6th Annual COVADIS Summit

Cardiac PET

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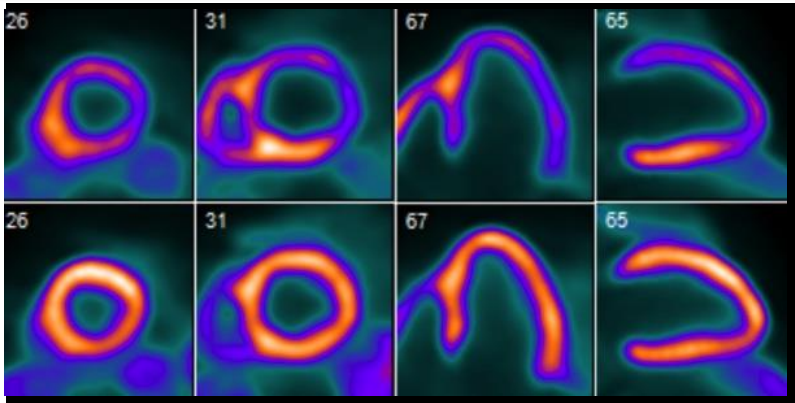
BWH BRIGHAM AND WOMEN'S HOSPITAL
| Heart & Vascular Center |

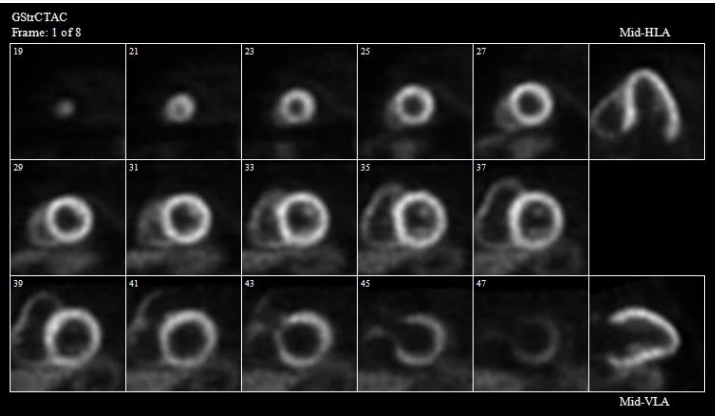
HARVARD MEDICAL SCHOOL
TEACHING AFFILIATE

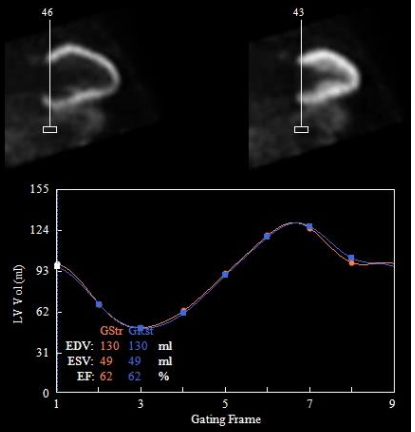
PET imaging in CMD

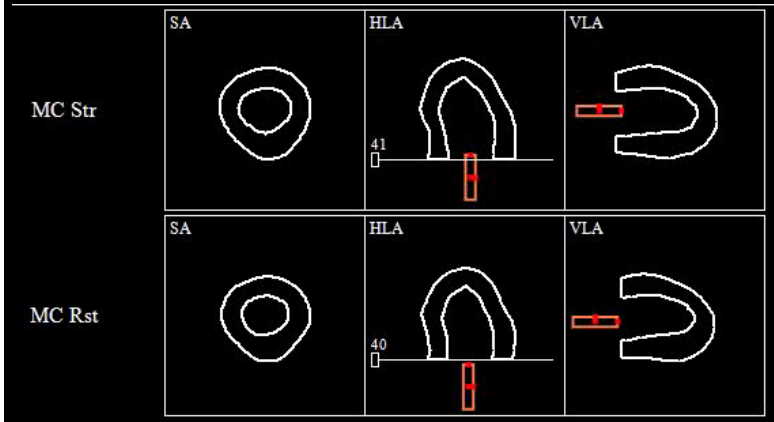
- Technical advances and integrated protocol

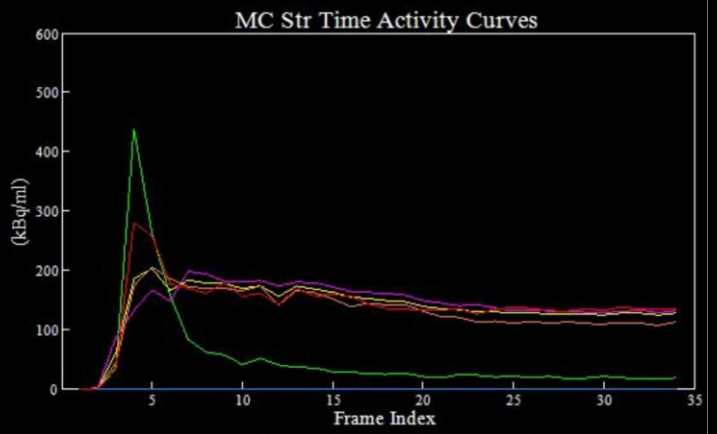
Technical innovation enabling clinical application of CFR quantification





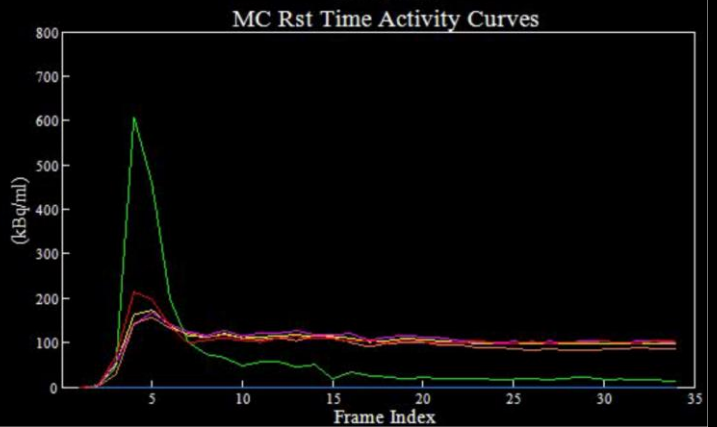




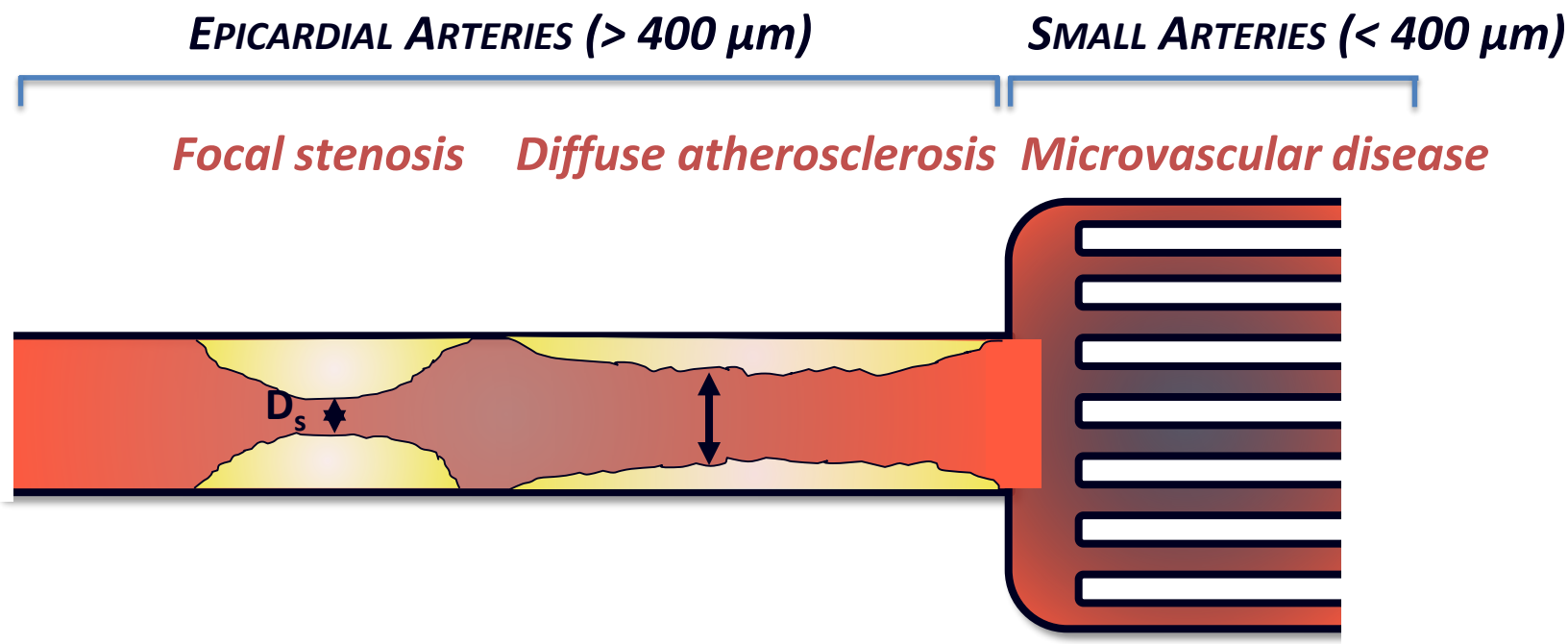


Global Results

Region	Mean Flow (ml/min/g) MC Str	MC Rst	MC Str	MC Rst	Reserve
LAD	87 %	88 %	2.76	1.14	2.42
LCX	71 %	73 %	2.99	1.06	2.82
RCA	87 %	88 %	3.90	1.04	3.76
TOT	82 %	84 %	3.03	1.09	2.78



Factors affecting the pathophysiology of myocardial ischemia and injury in stable IHD



Diffuse nonobstructive atherosclerosis: A common finding in CMD

- 70-80% of patients with CMD have diffuse athero by intravascular US or coronary CT
  - Contributes to myocardial ischemia and symptoms
  - May help explain low frequency of obstructive CAD in registries and clinical trials
  - Offers an opportunity for directing specialized testing for diagnosis and management

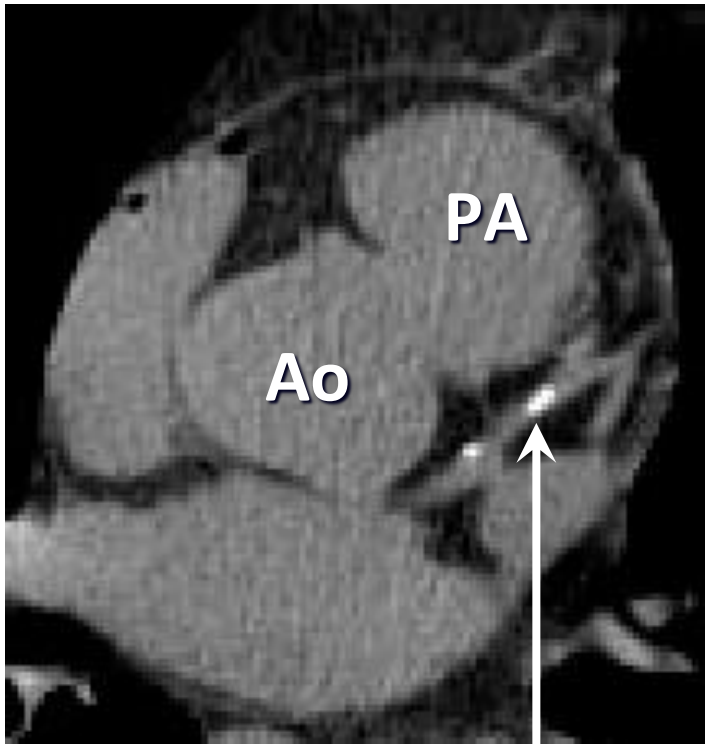
Sources: J Interv Cardiol 2010;23:511-9; Circulation 2014;129:2518-27; Circulation 2015;131:1054-60; Circulation 2001;104:2401-6

