Clinical Investigation Plan

A Prospective Study of Fractional Flow Reserve Assessment of Intermediate Coronary Stenoses in Severe Aortic Stenosis

Study Title	A Prospective Study of Fractional Flow Reserve Assessment of Intermediate Coronary Stenoses in Severe Aortic Stenosis
Study Site	Cleveland Clinic Heart & Vascular Institute
Study Design	Prospective, single-center. We anticipate enrolling 50 patients. Fractional flow reserve (iFR and FFR) assessment will be performed on all intermediate coronary stenoses using standard practice, immediately before TAVR (at the time of the procedure). Maximal hyperemia will be achieved utilizing intravenous adenosine. Immediately post-TAVR, the same lesions will be reassessed. We will compare pre- and post-TAVR iFR and FFR values, and assess short-term outcomes.
Study Objective	The purpose of the study is to determine whether iFR assessment gives a valid assessment of coronary hemodynamics in patients with severe aortic stenosis. Several factors confound the interpretation of fractional flow reserve (FFR) in patients with severe aortic stenosis (AS) and intermediate severity coronary stenoses, and the widely accepted cut-off value of 0.80 may not be applicable to this patient population. Coronary flow reserve is known to be attenuated under conditions of left ventricular hypertrophy and severe AS, with one study showing improvement in coronary flow reserve after aortic valve replacement. Left ventricular hypertrophy produces fixed resistance secondary to external compression of the coronary microcirculation. This potentially results in failure to achieve maximal hyperemia with adenosine and can lead to false negative FFR results. Neurohormonal influences in aortic stenosis can further attenuate vasodilator response and potentially result in false negative FFR values. Both of these conditions result in the potential deferral of lesions which may have been hemodynamically significant in the absence of severe AS. At present, there are no studies which have demonstrated validity of iFR/FFR measurement in patients with severe AS. Here, we propose a prospective study of iFR/FFR in patients with AS and indeterminate coronary lesions undergoing TAVR to understand the hemodynamic consequences of AS on iFR/FFR. We hypothesize that iFR/FFR values will be consistently and significantly higher pre-TAVR in comparison with post-TAVR for the same lesions.
Covariates of Interest	Demographics • Age • Sex Comorbid conditions

	• Diabetes • Hypertension • Hyperlipidemia • Kidney disease status • Previous PCI • Previous myocardial infarction • Stress test information Current medications Echocardiography data • Valve area • Aortic valve gradients • Dimensionless index of aortic valve • Stroke volume indexed • Ejection fraction • Wall motion abnormalities Frailty score Angiographic Characterisitcs • Lesion location • Lesion severity • Location • Presence and degree of calcification • Myocardial jeopardy score • Syntax score IVUS characteristics (if available) Fractional flow reserve characteristics • FFR value pre- and post-TAVR • Distal pressure & proximal pressure • Adenosine dose used to achieve hyperemia • Route of adenosine administration • Wave form • Coronary diastolic pressures differences during hyperemia
Enrollment	A maximum of 20-50 patients will be enrolled in the registry.
Clinical Sites	Cleveland Clinic Heart & Vascular Institute
Study Duration	Anticipated enrollment period: Q4 2016 and Q1 2017
Inclusion Criteria	Consecutive stable patients with at least one intermediate coronary stenosis and severe AS undergoing TAVR will be enrolled and followed in our registry. Severe aortic stenosis is defined by: • Presence of AVA < 1 cm^2 • Peak velocity > 4 m/s

	• Mean gradient > 40 mmHg • Dimensionless index < 0.25 • Low flow, low gradient, severe AS (increase in LVOT VTI of at least 20% with AVA <1 cm^2) Intermediate severity coronary stenosis is defined by percent stenosis 40-70%.
Exclusion Criteria	• Contraindication to adenosine. • Presence of cardiogenic shock. • Presence of acute coronary syndrome.
Principal Investigator	Samir R. Kapadia MD Director, Sones Cardiac Catheterization Laboratories Cleveland Clinic, Heart & Vascular Institute Cleveland, OH, USA

References:

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2. http://www.nature.com/nrcardio/journal/v13/n5/full/nrcardio.2016.9.html?WT.feed_name=subjects_interventional-cardiology