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Editorial

Go with the flow: physiological assessment of coronary artery stenosis severity in patients with severe aortic stenosis

Estudio fisiológico de la gravedad de las estenosis coronarias en pacientes con estenosis aórtica grave

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Coronary artery disease (CAD) frequently coexists with severe aortic valve stenosis (AVS) due to overlapping risk factors.[1] As both disease conditions may cause similar symptoms, the optimal strategy to assess and manage them can be challenging. Although the available evidence mainly comes from nonrandomized, observational studies with limitations due to different definitions of CAD, angiographic severity, completeness of revascularization and comorbidities,[2] the detrimental prognostic impact of CAD has recently been identified, especially among patients with severe CAD and high (residual) SYNTAX scores.[3,4] Current guidelines recommend concomitant myocardial revascularization in patients with severe AVS undergoing surgical aortic valve replacement or transcatheter aortic valve implantation (TAVI) and coronary artery diameter stenosis $>$ 70% in proximal segments (or $>$ 50% in case of left main stenosis) based on angiographic assessment of CAD.[5] In contrast, in chronic coronary syndromes without AVS, current guidelines recommend physiology-guided revascularization based on the results of randomized trials to improve symptoms and prognosis.[5] In patients with severe AVS, differentiation of symptoms against those originating from chronic coronary syndromes remains challenging, and both disease conditions also affect coronary hemodynamic status. AVS induces several functional alterations leading to oxygen supply-demand mismatch, which in turn is associated with lower microvascular resistance and greater vasodilatation as well as coronary blood flow at rest.[6,7] This adaptive process represents an important limitation of using physiological assessment in patients with AVS, especially of hyperemic indices, such as fractional flow reserve (FFR), as the pressure difference across coronary lesions is determined by microvascular resistance with reduced capacity for additional vasodilatation induced by adenosine.[8] In contrast, instantaneous wave-free ratio (iFR) and quantitative flow ratio (QFR) obviate the need for pharmacological hyperemia and consequently represent an attractive alternative to FFR in patients with severe AVS.

In a recent article published in *Revista Española de Cardiología*, Kleczynski et al.[9] report the results of a prospective registry designed to study application of QFR during evaluation of borderline coronary lesions in patients with severe AVS. The authors should be complemented for their endeavors to study an important unmet clinical need in patients scheduled to undergo TAVI, which is the management of coronary stenosis in the setting of severe AVS. QFR, which is based on computational assessment of contrast agent dynamics during coronary angiography, was assessed in 221 patients with severe AVS and compared with additional physiological and angiographic indices, such as FFR, iFR and resting Pd/Pa ratio. The main finding is that QFR showed better diagnostic accuracy and discriminatory function in determining the functional relevance of coronary stenosis compared with a previous study by Mejía-Rentería et al.,[10] when iFR instead of FFR was used as reference technology. The authors therefore postulate that nonhyperemic indices might be superior for coronary stenosis assessment in AVS patients. This is in line with previous studies, which demonstrated that iFR, but not FFR measurements, remain unchanged after valve replacement, suggesting that indices calculated during the wave-free period of diastole are less vulnerable to the confounding effect of AVS.[11,12] Although the findings of this study are of relevance to inform physiology-guided revascularization in the setting of AVS, there are some limitations that need to be mentioned: first and foremost, QFR was not assessed before and after treatment of AVS in this prospective registry; thus uncertainty remains about a possible change of this index pre- and post-AVS-treatment, with increase in coronary flow reserve and decrease in FFR.[10,13] This seems especially important in borderline lesions, where small changes may reclassify the functional severity of lesions. Second, ostial lesions not suitable for QFR were excluded from this analysis, which needs to be considered when interpreting these results. Third, validation of the results in larger studies with outcome data is required to establish cutoffs for intervention in this patient cohort.

Currently, there remain many unanswered questions regarding the optimal assessment and therapy of coronary artery stenosis in patients with severe AVS. In addition to angiographic and functional assessment of coronary lesions, intravascular imaging

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represents another option in the diagnostic armamentarium of CAD providing additional information on plaque and lesion morphology and is most likely not influenced by the confounding effects of AVS. Near-infrared spectroscopy intravascular ultrasound (NIRS-IVUS) is a novel, promising tool with the ability to identify patients and coronary segments at higher risk for future major adverse cardiovascular events (MACE)[14] and is currently investigated in the prospective, nonrandomized IMPACTavi trial (NCT04976062) regarding its ability to identify patients with MACE after successful TAVI. Moreover, several further randomized trials investigating the role of physiological assessment and optimal timing of revascularization procedures in patients with coexisting CAD and severe AVS undergoing TAVI are on the horizon, with the NOTION-3 (NCT03058627), FAITAVI (NCT03360591) and TAVI-PCI (NCT04310046) trials representative of many others.

To date, the significance of coexisting CAD needs to be carefully assessed on a case basis in patients undergoing (surgical or transcatheter) aortic valve replacement. An individualized treatment approach should take comorbidities, bleeding risk and the complexity of CAD into consideration when deciding whether, when and how to revascularize patients; in addition, careful assessment of coronary anatomy and valve morphology is required when selecting the optimal heart valve, as performing coronary interventions after TAVI can be technically challenging.[15]

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