Integrating atherosclerosis burden with CMD

No Calcification

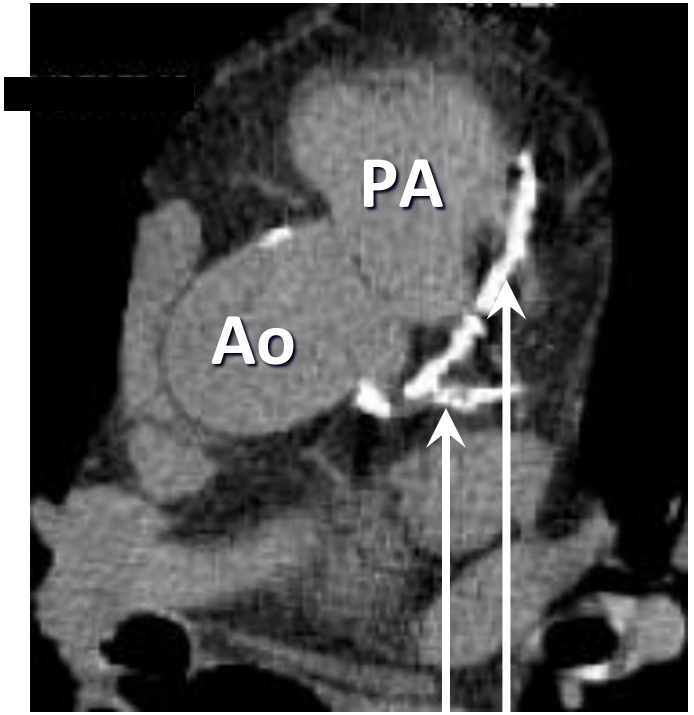
Left Main

Moderate Calcification



LAD

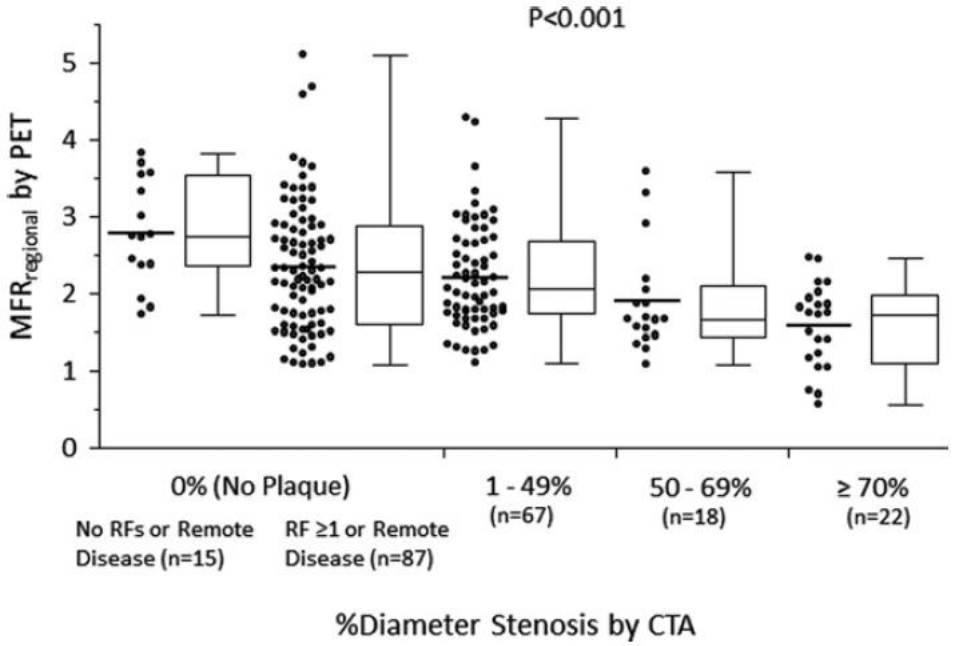
Severe Calcification

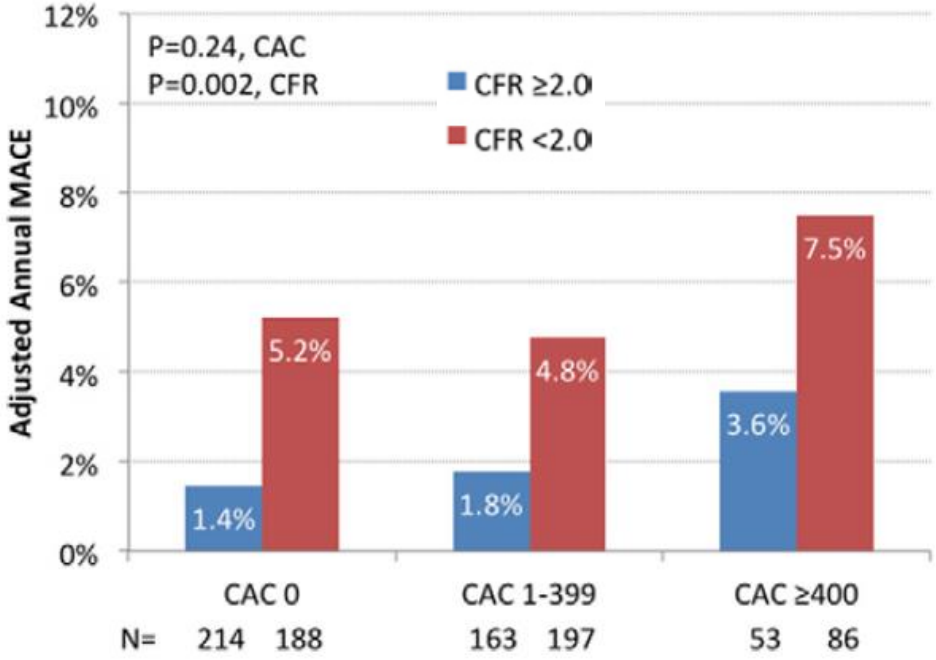


LAD

LCX

Interplay between atherosclerosis burden, CMD and clinical risk

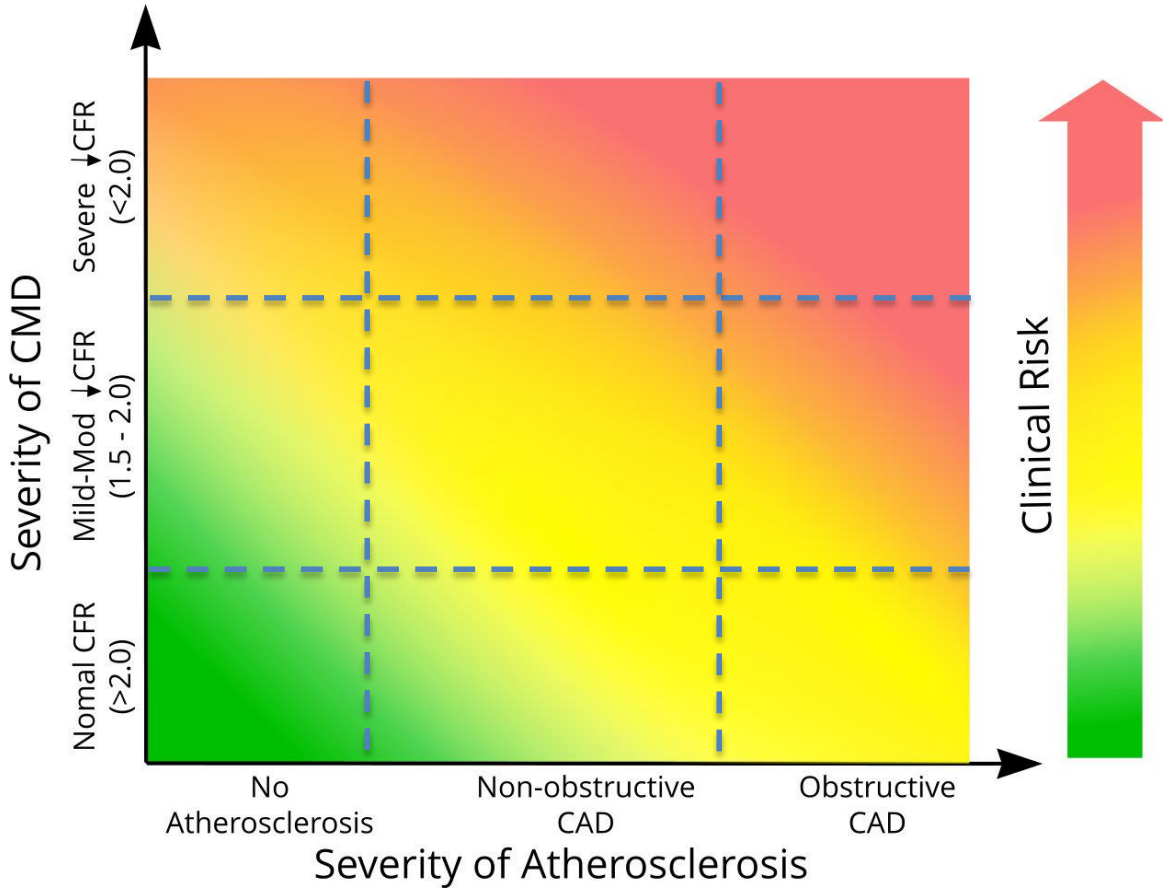




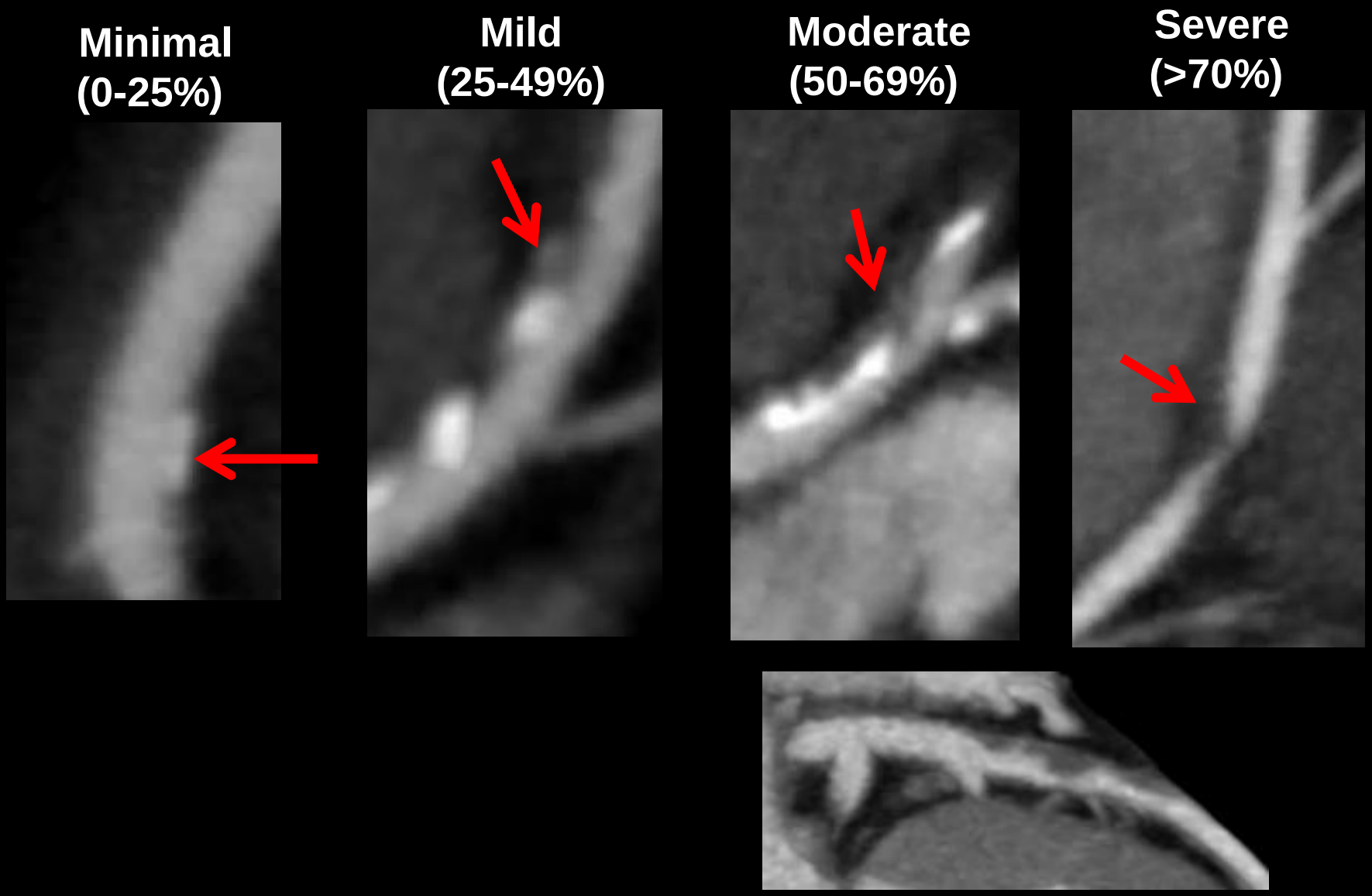
Sources: Naya M…Di Carli M. JACC 2011;58:1807–16 and JACC 2013;61: 2098–106

