this drug in improving cardiac function and potentially cardiovascular outcomes.[8] The overall effect of spironolactone was slightly reduced when adjusting for the obesity parameters and no effect modification of the treatment effects (i.e. 'interaction') was found by obesity, suggesting that spironolactone may be efficient both in obese and lean patients.

Supplementary Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Patient baseline characteristics: body mass index.

Table S2. Patient baseline characteristics: waist circumference.

Table S3. Patient baseline characteristics: waist-to-hip ratio.

Table S4. Analysis of Aldo-DHF endpoints adjusted for trial medication and obesity parameters. Main effects and interaction.

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Index of microcirculatory resistance assessment in patients with new diagnosis of left ventricular dilatation without significant coronary artery lesions: IMPAIRED pilot trial

According to Camici and Crea[1] coronary microvascular dysfunction can exist in the presence of myocardial diseases, particularly in patients with a new diagnosis of left ventricular (LV) dilatation without coronary artery lesions. The aim of the present study was to evaluate the index of microcirculatory resistance (IMR), coronary flow reserve (CFR) and fractional flow reserve (FFR) and their mutual interaction in patients with dilated cardiomyopathy. The study protocol was approved by the local Institutional Review Board, registered on ClinicalTrials.gov (NCT02705170), and all patients provided informed consent. Major inclusion criteria for the study were recent diagnosis of LV dilatation and absence of significant coronary artery stenosis (<40%) at coronary artery angiography. After coronary angiography, coronary physiological measurements (IMR, CFR, FFR) were performed on the left anterior descending artery (LAD). IMR and CFR were obtained according to the method described previously.[2,3] Cut-off values of abnormality were ≥25 for IMR, ≤2.5 for CFR and ≤0.80 for FFR. Coronary angiograms were reviewed by S.B., blinded to functional evaluation findings. Values were presented as median (interquartile range) and compared by Mann–Whitney U and Kruskal–Wallis tests. Data analysis was carried out by M.T. and A.M.L. Between March 2016 and November

Table 1 Baseline characteristics

	Normal IMR group ($n = 17$)	Abnormal IMR group ($n = 18$)	*P*-value
Age (years)	62.4 (48.5–71.4)	69.8 (54.8–80.3)	0.06
BSA (m^2)	1.9 (1.7–2.0)	2.2 (2.0–2.3)	0.003
LVEF (%)	31 (30–38)	35 (24–40)	0.9
EDD (cm)	6.2 (5.6–6.6)	6.0 (5.5–6.2)	0.19
EDV (mL)	180 (165–238)	170 (150–200)	0.19
LV mass (g)	120 (50–190)	114 (65–160)	0.08
CrCl (mL/min)	74.8 (72.8–142.1)	83.3 (59.3–130.9)	0.9
NYHA class			
I	10 (58.8)	9 (50.0)	0.6
II	7 (41.1)	9 (50.0)	
III	0	0	
IV	0	0	
Coronary physiological measurement			
Pa (mmHg)	71 (65–80)	87 (72–95)	0.02
Pd (mmHg)	60 (37–61)	78 (61–88)	0.003
FFR	0.80 (0.66–0.85)	0.89 (0.86–0.91)	0.005
CFR	2.7 (1.3–3.0)	1.15 (0.80–1.20)	0.0003
Hyperaemia	0.34 (0.26–0.38)	0.93 (0.56–1.21)	0.000001
IMR	18.1 (15.3–23.1)	56.7 (43.6–106.4)	0.0001

Values are given as median (interquartile range), or *n* (%).
BSA, body surface area; CFR, coronary flow reserve; CrCl, creatinine clearance; FFR, fractional flow reserve; LVEF, left ventricular ejection fraction; EDV, end-diastolic volume; EDD, end-diastolic diameter; IMR, index of microvascular resistance; LV, left ventricular; NYHA, New York Heart Association; Pa, aortic pressure; Pd, distal pressure.

2017, 35 patients were enrolled; 54% were male with a median age of 69.8 (54.8–74.6); 21 patients (60%) had hypertension, 2 (6%) had diabetes, 7 (20%) had dyslipidaemia, and 8 (23%) were current smokers. LV ejection fraction, end-diastolic volume and end-diastolic diameter were 35% (24–40), 170 mL (150–200) and 6.0 cm (5.5–6.2), respectively. Regarding indexes of coronary physiology, median values of IMR, CFR and FFR were 27.2 (18.1–56.7), 1.2 (1.1–2.7) and 0.86 (0.80–0.90), respectively. Patients were divided into two groups on the basis of the IMR value (normal IMR group vs. abnormal IMR group), indicating, respectively, the absence and the presence of significant microvascular dysfunction. Interestingly, patients in the normal IMR group had a lower FFR value and a higher CFR value as compared to the abnormal IMR group [0.80 (0.66–0.85) vs. 0.89 (0.86–0.91), $P = 0.005$; and 2.7 (1.3–3.0) vs. 1.15 (0.80–1.20), $P = 0.0003$, respectively] (*Table 1*). In summary, in our population of patients with LV dilatation without coronary artery lesions, those without coronary microvascular dysfunction (IMR < 25) (normal IMR group) presents on average an 'ischaemic' FFR value and a normal CFR value, whereas those with microvascular dysfunction (IMR ≥ 25) (abnormal IMR group) show a normal FFR value and an abnormal CFR value. While the findings in the abnormal IMR group clearly depict the expected scenario of the absence of epicardial disease (normal FFR) with significant microvascular disease (abnormal CFR), it is more complex to explain the findings in the normal IMR group. In the latter, we found an 'ischaemic' FFR associated with normal CFR. Basically, this means that a large increase in flow is not adequately sustained by the conductance of the epicardial artery. This generates a pressure gradient throughout the course of a vessel apparently normal. Although we cannot dismiss the possibility that a diffuse disease could have played a role in this phenomenon, especially considering that we did not perform any intravascular imaging, the lack of any angiographic disease could be quite reassuring about the possibility that this phenomenon could be related to a pathophysiological mechanism instead of a technical pitfall of FFR.[4] We may hypothesize that this could be related to LV dilatation and possibly to increased LV mass[5] that is not adequately supported by a coronary system intrinsically undersized. This is indirectly confirmed by the evidence of a significantly lower body surface area (with non-significantly higher LV dimensions), but further confirmations are clearly on demand. In conclusion, the interpretation of our data suggests that, in patients with dilated cardiomyopathy, invasive functional indexes could produce results that are not easily interpretable. This does not imply that IMR, CFR and, more importantly, FFR cannot be used or are not reliable in this setting, but, more generally, that in these patients, that originally were excluded in the validation process of these techniques, there is a complex interplay between epicardial vessels, microcirculatory system and LV structure. Further studies are warranted to deeply understand the pathophysiological mechanisms responsible for this apparent coronary incompetence.

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