

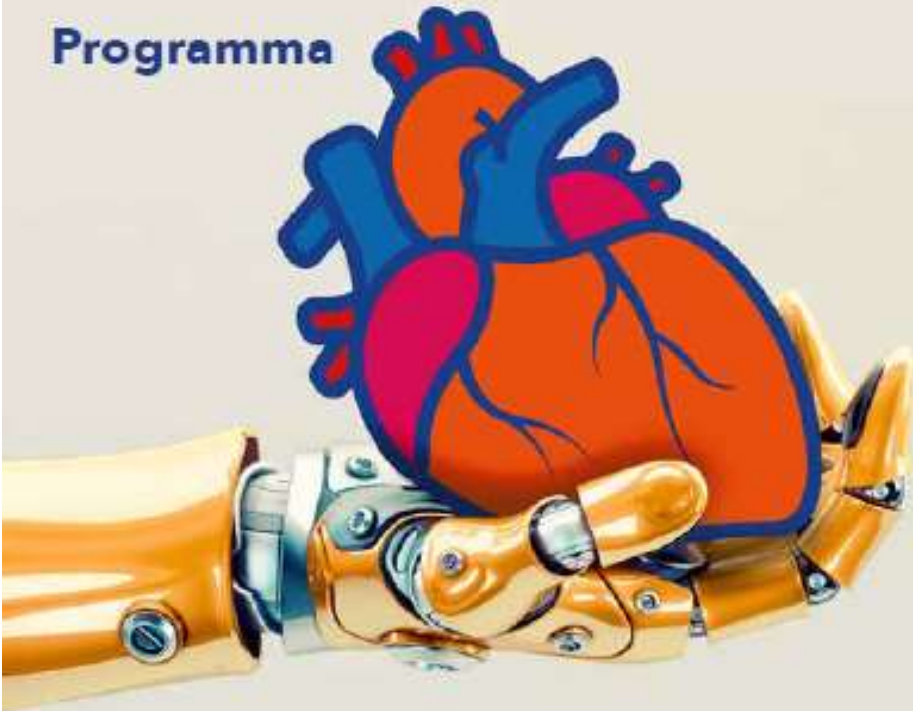
17° Meeting



CardioLucca

Heart Brings Heart 2023

Programma



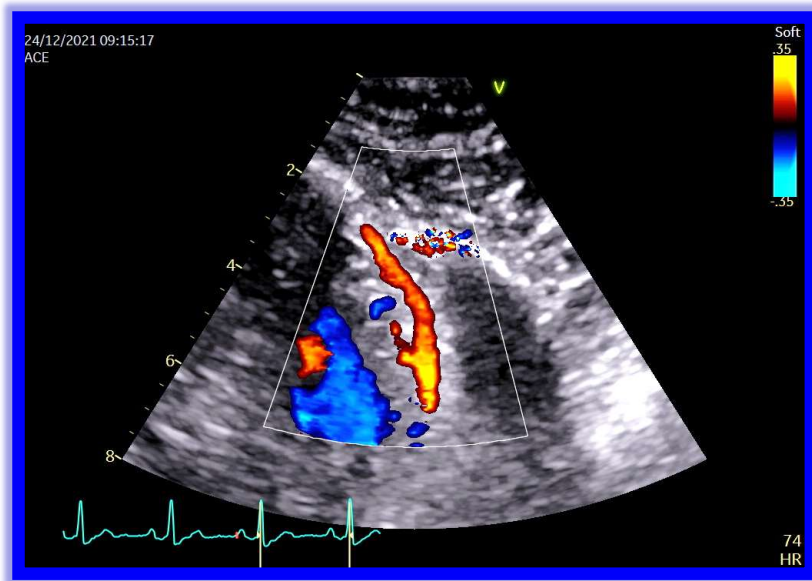
Lucca, 22-24 Giugno 2023

Centro Congressi Auditorium San Francesco

**Flusso coronarico a riposo:
limite di velocità a 32 ?**

Lauro Cortigiani

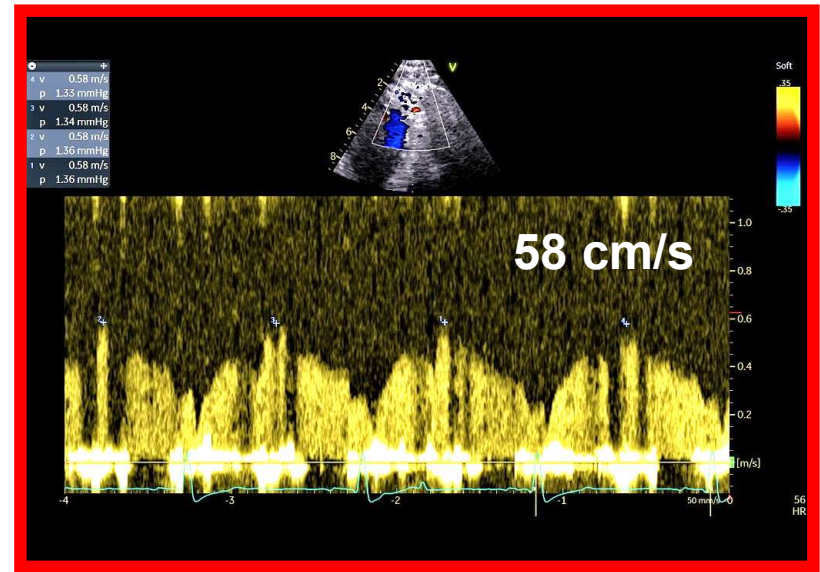
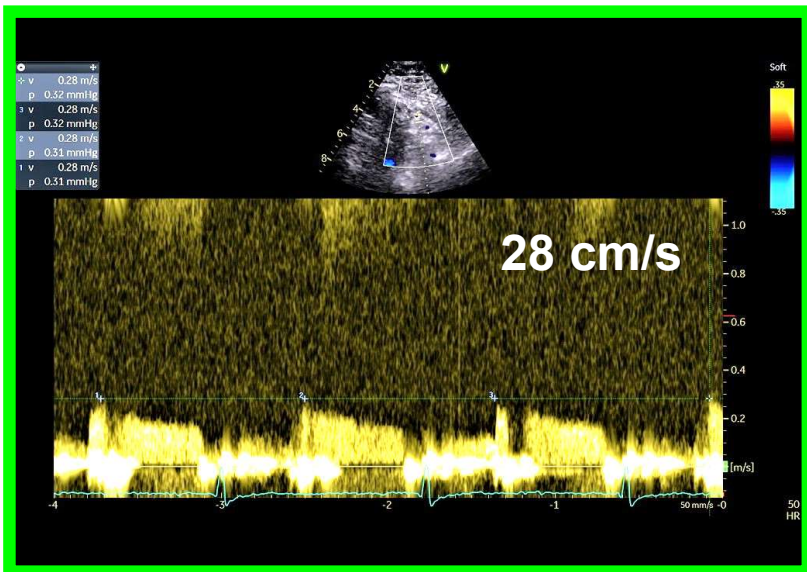
UO Malattie Cardiovascolari, Lucca

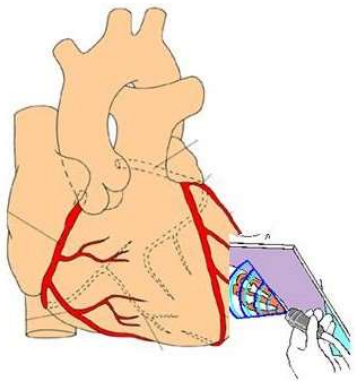


<32 cm/s

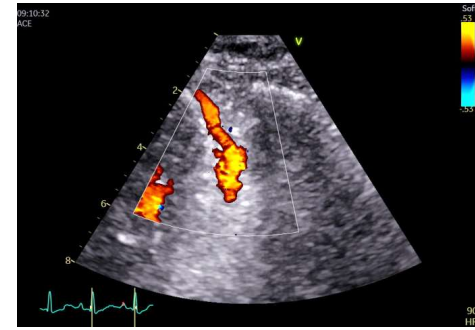


>32 cm/s





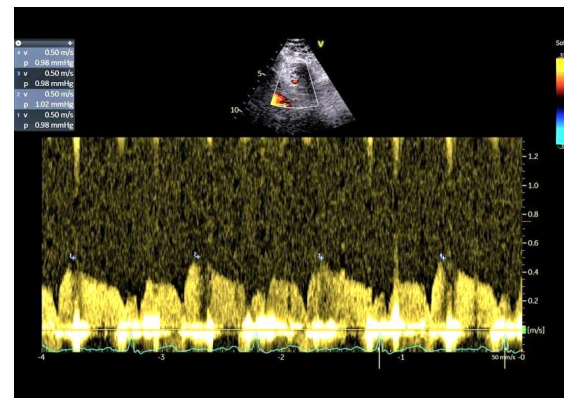
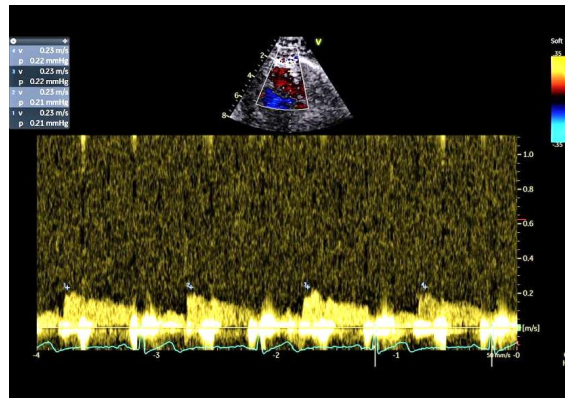
Coronary Flow Velocity Reserve



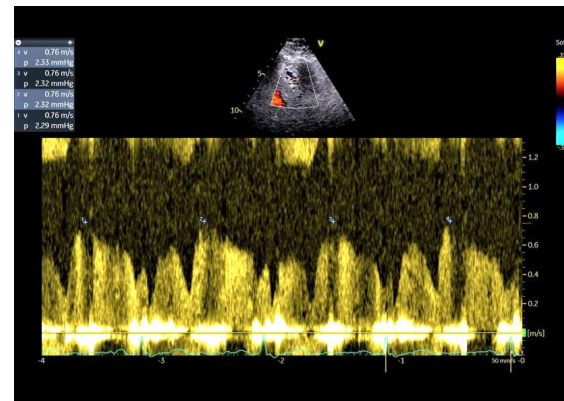
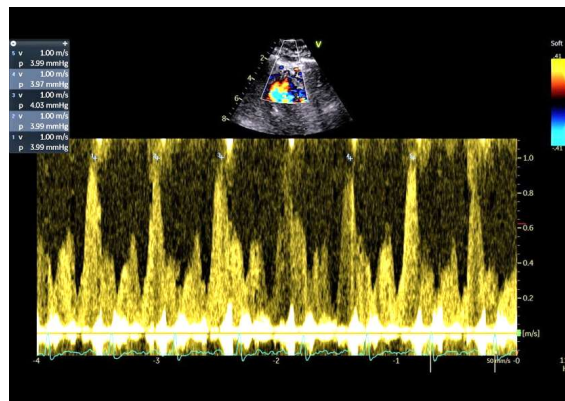
Normal CFVR

