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Editorial

Challenges in risk stratification for TAVI☆

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In the last decade, trans-catheter aortic valve implantation (TAVI) greatly implemented the treatment strategy of degenerative aortic stenosis. Current guidelines [1,2] recommend TAVI for patients with severe aortic stenosis and moderate to high surgical risk. Despite that, risk stratification of such frail and vulnerable older patients, such those nowadays presenting with severe aortic stenosis, is not well established, nor fully reliable.

Many efforts have been made in order to better stratify the operative risk of patients scheduled for TAVI [3]. That because the available tools, namely the European Score for Cardiac Operative Risk Evaluation (EuroSCORE) and the Society of Thoracic Surgeons (STS) risk score, having been developed upon surgical populations, clearly overestimates the operative risk of TAVI [4].

In addition, none of the latter risk models consider the frailty of those elderly patients, not taking into account their ability and independence in the daily activities, cognitive impairment, and so on. For this purpose, dedicated models have been developed and applied to TAVI series [4], hence demonstrating that frailty indeed is well correlated with both peri-procedural and 1-year clinical outcomes [5]. Therefore, decision-making is often challenging and the so-called Heart-team needs deep and complex examination of each single case to reliably stratify risks and benefits.

In this scenario, the present paper from Jung and colleagues [6] was intended to identify a novel outcomes predictor suitable for TAVI patients. The Insulin-like growth factor binding protein 2 (IGFBP-2) exerts many different metabolic effects and has already been correlated with the risk of stroke, left ventricular systolic function and long-term mortality of patients with different cardiovascular diseases [6]. Jung and colleagues tested IGFBP-2 as an outcome predictor among patients undergoing TAVI and found a strong correlation between this biomarker and 1-year mortality.

That strong correlation showed by IGFBP-2 with regards to 1-year mortality is surprisingly higher than historical hard predictors such as age, coronary artery disease, left ventricular ejection fraction, and B-type natriuretic peptide levels. The authors argue that this unexpected result may be referred to the fact that the study population was a high-risk very homogenous cohort of patients with similar baseline characteristics.

Even if that sounds acceptable from a statistical point of view, it would be very interesting to assess whether IGFBP-2, given its several metabolic effects, may enhance apoptosis and fibrosis in the context of the myocardium. Indeed, histopathological studies have demonstrated fibrosis in the left ventricle of patients with aortic stenosis, and it has been postulated that increasing myocyte size eventually leads them to apoptosis and replacement fibrosis; a sequence, the latter, responsible for the progression to ventricular hypertrophy and heart failure, with increasing risk of arrhythmias and sudden cardiac death [7].

From this point of view, if the metabolic modulations exerted by IGFBP-2 could be linked to the myocardial fibrosis process, IGFBP-2 itself could be considered such a surrogate of the morphological and haemodynamic sequelae of long-standing severe aortic stenosis, which is the case of those high-risk patients currently scheduled for TAVI, in whom ejection fraction estimates may not correctly assess left ventricular function [7]. Hence, if IGFBP-2 is really correlated with the degree of myocardial fibrosis of those patients, it somehow overlaps with that cited hard predictors such as age, left ventricular ejection fraction, and B-type natriuretic peptide levels. In my opinion, that surely set the stage for further investigations aimed to identify hypothetical metabolic patterns through which IGFBP-2 eventually affects myocardial remodelling and fibrosis.

In addition, getting back to the results presented by Jung and colleagues, it has to be pointed out that, unfortunately, functional parameters of the implanted aortic prosthesis were not addressed in the study. It is well known that trans-valvular gradients and prosthetic area are important determinant of outcomes in the settings of aortic valve replacement, not only in terms of functional capacity and quality of life, but also in terms of survival [8]. As a consequence, it has to be disclosed that the independent correlation between IGFBP-2 and 1-year mortality found by Jung and colleagues was not corrected for those important variables, notably prosthetic aortic valve area, mean and peak pressure gradients. That is a point that should be addressed

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in upcoming investigations, in order to strengthen the proposed predictive power of IGFBP-2.

In conclusion, notwithstanding the argued issues, in the study of Jung and colleagues IGFBP-2 resulted as a strong predictor of mortality after TAVI thus proposing a novel, easy, and cost-effective tool to better stratify the individual risk of patients with aortic stenosis scheduled for TAVI. Whenever further larger investigations can confirm this major finding, the so-called Heart-team will be provided with a novel, feasible and reliable tool to ameliorate and ease risk stratification of patients undergoing TAVI.

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

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