Updating sulla diagnostica di ischemia

Piercarlo Ballo - S.C. Cardiologia
Ospedale S. Maria Annunziata - Firenze

European Heart Journal (2013) **34**, 2949–3003
doi:10.1093/eurheartj/eht296

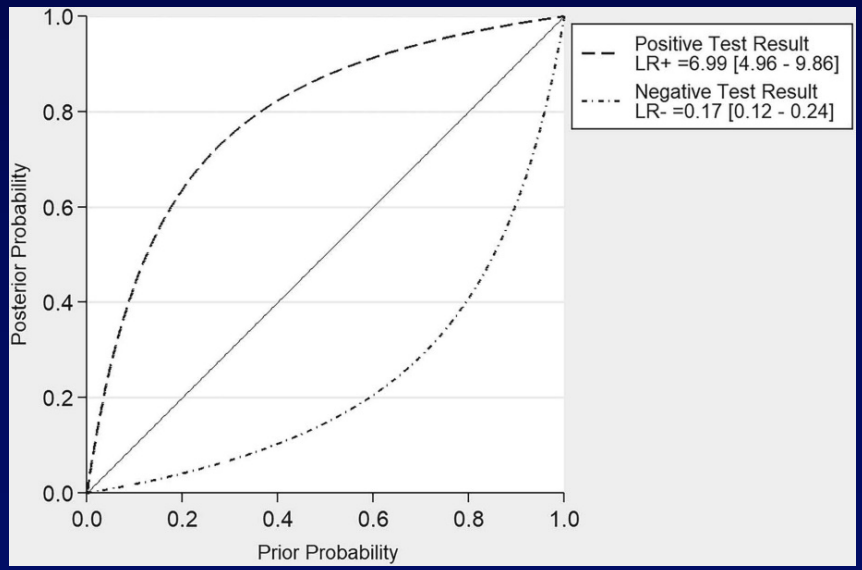
ESC GUIDELINES

2013 ESC guidelines on the management of stable coronary artery disease

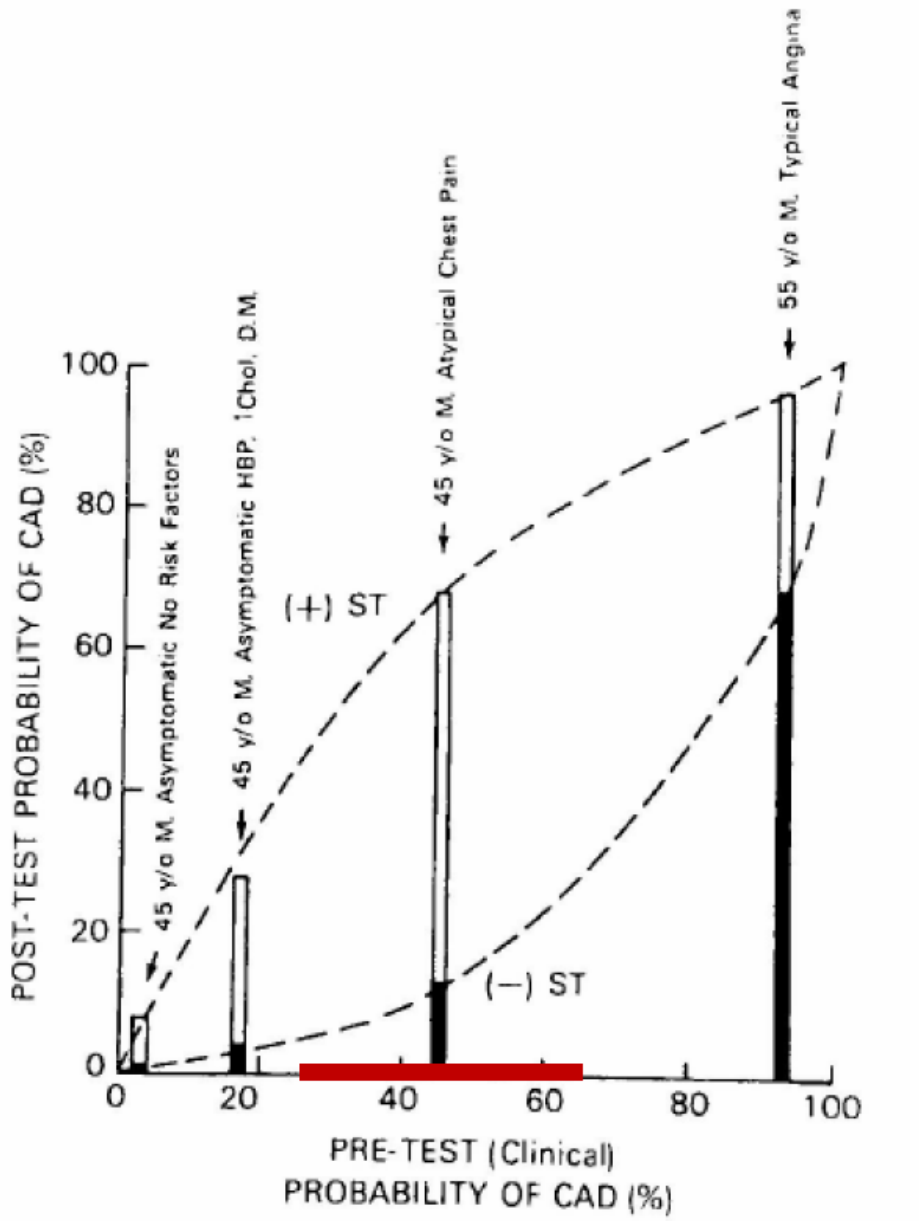
The Task Force on the management of stable coronary artery disease of the European Society of Cardiology

"Interpretation of non-invasive cardiac tests requires a Bayesian approach to diagnosis"

The probability of an event (in our case a "true" positive for the diagnosis of myocardial ischemia) depends on the pre-test probability



Probability of Coronary Artery Disease



1350 THE NEW ENGLAND JOURNAL OF MEDICINE June 14, 1979

ANALYSIS OF PROBABILITY AS AN AID IN THE CLINICAL DIAGNOSIS OF CORONARY-ARTERY DISEASE

GEORGE A. DIAMOND, M.D., AND JAMES S. FORRESTER, M.D.

