Comprehensive Functional Coronary Assessment

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Expanding the Clinical Paradigm

Structural Coronary Artery Disease

- Obstructive (≥ 50%) lesion
- Atherothrombotic processes

Adapted from Beltrame et al (2016) Circ J

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Functional Coronary Artery Disease

- Coronary Artery Spasm
- Presence/absence atherosclerosis

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Coronary Microvascular Disorders

- Not visible on angiography
- Microvascular Dysfunction

Coronary Vasomotor Disorders

Adapted from Beltrame et al (2016) Circ J

Beyond Structural Angiography The Emergence of Functional Angiography

Comprehensive Coronary Evaluation of Suspected Cardiac Pain

Structural Coronary Angiography

Macrovascular	 Is there a tight stenosis?
(Epicardial)	(check for late filling vessels - collaterals) What are the lesion characteristics?
Dysfunction	(IVUS / OCT) Is there a muscle bridge?
Microvascular	 Is there impaired contrast flow?
Dysfunction	(TIMI-2 flow / TIMI Frame Count)

IVUS = Intravascular Ultrasound, OCT = Optical Coherence Tomography, iv = intravenous, ic = intracoronary, ACh = Acetylcholine

Beltrame et al (2022) JACC 79:2379-82

Beyond Structural Angiography The Emergence of Functional Angiography					
Comp	orehensive Coronary Evalua Structural Coronary Angiography	tion of Suspected Cardiac Pain Functional Coronary Angiography			
Macrovascular (Epicardial) Dysfunction	 Is there a tight stenosis? (check for late filling vessels - collaterals) What are the lesion characteristics? (IVUS / OCT) Is there a muscle bridge? 	 Is the stenosis obstructive? (Fractional Flow Reserve) Is the stenosis fixed or dynamic? (lesion response to ic nitrates) Is there inducible spasm? (>90% constriction to icACh bolus) 			
Microvascular Dysfunction	 Is there impaired contrast flow? (TIMI-2 flow / TIMI Frame Count) 	 Is there appropriate microvascular hyperemia? (iv adenosine – Coronary Flow Reserve, Microvascular Resist) Is there inappropriate microvascular constrictor? (icACh bolus – ischemia in absence of epicardial spasm) 			

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Functional Coronary Angiography Protocol

1. Coronary Angiogram Imaging

- *Structural*: Exclude obstructive CAD (no stenosis \geq 50%)
- Dynamic: Coronary Slow Flow, Myocardial Bridge

2. Coronary Hyperaemic Indices (Adenosine)

- Large Vessel: Intermediate Coronary Stenosis (FFR)
- *Microvessels*: Microvascular Angina (CFR, iMR, hMR)

3. Coronary Spasm Provocation (ACh bolus)

- Inducible Coronary Spasm: Vasospastic Angina
- No inducible Coronary Spasm: Microvascular Spasm

4. Coronary Endothelial Function (ACh infusion)

- Mechanism: Endothelial integrity
- *Prognosis*: Endothelial function studies

Value of Functional Angiography

- Diagnostic Value is there a cardiac abnormality?
- Pathophysiological Value macro vs microvascular?
- Prognostic Value guarded prognosis?
- Therapeutic Value identify target?

Value of Functional Angiography Diagnostic Guideline Recommendations

ESC Chronic Coronary Syndrome

IIa Recommendation

- Guidewire-base CFR or microcirculatory resistance measurements should be considered in patients with persistent symptoms, but coronary arteries that are either angiographically normal or moderate stenoses with preserved FFR.
- Intracoronary acetylcholine with ECG monitoring may be considered during angiography, if coronary arteries are either angiographically normal or have moderate stenoses with preserved FFR, to assess microvascular vasospasm.

AHA/ACC Chest Pain Evaluation

• Ila Recommendation (Evidence-B)

 For patients with persistent stable chest pain and nonobstructive CAD and at least mild myocardial ischemia on imaging, it is reasonable to consider *invasive* coronary function testing to improve the diagnosis of coronary microvascular dysfunction and to enhance risk stratification.