CMD, atherosclerosis burden and clinical risk

- CMD w/o atherosclerosis
  - Hypertensive and valvular heart disease, and cardiomyopathies
- CMD w/ nonobstructive CAD
- CMD w/ obstructive CAD



Nonobstructive atherosclerosis: A common finding in CMD

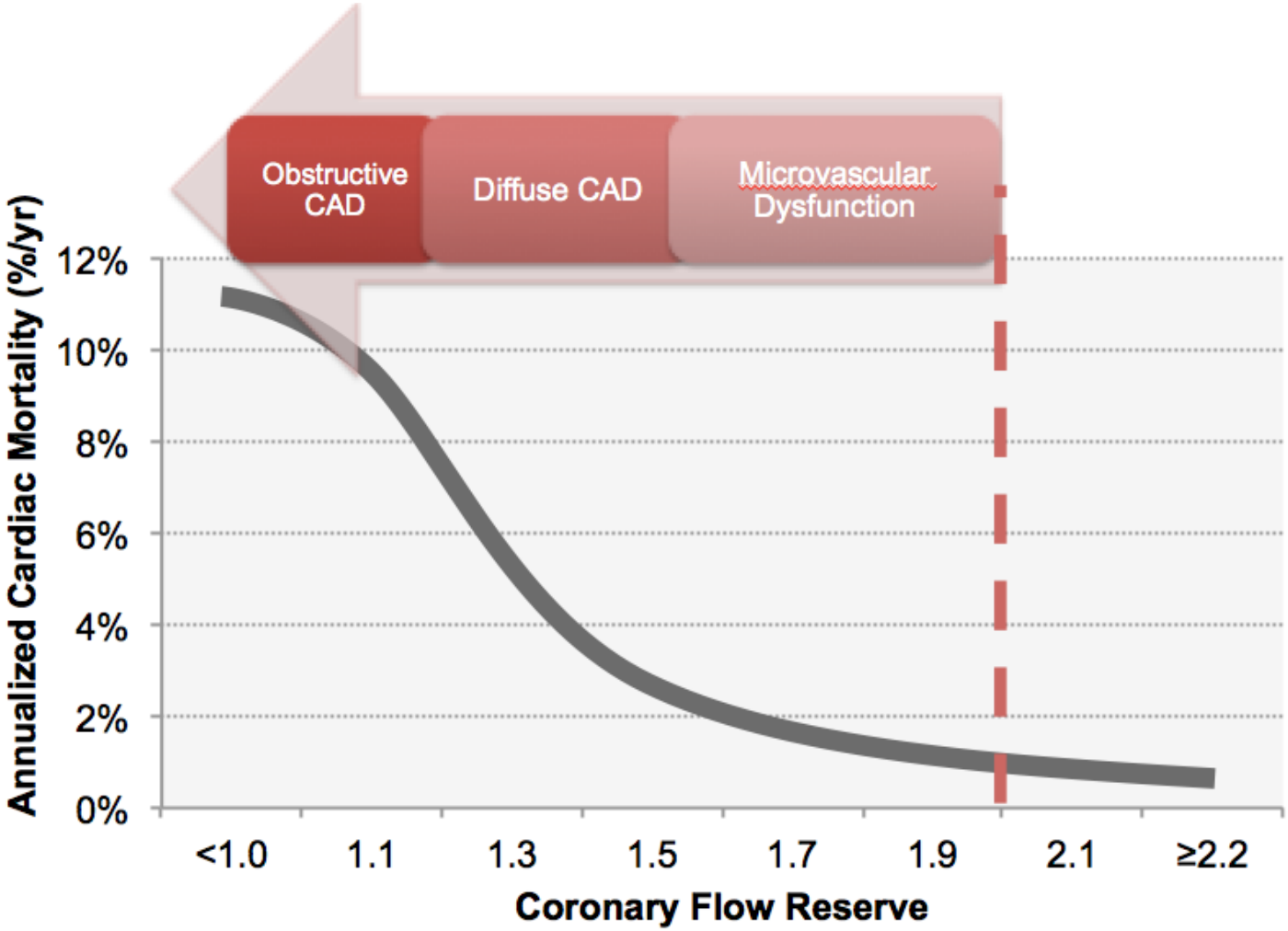


Courtesy of Ron Blankstein

PET imaging in CMD

- Technical advances and integrated protocol
- Diagnostic features of CMD

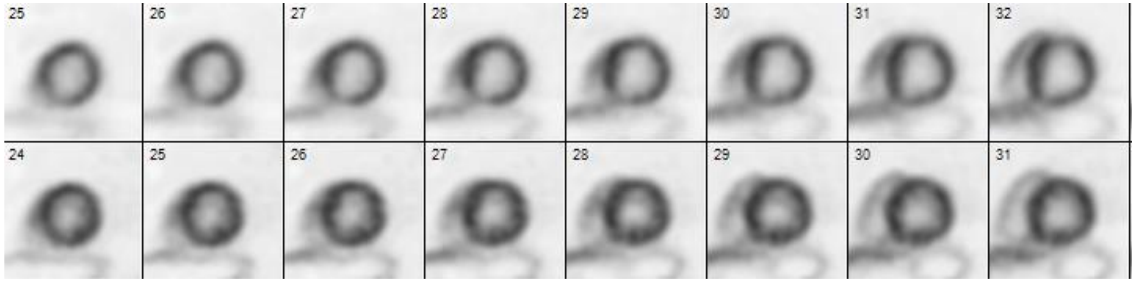
Risk-based threshold of CFR for diagnosis of CMD

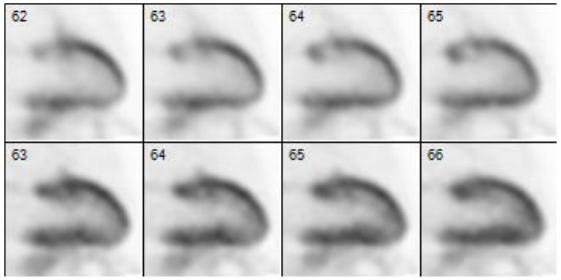


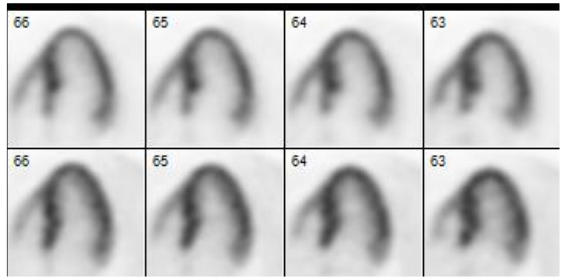
- Nonobstructive CAD
- Obstructive CAD
- Isch and non-isch cardiomyopathy
- Diabetes
- Met syndrome
- CKD

Sources: Murthy VL et al. JNM 2014; 2014;55:1952-8; Taqueti & Di Carli, Curr Probl Cardiol 2016; Murthy VL, et al. Circulation. 2011;124:2215-24; Herzog et al. JACC 2009;54:150; Ziadi et al. JACC 2011;58:740; Fukushima et al. JNM 2011;52:726; Shah NR, et al. JASN 2016 Jun;27:1823-9; Taqueti VR, et al. Circulation 2015;131(6):528-35 & Circulation 2015;131(1):19-27

51 yo M with CAD, recent STEMI and DES to pLAD in 2/16, HTN, Type 1 DM, diabetic nephropathy s/p renal transplant in 2008, p/w several hours of chest pain and dyspnea.



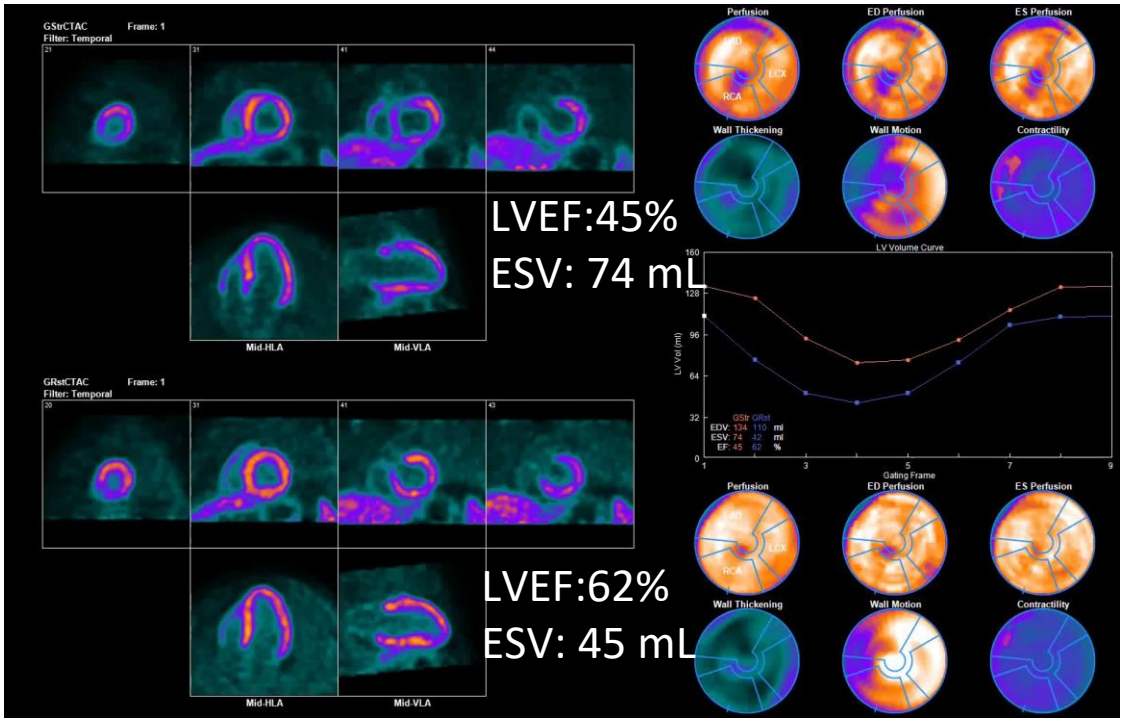


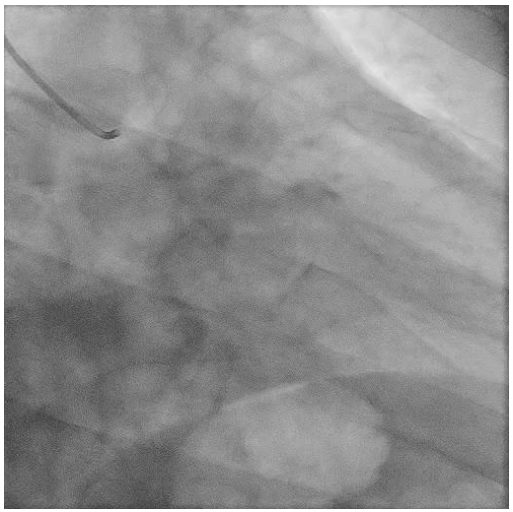


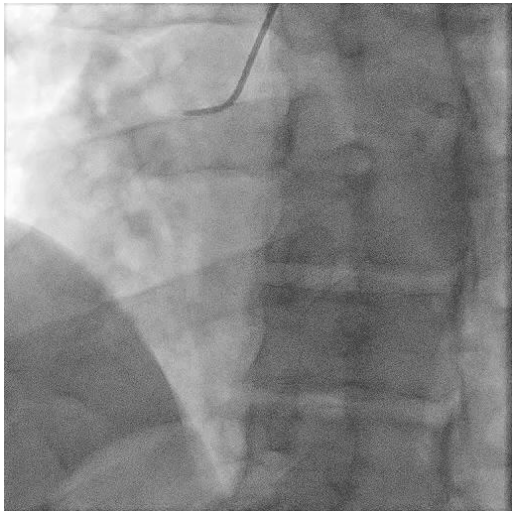
Quantitative myocardial blood flow and CFR