Abstract The diagnosis of coronary-artery disease has become increasingly complex. Many different results, obtained from tests with substantial imperfections, must be integrated into a diagnostic conclusion about the probability of disease in a given patient.

To approach this problem in a practical manner, we reviewed the literature to estimate the pretest likelihood of disease (defined by age, sex and symptoms) and the sensitivity and specificity of four diagnostic tests: stress electrocardiography, cardiokymography, thallium scintigraphy and cardiac fluoroscopy. With this information, test results can be analyzed by use of Bayes theorem of conditional probability. This approach has several advantages. It pools the diagnostic experience of many physicians and integrates fundamental pretest clinical descriptors with many varying test results to summarize reproducibly and meaningfully the probability of angiographic coronary-artery disease. This approach also aids, but does not replace, the physician's judgment and may assist in decisions on cost effectiveness of tests. (N Engl J Med 300:1350-1358, 1979)

European Heart Journal (2011) 32, 1311–1312
doi:10.1093/eurheartj/ehr015

EDITORIAL

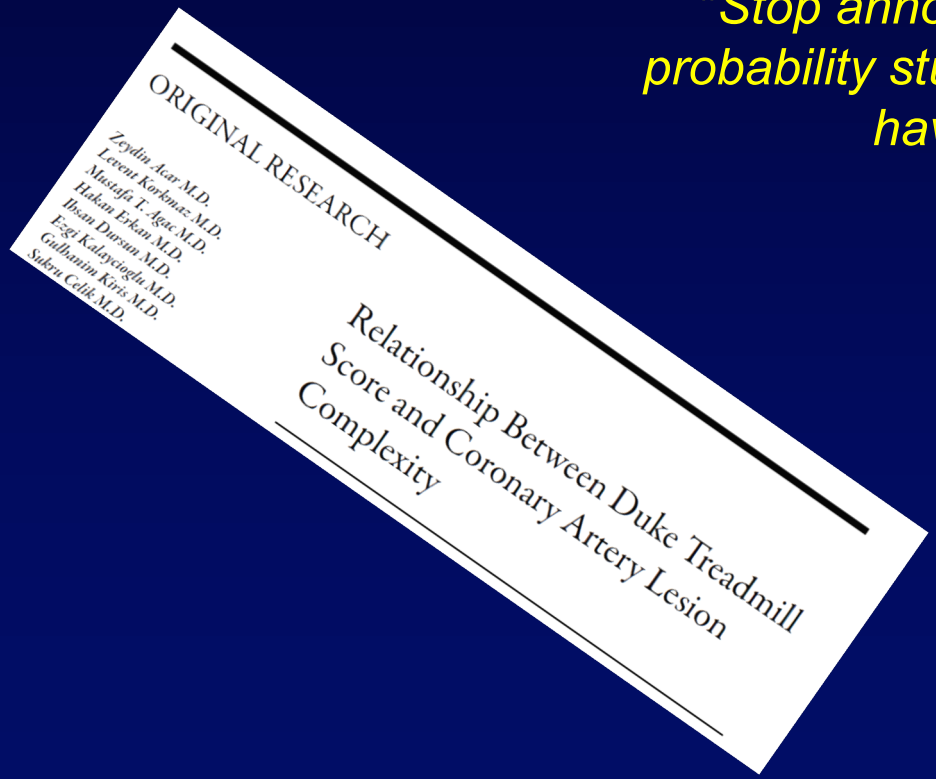
Diagnosing coronary artery disease—the Diamond and Forrester model revisited

Ian M. Graham*

Trinity College, Dublin, Ireland

Online publish-ahead-of-print 11 March 2011

"Stop annoying me with this probability stuff. Does my patient have CAD?"



ORIGINAL RESEARCH

Zeydin Acar M.D.
Levent Korkmaz M.D.
Mustafa T. Agac M.D.
Hakan Erkan M.D.
Ihsan Dursun M.D.
Ezgi Kalaycioglu M.D.
Gulhanim Kiris M.D.
Sukru Celik M.D.

Relationship Between Duke Treadmill Score and Coronary Artery Lesion Complexity

200

CARDIAC IMAGING AND NON-INVASIVE TESTING

A pretest prognostic score to assess patients undergoing exercise or pharmacological stress testing

Anthony Morise, Matthew Evans, Farrukh Jalisi, Rajendra Shetty, Marc Stauffer

Heart 2007;93:200–204. doi: 10.1136/hrt.2006.093799

European Heart Journal
doi:10.1093/eurheartj/ehr014

CLINICAL RESEARCH

A clinical prediction rule for the diagnosis of coronary artery disease: validation, updating, and extension

Tessa S.S. Genders[1,2], Ewout W. Steyerberg[3], Hatem Alkadhi[4], Sebastian Leschka[4], Lotus Desbiolles[4], Koen Nieman[2,5], Tjebbe W. Galema[5], W. Bob Meijboom[2,5], Nico R. Mollet[2,5], Pim J. de Feyter[2,5], Filippo Cademartiri[2,6], Erica Maffei[6], Marc Dewey[7], Elke Zimmermann[7], Michael Laule[8], Francesca Pugliese[9,10], Rossella Barbagallo[9], Valentin Sinitsyn[11], Jan Bogaert[12], Kaatje Goetschalckx[13], U. Joseph Schoepf[14], Garrett W. Rowe[14], Joanne D. Schuijf[15], Jeroen J. Bax[15], Fleur R. de Graaf[15], Juhani Knuuti[16], Sami Kajander[16], Carlos A.G. van Mieghem[17], Matthijs F.L. Meijs[18,19], Maarten J. Cramer[18], Deepa Gopalan[20], Gudrun Feuchtner[21], Guy Friedrich[22], Gabriel P. Krestin[2], and M.G. Myriam Hunink[1,2,23]*, The CAD Consortium

CAD consortium - Prospective data from 14 European and US hospitals on 2260 patients with chest pain without a history of CAD and referred for coronary angiography.

