due to an excess number of adverse events in the transapical TAVI group. Primary endpoint events occurred in 5 patients in the transapical TAVI group and 1 patient in the SAVR group within 3 months (p=0.07; Table 1).

Table 1. Primary Endpoint Events.

Allocation	Event	Time of event	Outcome
Transapical TAVI	Death	On waiting list	Not treatment related
Transapical TAVI	Left coronary artery blockage	Perioperative	Acute CABG/ SAVR, death Day 1
Transapical TAVI	Major stroke	Day 27	Severe disability, death Day 34
Transapical TAVI	Major stroke	Day 16	Severe disability
Transapical TAVI	Renal failure requiring dialysis	Day 8	Hemodialysis
SAVR	Major stroke	Perioperative	Severe disability

After treatment, the mean aortic valve area increased from baseline in the transapical TAVI group from 0.66 cm^2 to 1.4 cm^2 (p<0.0001) and in the SAVR group from 0.71 cm^2 to 1.3 cm^2 (p <0.0001). Baseline peak aortic gradient was higher in the transapical TAVI group compared with the SAVR group. Both groups had lower gradients after treatment (p<0.0001), with a lower gradient in the transapical TAVI group than in the SAVR group (p=0.07). Paravalvular leakage after treatment was more frequent with transapical TAVI than SAVR (p<0.001; Table 2). The NYHA class was significantly improved from baseline in both the transapical TAVI (p=0.01) and SAVR (p=0.001) groups.

Table 2. Paravalvular Leakage.

	Transapical TAVI	SAVR	p value
Aortic valve area (cm^2)			
Baseline	0.66	0.71	<0.0001*
After treatment	1.4**	1.3**	
Peak aortic gradient (mm Hg)			
Baseline	80	67	<0.0001*
After treatment	20	24	
Paravalvular leakage after treatment n (%)			
Moderate to severe	4 (13)	0	<0.001†
Minimal	13 (43)	2 (6)	
None	13 (43)	33 (94)	

*change from baseline to after treatment; **estimated from Figure; †difference between groups.

The study was limited by the inclusion of only two enrolling centers with some experience in performing transapical TAVI. Furthermore, preoperative use of multislice CT was not utilized to optimize valve sizing and positioning relative to the left main. Since the trial was terminated early, the estimates of the risks and benefits may be less precise due to a smaller sample size than had been planned.

Prof. Thuesen concluded that in its present phase of development, transapical TAVI appears to be inferior to SAVR in low-risk, operable, elderly patients. This study highlights the importance of patient selection, noninvasive preprocedural assessment, and the current indications for the procedure; TAVI should be used in nonoperable or surgically very high-risk patients. The role of transapical TAVI requires further investigation to determine what clinical role it may have.

Primary Results of ADVISE: Validation of a Vasodilator Independent Measure of Coronary Fractional Flow Reserve

Fractional flow reserve (FFR) is a diagnostic tool that is utilized during coronary angiography to determine the physiological significance of a coronary artery stenosis. FFR is defined as the ratio of the pressure that is distal to a stenosis relative to the pressure before the stenosis during maximal hyperemia. Although FFR has been validated in clinical trials and correlated with improved outcomes, recent evidence has shown that only 6% of percutaneous coronary interventions (PCIs) in the United States are performed with FFR guidance [Kleiman NS et al. *J Am Coll Cardiol* 2011]. A major barrier to its use is the current requirement for vasodilator drugs, such as adenosine, which may be contraindicated or disliked by patients, and it adds to procedural time and costs, inconvenience, and risk [Pijls N. *J Am Coll Cardiol Interv* 2011].

Justin Davies, MD, PhD, Imperial College, London, UK, presented the results of the ADVISE trial, which evaluated instantaneous wave-free ratio (iFR), a new technology that assesses coronary stenosis using pressure as a surrogate for coronary flow during a period of naturally occurring stable resistance, thereby avoiding the need for adenosine or other vasodilators.

The first part (proof-of-concept) of the ADVISE study evaluated resting wave-free resistance versus mean hyperemic resistance in 39 patients. Study assessments included intracoronary pressure and flow velocity measurements, baseline resistance assessment, and resistance assessment under pharmacological

vasodilatation. The investigators found that resistance that was measured at rest during the wave-free period was similar in both stability (p=0.96) and magnitude (p=0.70) to values that were achieved under adenosine hyperemia.

The second part of the study evaluated whether the assessment of the significance of a coronary stenosis was numerically similar using iFR and FFR in 157 patients. iFR is defined as an instantaneous pressure ratio across a stenosis during the wave-free period, when resistance is constant and minimized in the cardiac cycle. The FFR was measured following administration of intravenous adenosine to achieve maximal hyperemia.