Abnormal CFVR

Rest CFV



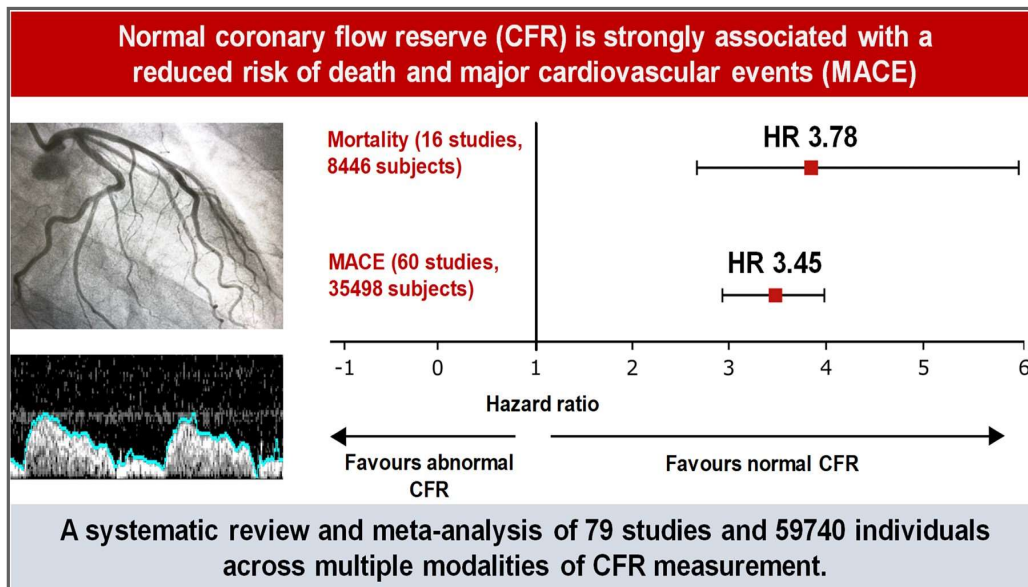
Stress CFV



CFVR: $100/23 = 4.34$

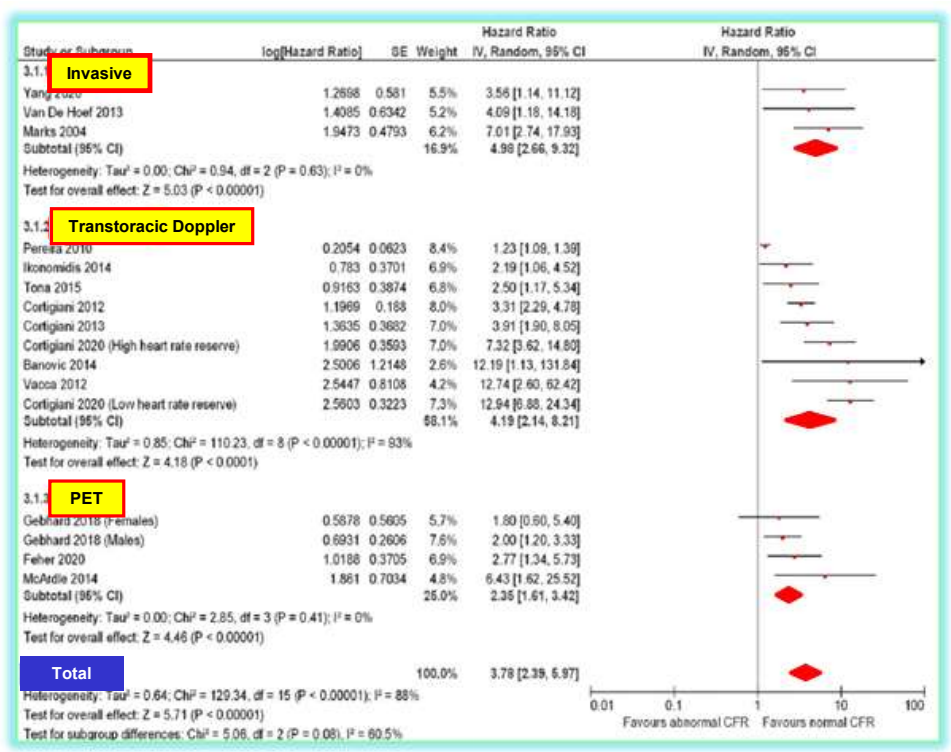
CFVR: $76/50 = 1.52$

Coronary Flow Reserve: prognostic value

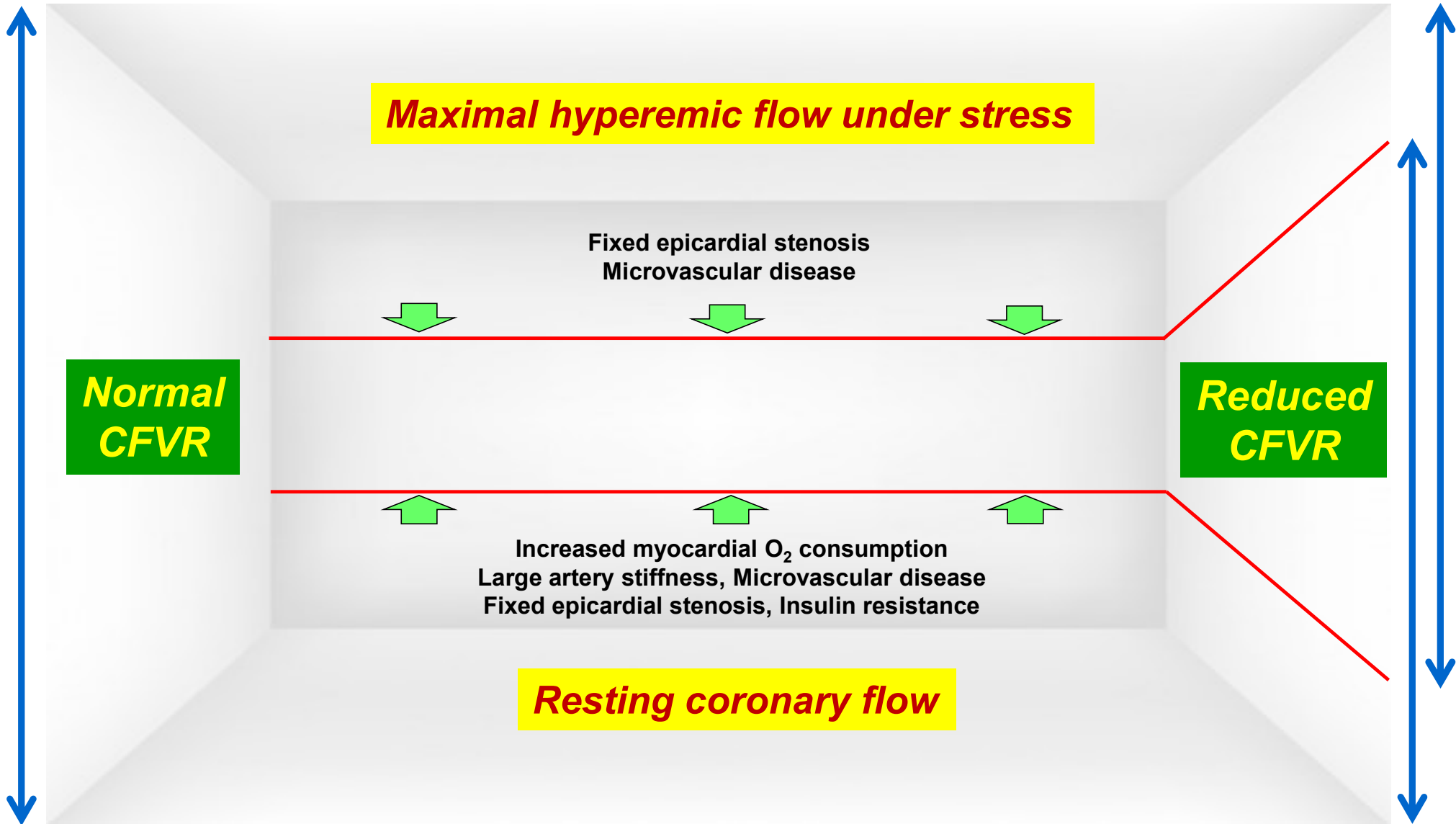


Techniques

49% Transthoracic Doppler
23% Invasive evaluation
23% PET
5% CMR



The room of coronary physiology



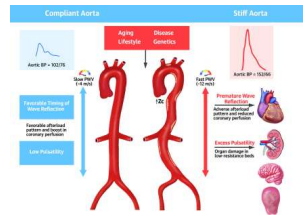
Mechanisms of increased resting coronary flow

Increased O₂ consumption or decreased O₂ supply



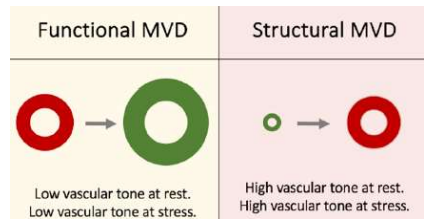
Heusch. Am J Physiol 2019;316:1439

Large artery stiffness

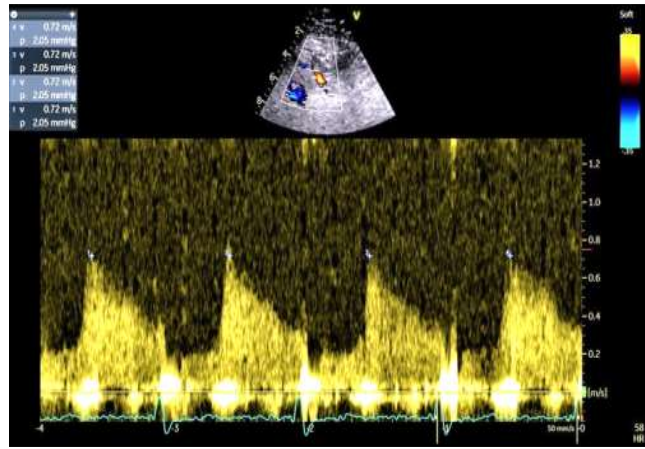


Chirinos. JACC 2019;74:1237

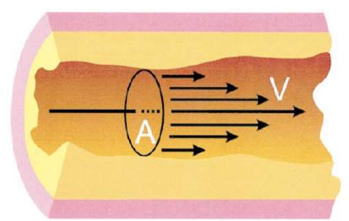
Microvascular disease



Rahman. Circulation 2019;140:1805

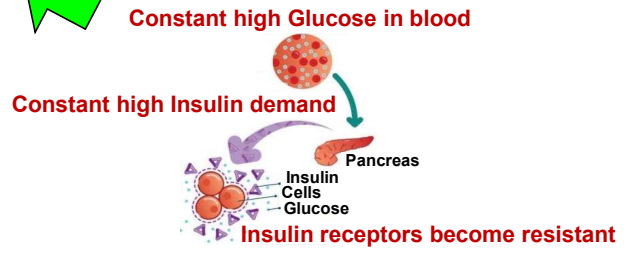


Coronary stenosis



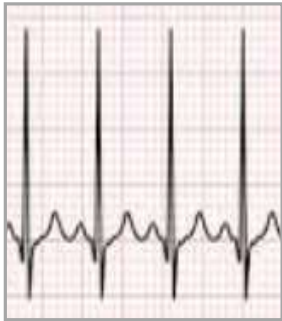
Anderson. Circulation 2000;102:48

Insulin resistance



Picchi. Am J Physiol 2011;301:2279

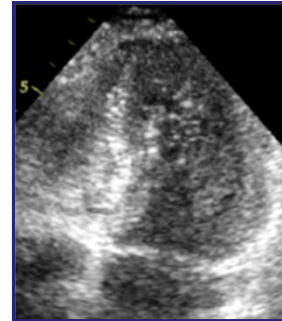
Increase in resting myocardial O_2 consumption or decrease in myocardial O_2 supply