Primary outcome: obstructive CAD (≥50% stenosis in one or more vessels)

Update and recalibration of the original Diamond/Forrester pretest risk score

Updated Diamond and Forrester score

Chest Pain Criteria:

1. Sub-sternal chest discomfort with characteristic quality and duration
2. Provoked by exertion or emotional stress
3. Relieved promptly by rest or nitroglycerin

	Typical angina		Atypical angina		Non-anginal pain	
Age	Men	Women	Men	Women	Men	Women
30–39	59	28	29	10	18	5
40–49	69	37	38	14	25	8
50–59	77	47	49	20	34	12
60–69	84	58	59	28	44	17
70–79	89	68	69	37	54	24
>80	93	76	78	47	65	32

Genders T et al. *Eur Heart J* 2011

CAD consortium score

BMJ

BMJ 2012;344:e3485 doi: 10.1136/bmj.e3485 (Published 12 June 2012) Page 1 of 13

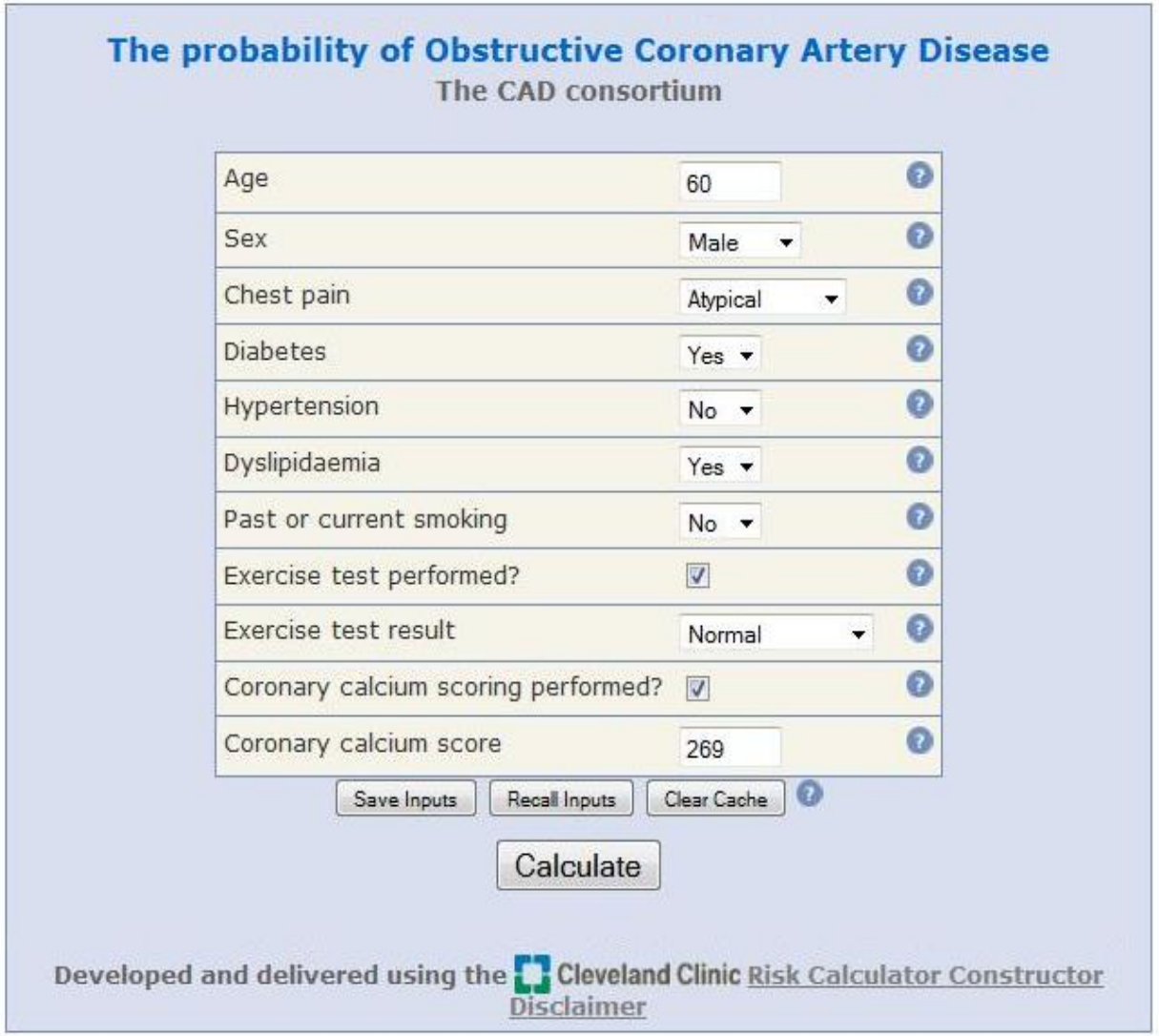
Prediction model to estimate presence of coronary artery disease: retrospective pooled analysis of existing cohorts

Validated on 5677 patients with stable chest pain without evidence for previous CAD, referred for TC-based or catheter-based coronary angiography

Primary outcome: obstructive CAD (≥50% stenosis in any coronary artery by catheter-based coronary angiography)

Two versions:
"basic" and "clinical"