	Rest	Stress	CFR
LAD	0.82	1.23	1.50
LCX	0.83	1.34	1.62
RCA	0.81	1.13	1.39
Global LV	0.82	1.23	1.50

Normal CFR >2

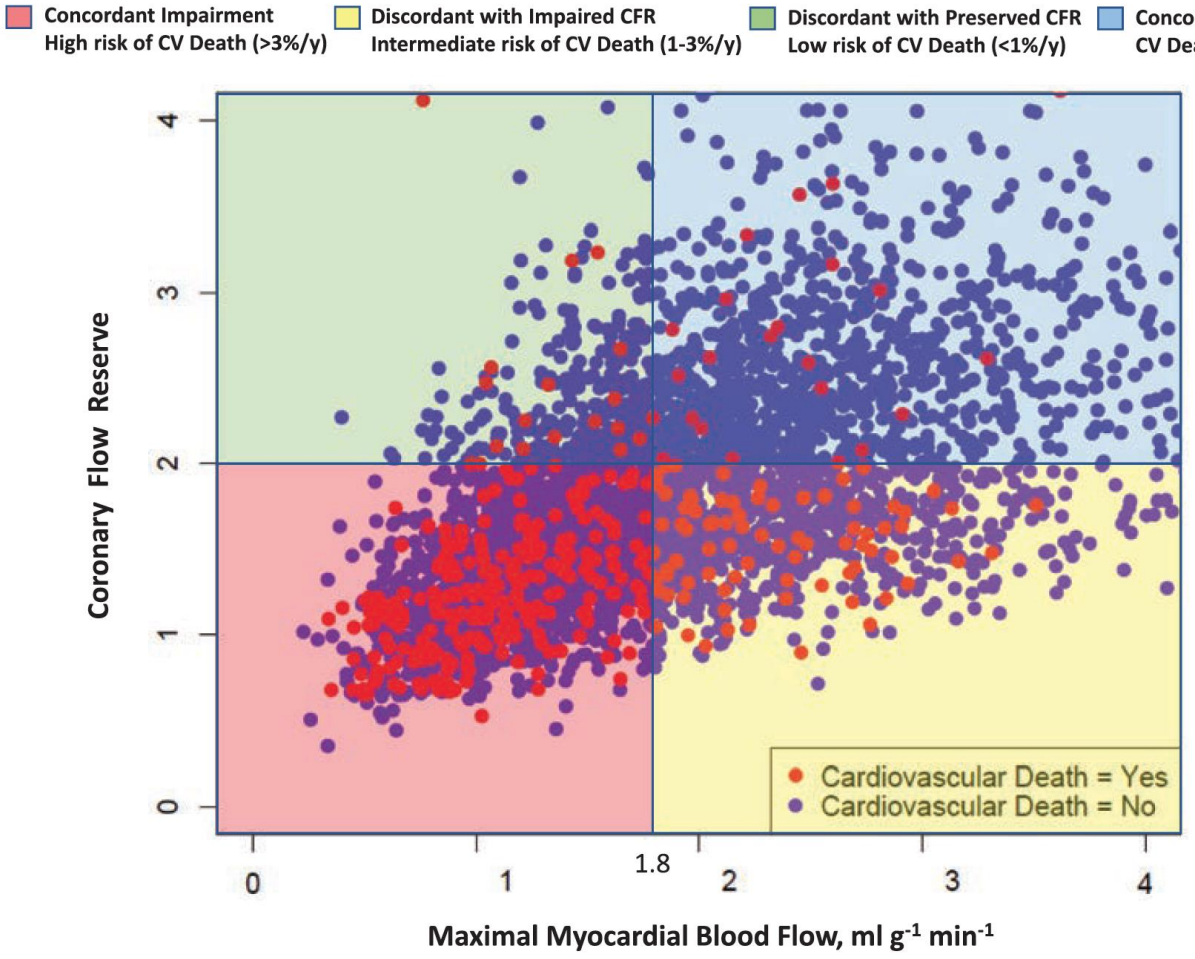


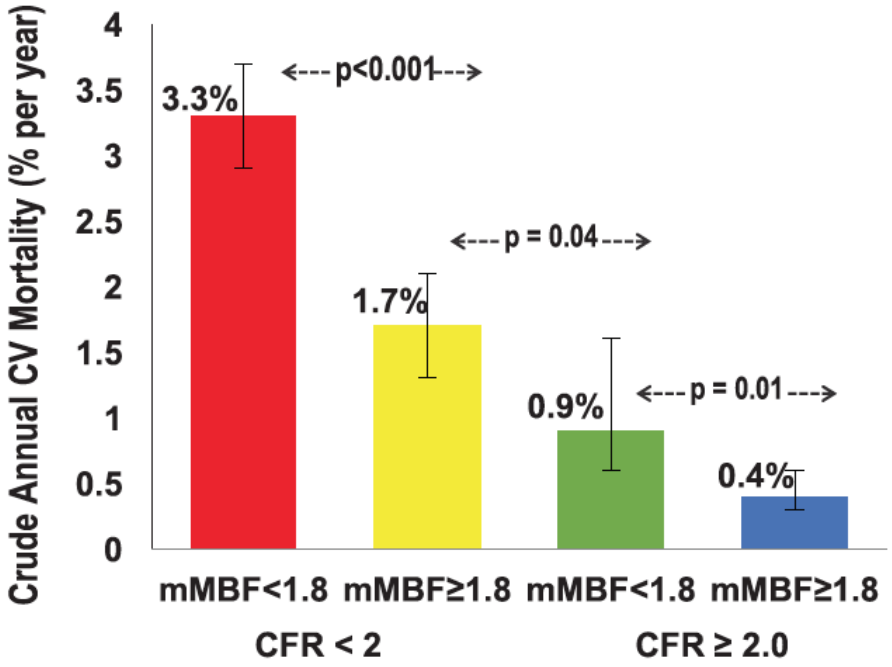




Coronary hemodynamic profile and risk of cardiac death

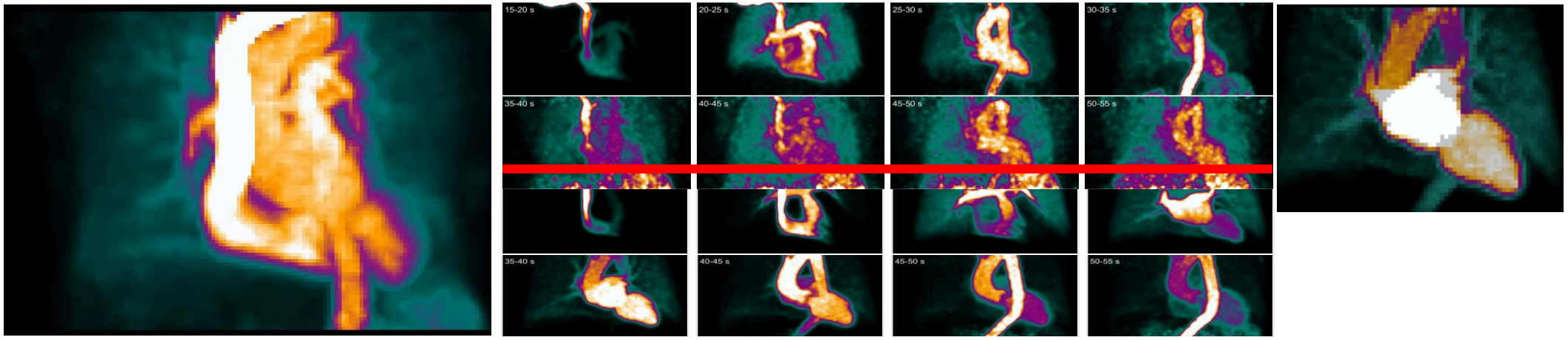
N= 4,029
CD= 392
FU= 5.6 yrs



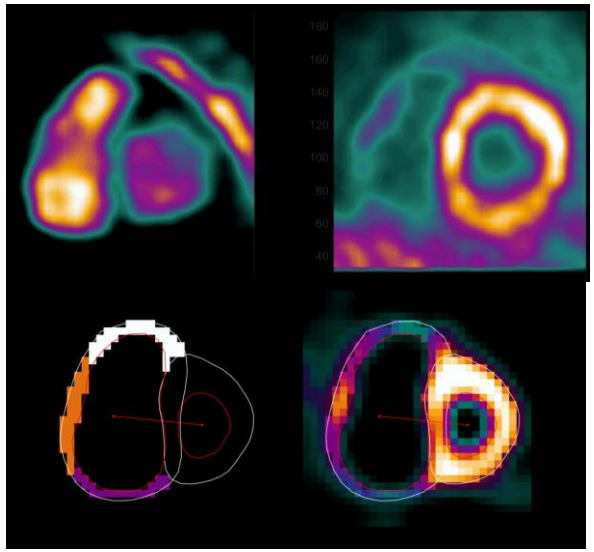


Source: Gupta A...Di Carli M. Circulation. 2017 Dec 12;136(24):2325-36.

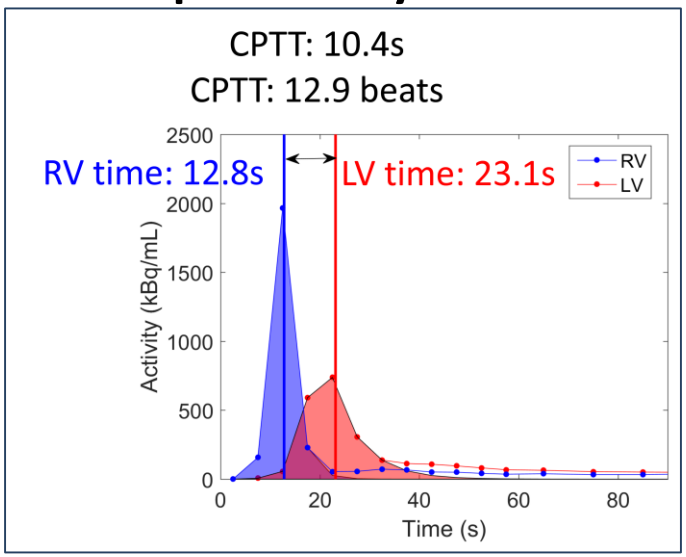
Quantification of integrated cardiopulmonary function from dynamic PET



RV function and flow



Cardio-pulmonary transit time



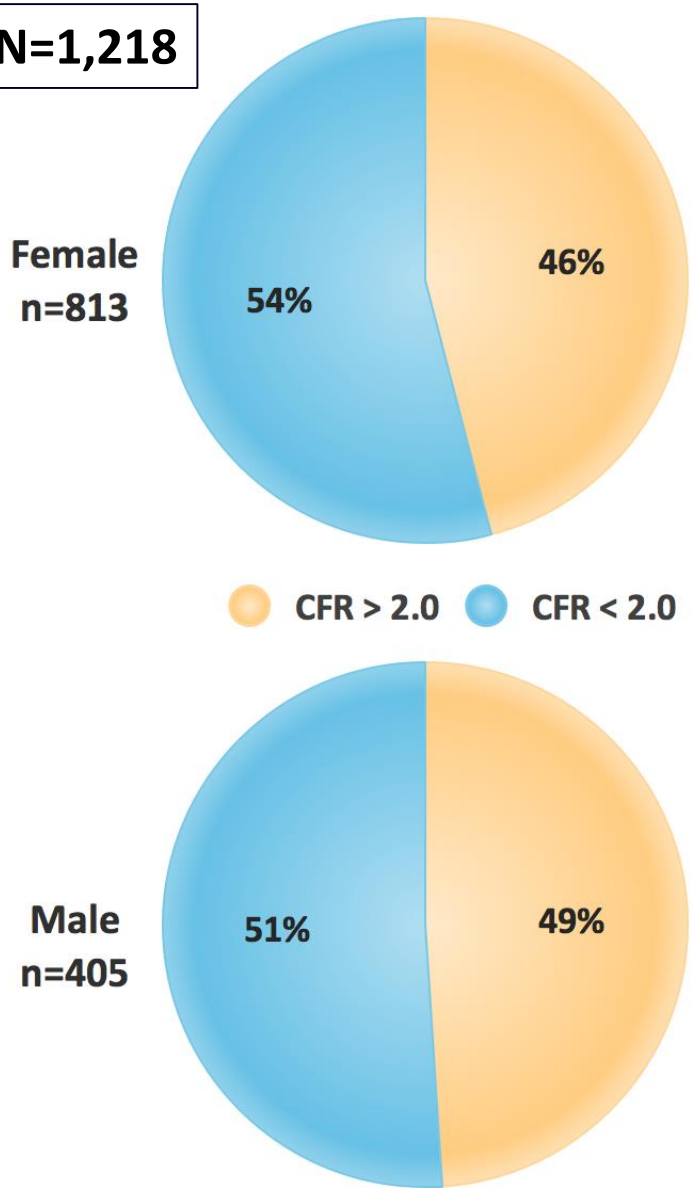
Source: Hans Harms, PhD., University of Denmark and Brigham and Women's Hospital