Measurement of iFR during the wave-free period provided a measure of stenosis severity that was similar to the FFR measurement (r=0.90, regression coefficient y=1.022x + 0.03; Figure 1). The small difference between iFR and FFR was not explained by the magnitude of hyperemia (Figure 2).

Figure 1. Close relationship between iFR and FFR.

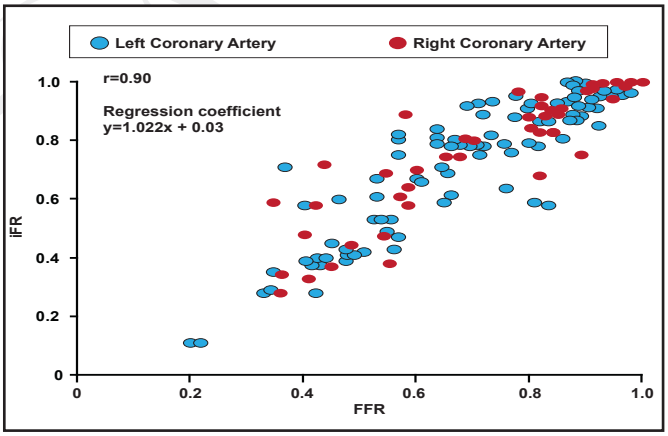

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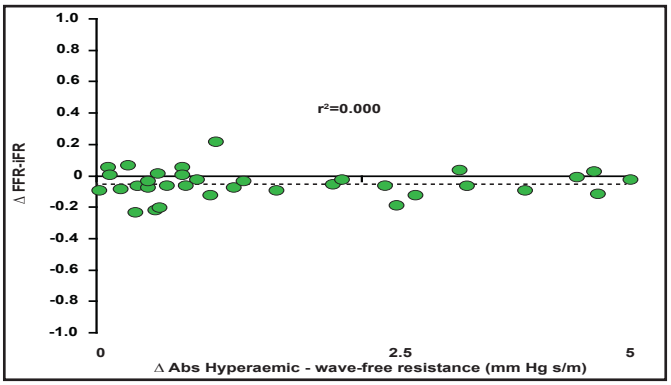
Figure 2. Magnitude of Hyperemia.



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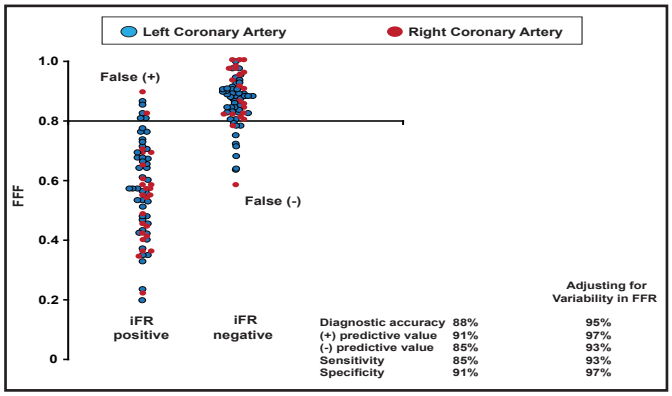
Assessment of the diagnostic efficiency of iFR demonstrated a diagnostic accuracy of 88%, positive predictive value of 91%, negative predictive value of 85%, sensitivity of 85%, and specificity of 91%. After adjustment for the inherent variability in FFR, diagnostic accuracy was 95%, positive predictive value was 97%, negative predictive value was 93%, sensitivity was 93%, and specificity was 97% (Figure 3).

Figure 3. Assessment of Diagnostic Efficiency of iFR After Adjustment for Inherent Variability in FFR.



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The ADVISE study identified a wave-free period in the cardiac cycle when resistance is naturally stabilized and minimal, obviating the need for administration of adenosine. iFR that is measured during this wave-free period gives a measure of stenosis severity that is similar to that provided by FFR. The clinical implications of these results include removal of barriers to adoption of physiological assessment, increased applicability, improved work flow in the catheter laboratory, and improved patient experience.

Point-of-Care Genetic Testing Facilitates Rapid Personalization of Antiplatelet Therapy

Previous studies suggest that *CYP2C19* loss-of-function alleles affect clopidogrel metabolism and are associated with major adverse cardiac events (MACE) and stent thrombosis. *CYP2C19**2 accounts for 95% of *CYP2C19* loss-of-function alleles and occurs in up to 25% of Caucasian populations and 40% of Asian populations.

Currently, most genetic testing is done in central laboratories, with a turnaround time of 2 to 7 days. This delay has prevented the prospective evaluation of genetic testing in percutaneous coronary intervention (PCI) studies. The University of Ottawa Heart Institute, in collaboration with Spartan Biosciences, created the first