Genders T et al. *BMJ* 2012



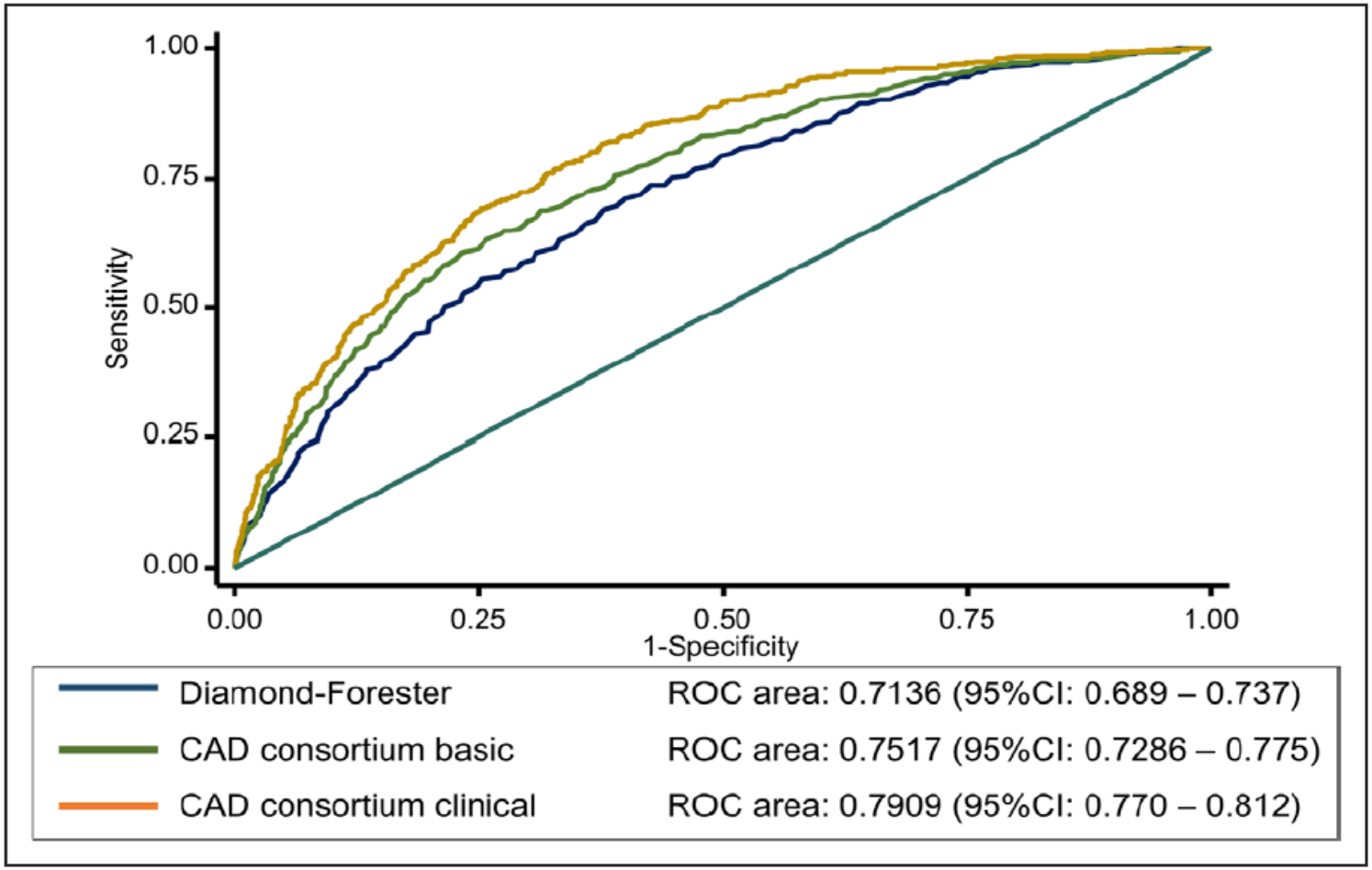
ORIGINAL RESEARCH ARTICLE

European Society of Cardiology–Recommended Coronary Artery Disease Consortium Pretest Probability Scores More Accurately Predict Obstructive Coronary Disease and Cardiovascular Events Than the Diamond and Forrester Score

The Partners Registry

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®



Bittencourt M, et al. *Circulation* 2016

CLINICAL RESEARCH STUDY

THE AMERICAN JOURNAL of MEDICINE®

Medical History for Prognostic Risk Assessment and Diagnosis of Stable Patients with Suspected Coronary Artery Disease

James K. Min, MD,[a] Allison Dunning, MS,[b] Heidi Gransar, MS,[c] Stephan Achenbach, MD,[d] Fay Y. Lin, MD,[e] Mouaz Al-Mallah, MD,[f] Matthew J. Budoff, MD,[g] Tracy Q. Callister, MD,[h] Hyuk-Jae Chang, MD,[i] Filippo Cademartiri, MD,[j,k] Erica Maffei, MD,[j,k] Kavitha Chinnaiyan, MD,[l] Benjamin J.W. Chow, MD,[m] Ralph D'Agostino, PhD,[n] Augustin DeLago, MD,[o] John Friedman, MD,[c] Martin Hadamitzky, MD,[p] Joerg Hausleiter, MD,[q] Sean W. Hayes, MD,[c] Philipp Kaufmann, MD,[r] Gilbert L. Raff, MD,[l] Leslee J. Shaw, PhD,[s] Louise Thomson, MD,[c] Todd Villines, MD,[t] Ricardo C. Cury, MD,[u] Gudrun Feuchtner, MD,[v] Yong-Jin Kim, MD,[w] Jonathon Leipsic, MD,[x] Hugo Marques, MD,[y] Daniel S. Berman, MD,[c] Michael Pencina, PhD[z]

CONFIRM Score

Recent score validated on 14.000 adults with suspected CAD referred for cardiac CT imaging

Primary outcome: obstructive CAD (≥50% stenosis in any coronary artery ≥1.5 mm in diameter)