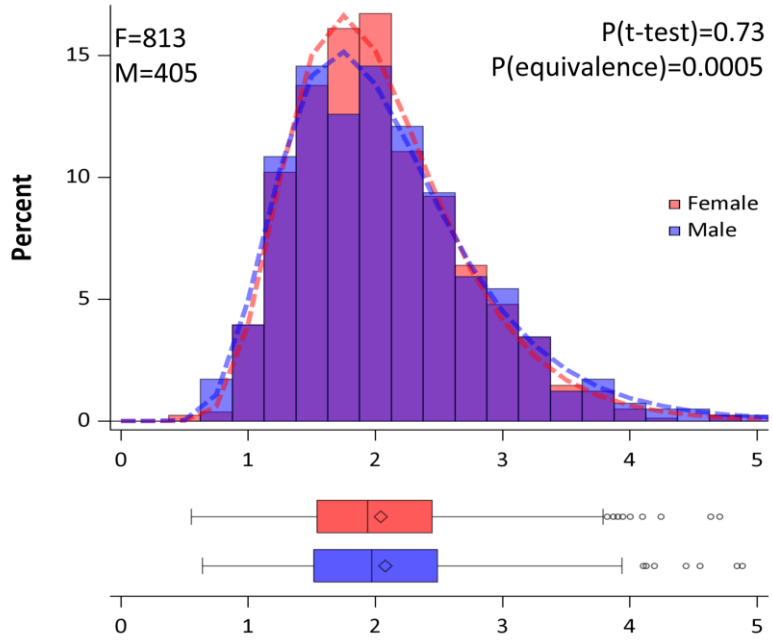
PET imaging in CMD

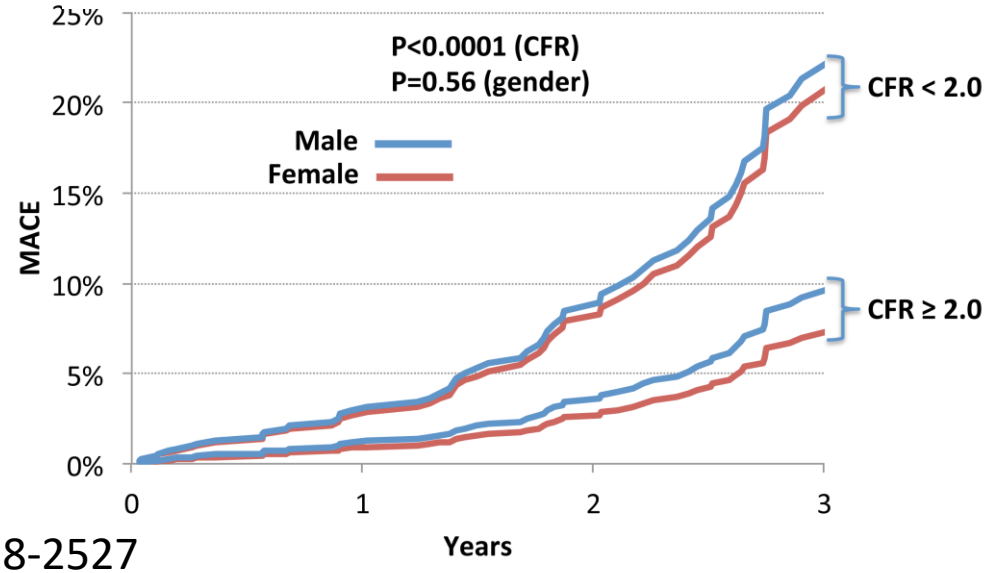
- Technical advances and integrated protocol
- Diagnostic features of CMD
- Prognostic data

High prevalence of CMD in patients without obstructive CAD

N=1,218

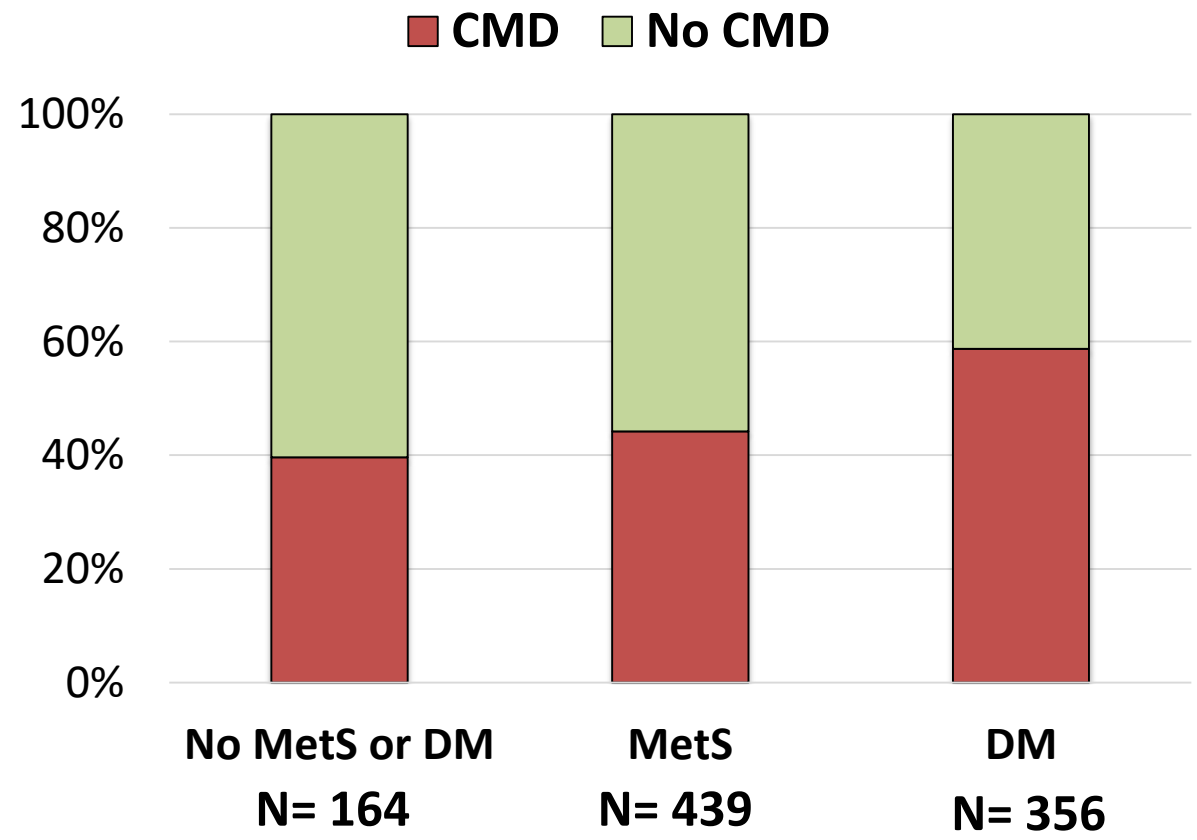


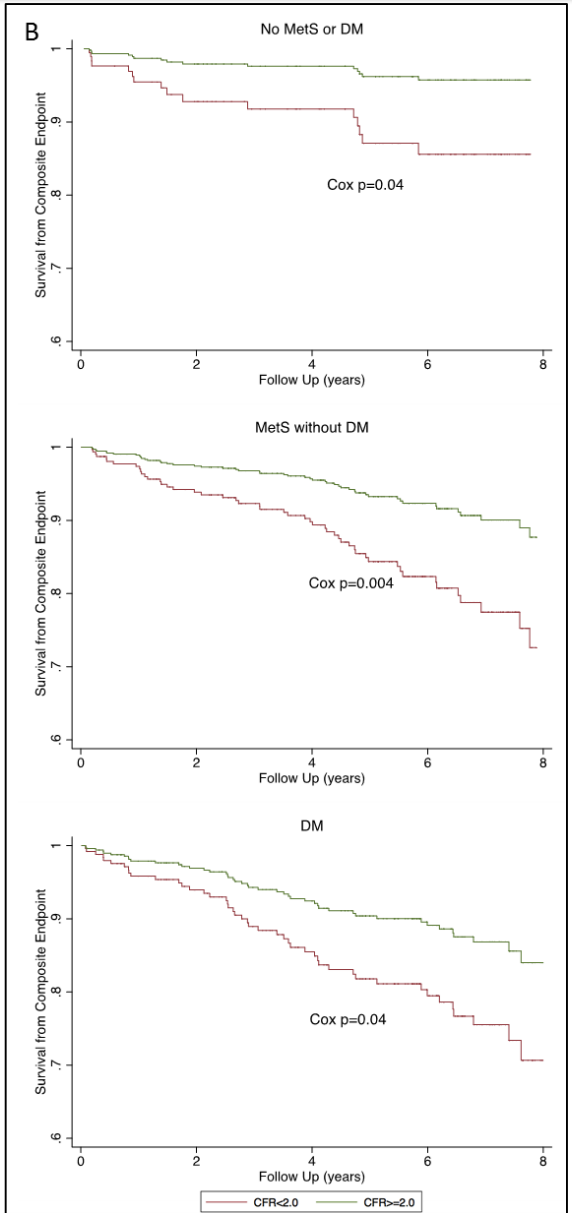




Source: Murthy V, et al. Circulation 2014;129:2518-2527

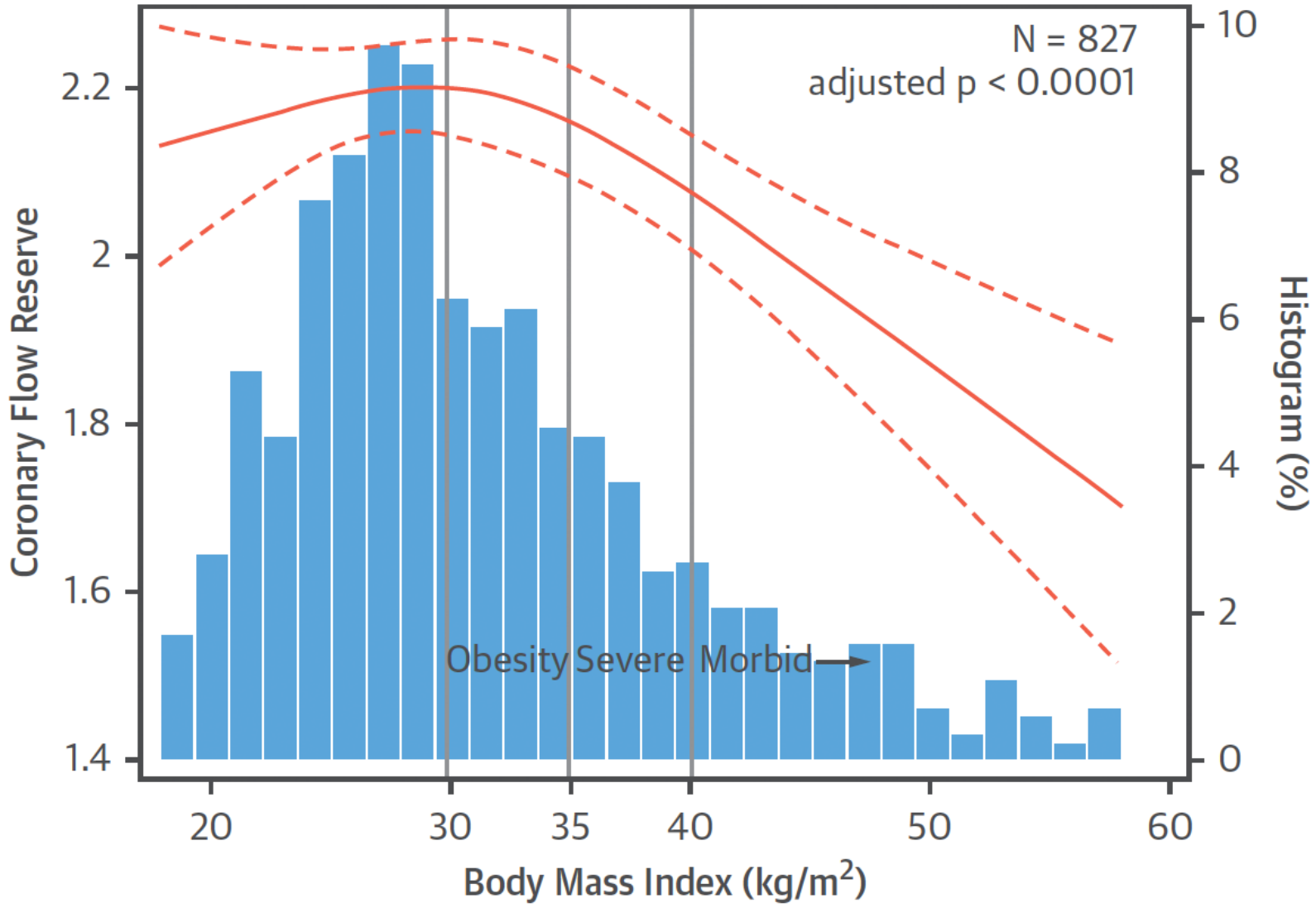
Prevalence of CMD and outcomes across the spectrum of cardiometabolic risk