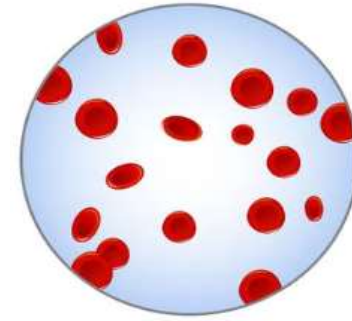
HR increase



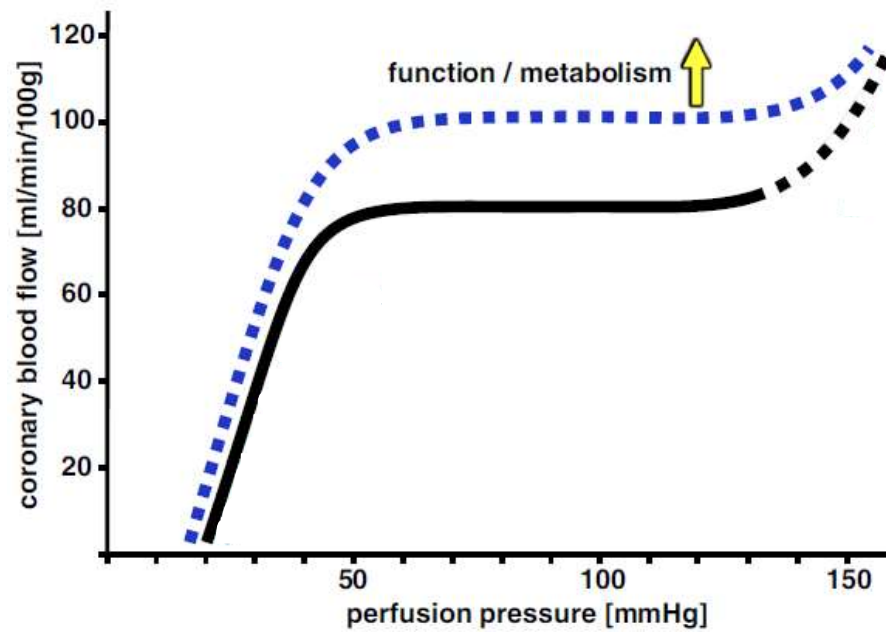
SBP increase



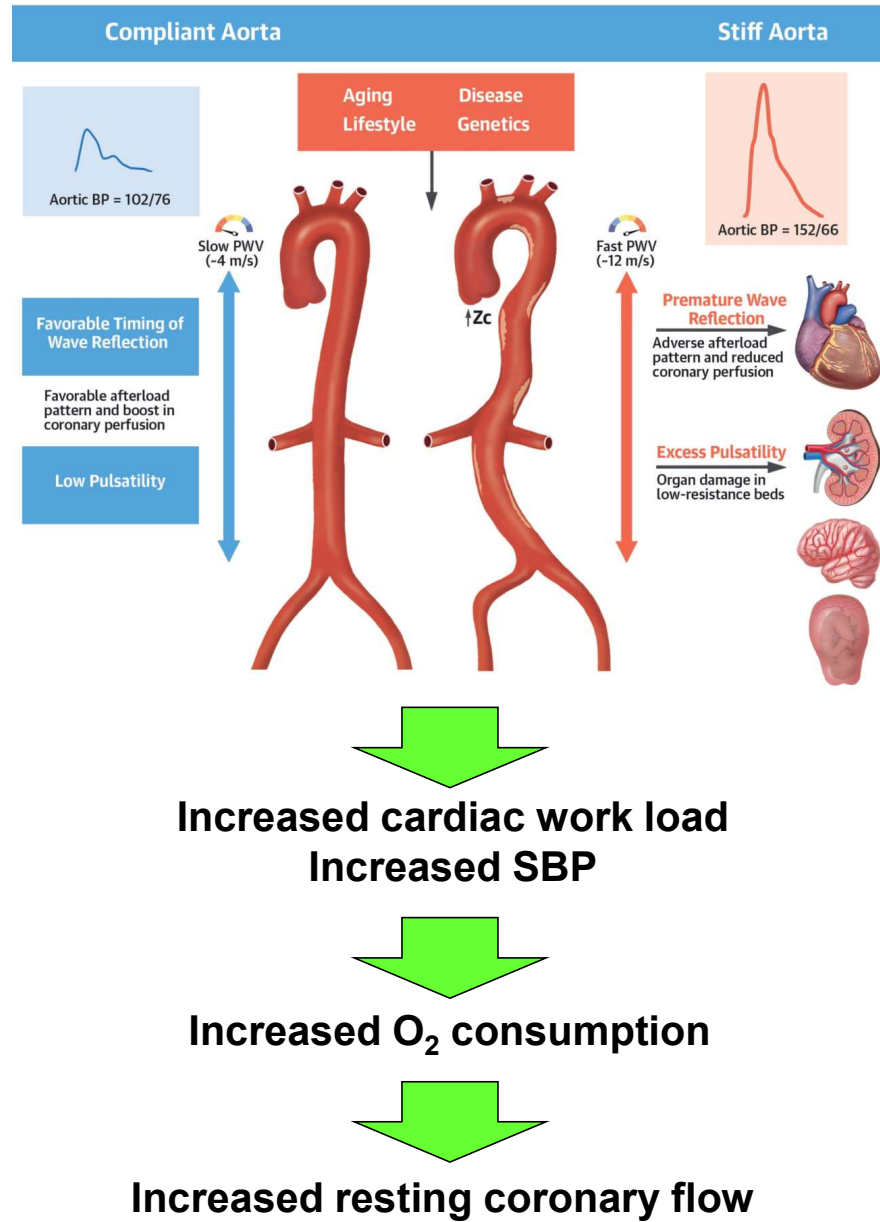
Contractility increase



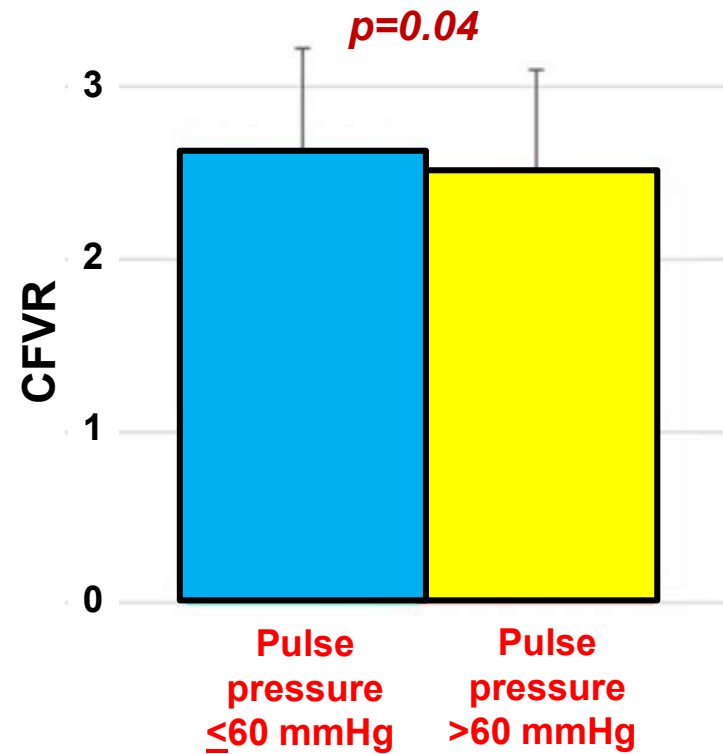
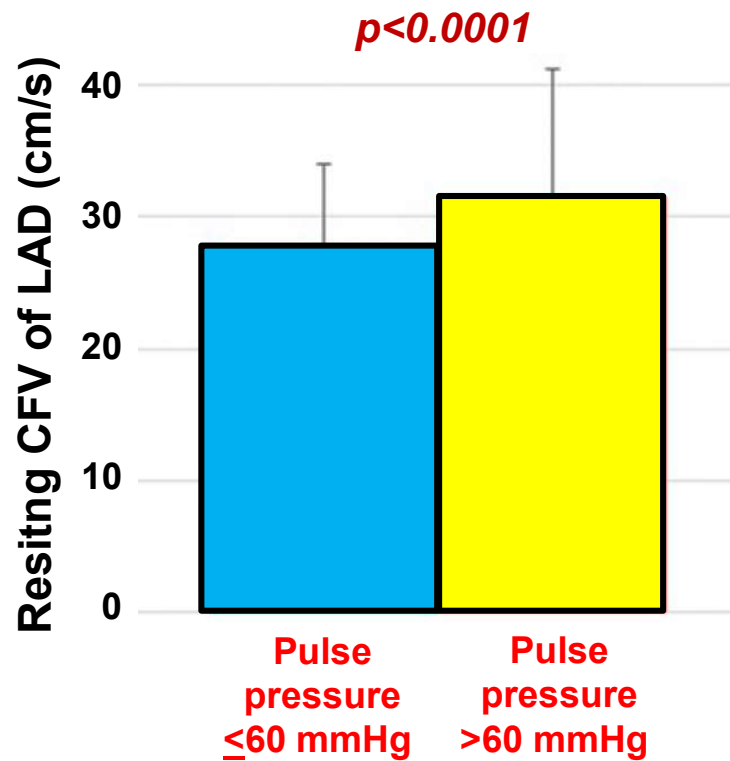
Anemia



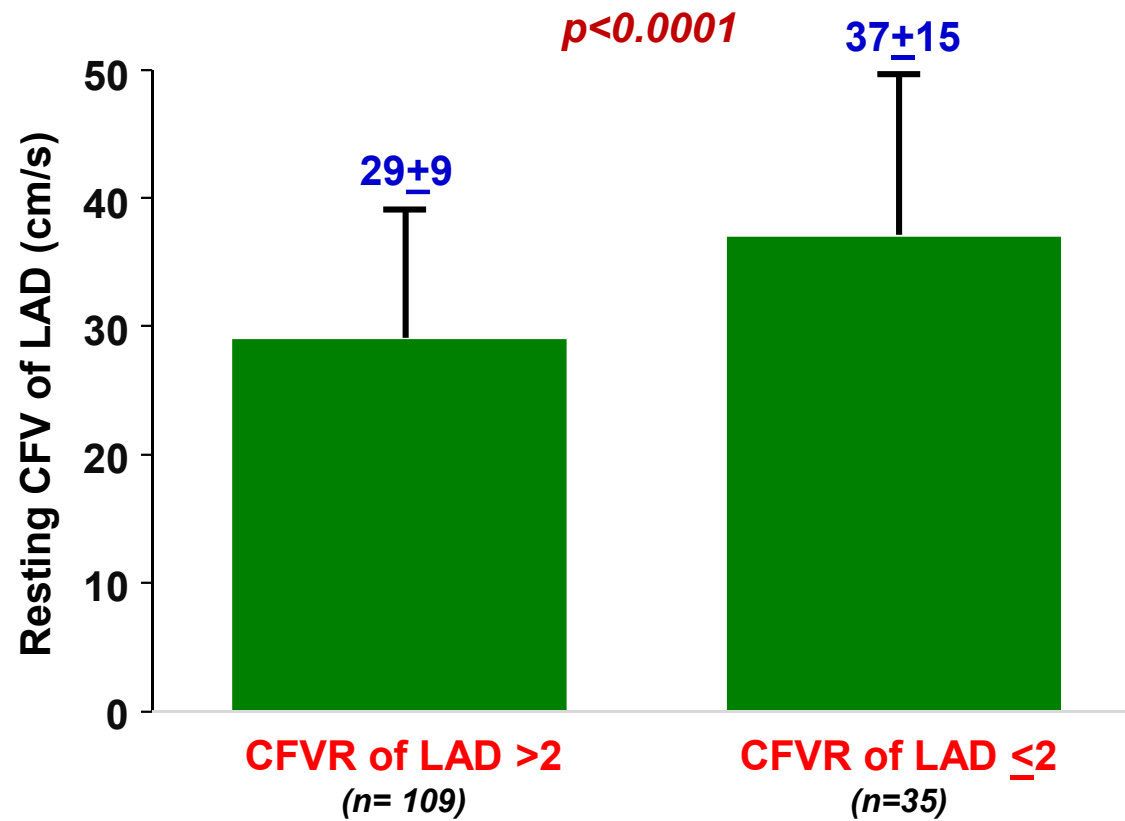
Large artery stiffness




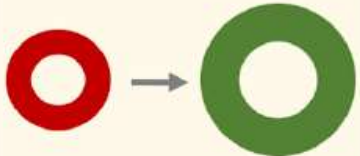


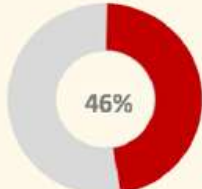
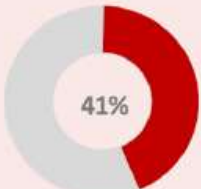
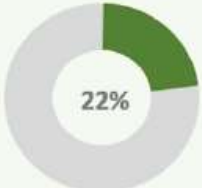