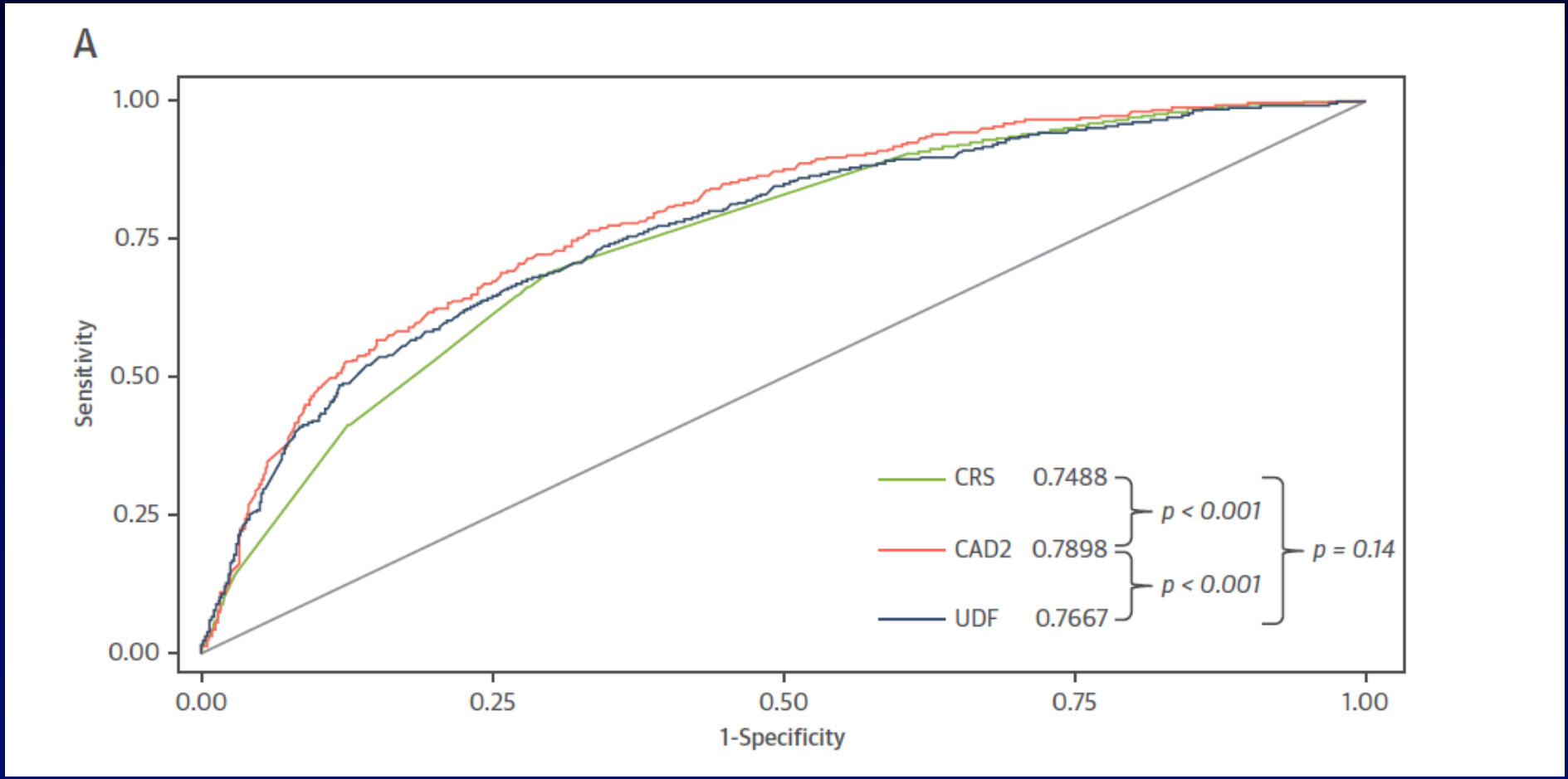
Min JK, et al. Am J Med 2015

Risk Factor	Categories	Points
Age		
	18-39	3
	40-49	4
	50-59	5
	60-69	6
	Great than 70	7
Sex		
	Male	1
	Female	0
Symptom		
	Non-typical	0
	Typical	1
Diabetes		
	Non-Diabetic	0
	Diabetic	1
Hypertension		
	Normotensive	0
	Hypertensive	1
Family History of CAD		
	No Family History	0
	Family History	1
Current Smoking		
	Non-Smoker	0
	Current Smoker	1

