Conclusions: FFR guided PCI showed the similar clinical outcomes with concurrent CABG with different safety and efficacy profile. Our results should be confirmed in the ongoing randomized clinical trial.

TCT-321
Invasively Derived Coronary Flow Capacity: Diagnostic Implications of a Cross-modality Physiological Concept
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Background: Coronary flow capacity (CFC) is a cross-modality physiological concept, which integrates both CFR and hyperemic flow to depict the ischemic burden of the myocardium. Originally derived from positron emission tomography (PET) imaging, moderate to severe impairment of CFC has been strongly linked to electrical and clinical manifestations of myocardial ischemia, while no ischemia occurs with normal or mildly reduced CFC. Analogous to PET-derived CFC, we derived an invasive CFC concept, and studied the relationship of fractional flow reserve (FFR) and hyperemic stenosis resistance (HSR) with CFC-defined blood flow impairment.

Results: Coronary pressure and flow velocity were measured in 299 stenoses. After stratification in normal, mildly reduced, moderately reduced, and severely reduced CFC using literature-derived CFR cut-offs and the corresponding hyperemic flow velocity percentiles, FFR and HSR outcomes were evaluated across the four CFC groups.

Results: Identification of severely reduced CFC was excellent for FFR<0.80 (90% agreement) and HSR>0.80 mm Hg/cm/s (92% agreement). However, 40% and 43% of vessels with normal or mildly reduced CFC had a positive FFR (≤0.80). Notably, FFR decreased to 0.77 (0.71-0.81) and 0.49 (0.40-0.64) in the moderately and severely reduced CFC categories (P<0.05 compared with all other CFC categories), where 75% of stenoses with severely reduced CFC had FFR<0.65. HSR increased significantly with decreasing CFC, and showed less discordance with CFC than FFR (6% and 11% for normal or mildly reduced CFC). Notably, 13 out of 15 stenoses associated with moderately or severely reduced CFC not identified by FFR<0.80, were characterized by high HMR (3.24 mm Hg/cm/s [2.69 - 3.37 mm Hg/cm/s]), and low HSR (0.53 mm Hg/cm/s [0.46 - 0.60 mm Hg/cm/s]), suggestive of microcirculatory disease or low-flow ischemia.

Conclusions: Coronary flow characteristics that determine signs of ischemia are associated with FFR values far below contemporary interventional thresholds. FFR seems oversensitive in high-flow settings, and insensitive in low-flow settings. These findings corroborate concerns using a pressure-derived estimate of coronary flow impairment.

TCT-322
Implications Of Human Coronary Autoregulation On Functional Assessment Of Coronary Artery Stenosis Significance Under Baseline Conditions
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Background: Recently, several parameters (iFR, Pa/Pa and BSR) were proposed to detect functional significance of coronary artery disease (CAD) using coronary pressure, obviating the need for hyperemia. These parameters show a good correlation with hyperemic fractional flow reserve (FFR). Coronary autoregulation, i.e. more dilatation in case of more severe epicardial stenosis could be an explanation. Although some experimental data point in this direction, the hypothesis has never been tested in humans.

Methods: Simultaneous measurements of coronary pressure and Doppler flow velocity were obtained in 253 vessels in patients with suspected CAD. FFR was used to indicate functional stenosis severity, while baseline Pa/Pa determined the transmural pressure ratio. Coronary resistance reserve (CRR) was defined as the ratio of hyperemic and basal microvascular resistance, indicating the degree of autoregulation.

Results: The figure shows that with increasing stenosis severity (by FFR), baseline Pa/Pa shows a concomitant progressive decline (P<0.001 for trend). Also, CRR decreases with increasing stenosis severity (P<0.001 for trend) and a stable baseline APV was maintained (P=0.25 for trend).

Conclusions: With progressive stenosis severity, baseline coronary flow is preserved by microvascular resistance reduction (coronary autoregulation), resulting in decreased perfusion pressure. This explains in part the good performance of resting pressure measurements to detect significant CAD.