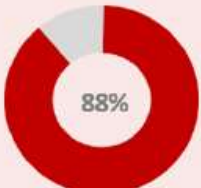
Increased resting CFV in patients with normal coronary arteries and elevated pulse pressure



Increased resting CVF in ANOCA type 2 diabetics with reduced CFVR



Miscovascular dysfunction endotypes in ANOCA patients

		Controls	Functional MVD	Structural MVD
Mechanism		 <p>High vascular tone at rest. Low vascular tone at stress.</p>	 <p>Low vascular tone at rest. Low vascular tone at stress.</p>	 <p>High vascular tone at rest. High vascular tone at stress.</p>
Myocardium	NT-pro BNP	34 pgmL ⁻¹	69 pgmL ⁻¹	132 pgmL ⁻¹
	Exercise Coronary Perfusion Efficiency	 <p>65%</p>	 <p>46%</p>	 <p>41%</p>
	Inducible Ischaemia	 <p>22%</p>	 <p>77%</p>	 <p>88%</p>

Elevated resting flow

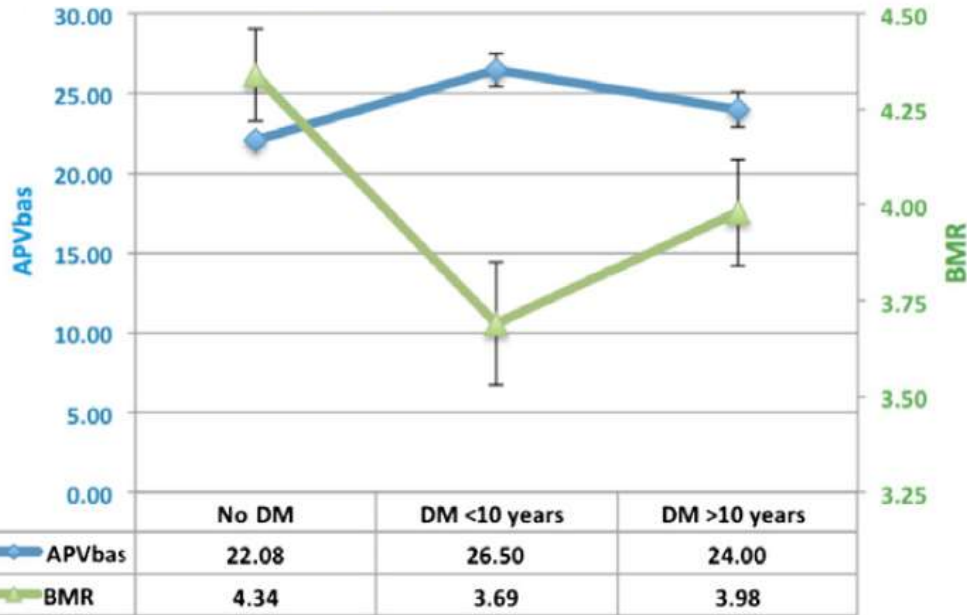
Impaired stress flow

Reduced CFR

Baseline and hyperemic coronary flow and microvascular resistance in patients with short and long duration of diabetes

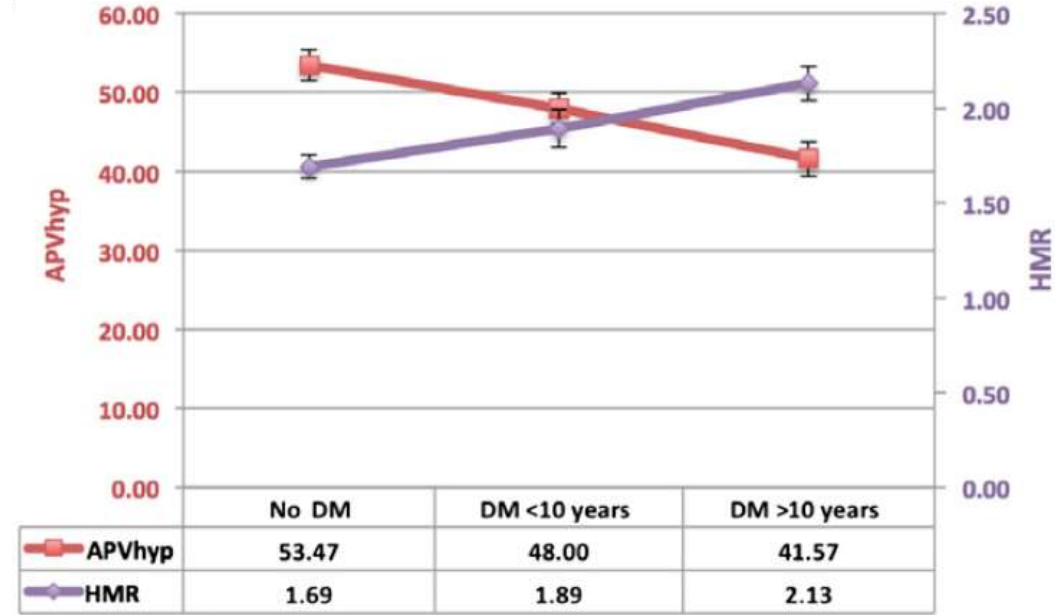
Baseline parameters

APV_{bas} = Baseline average peak velocity
BMR = Baseline microvascular resistance

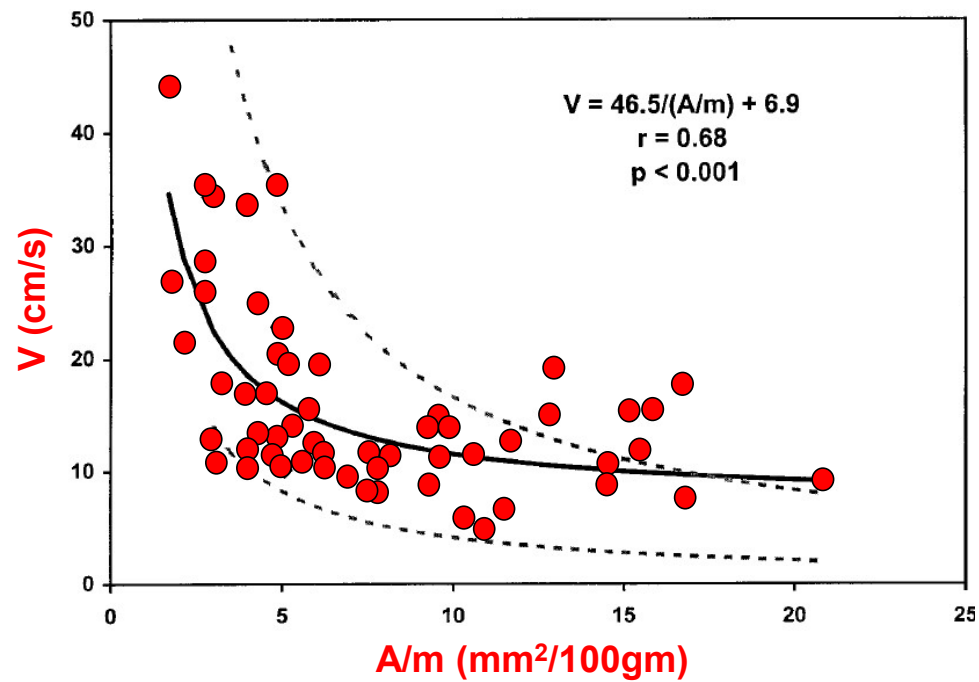
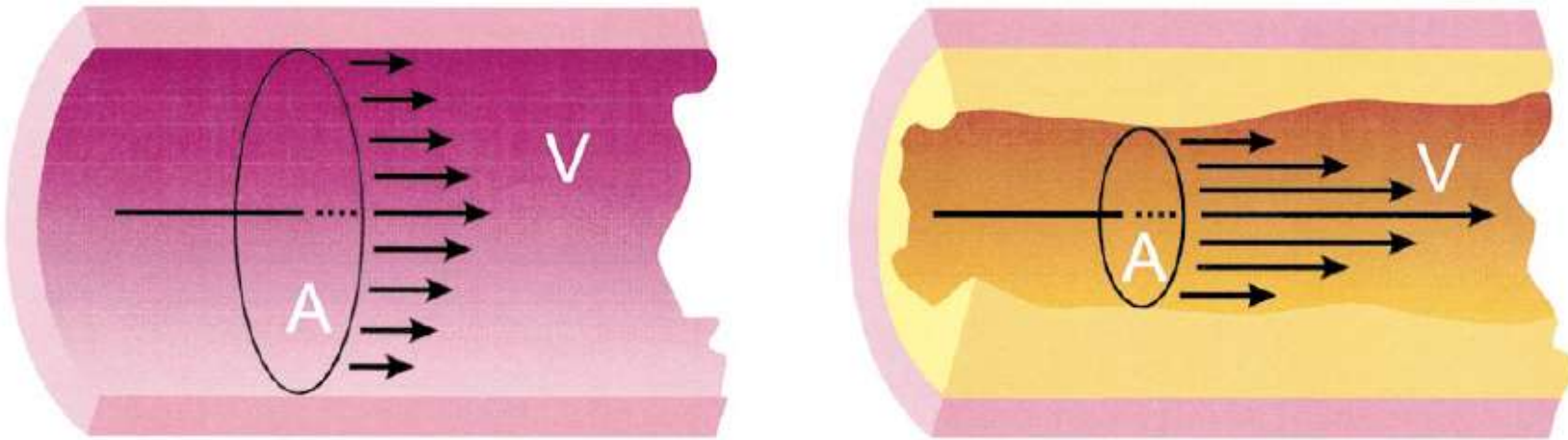


Hyperemic parameters

APV_{hyp} = Hyperemic average peak velocity
HMR = Hyperemic microvascular resistance

