# **Reply: Coronary physiology in severe aortic stenosis: solely a matter of increased coronary resting flow?**

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We would like to thank Drs Minten, Bennett and Dubois for their interest in our work and their careful commentary<sup>1</sup>. Broadly we agree with their comments; for the sake of clarity, we will address them individually. It is now widely recognised that bolus thermodilution produces more variable results than continuous thermodilution. Unfortunately, it was not until the very end of our study that measuring resting flow by continuous thermodilution was demonstrated to be feasible by Gallinoro et al<sup>2</sup>.

We acknowledge that one should be cautious with firm conclusions on resting flow based on measured transit times. However, the finding of a statistically significant increase in coronary flow reserve, combined with a highly significant increase in serial measurements of transit time and a non-significant increase in absolute hyperaemic flow, strongly suggests that resting flow did indeed change and is the major reason for the improved coronary flow reserve. Having stated that, we agree that the trend of increased hyperaemic flow and decreased minimal microvascular resistance may in fact be real phenomena, at least for some patients, as evidenced by the patient level changes shown in **Figure 1** of the paper.

The index of hyperaemic flow to left ventricular mass increased by 39% (p<0.001), as reported in the text, while mass-indexed resistance was reduced by 30% (p<0.001, not reported in the original paper). Because of variation in the proportion of the myocardium subtended by the left anterior descending artery, we only reported the relative change in indexed flow and resistance – under the assumption that the proportion of myocardium subtended remained constant before and after regression of left ventricular hypertrophy in the individual patient.

The correlation between left ventricular stroke work and absolute resting flow would most likely have been stronger than the reported correlation using transit mean time – we agree.

We have now demonstrated in two separate cohorts of patients with severe aortic stenosis that hyperaemic flow is stable after aortic valve replacement<sup>3,4</sup>. Although these are the

largest cohorts to date with long-term repeated invasive measurements, they are small in absolute terms. The final verdict may, therefore, be contingent on data from a larger sample. The obvious challenge, as recognised by Dr Minten et al, lies in the repeated invasive assessment of these patients. We look forward to the results of their ongoing study which aims to include 100 patients<sup>5</sup>.

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## **Conflict of interest statement**

The authors have no conflicts of interest to declare.

### References

1. Minten L, Bennett J, Dubois C. Letter: Coronary physiology in severe AS: solely a matter of increased coronary resting flow? *EuroIntervention*. 2023;18:1295.

2. Gallinoro E, Candreva A, Colaiori I, Kodeboina M, Fournier S, Nelis O, Gioia G di, Sonck J, van't Veer M, Pijls NHJ, Collet C, De Bruyne B. Thermodilution-derived volumetric resting coronary blood flow measurement in humans. *EuroIntervention*. 2021;17:e672-9.

3. Sabbah M, Joshi FR, Minkkinen M, Holmvang L, Tilsted H-H, Pedersen F, Ahtarovski K, Sørensen R, Thue Olsen N, Søndergaard L, De Backer O, Engstrøm T, Lønborg J. Long-Term Changes in Invasive Physiological Pressure Indices of Stenosis Severity Following Transcatheter Aortic Valve Implantation. *Circ Cardiovasc Interv.* 2022;15:e011331.

4. Sabbah M, Olsen NT, Holmvang L, Tilsted HH, Pedersen F, Joshi FR, Sørensen R, Jabbari R, Arslani K, Sondergaard L, Engstrøm T, Lønborg JT. Long-term changes in coronary physiology after aortic valve replacement. *EuroIntervention.* 2023;18: 1156-64.

5. Minten L, McCutcheon K, Jentjens S, Vanhaverbeke M, Segers VFM, Bennett J, Dubois C. The coronary and microcirculatory measurements in patients with aortic valve stenosis study: rationale and design. *Am J Physiol Heart Circ Physiol.* 2021;321:H1106-16

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