TCT-323
Diastolic fractional flow reserve (FFR) closely tracks whole-cycle FFR
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Background: FFR explicitly selected whole-cycle measurements to focus on epicardial resistance while minimizing capacitive and inductive effects. However, subsequent work proposed diastolic FFR because coronary flow occurs predominately during this phase of the cardiac cycle.

Methods: VERIFY enrolled consecutive patients from 5 global sites and used IV adenosine hyperemia. Each FFR measurement was repeated following a 2 minute rest period. Whole-cycle and diastolic FFR were computed at a central core lab by averaging 5 consecutive cycles. Diastolic began at the dicrotic notch and ended at the anacrotic limb.

Results: In 206 patients, test/retest repeatability was excellent for both whole-cycle and diastolic FFR. An extremely linear relationship existed between the two FFR metrics, implying that whole-cycle FFR explains 95% of the variation in diastolic FFR. ROC analysis demonstrated an AUC over 98% for diastolic FFR to predict FFR<0.8.
Table. Statistics for repeated whole-cycle and diastolic FFR measurements

<table>
<thead>
<tr>
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<th>1st measurement</th>
<th>2nd measurement</th>
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<tbody>
<tr>
<td>Pearson correlation coefficient (r)</td>
<td>0.980 (p&lt;0.001)</td>
<td>0.976 (p&lt;0.001)</td>
</tr>
<tr>
<td>Coefficient of determination (R²)</td>
<td>96.0%</td>
<td>95.3%</td>
</tr>
<tr>
<td>Area under ROC curve for FFR&lt;0.8</td>
<td>0.988</td>
<td>0.985</td>
</tr>
<tr>
<td>Linear fit (slope)</td>
<td>1.222</td>
<td>1.220</td>
</tr>
<tr>
<td>Linear fit (intercept)</td>
<td>-0.262</td>
<td>-0.257</td>
</tr>
<tr>
<td>Test/retest repeatability of FFR (bias/SD)</td>
<td>-0.003 +/- 0.020</td>
<td></td>
</tr>
<tr>
<td>Test/retest repeatability of diastolic FFR</td>
<td>-0.003 +/- 0.030</td>
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Conclusions: Diastolic and whole-cycle FFR show a highly linear relationship and close diagnostic agreement. Therefore, it would be very difficult to demonstrate a difference between the two metrics in terms of diagnostic accuracy or clinical performance. Fundamentally, greater differences exist between rest and hyperemia than between whole-cycle and diastole at each flow level.

TCT-324
Influence Of Heart Rate On A Fractional Flow Reserve Measurement In Different Epicardial Territories – A Theoretical And Experimental Study

In The Stenosis Model Of Porcine Coronaries

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Background: Coronary blood flow occurs primarily during diastole, therefore we hypothesize that heart rate (HR) by affecting the diastolic/stenosis ratio may exert a significant effect on the fractional flow reserve (FFR). The aim of the study was to develop a mathematical formula describing the relationship between FFR and HR and to verify the results in an in vivo experimental setting using porcine model of coronary stenosis.

Methods: Literature data regarding the diastolic/stenosis ratio and assumption that coronary blood flow occurs during diastole were used to develop the mathematical model. The formula was then verified experimentally. Serial FFR measurements were performed in porcine coronary arteries. Coronary stenosis was obtained with the use of balloon inflation on a pressure wire within previously placed stents in LAD and RCA respectively. Subsequently, cardiac pacing was initiated and serial FFR measurements were made for achievable HR range of 60-180 per minute.

Results: The results are presented in fig. 1. In the experimental part 35 FFR measurements (14 RCA and LAD 19) were performed, which indicated a significant correlation of FFR and HR in LAD (r² = 0.79, p < 0.0001), which agreed with in silico model (p<0.11). In opposite, the results obtained in RCA indicate a lack of correlation between FFR and HR (r² = 0.03, p = 0.52).

Conclusions: Our study generates hypothesis that HR influences FFR in LAD, suggesting the necessity for clinical validation and algorithm correction. Although the formula of FFR-HR dependency developed during the study is ready to implement in existing FFR modalities.