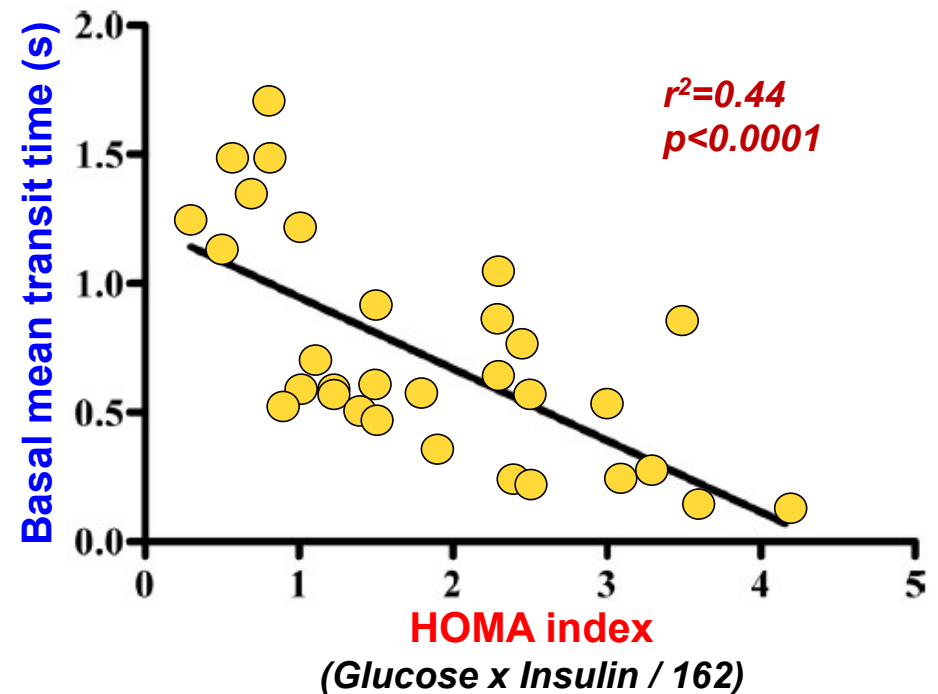
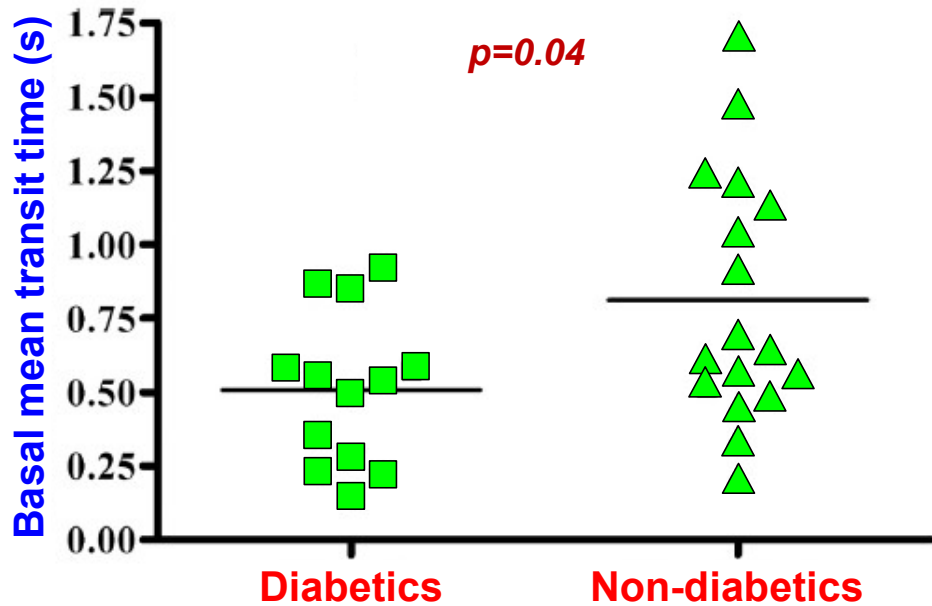


Reduced coronary lumen area and coronary flow



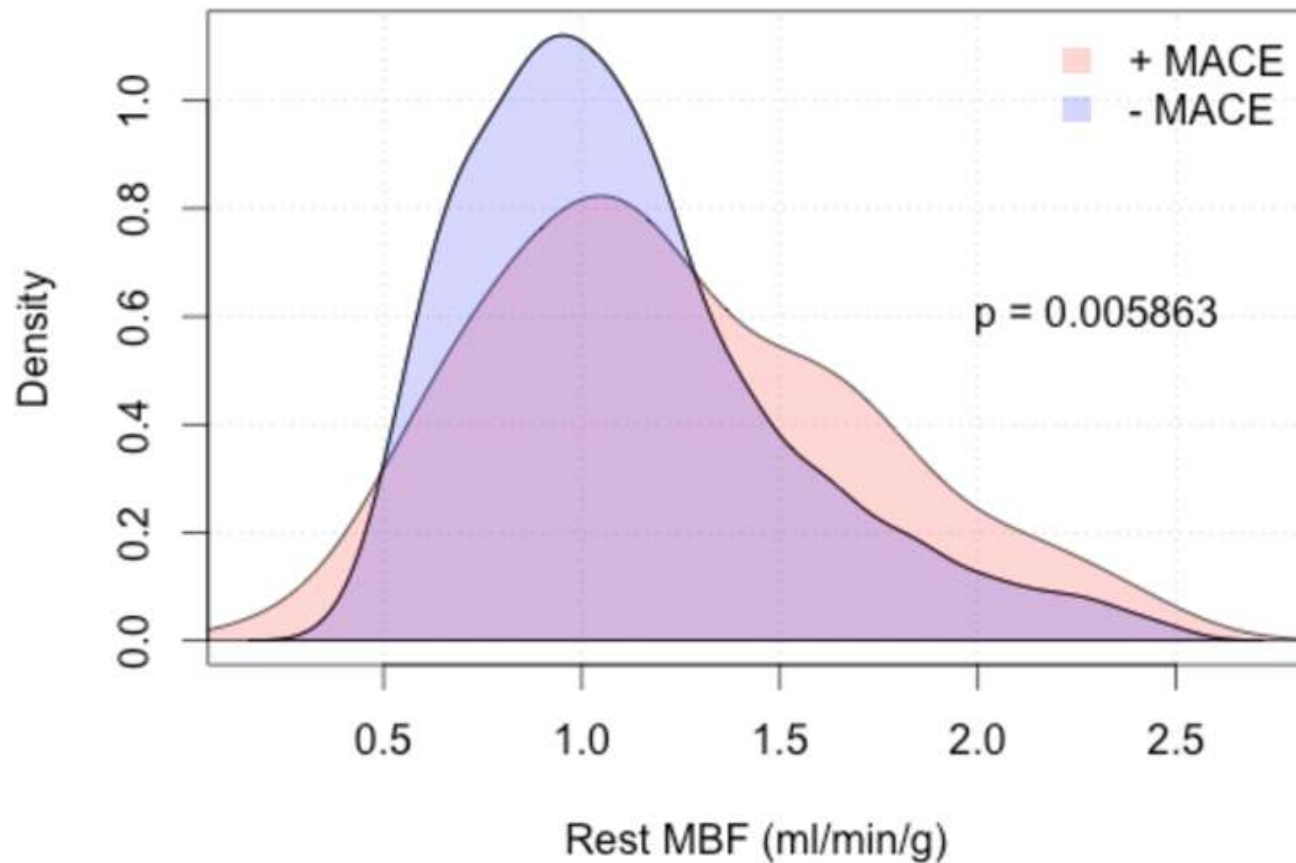
Insulin resistance and coronary flow in type 2 diabetic patients

A cellular reduction in glucose uptake due to insulin resistance may result in a metabolic shift towards increased fatty acid oxidation, with a consequent decrease of ATP produced per molecule of oxygen consumed leading to the need for higher resting coronary blood flow



Prognostic value of high resting coronary flow at PET

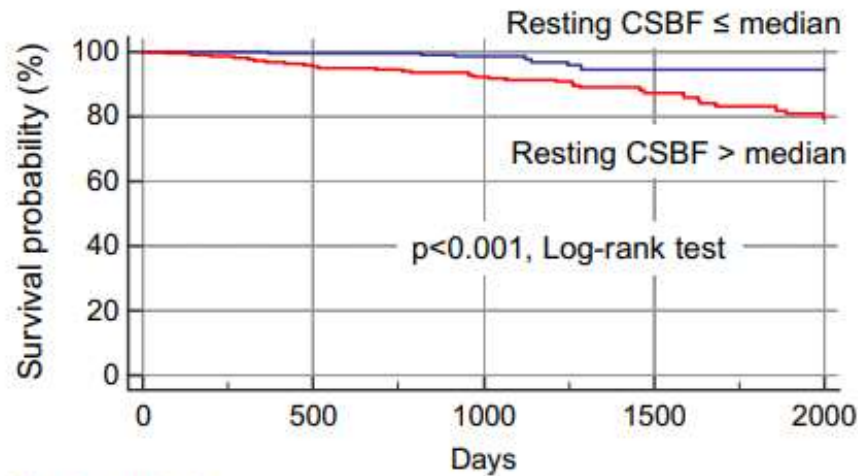
MACE: Death, NSTEMI, STEMI, unstable angina, stroke



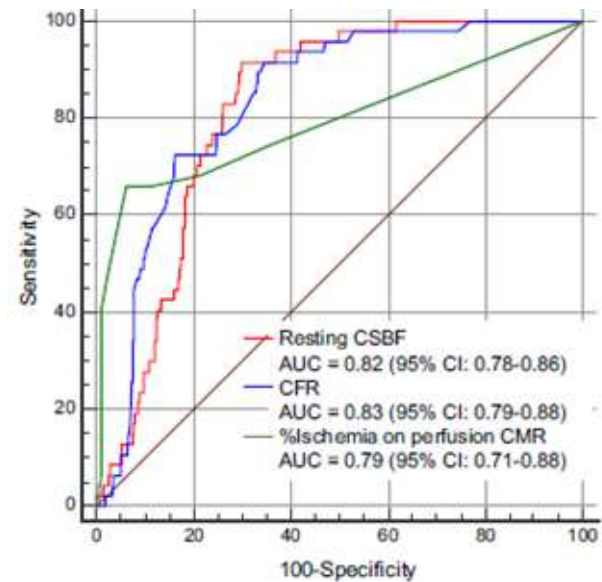
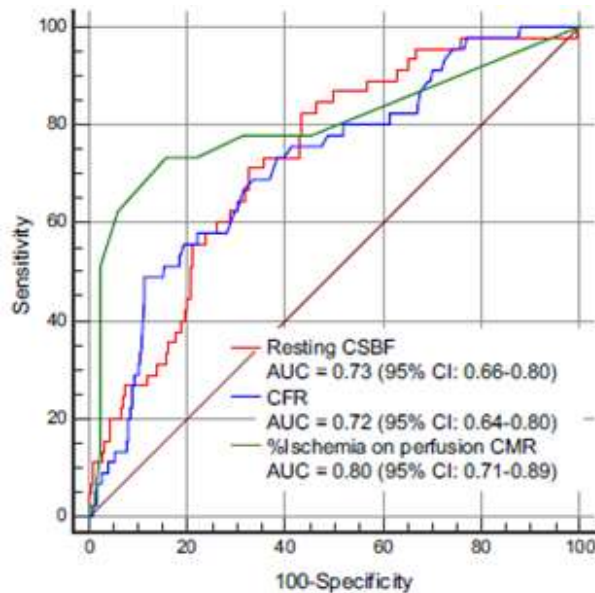
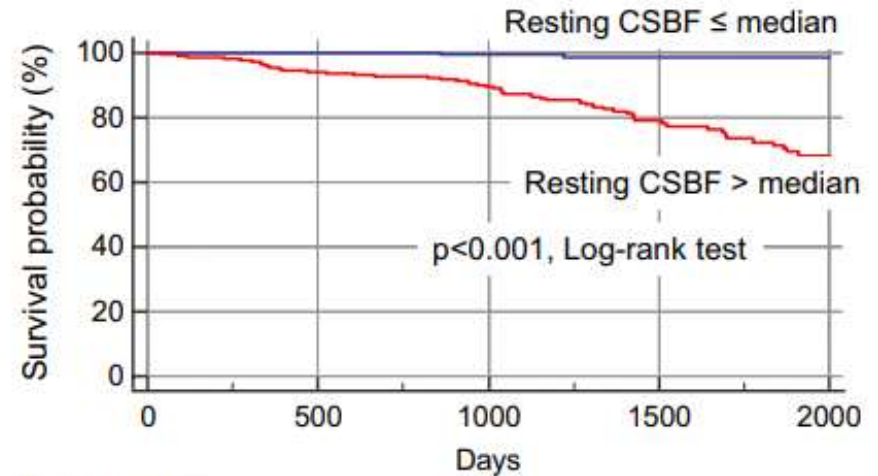
$n = 1,283$