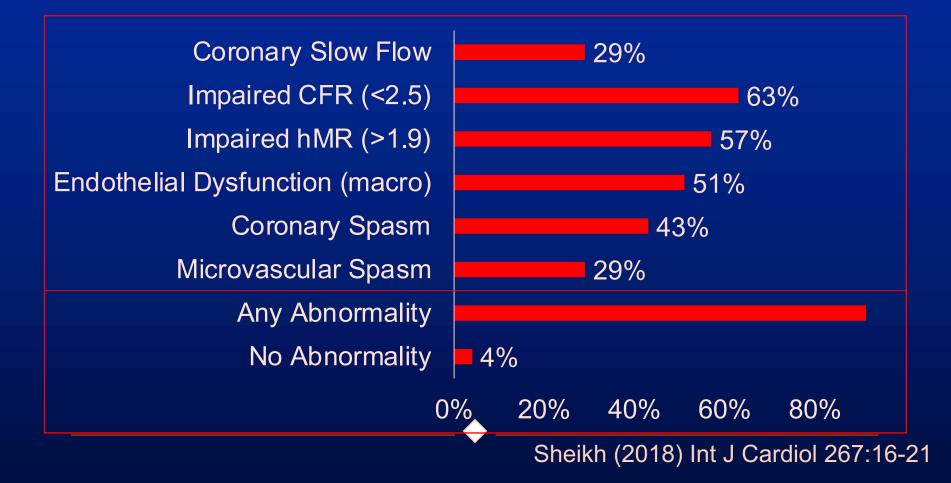
Knuuti (2020) EHJ 41:407

Gulati (2021) Circulation 144:e368

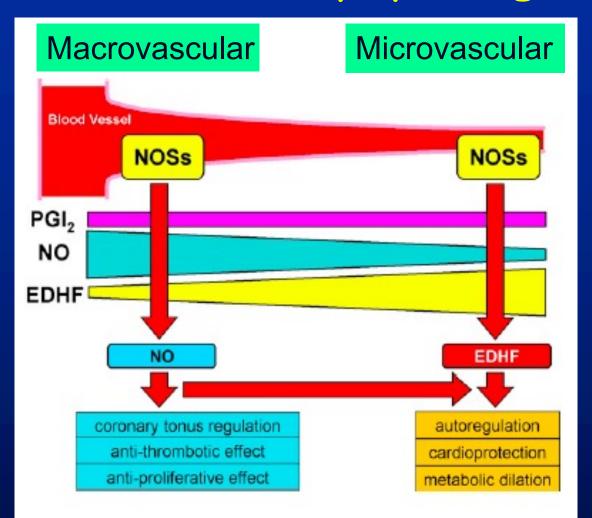
Value of Functional Angiography Diagnostic Value

49 pts with angina and non-obstructive CAD

• Angio, pressure-Doppler sensor guidewire, ACh test



Value of Functional Angiography Pathophysiological Value



Pathophysiological Insights
Vascular Site:
➤ Macrovascular

Microvascular

Both

Nature of Dysfunction:

- Hyperconstriction
- Impaired Dilation
- Both

Shimokawa (2008) EHJ 35:3180-93

Value of Functional Angiography Prognostic Value

Japanese Coronary Spasm Association Risk Score

- 1,429 vasospastic angina pts followed for median period of 32mths
- MACE Predictors (cardiac death, non-fatal MI, appropriate ICD shock)
 - Low Risk (0-2): 0.5% MACE/5yrs
 - Intermediate Risk (3-5): 0.8% MACE/5yrs
 - High Risk 6-9):

3.1% MACE/5yrs

Table 3. Coronary Spasm Association Risk Score				
Clinical determinant	Hazard ratio (95% CI)	Assigned score		
Out-of-hospital cardiac arrest	3.79 (1.61–8.94)	4		
Significant organic stenosis	2.24 (1.33-3.78)	2		
Rest angina alone	1.71 (1.08–2.72)	2		
Smoking	1.71 (1.04–2.79)	2		
Multivessel spasm	1.69 (1.03–2.78)	2		
ST elevation during angina attack	1.54 (0.95–2.50)	1		
Use of β-blockers	2.00 (0.88–4.54)	1		

