Demystifying Complex Coronary Hemodynamics in Patients Undergoing Transcatheter Aortic Valve Replacement

Sowing the Seeds for Coronary Physiological Assessment in the Future?

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Transcatheter aortic valve replacement (TAVR) has revolutionized the treatment of patients with severe aortic stenosis who are at high risk for traditional surgical intervention. As the technology matures and experience grows, the applicability of TAVR to lower risk populations is likely and is already being explored. These patients often present with chest pain or exertional dyspnoea in the context of varying degrees of coronary artery disease. An understanding of how the aortic valve affects coronary hemodynamics is becoming increasingly clinically relevant in determining how to manage this coexisting coronary disease.

See Article by Wiegerinck et al

Creating a model of aortic stenosis is challenging. The pressure loading of the ventricle and coronary arteries varies according to the location of the stenosis. Stenosis at the level of the aortic valve is anatomically below coronary artery inflow; this results in increased afterload of the left ventricle but reduces coronary perfusion pressure. Relief of the stenosis therefore results in an acute reduction in left ventricular end-diastolic pressure, and in most cases, it results in an increase in coronary perfusion pressure. This differs from the traditional systemic hypertension model often generated experimentally in animal models in which a restrictive band is placed around the aorta. In such cases, the stenosis is positioned in the aorta distal to coronary artery inflow; this results in an increase in both left ventricular end-diastolic pressure and coronary perfusion. After removal of the aortic band, both left ventricular end-diastolic pressure and coronary perfusion fall; as a result, the traditional banding model cannot be used to make inferences on the acute effect of relieving aortic stenosis on coronary hemodynamics.

The development of TAVR therefore provides a unique model to delineate the coronary hemodynamics of patients with aortic stenosis. In addition to being a model of true aortic stenosis, it permits easy access to the coronaries before and after the procedure for rapid hemodynamic assessment. Previously, TAVR had been performed under general anesthesia, and whilst recently, conscious sedation is increasingly used. Conscious sedation avoids the potentially confounding effect of a general anesthetic, which can manipulate myocardial preload and after-load, and therefore, it may provide a better model to study the effect of severe aortic stenosis on coronary artery hemodynamics.

In this issue of Circulation: Cardiovascular Interventions, Wiegerinck et al use the TAVR model to determine how relief of aortic stenosis alters coronary hemodynamics. In a study of 27 patients with aortic stenosis and 28 control patients without aortic stenosis, detailed assessment of coronary flow and microvascular resistance was performed at rest and after intracoronary adenosine administration pre and post TAVR.

They demonstrate that in the cohort of patients with no aortic regurgitation post TAVR, hyperemic flow, coronary flow reserve, and hyperemic microvascular resistance are significantly improved. These are in keeping with the findings of others but extend those findings to patients undergoing TAVR with conscious sedation rather than general anesthetic.

Their results also provide insights to the importance of aortic regurgitation post TAVR, the differences between baseline and hyperemic coronary flow in these patients, and perhaps the effect of residual left ventricular hypertrophy on coronary hemodynamics.

Aortic Regurgitation Post TAVR

Aortic regurgitation post TAVR has been noted to be a significant predictor of adverse outcomes, and as a result, it has been a major focus of the development of the second generation of TAVR valves. Wiegerinck et al provide useful insight into this cohort of patients. They demonstrate that patients with aortic regurgitation post TAVR do not benefit from the favorable improvement in coronary flow reserve realized in the TAVR patients who are not complicated by postprocedural aortic regurgitation. Could this be the reason why patients with aortic regurgitation post TAVR have worse outcomes?

It is known that an impaired coronary flow reserve even in the context of unobstructed epicardial coronaries is a powerful predictor of cardiovascular events. Patients with an abnormal coronary flow reserve have a much higher cardiovascular event rate than those with a normal coronary flow reserve regardless of any epicardial stenosis. Therefore, the impaired microvascular function secondary to residual aortic regurgitation demonstrated in this study could provide a mechanistic explanation for higher event rates in this population. It also provides further justification for operators to...
aim for as little aortic regurgitation post TAVR as possible and for the need for valves that minimize the potential of aortic regurgitation.

Effect of Residual Left Ventricular Hypertrophy on Coronary Hemodynamics
Despite a significant improvement in coronary flow reserve post TAVR (in patients not complicated by aortic regurgitation), the absolute value differed significantly from that of the control group in this study. It is suggested that this may represent the effect of residual left ventricular hypertrophy in this population. However, interpretation of this finding should be treated cautiously because there are significant differences in patient characteristics between the TAVR group and the control group. The control group was significantly younger, had more men, and had significant differences in statin and β-blocker usage. Each of these variables can significantly alter coronary flow reserve, and therefore, any conclusions on the observed differences in coronary flow between the 2 groups should be made cautiously. As the indications for TAVR become less stringent, the identification of a better-matched control group in future studies should be easier. Until then, the residual effect of left ventricular hypertrophy on coronary hemodynamics in patients post TAVR could be ascertained by longitudinal follow-up of the TAVR group.

Baseline and Hyperemic Flow in Aortic Stenosis
The differences between baseline and hyperemic flow has been a subject of much debate in recent years.2-11 This study provides a timely addition to the literature comparing the characteristics of flow under these 2 conditions but on this occasion in the context with aortic stenosis. A significant proportion of these patients have coronary artery disease and, as the population undergoing TAVR increases, determining the significance of this disease will become clinically important, especially, in border line cases, when it is unclear whether the valve or coronary disease is responsible for symptoms.

Wiegnerck et al1 clearly demonstrate that baseline hemodynamics are stable pre and post TAVR, whereas hyperemic parameters significantly changed. These findings are consistent with an increasing body of literature pertaining to the stability of baseline coronary flow and have clinical implication for the assessment of coronary disease in this patient population in which the administration of vasodilators is fraught with risk and should be avoided. However, it should be noted that the presence of aortic stenosis adds an extra layer of complexity on stenosis assessment, and it remains to be seen if any index of stenosis severity is able to isolate the hemodynamics of a stenosis in an epicardial artery from that of the complex interplay between epicardial flow and the altered myocardial–microvascular interaction in this context.

As new innovations are introduced, it is vital that investigators take the opportunity that such technology affords to improve our understanding of human physiology. Wiegnerck et al1 have performed an elegant study that adds significantly to a growing body of literature using the TAVR model to unpick the complex interplay between coronary blood flow and the myocardial–microvascular interaction in patients with severe aortic stenosis. As TAVR technology matures and its indications expand, a better understanding of underlying physiology may help to improve clinical outcomes. The development of new diagnostic tools for this complex group of patients will be based on continued detailed research such as this.

Disclosures
Dr Davies is a consultant for Volcano Corporation and has intellectual property pertaining to iFR technology which is under license. Dr Sen reports no conflict.

References


**KEY WORDS:** Editorials • aortic valve insufficiency • aortic valve stenosis • coronary circulation • hemodynamics • transcatheter aortic valve implantation
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Circ Cardiovasc Interv. 2015;8:e002909
doi: 10.1161/CIRCINTERVENTIONS.115.002909

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