weight BMI 18.5–24.9 kg/m <sup>2</sup> (n = 9)	Obesity BMI >30 kg/m <sup>2</sup> (n = 18)	P-value
Age, years	40 ± 9	47 ± 9	0.09
Height, cm	168 ± 6	168 ± 10	0.94
Weight, kg	60 ± 6	97 ± 15	<0.001
BMI, kg/m <sup>2</sup>	22 ± 1	35 ± 5	NA
Systolic BP, mmHg	111 ± 10	108 ± 27	0.08
Diastolic BP, mmHg	70 ± 10	74 ± 6	0.08
Fat mass total, kg	19.6 ± 9	49.1 ± 16	<0.001
Total cholesterol, mmol/L	4.9 ± 0.7	5.4 ± 2.2	0.18
Fasting triglycerides, mmol/L	0.8 ± 1	1.3 ± 1	0.04
Fasting glucose, mmol/L	4.7 (4.6–5.0)	5.2 (4.6–5.9)	0.18
C-reactive protein, mg/L	0 (0–0)	0.1 (0–0.7)	0.07
Interleukin 6, ng/mL	1.8 (0–4.0)	5.9 (1.0–8.7)	0.07
Fasting Insulin, mIU/L	2.1 ± 2	8.4 ± 6	0.01
Leptin, ng/mL	30 ± 30	91 ± 60	0.12
Non-esterified fatty acids, mmol/L	0.6 ± 0.4	0.4 ± 0.3	0.15

Downloaded from <https://academic.oup.com/enjicimaging/article/23/10/1383/6359103> by guest on 06 January 2023





15. Park HS, Park JY, Yu R. Relationship of obesity and visceral adiposity with serum concentrations of CRP, TNF- $\alpha$  and IL-6. *Diabetes Res Clin Pract* 2005;**69**:29–35.
16. Rider OJ, Lewis AJ, Lewandowski AJ, Ntusi N, Nethononda R, Petersen SE et al. Obese subjects show sex-specific differences in right ventricular hypertrophy. *Circ Cardiovasc Imaging* 2015;**8**:e002454.
17. Guazzi M, Borlaug BA. Pulmonary hypertension due to left heart disease. *Circulation* 2012;**126**:975–90.
18. Verbrugge FH, Guazzi M, Testani JM, Borlaug BA. Altered hemodynamics and end-organ damage in heart failure: impact on the lung and kidney. *Circulation* 2020;**142**:998–1012.
19. Sheu EG, Channick R, Gee DW. Improvement in severe pulmonary hypertension in obese patients after laparoscopic gastric bypass or sleeve gastrectomy. *Surg Endosc* 2016;**30**:633–7.
20. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J* 2016;**37**:2129–200.
21. Curtis JP, Selzer JG, Wang Y, Rathore SS, Jovin IS, Jadbabaie F et al. The obesity paradox: body mass index and outcomes in patients with heart failure. *Arch Intern Med* 2005;**165**:55–61.
22. Oga EA, Eseyin OR. The obesity paradox and heart failure: a systematic review of a decade of evidence. *J Obes* 2016;**2016**:9040248.
23. Sundström J, Bruze G, Ottosson J, Marcus C, Näslund I, Neovius M. Weight loss and heart failure: a nationwide study of gastric bypass surgery versus intensive lifestyle treatment. *Circulation* 2017;**135**:1577–85.
24. Rayner J, Neubauer S, Rider O. The paradox of obesity cardiomyopathy and the potential for weight loss as a therapy. *Obes Rev* 2015;**16**:679–90.