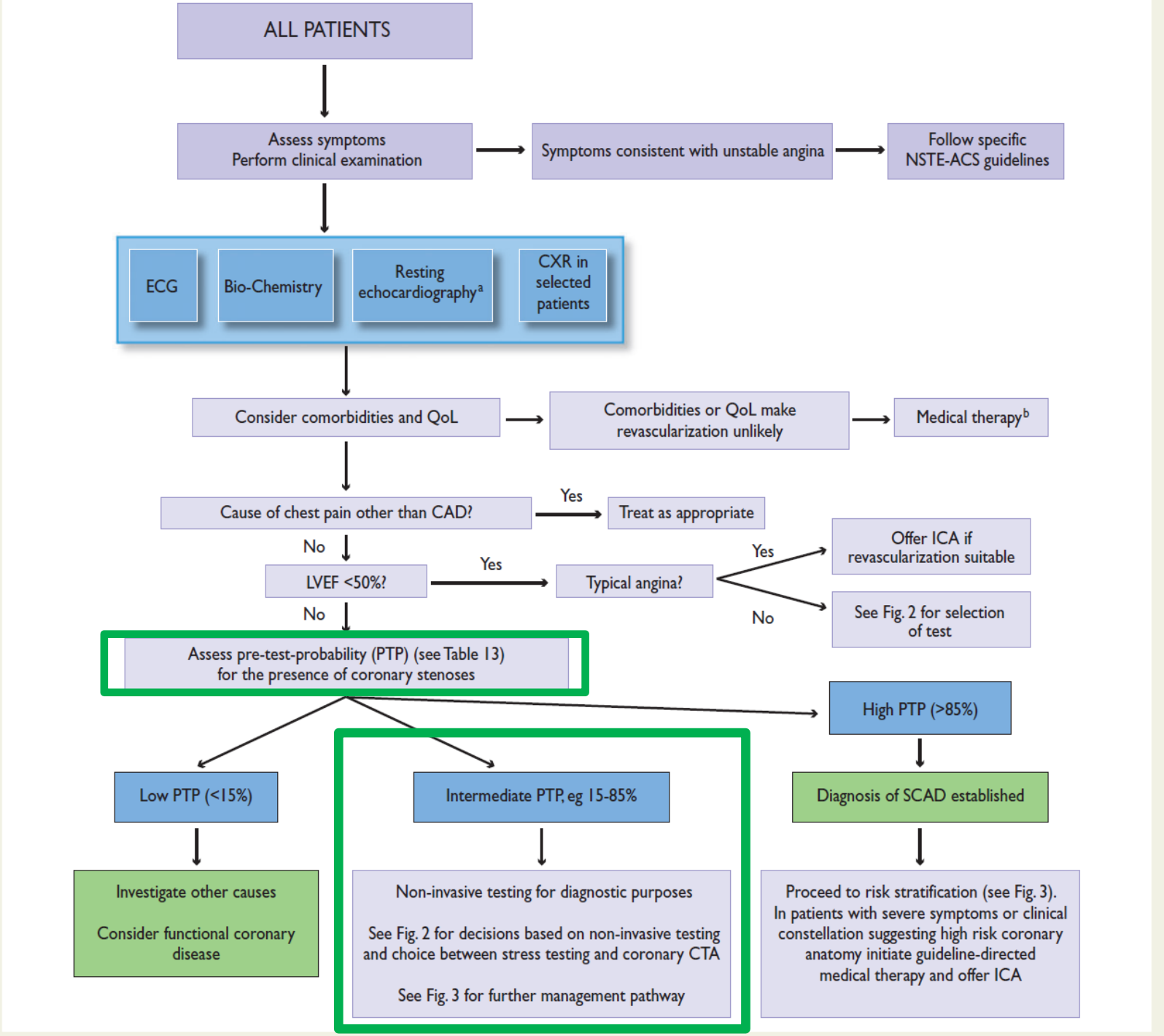
JACC: CARDIOVASCULAR IMAGING
© 2018 PUBLISHED BY ELSEVIER ON BEHALF OF THE
AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
VOL. ■, NO. ■, 2018

A Comparison of the Updated Diamond-Forrester, CAD Consortium, and CONFIRM History-Based Risk Scores for Predicting Obstructive Coronary Artery Disease in Patients With Stable Chest Pain

The SCOT-HEART Coronary CTA Cohort



Baskaran L, et al. *JACC Cardiovasc Imag* 2018


ALL PATIENTS
Assess symptoms
Perform clinical examination
Symptoms consistent with unstable angina
Follow specific NSTE-ACS guidelines
ECG
Bio-Chemistry
Resting echocardiography[a]
CXR in selected patients
Consider comorbidities and QoL
Comorbidities or QoL make revascularization unlikely
Medical therapy[b]
Cause of chest pain other than CAD?
Yes
Treat as appropriate
No
LVEF <50%?
Yes
Typical angina?
Yes
Offer ICA if revascularization suitable
No
See Fig. 2 for selection of test
No
Assess pre-test-probability (PTP) (see Table 13) for the presence of coronary stenoses
High PTP (>85%)
Low PTP (<15%)
Intermediate PTP, eg 15-85%
Diagnosis of SCAD established
Investigate other causes
Consider functional coronary disease
Non-invasive testing for diagnostic purposes
See Fig. 2 for decisions based on non-invasive testing and choice between stress testing and coronary CTA
See Fig. 3 for further management pathway
Proceed to risk stratification (see Fig. 3). In patients with severe symptoms or clinical constellation suggesting high risk coronary anatomy initiate guideline-directed medical therapy and offer ICA