TCT-325
Influence of the amount of myocardium subtended by an intermediate coronary artery stenosis on FFR and iFR

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Background: Fractional Flow Reserve (FFR) has been shown to be related to the amount of myocardium subtended by a coronary stenosis; this has never been shown for the instantaneous wave-free pressure ratio (iFR). In addition, myocardial hyperemia during the wave-free period has been shown to be nearly the same of that measured during adenosine induced maximal hyperemia, but it is still not clear whether this equivalence is also depending of the amount of myocardium subtended to the coronary stenoses.

Methods: Consecutive patients with at least one equivocal stenosis in one major coronary artery were enrolled. Both FFR, iFR and iFR with adenosine administration (iFRa) were measured. Δ%iFR was defined as the difference in percentage of Pa/Pd ratio assessed during conventional iFR measurement and iFR measurement during intra-coronary adenosine infusion (iFRa). The amount of jeopardized myocardium was evaluated using the Duke Jeopardy Score (DJS). Two-dimensional quantitative coronary angiography (QCA) was used to assess the angiographic features of the coronary stenosis and both reference diameter (RD) and minimal lumen diameter (MLD) were calculated.

Results: We evaluated 42 intermediate coronary artery stenoses in 38 patients. Both FFR, iFR and iFRa were inversely correlated with DJS/MLD ratio (respectively, r² = 0.32, p < 0.001, r² = 0.53, p < 0.001, and r² = 0.64, p < 0.001). Moreover, the Δ%iFR was significantly correlated with the DJS/MLD ratio (r² = 0.22, p = 0.03), suggesting that myocardial residual function cannot be considered negligible during the wave-free period particularly in larger territories. Of note, DJS/MLD ratio had higher accuracy in predicting FFR value (ROC analysis: 0.89 [0.79-1.00], p < 0.001).

Conclusions: Both FFR and iFR are related to the amount of myocardium subtended by a coronary artery stenosis and DJS/MLD ratio can reliably predict a positive FFR value. In addition, because of the not negligible resistance during the wave-free period, iFR should not be used for the assessment of coronary stenosis subtending larger myocardial territories.

TCT-326
Utility of Fractional Flow Reserve Assessment in Aortic Stenosis

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Background: Assessment of the significance of coronary stenosis in patients undergoing aortic valve replacement is important as concomitant revascularization increases procedural mortality risk. Fractional flow reserve (FFR) is an essential tool for evaluating the functional significance of coronary artery stenosis that has been validated in patients without valvular disease. Its diagnostic utility has not been assessed in patients with symptomatic aortic stenosis (AS).

Methods: We retrospectively analyzed all patients with moderate to severe AS from July 1, 2005 to October 31, 2013 who underwent coronary angiography and FFR assessment at our institution. Clinical, echocardiographic, hemodynamic, and angiographic data were collected. Patients were stratified by the hemodynamic significance of their coronary artery disease (FFR ≥0.8). Longitudinal follow up was performed to determine the primary outcomes of death, myocardial infarction (MI), target lesion revascularization (TLR), or its combination (MACE).

Results: Patients (n=54) with moderate to severe AS (mean aortic valve area 0.88±0.23 cm², mean gradient of 32±14 mmHg) underwent FFR assessment of 76 coronary lesions. The mean angiographic severity was 64%. Mean duration of follow-up was 853 days. Of the lesions that underwent FFR assessment, 13(17.1%) lesions were treated with percutaneous intervention, 23(30.3%) were bypassed during cardiac surgery, and 40(52.6%) were treated medically. There was no difference between MACE or individual outcomes between lesions with an FFR<0.80 versus FFR≥0.80: MACE 27.9% vs 33.3% p = 0.610, TLR 7.0% vs 0.0% p = 0.122, MI 9.3% vs 15.2% p = 0.434, Death 20.9% vs 27.3% p = 0.519. Utilization of a cutoff of >0.80 for medical management had a negative predictive value of 100% [95%CI 89.32%–100.00%] for freedom from TLR. Furthermore, there was no correlation in FFR result with severity of AS (p=0.730), even after adjusting for the degree of angiographic severity (p=0.530).

Conclusions: FFR can be utilized to diagnose hemodynamic significance of coronary artery disease in patients with moderate and severe AS. There appears to be no influence of the severity of AS on FFR results nor on clinical outcomes.