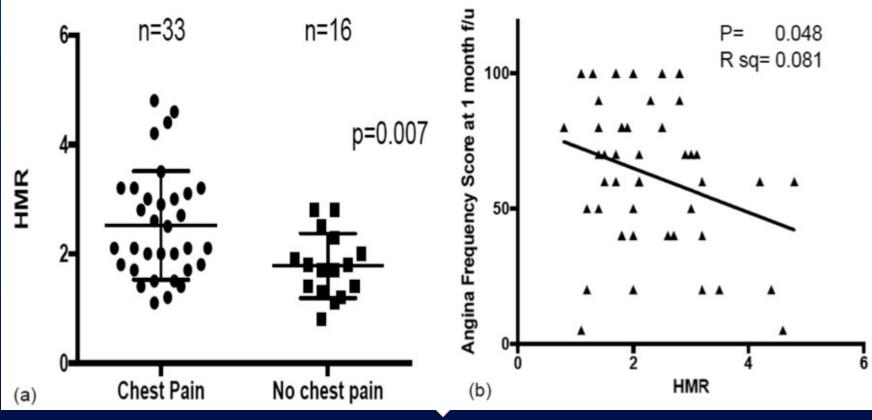
Takagi (2013) JACC 62:1144-53

Value of Functional Angiography Prognostic Value

• Functional coronary angiography for chest pain (n=49)

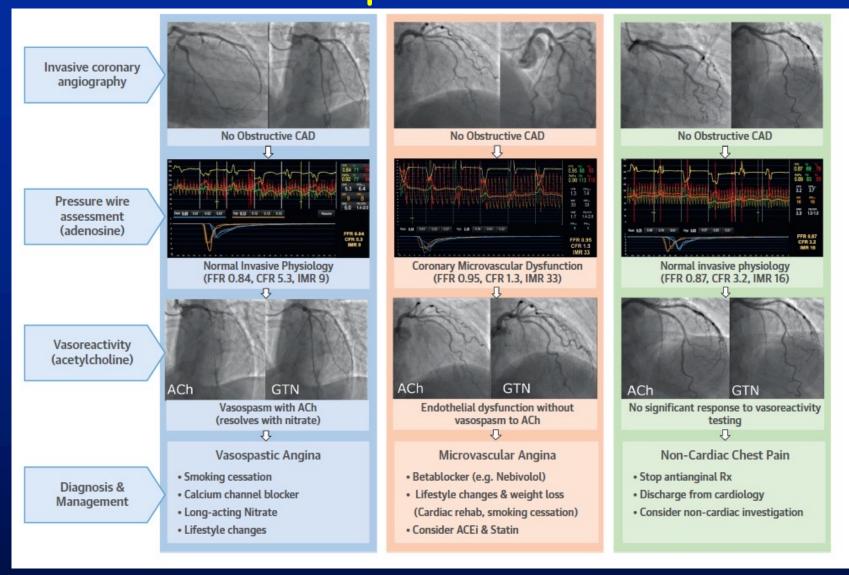
• Predictors of chest pain at 30-days: Previous unstable angina

hMR



Sheikh (2018) Int J Cardiol 267:16-21

Value of Functional Angiography Therapeutic Value



Ford et al (2018) JACC 72:2841-55

Interventional Cardiologist Role

- Unique diagnostic role (not provided by other subspecialties)
- Comprehensive coronary evaluation of chest pain mechanism:
 - > INOCA
 - > MINOCA
 - Secondary Coronary Vasomotor Dysfunction
- Obstructive CAD
 - Cardiomyopathies
 - Other
- Improve Patient Outcome: Confirm Diagnosis
 - Prognostic Implications
 - Guide therapy