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Hyperaemic and non-hyperaemic indices for functional assessment of coronary lesions in patients with severe aortic valve stenosis

We read with great enthusiasm the elegantly written case from Minten *et al.*[1] regarding the use of coronary physiology for invasive functional assessment of coronary lesions in patients with severe aortic stenosis (AS). The authors measured the haemodynamic significance of a lesion in the mid-right coronary artery (RCA) in a patient with severe AS, by using fractional flow reserve (FFR) and the non-hyperaemic resting full-cycle ratio (RFR) before and after transcatheter aortic valve implantation (TAVI). Fractional flow reserve pre-TAVI was negative (0.84) with a significant decrease after TAVI (0.72) while the RFR remained positive and stable pre- and post-TAVI (0.80). Eventually, percutaneous coronary intervention (PCI) of the RCA was performed after TAVI.

Previous studies have reported that the combination of severe AS and coronary artery disease (CAD) behaves like 'serial stenoses'.[2,3] In particular, severe AS (upstream lesion) reduces flow across the coronary stenosis (downstream lesion) making it appear less severe than when measured in isolation.[3] Thus, FFR of the coronary stenosis after TAVI might be lower than before TAVI[2]. In addition, researchers have proposed the use of the 'grey zone' FFR concept[4] in patients with concomitant severe AS and CAD.[2] In this population, FFR values pre-TAVI between 0.80 and 0.85 demarcate the 'grey zone', that might drop to <0.75 post-TAVI.[2] Application of the aforementioned cut-offs in this case, where pre-TAVI FFR was measured 0.84, reclassifies the patient in the 'grey zone' FFR for severe AS and CAD (0.80–0.85). The reclassified 'grey zone' FFR in combination with the clearly positive non-invasive testing (reversible ischaemia of 15%) could have indicated the performance of PCI of the RCA before TAVI. Timely revascularization of a severe coronary lesion is crucial especially in healthcare systems where TAVI waiting lists are long.

Additionally, as nicely stated by the authors, there are conflicting data in the literature regarding the use of RFR when assessing the severity of CAD in severe AS. Studies report stable or increased RFR values after TAVI, emphasizing that even the resting indices, can change due to a lower resting coronary flow after TAVI.[1] Moreover, in the VALIDATE-RFR study the sensitivity of both RFR and instantaneous wave-free ratio (iFR) were notably lower for the RCA.[5] Even though coronary perfusion is predominantly diastolic, the RCA perfuses in systole to a greater degree than the left coronary system, probably due to the thinner-walled right ventricle, which results in less systolic compression.[5] Furthermore, the RCA has a smaller diastolic suction wave.[5] Subsequently, this variability of resting gradients in patients with AS mandates for cautious interpretation of the results provided, especially in the assessment of RCA lesions, as in this case.

In conclusion, severe AS and TAVI produce massive changes in the physiology of the myocardium. Ventricular hypertrophy, subendocardial ischaemia, microvascular dysfunction, and impaired hyperaemic flow may affect functional assessment of CAD in patients with severe AS. In the light of upcoming studies, the interpretation of coronary physiology measurements in this population should be meticulous.

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