Prognostic value of high resting coronary flow at MRI

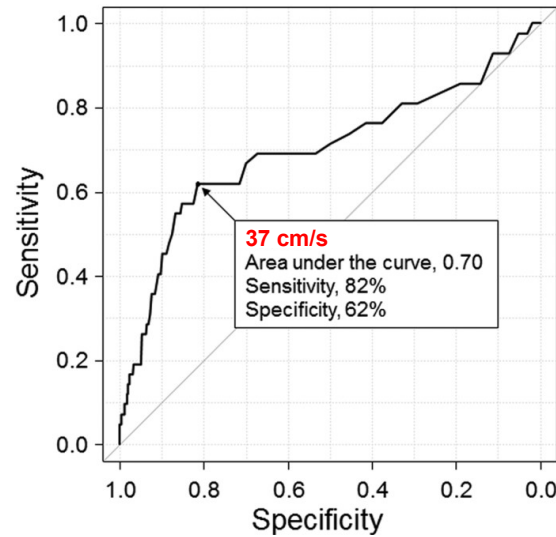
Known CAD (n=693)



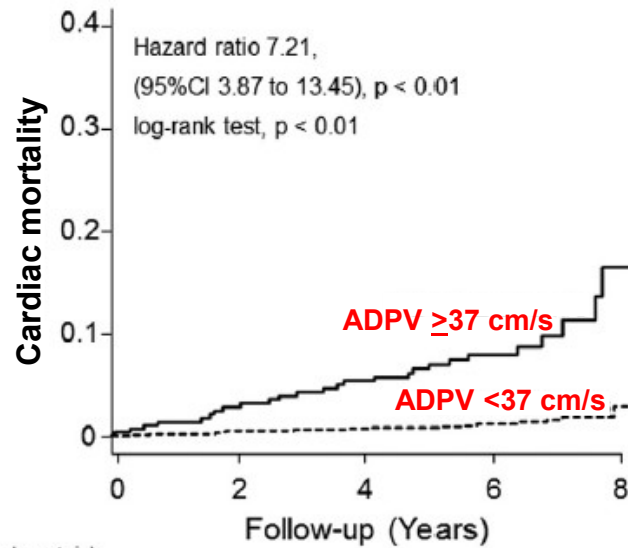
Suspected CAD (n=519)



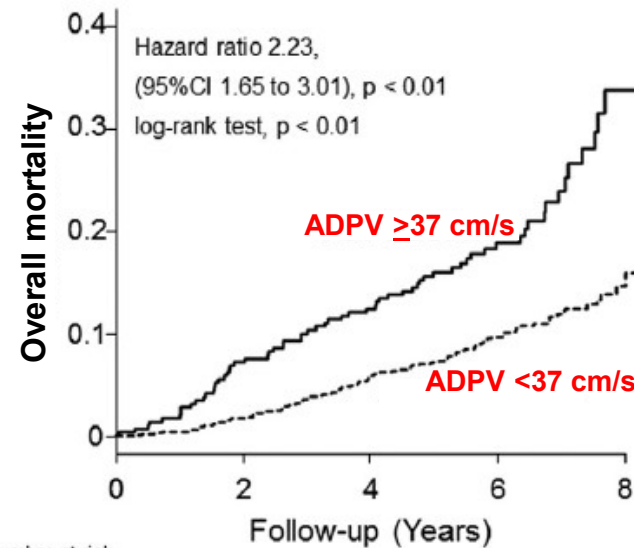
Prognostic value of CFV of proximal LAD at Doppler TTE



N = 1,472



Number at risk	0	2	4	6	8
ADPV < 37 cm/s 1181	1161	1112	697	79	
ADPV ≥ 37 cm/s 291	270	255	149	17	



Number at risk	0	2	4	6	8
ADPV < 37 cm/s 1181	1161	1112	697	79	
ADPV ≥ 37 cm/s 291	270	255	149	17	

Prognostic value of CFV of LAD in patients with preserved LVEF

Aims

To assess the relationship between resting CFV, CFVR, and outcome in patients with chronic coronary syndromes and preserved LVEF.

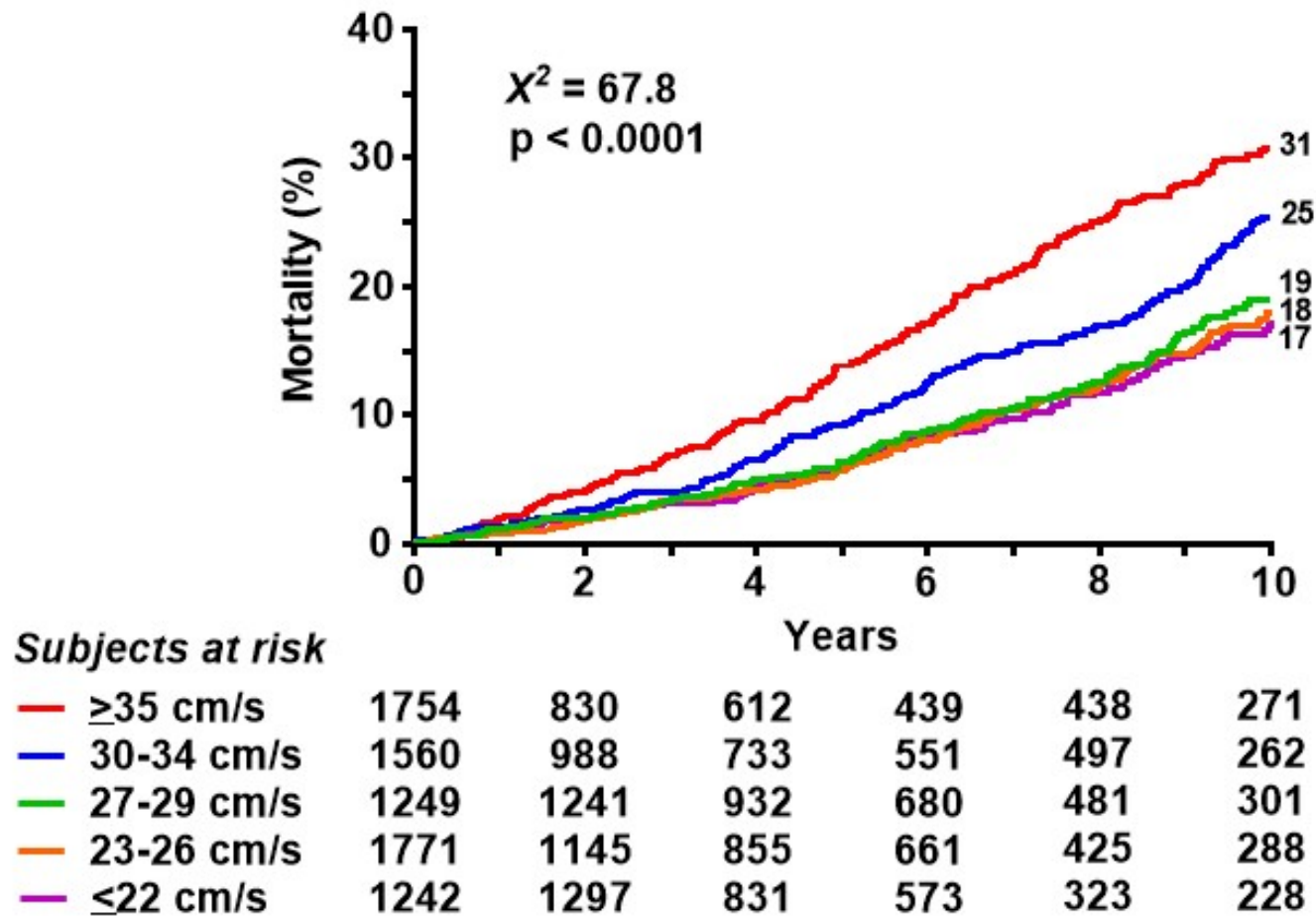
Methods

- ❑ In a prospective multicenter study design, we enrolled **7,576 patients** (age 66 ± 11 years; 3,312 men) with LVEF $\geq 50\%$.
- ❑ Recruitment (years 2004-2022) involved **7 accredited laboratories**, (**Lucca, Benevento, Parma, Mestre, Pisa, Lodz, Mexico City**) with inter-observer variability $< 10\%$ or CFV measurement at study entry.
- ❑ Baseline peak diastolic CFV and CFVR were obtained by **pulsed-wave Doppler in mid-distal LAD** during dipyridamole stress echo.
- ❑ Duration of follow-up: **5.9 ± 4.3 years.**
- ❑ **All-cause death** was the only end-point.

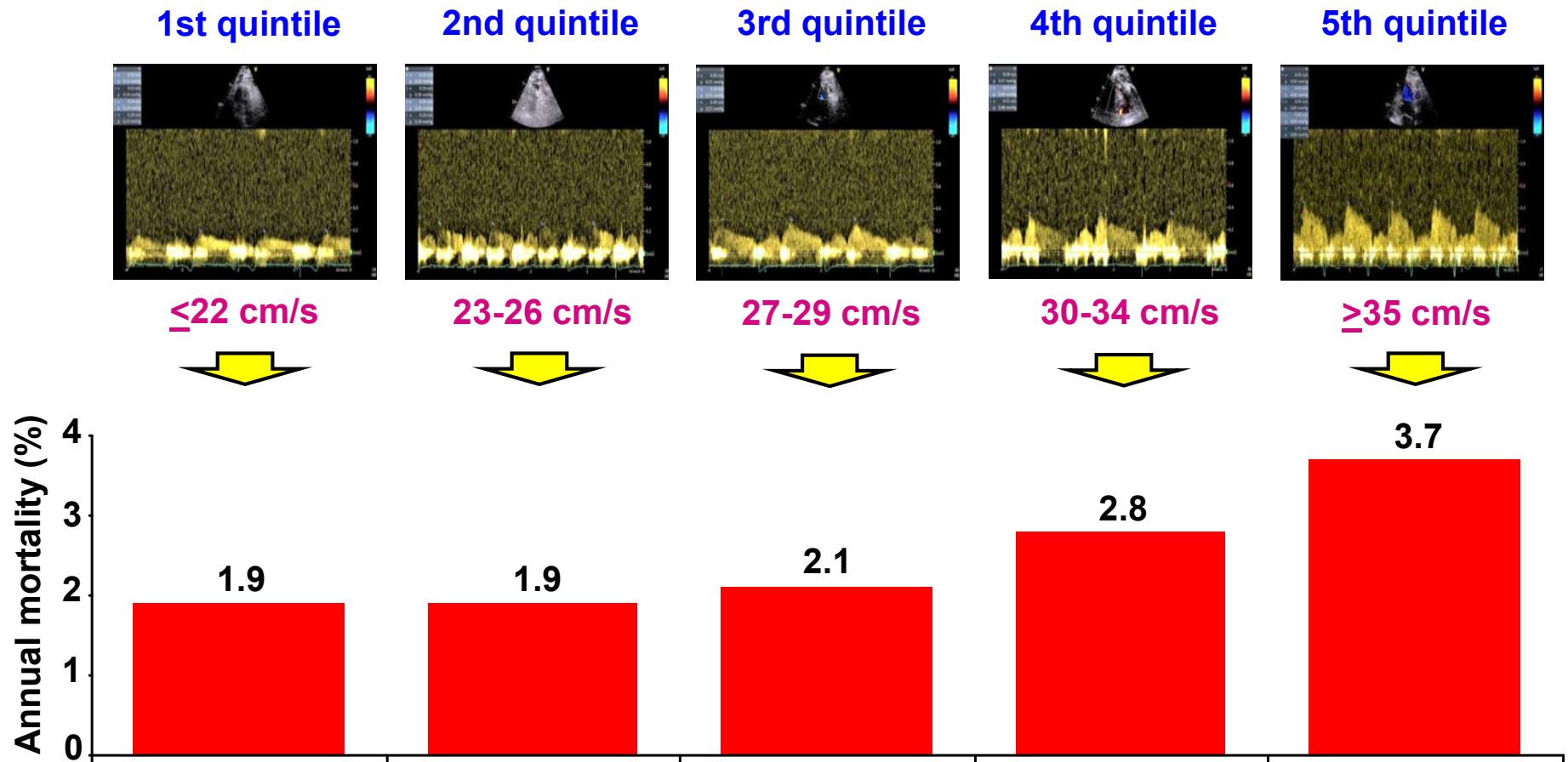
Clinical and echo findings according to quintiles of CFV