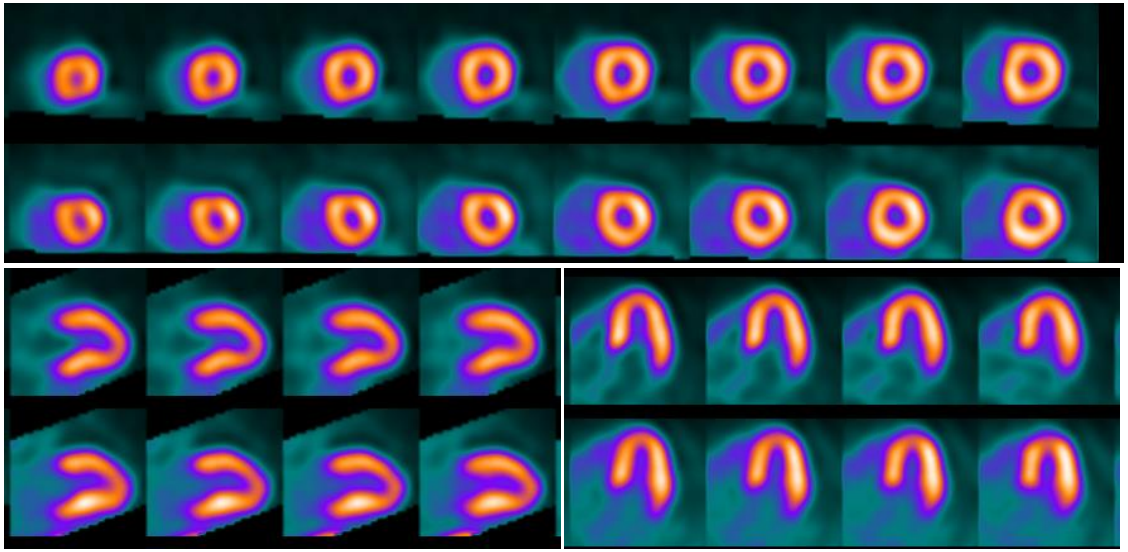
Source: Osborne M…Di Carli M. JACC 2017, Dec 5;70(22):2835-37

High prevalence of CMD in obese patients



Source: Bajaj N… Di Carli M, Taqueti V. 2017. JACC 2018, in press

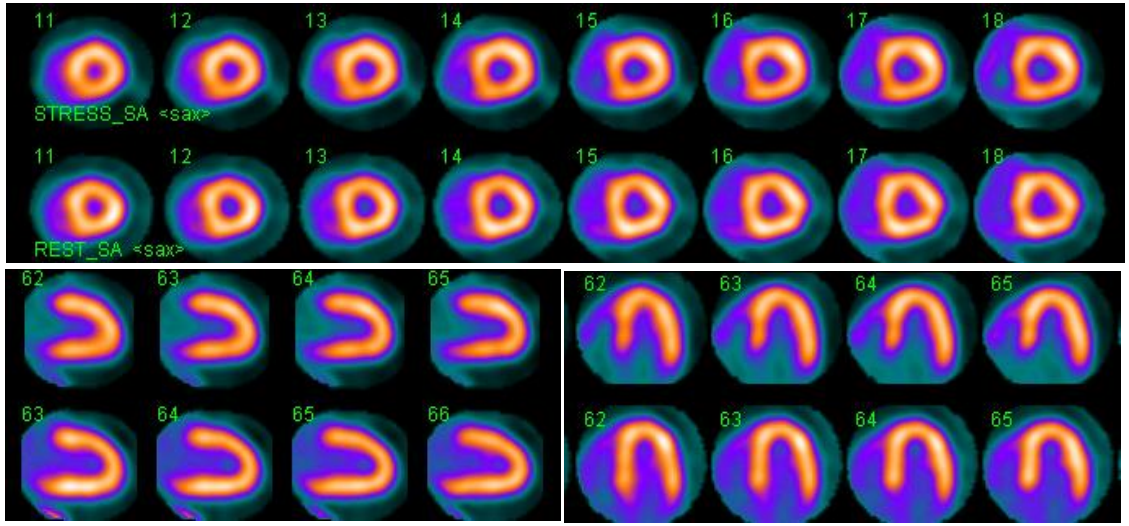
58 yo male with HTN and diabetes evaluated for atypical chest pain



Quantitative myocardial blood flow and CFR

	Rest	Stress	CFR
LAD	0.91	2.1	2.3
LCX	0.87	1.98	2.2
RCA	0.92	1.87	2.0
Global LV	0.89	1.98	2.1

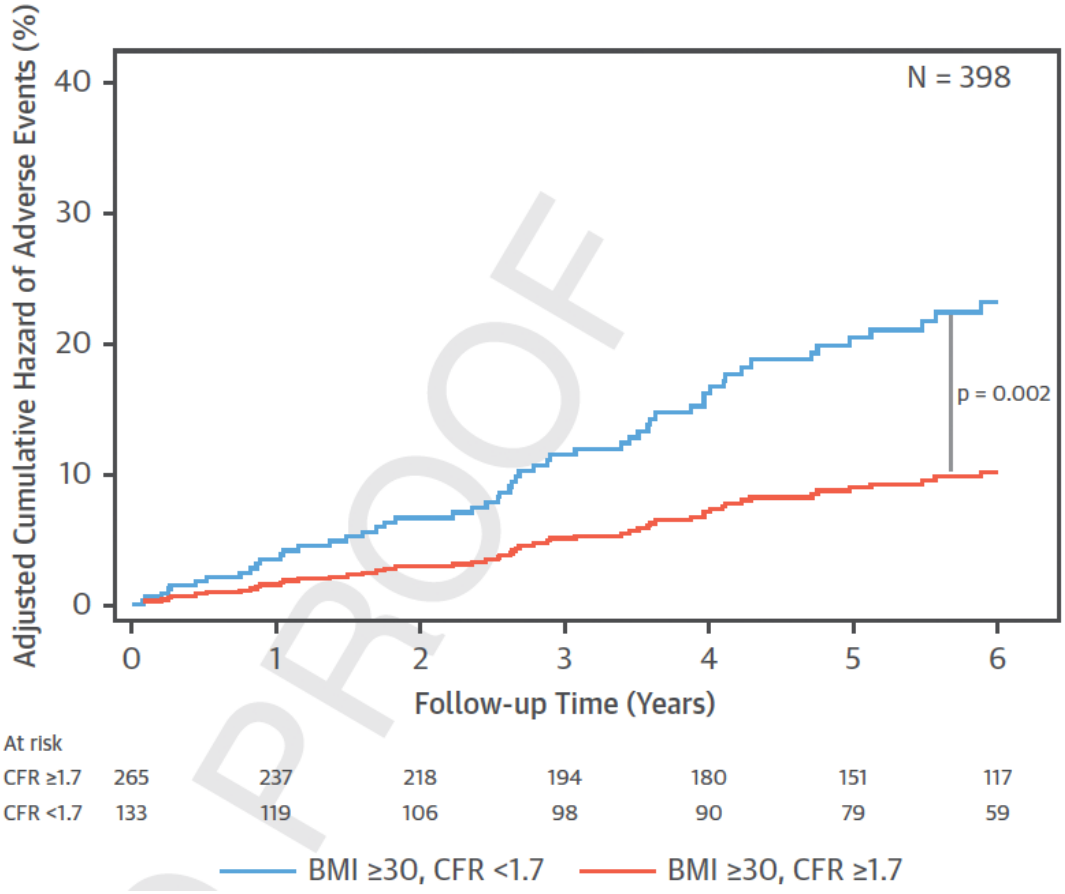
63 yo male with HTN, diabetes and high cholesterol evaluated for dyspnea

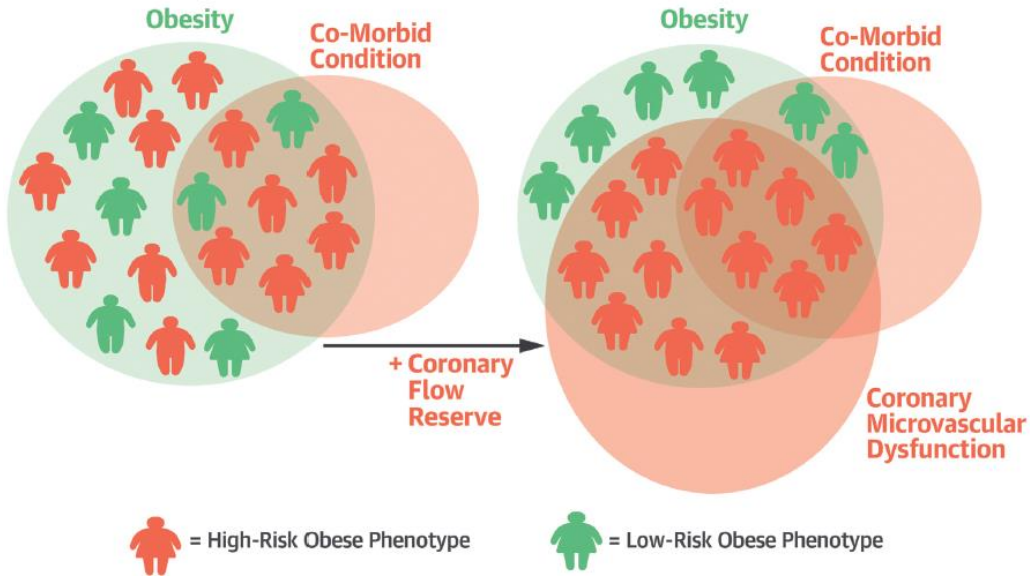


Quantitative myocardial blood flow and CFR

	Rest	Stress	CFR
LAD	1.0	1.48	1.48
LCX	0.94	1.41	1.50
RCA	0.97	1.39	1.43
Global LV	0.97	1.42	1.47