Algorithm for the management of patients with intermediate pre-test probability

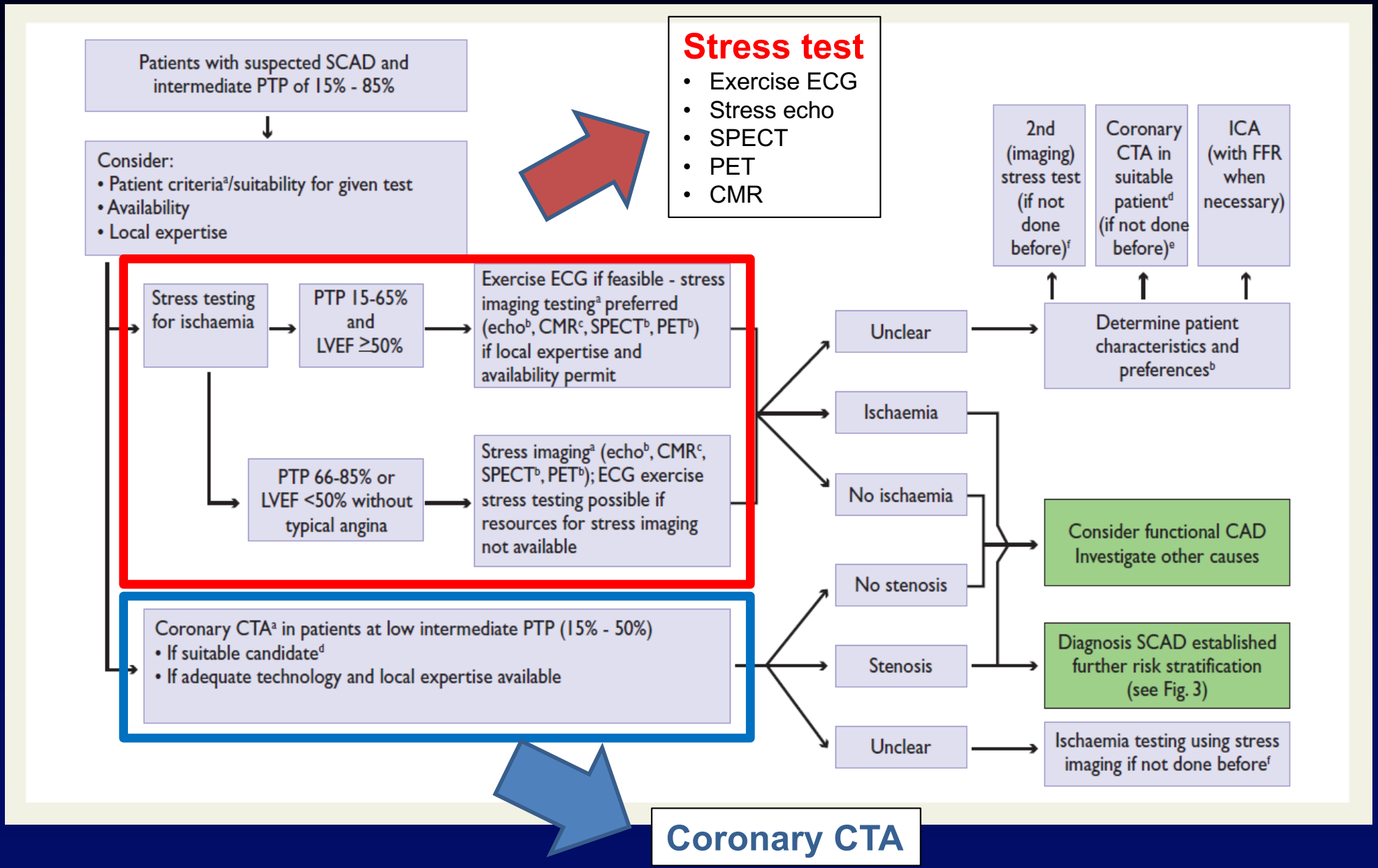


Table 12 Characteristics of tests commonly used to diagnose the presence of coronary artery disease

	Diagnosis of CAD	
	Sensitivity (%)	Specificity (%)
Exercise ECG [a, 91, 94, 95]	45–50	85–90
Exercise stress echocardiography[96]	80–85	80–88
Exercise stress SPECT[96-99]	73–92	63–87
Dobutamine stress echocardiography[96]	79–83	82–86
Dobutamine stress MRI[b,100]	79–88	81–91
Vasodilator stress echocardiography[96]	72–79	92–95
Vasodilator stress SPECT[96, 99]	90–91	75–84
Vasodilator stress MRI[b,98, 100-102]	67–94	61–85
Coronary CTA[c,103-105]	95–99	64–83
Vasodilator stress PET[97, 99, 106]	81–97	74–91

Why no exercise ECG in patients with pretest probability >65%?

Exercise ECG has a very low sensitivity (only 50%) despite a good specificity of 90%
(confirmed by studies avoiding verification bias)

Low sensitivity = High rate of false negatives

This limitation is not acceptable in patients with relatively higher risk

Table 14 **Performing an exercise electrocardiogram for initial diagnostic assessment of angina or evaluation of symptoms**

Recommendations	Class [a]	Level [b]	Ref. [c]
Exercise ECG is recommended as the initial test for establishing a diagnosis of SCAD in patients with symptoms of angina and intermediate PTP of CAD (Table 13, 15–65%), free of anti-ischaemic drugs, unless they cannot exercise or display ECG changes which make the ECG non evaluable.	I	B	115, 116
Exercise ECG should be considered in patients on treatment to evaluate control of symptoms and ischaemia.	IIa	C	-
Exercise ECG in patients with ≥0,1 mV ST-depression on resting ECG or taking digitalis is not recommended for diagnostic purposes.	III	C	-

Table 15 Use of exercise or pharmacologic stress testing in combination with imaging

Recommendations	Class [a]	Level [b]	Ref. [c]
An imaging stress test is recommended as the initial test for diagnosing SCAD if the PTP is between 66–85% or if LVEF is <50% in patients without typical angina.	I	B	143, 144
An imaging stress test is recommended in patients with resting ECG abnormalities which prevent accurate interpretation of ECG changes during stress.	I	B	117, 145
An imaging stress test should be considered in symptomatic patients with prior revascularization (PCI or CABG).	IIa	B	146, 147
An imaging stress test should be considered to assess the functional severity of intermediate lesions on coronary arteriography.	IIa	B	148, 149