	1 st quintile ≤22 cm/s (n = 1,242)	2 nd quintile 23-26 cm/s (n = 1,771)	3 rd quintile 27-29 cm/s (n = 1,249)	4 th quintile 30-34 cm/s (n = 1,560)	5 th quintile ≥35 cm/s (n=1,754)	p value
Age (years)	64.6±11.8	64.4±11.7	64.9±11.4	65.5±11.3	67.4±11.5	<0.0001
Males	825 (66%)	1,021 (58%)	669 (54%)	837 (54%)	960 (55%)	<0.0001
Diabetes mellitus	361 (29%)	524 (30%)	351 (28%)	401 (26%)	570 (33%)	0.0007
Arterial hypertension	873 (70%)	1,112 (63%)	796 (64%)	1,045 (67%)	1,235 (70%)	<0.0001
Hypercholesterolemia	768 (62%)	972 (55%)	705 (56%)	884 (57%)	984 (56%)	0.003
Current smoker	325 (26%)	416 (24%)	304 (24%)	396 (25%)	484 (28%)	0.06
LBBB	34 (3%)	56 (3%)	47 (4%)	82 (5%)	77 (4%)	0.004
Prior myocardial infarction	189 (23%)	331 (19%)	235 (19%)	308 (20%)	401 (23%)	0.0005
Prior CABG	87 (7%)	89 (5%)	62 (5%)	72 (5%)	83 (5%)	0.03
Prior PCI	393 (32%)	409 (23%)	278 (22%)	335 (22%)	416 (24%)	<0.0001
LVEF (%)	60.3±5.1	60.1±4.8	59.6±4.5	59.6±4.8	59.1±5.1	<0.0001
β-blocker therapy	506 (41%)	598 (34%)	430 (34%)	527 (34%)	579 (33%)	0.0001
Heart rate (beats/min)	64.8±9.9	67.1±11.5	68.8±11.3	69.3±11.2	71.0±11.8	<0.0001
SBP (mmHg)	131.7±17.3	133.4±16.8	135.2±17.4	137.4±16.7	140.1±17.9	<0.0001
DBP (mmHg)	77.2±8.9	78.2±9.0	79.4±8.9	79.8±8.7	80.0±9.0	<0.0001
Inducible ischemia	92 (7%)	131 (7%)	117 (9%)	135 (9%)	248 (14%)	<0.0001
CFV of LAD (cm/s)	19.7±2.0	24.6±1.1	28.0±0.8	31.6±1.4	45.8±15.5	<0.0001
CFVR of LAD	2.5±0.7	2.4±0.6	2.3±0.5	2.3±0.6	2.1±0.6	<0.0001
CFVR of LAD ≤2.0	258 (21%)	427 (24%)	282 (23%)	430 (28%)	767 (44%)	<0.0001

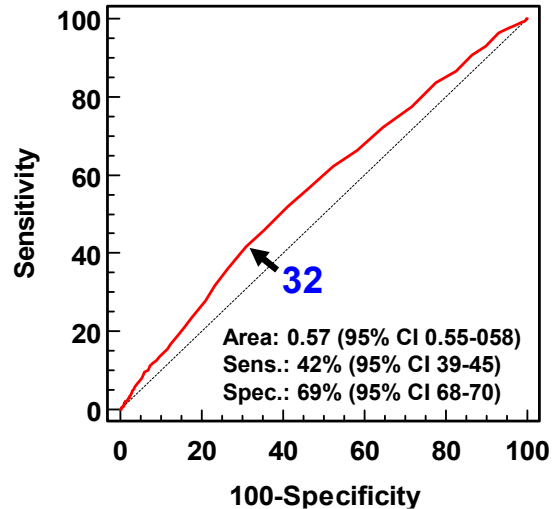
10-year mortality according to quintiles of CFV



Annualized mortality rate according to quintiles of CFV



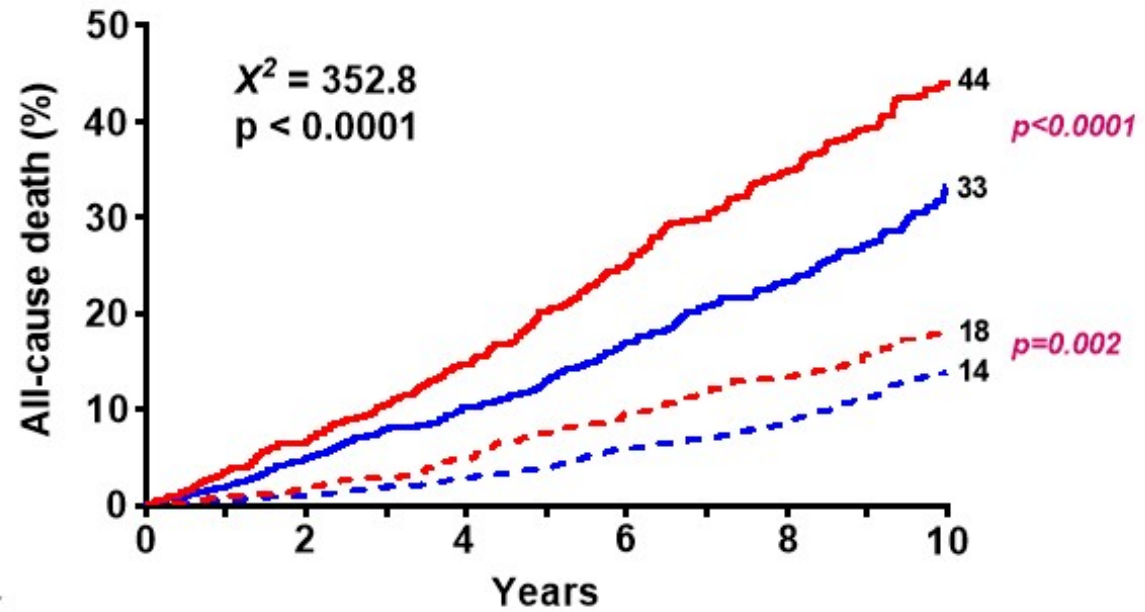
Predictors of all-cause mortality



Resting CFV of LAD ≥ 32 cm/s
best predictor of mortality

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p value	HR (95% CI)	p value
Age	1.10 (1.09-1.10)	<0.0001	1.09 (1.08-1.10)	<0.0001
Male sex	1.06 (0.94-1.19)	0.38		
Diabetes mellitus	1.50 (1.33-1.69)	<0.0001	1.37 (1.21-1.55)	<0.0001
Arterial hypertension	1.41 (1.24-1.61)	<0.0001		
Hypercholesterolemia	0.94 (0.83-1.05)	0.26		
Current smoker	1.05 (0.92-1.20)	0.47		
Left bundle branch block	1.44 (1.03-1.77)	0.03		
Prior myocardial infarction	1.54 (1.35-1.75)	<0.0001		
Prior CABG	1.89 (1.55-2.30)	<0.0001	1.58 (1.33-1.93)	<0.0001
Prior PCI	1.08 (0.95-1.23)	0.26		
β -blocker therapy	1.24 (1.10-1.41)	0.001		
LVEF	0.95 (0.94-0.97)	<0.0001	0.98 (0.97-1.00)	0.03
Resting RWMA	1.64 (1.42-1.89)	<0.0001		
Inducible ischemia	1.34 (1.10-1.64)	0.004		
Resting CFV of LAD ≥ 32 cm/s	1.63 (1.45-1.84)	<0.0001	1.24 (1.10-1.40)	<0.0001
CFVR of LAD ≤ 2	2.80 (2.49-3.15)	<0.0001	1.78 (1.57-2.02)	<0.0001

Mortality rate according to resting CFV and CFVR of LAD



	Subjects at risk					
	0	2	4	6	8	10
— CFVR ≤ 2 / CFV ≥ 32 cm/s	995	680	529	401	288	193
— CFVR ≤ 2 / CFV < 32 cm/s	1169	936	760	594	413	184
- - CFVR > 2 / CFV ≥ 32 cm/s	1541	1033	735	524	426	299
- - CFVR > 2 / CFV < 32 cm/s	3871	3270	2255	1627	1229	771

