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Response to Letter Regarding Article, "Effects of sildenafil on ventricular and vascular function in heart failure with preserved ejection fraction"

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We appreciate the comments from Drs. Brutsaert and De Keulenaer regarding our recent publication on the ventricular and vascular effects of sildenafil in people with heart failure with preserved ejection fraction (HFpEF) enrolled in the RELAX trial.[1, 2] The authors suggest that different results might have been observed had HFpEF subjects been sub-grouped according to characteristics such as age, sex, body composition and comorbidities. We agree that this concept has merit, but many or most of these characteristics coexist within the typical HFpEF patient, and while the comorbid conditions influence cardiovascular properties, fundamental disease-specific changes have been shown to underlie HFpEF, irrespective of comorbidities.[3]

Drs. Brutsaert and De Keulenaer make the point that changes in arterial afterload can affect ventricular function, going on to suggest that reduction in arterial wave reflections might have affected the timing of relaxation to cause or contribute to the observed decrease in peak ventricular pump performance. This is an intellectually appealing theory, but our data do not support it. There was no effect of sildenafil on wave reflections, assessed by aortic augmentation index, and there was no effect of sildenafil on left ventricular relaxation, at least as estimated by left ventricular diastolic tissue velocities.[1] Therefore we are not convinced that changes in loading sequence completely explain the findings in our study.

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Disclosures

None.

The authors further suggest that a lower sildenafil dose might have been more effective. This was not observed at the 20 mg dosage,[1] though lower doses were not examined in the RELAX trial.[2] Stroke work and peak power are both independent of afterload, but vary directly with preload (end diastolic volume).[4] Because both were divided by end diastolic volume, these indices can be considered as measures of ventricular contractility,[4] but we agree with Drs. Brutsaert and De Keulenaer that chamber contractility is distinct from myocardial contractility.[5]

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