Risk reclassification by identification of CMD in symptomatic obese individuals

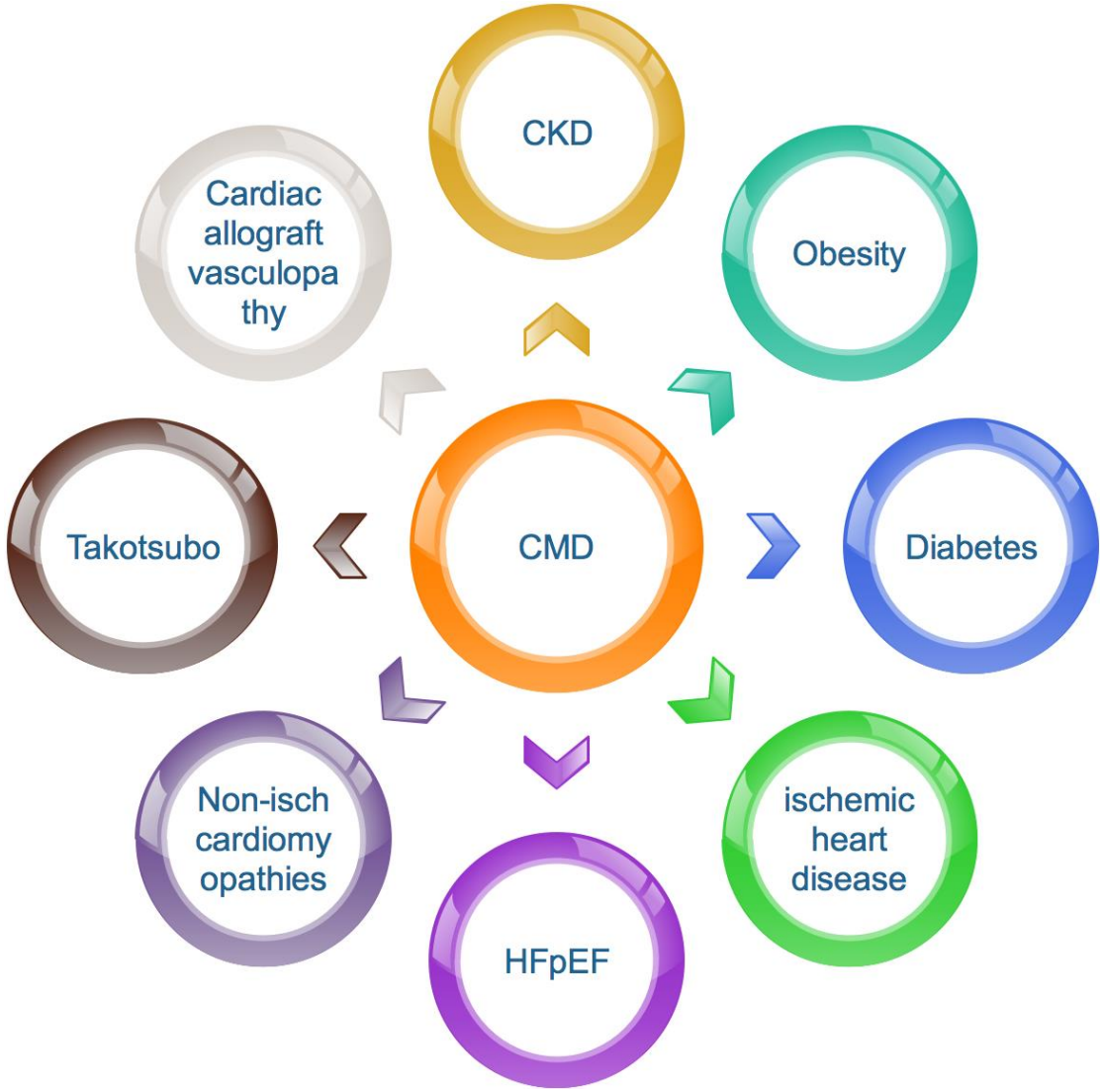




Source: Bajaj N… Di Carli M, Taqueti V. 2017. JACC 2018, in press

CMD is prevalent in a wide range of patients groups

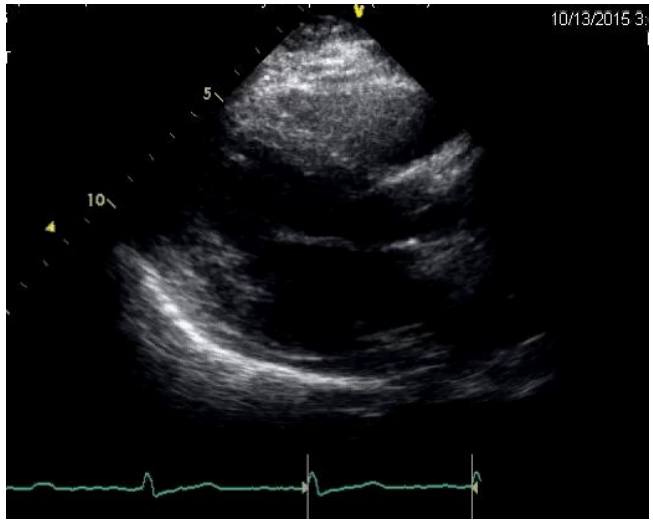
- **In all groups, CMD associated with worse clinical outcome**

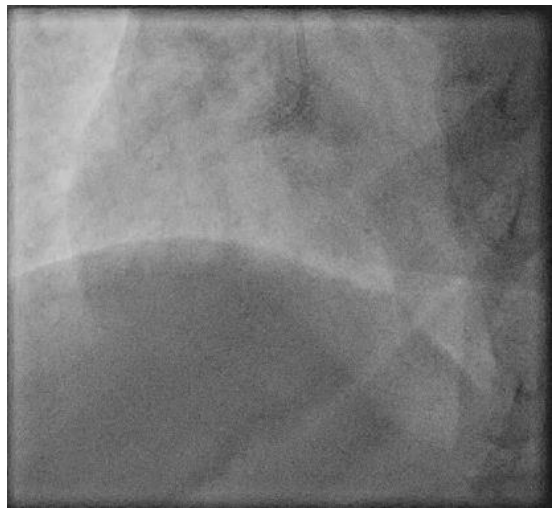


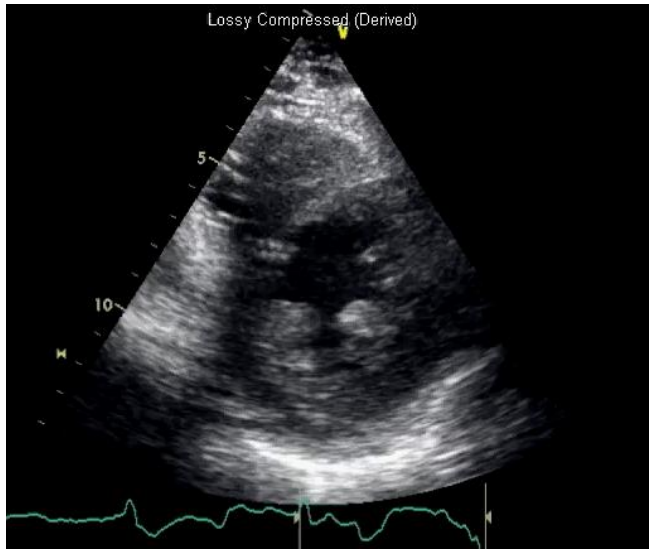
PET imaging in CMD

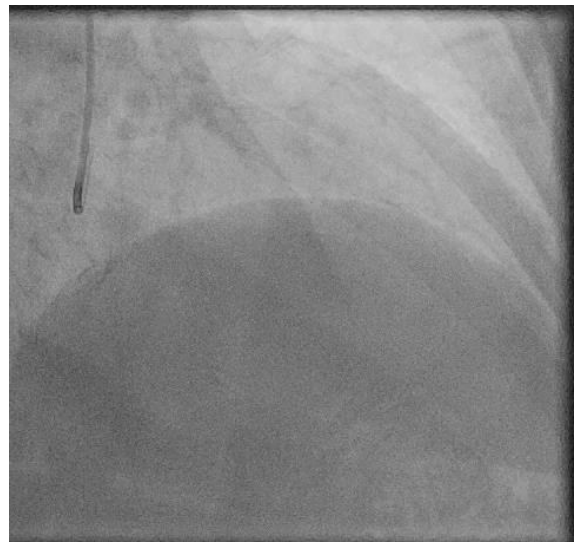
- Technical advances and integrated protocol
- Diagnostic features of CMD
- Prognostic data
- Impaired CFR, adverse remodeling and outcomes

73 female, CAD s/p PCI, IDDM, HTN, hyperlipidemia, CKD (GFR ~35), OSA, presenting with chest pain and HFpEF









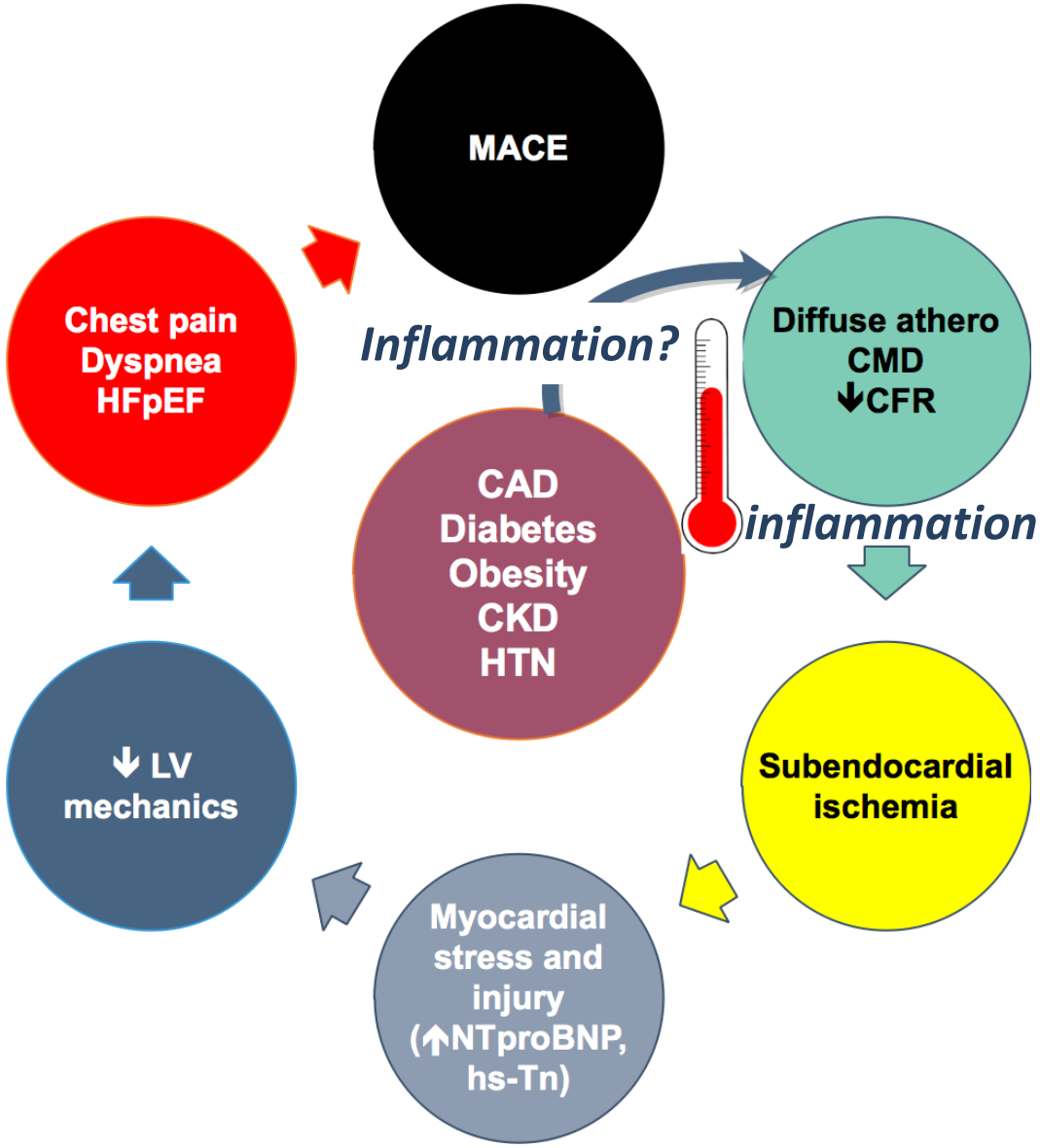
Quantitative myocardial blood flow and CFR

	Rest	Stress	CFR
LAD	0.90	1.40	1.56
LCX	0.84	1.19	1.42
RCA	0.83	0.99	1.20
Global LV	0.86	1.21	1.41

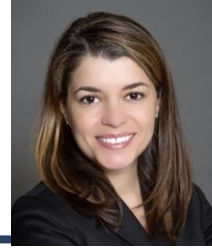
Normal CFR >2

Courtesy of Alec Schmaier

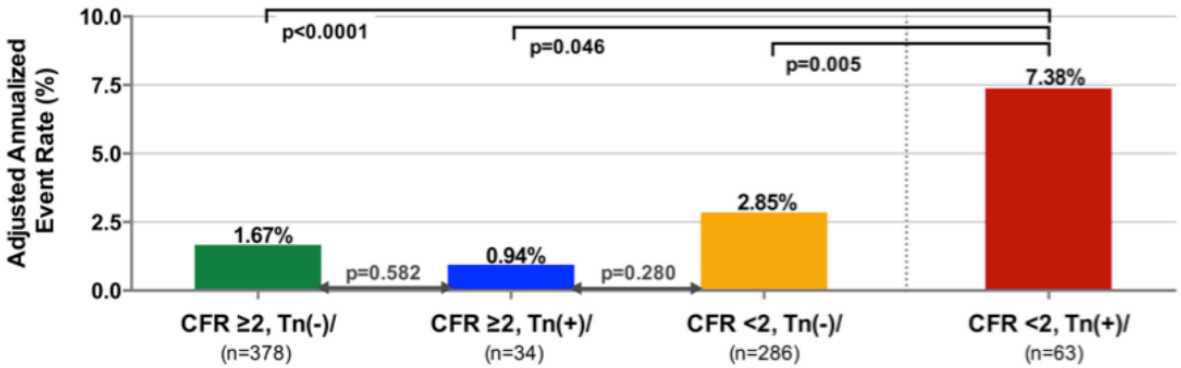
Proposed pathophysiologic link between atherosclerosis and CMD and clinical outcomes



Microvascular ischemia, myocyte injury, and outcomes in patients w/o obstructive CAD



N=761



Annualized event rates adjusted for pretest clinical score, LVEF, and estimated glomerular filtration rate <60 mL.min^{-1}.1.73 m^{-2}.