Prognostic predictors in heart failure with reduced LVEF

1,408 HF patients (66±11 yy), LVEF <50%, 8 echo lab

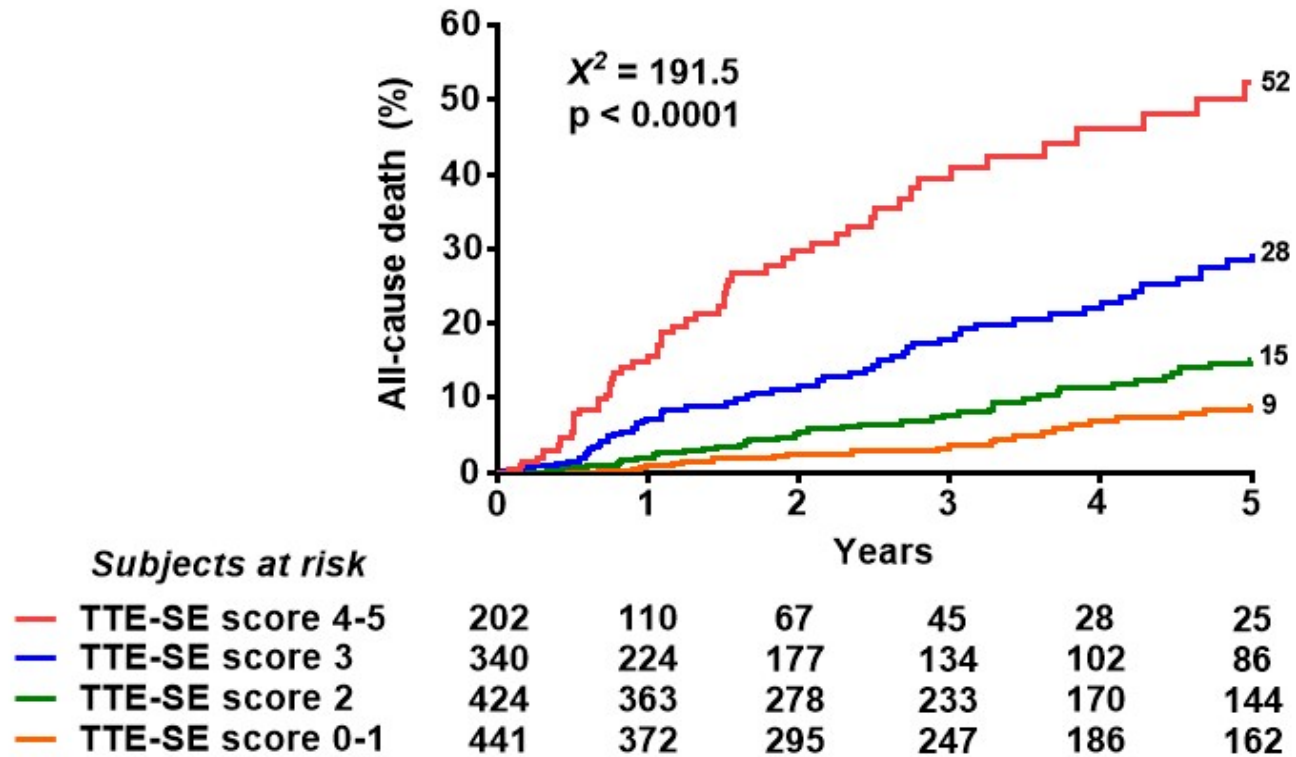
SE: Vasodilator 86%, Exercise 7%, Dobutamine 7%

Median FU: 2.7 years

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p value	HR (95% CI)	p value
Age	1.06 (1.05-1.08)	<0.001	1.05 (1.04-1.07)	<0.001
Male sex	1.20 (0.90-1.60)	0.21		
Hypertension	1.19 (0.91-1.55)	0.20		
β-blockers therapy	1.17 (0.91-1.50)	0.22		
Diabetes mellitus	1.22 (0.95-1.57)	0.12		
Prior myocardial infarction	1.04 (0.81-1.33)	0.77		
LVEF	0.96 (0.94-0.97)	<0.001	0.96 (0.95-0.98)	<0.001
CFV of LAD ≥32 cm/s	2.41 (1.87-3.10)	<0.001	1.75 (1.34-2.27)	<0.001
CFVR of LAD ≤2.0	3.91 (2.90-5.25)	<0.001	2.31 (1.68-3.18)	<0.001
LVCR	0.52 (0.32-0.85)	<0.001	0.51 (0.30-0.85)	0.010

TTE-SE score

Mortality rate according to the composite TTE-SE score

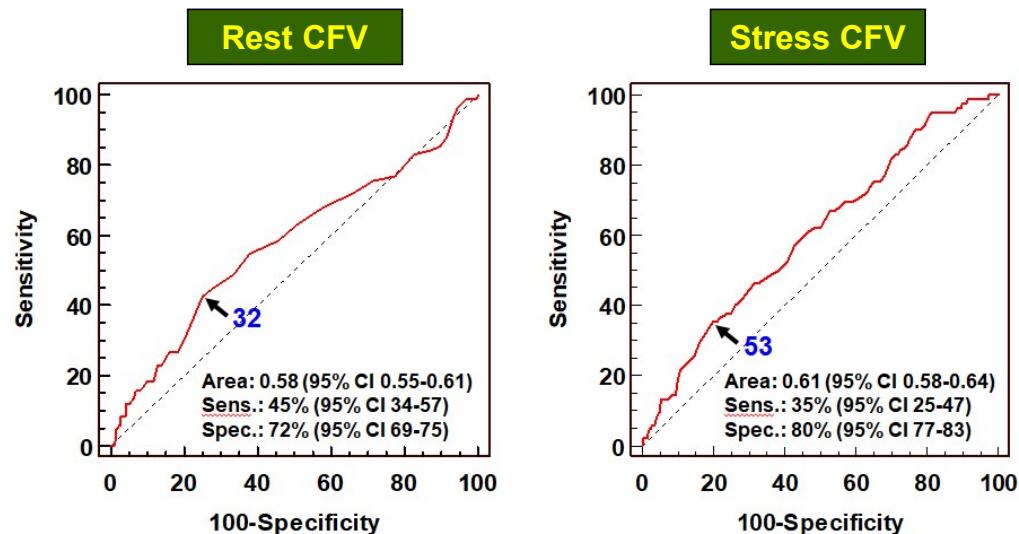


Rest and stress CFV to assess different endotypes and risk classes in ANOCA patients

1,033 ANOCA patients

Age 63 ± 11 yy, 22% diabetics, LVEF $59 \pm 5\%$, FU 4.8 ± 4.1 yy

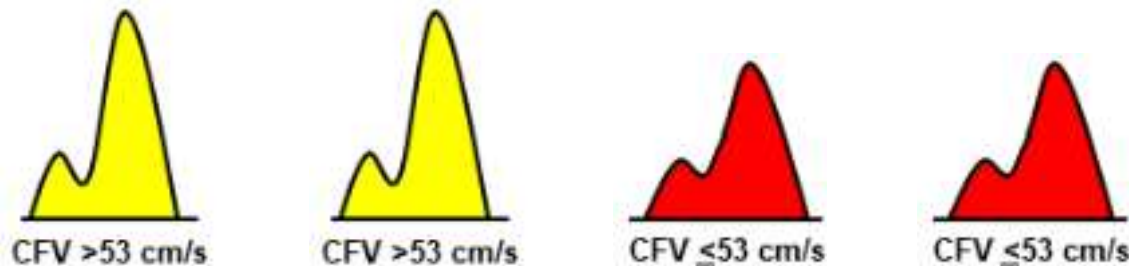
SE: Dipyridamole, 4 accredited echo lab



Rest CFV



Stress CFV



n=465
(45%)

n=350
(34%)

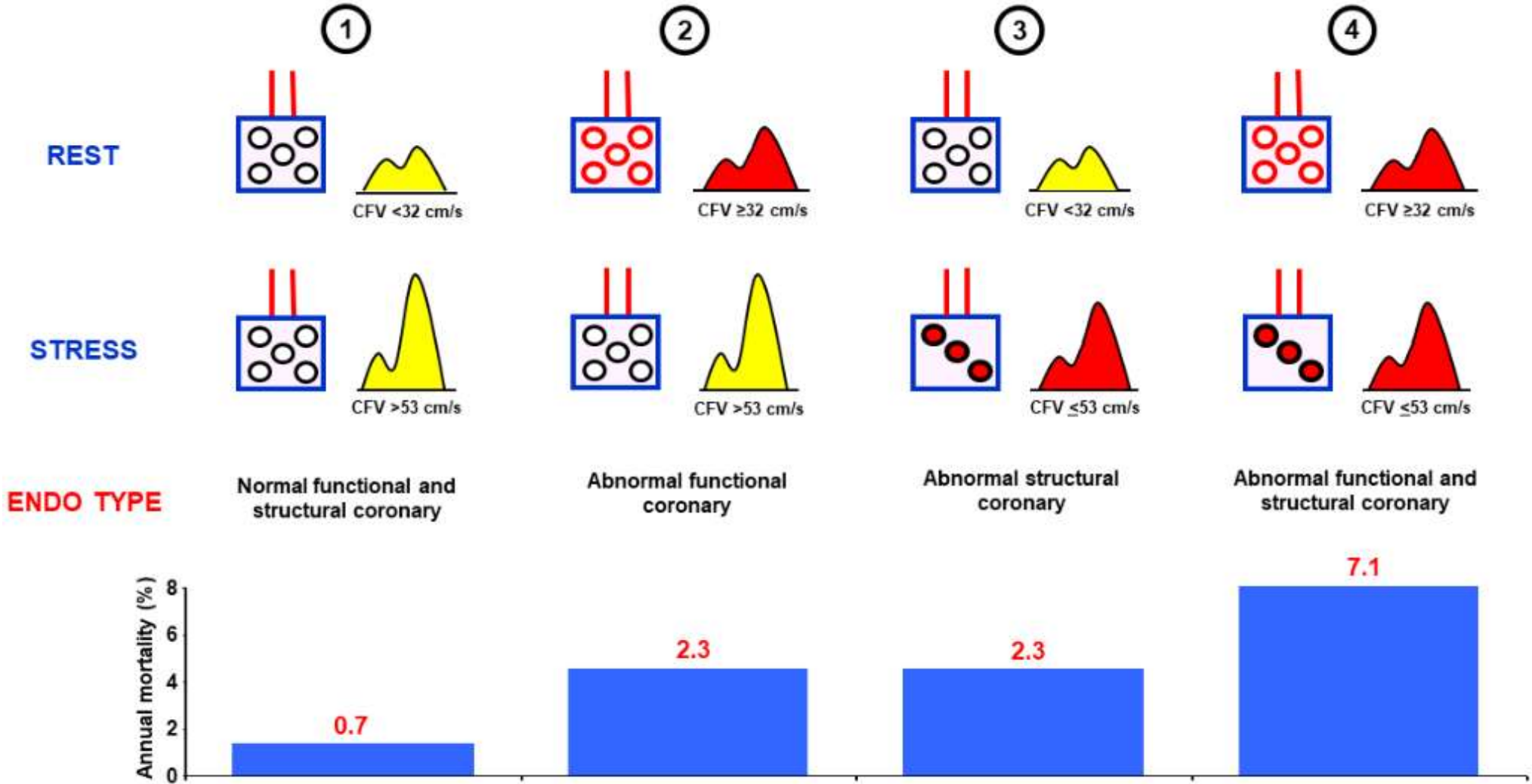
n=210
(20%)

n=8
(1%)

Predictors of all-cause mortality in ANOCA patients

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p value	HR (95% CI)	p value
Age	1.14 (1.10-1.17)	<0.0001	1.14 (1.10-1.17)	<0.0001
Female sex	1.47 (0.95-2.28)	0.09		
Diabetes mellitus	1.17 (0.74-1.85)	0.49		
Arterial hypertension	1.15 (0.73-1.82)	0.54		
Hypercholesterolemia	0.88 (0.57-1.36)	0.58		
Current smoker	0.75 (0.45-1.25)	0.47		
Left bundle branch block	2.08 (0.90-4.09)	0.08	2.57 (1.11-5.96)	0.03
Beta-blocker therapy	1.10 (0.69-1.74)	0.001		
LVEF	0.98 (0.93-1.02)	0.31		
Resting CFV \geq32 cm/s	1.80 (1.16-2.77)	0.008	1.77 (1.05-2.97)	0.03
Stress CFV \leq53 cm/s	1.63 (1.03-2.56)	0.04		

Different endotypes and mortality rate in ANOCA patients



Conclusions

- **Resting CFV of LAD provides useful information on coronary blood flow physiology as well as independent prognostic information in patients with either preserved and reduced LVEF and in ANOCA patients.**
- **In patients with preserved LVEF the prognostic value of CFV is incremental to that of CFVR.**
- **No stress, no contrast, no cost and no hazard are needed to obtain the information on resting CFV.**
- **Therefore, it seems reasonable to add the evaluation of resting CFV to the resting TTE and not to consider it only an ancillary parameter for CFVR assessment.**