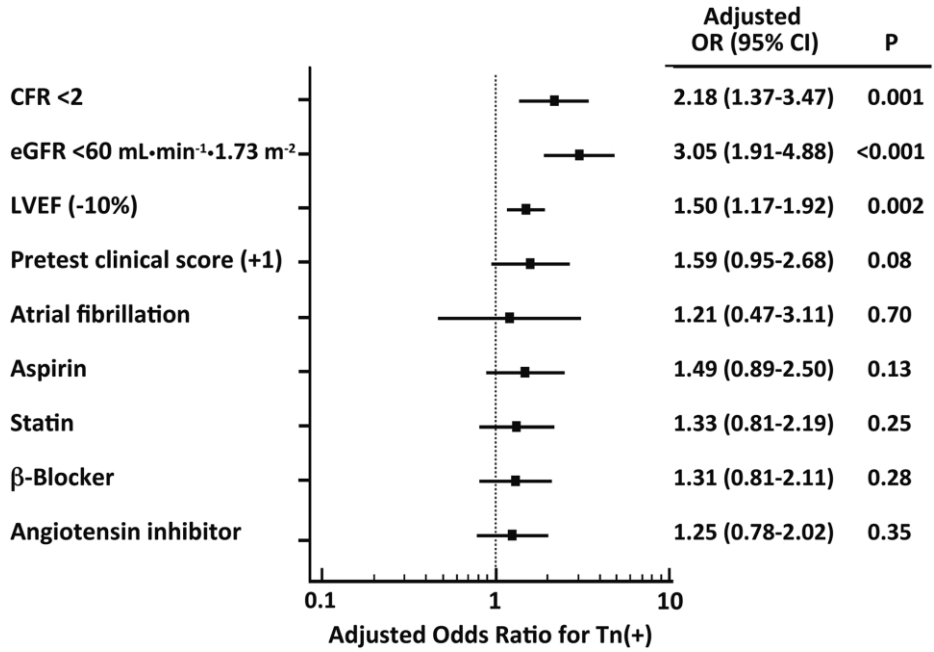


Table 2. Association Between CFR and Positive Troponin

	Univariable Model		Multivariable Model*	
Covariate	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
CFR_{binary}†	2.45 (1.57–3.82)	<0.0001	2.18 (1.37–3.47)	0.001
$CFR_{continuous}$‡	1.80 (1.34–2.43)	0.0001	1.62 (1.19–2.20)	0.002

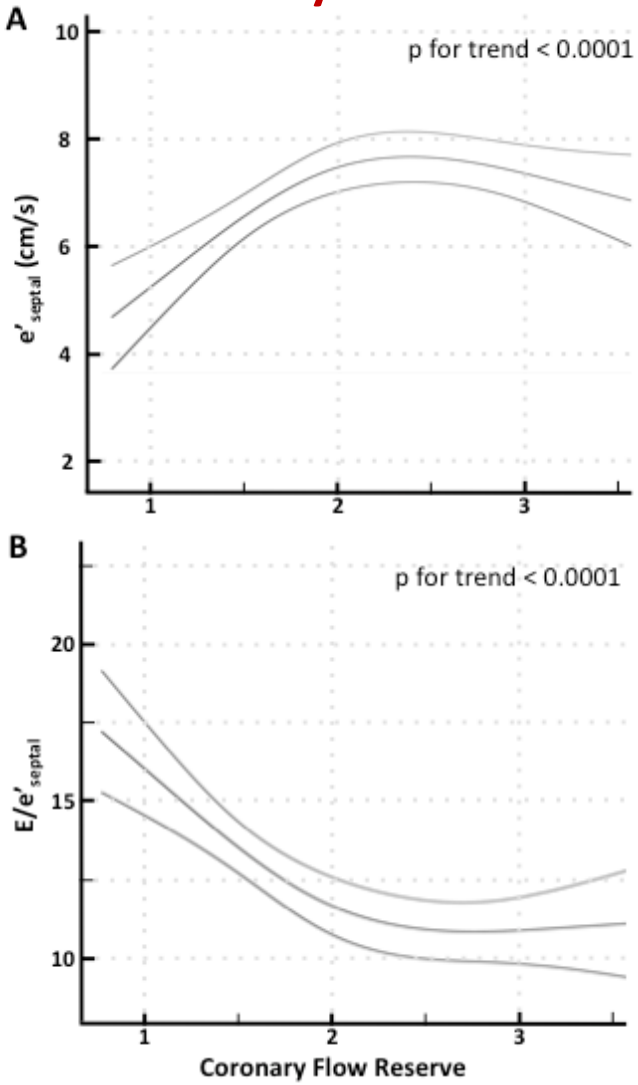
CFR indicates coronary flow reserve; CI, confidence interval; and OR, odds ratio.

*Adjusted for pretest clinical score, left ventricular ejection fraction, estimated glomerular filtration rate <60 mL·min^{-1}·1.73 m^{-2}, history of atrial fibrillation, and use of aspirin, β-blocker, statin, or angiotensin inhibitor.

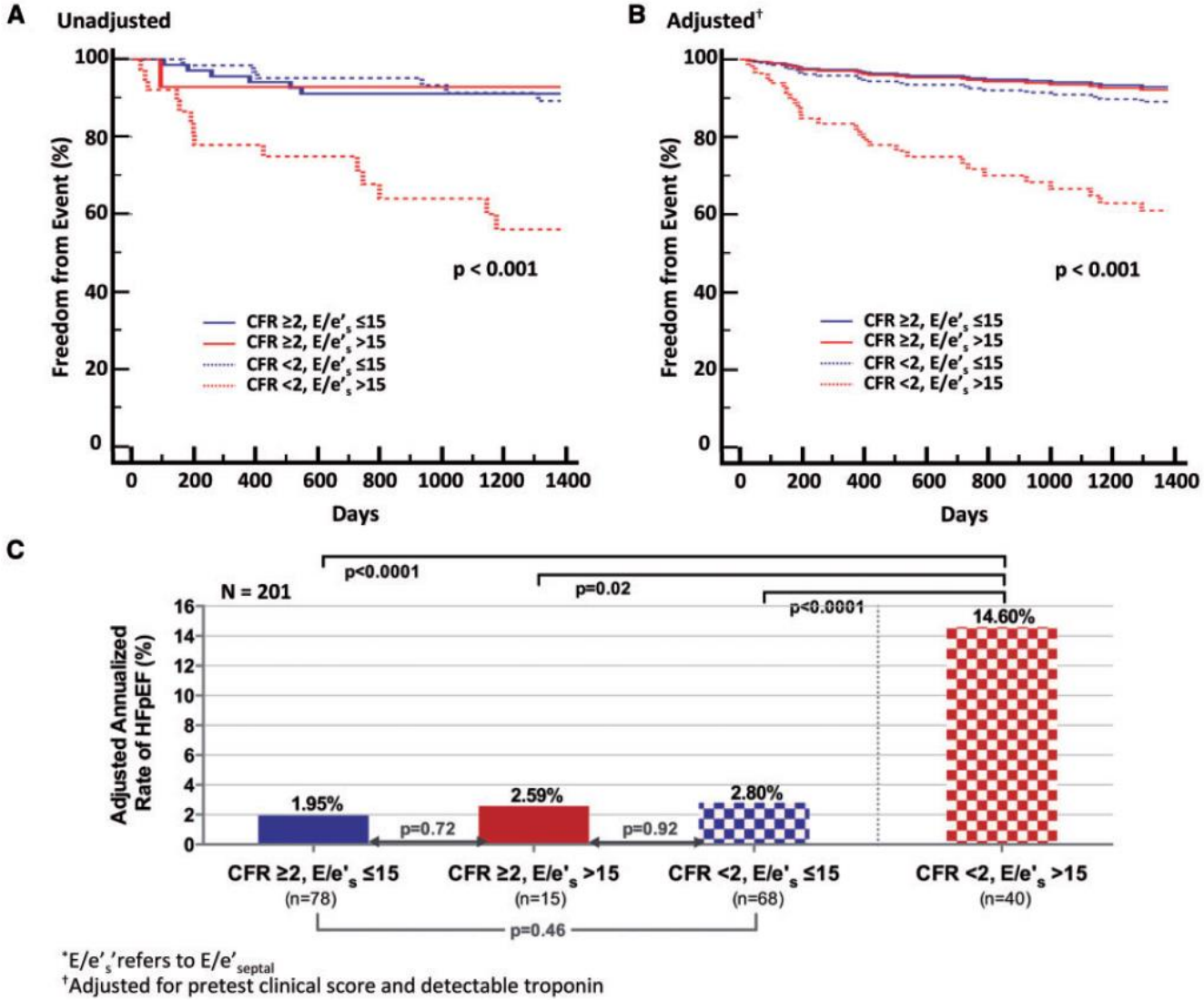
Source: Taqueti VR, et al. Circulation. 2015 Feb 10;131(6):528-35

CMD, diastolic dysfunction, and HF hospitalizations

CFR and markers of diastolic dysfunction



Freedom from Hospitalization for HF by CFR and E/e'



*E/e's refers to E/e'septal
†Adjusted for pretest clinical score and detectable troponin

Source: Taqueti VR…Di Carli M. EHJ 2018;39:840–849.

PET imaging in CMD

- Technical advances and integrated protocol
- Diagnostic features of CMD
- Prognostic data
- Impaired CFR, adverse remodeling and outcomes
- Integrating PET in multicenter trials

Opportunities and challenges for PET imaging of CMD

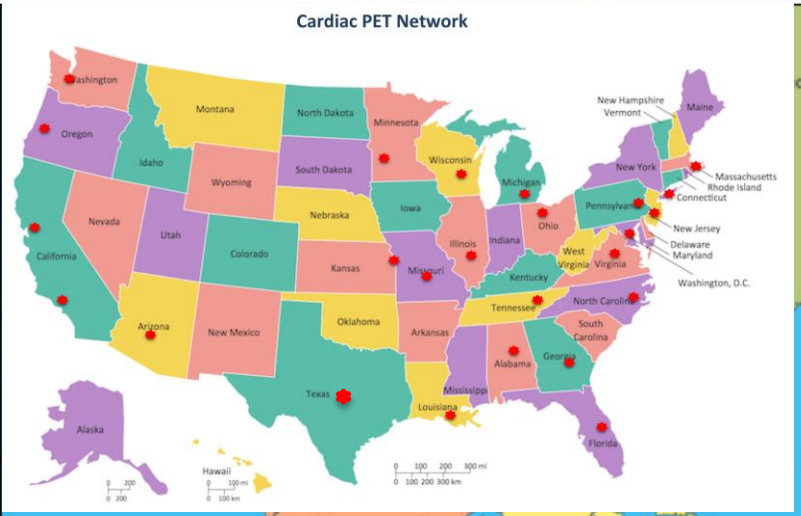
Opportunities

- Robust quantification and excellent reproducibility
- Strong association with outcomes including CV death and HFpEF
- Myocardial perfusion imaging is part of the continuum of care and easy to translate into practice

Challenges

- Reasonable network of PET scanners worldwide
- Increasing access to perfusion agents

Cardiac PET Network



15 countries, 4 continents, 25 centers