Stress echocardiography

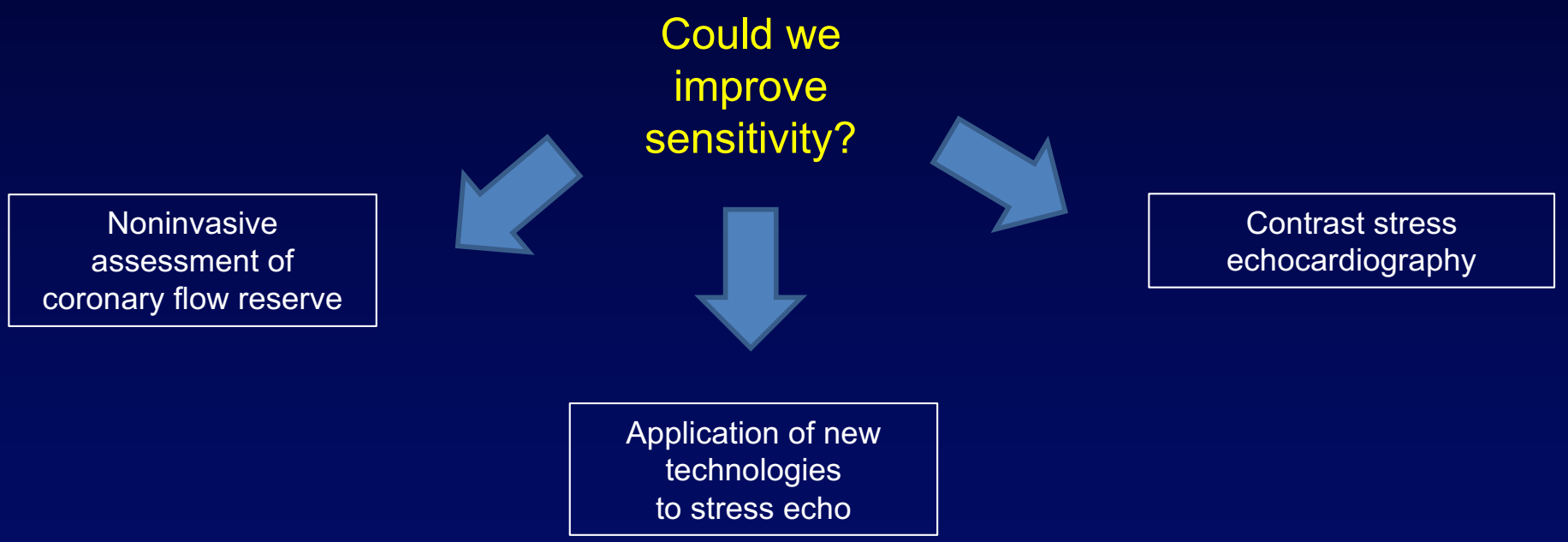
Advantages

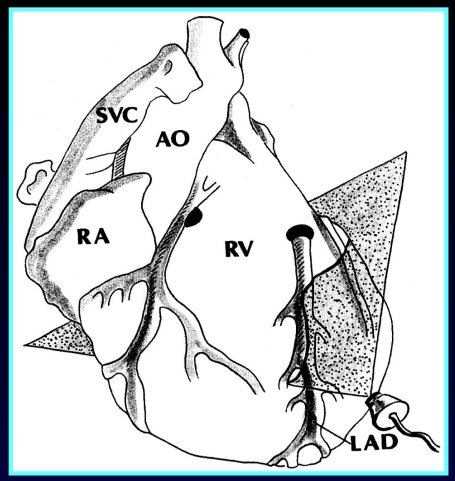
- Readily available
- Provides direct visualization of wall motion, LV function, and anatomy
- Can localize region of abnormality
- May detect valvular abnormalities
- Higher specificity than perfusion imaging (77-89% vs 70-88%)
- Higher sensitivity than Treadmill alone (70-85% vs 61-68%)
- No radiation

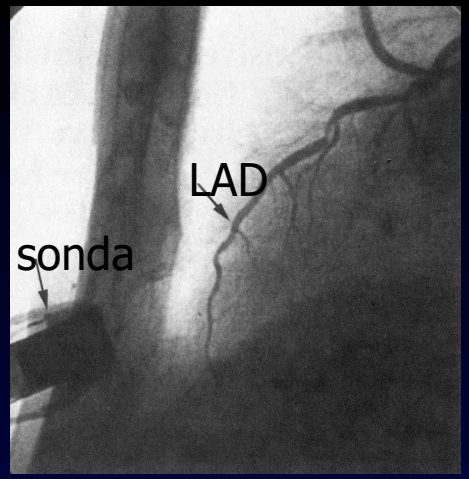
Limitations

- Technically difficult with poor acoustic windows
- Requires an experienced sonographer
- Less sensitive than myocardial perfusion imaging (requires ischemia)
- Fewer clinical data than perfusion imaging
- Interpretation is subjective
- Interpretable image quality may be obtained during submaximal HR

Stress echocardiography







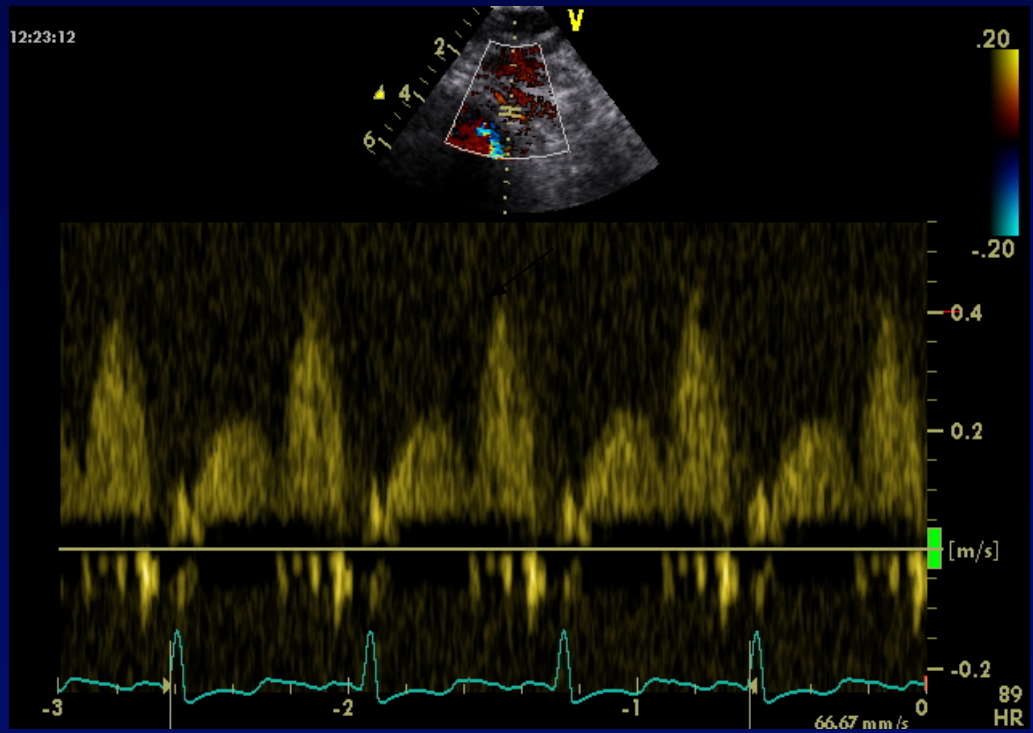
Noninvasive coronary flow reserve

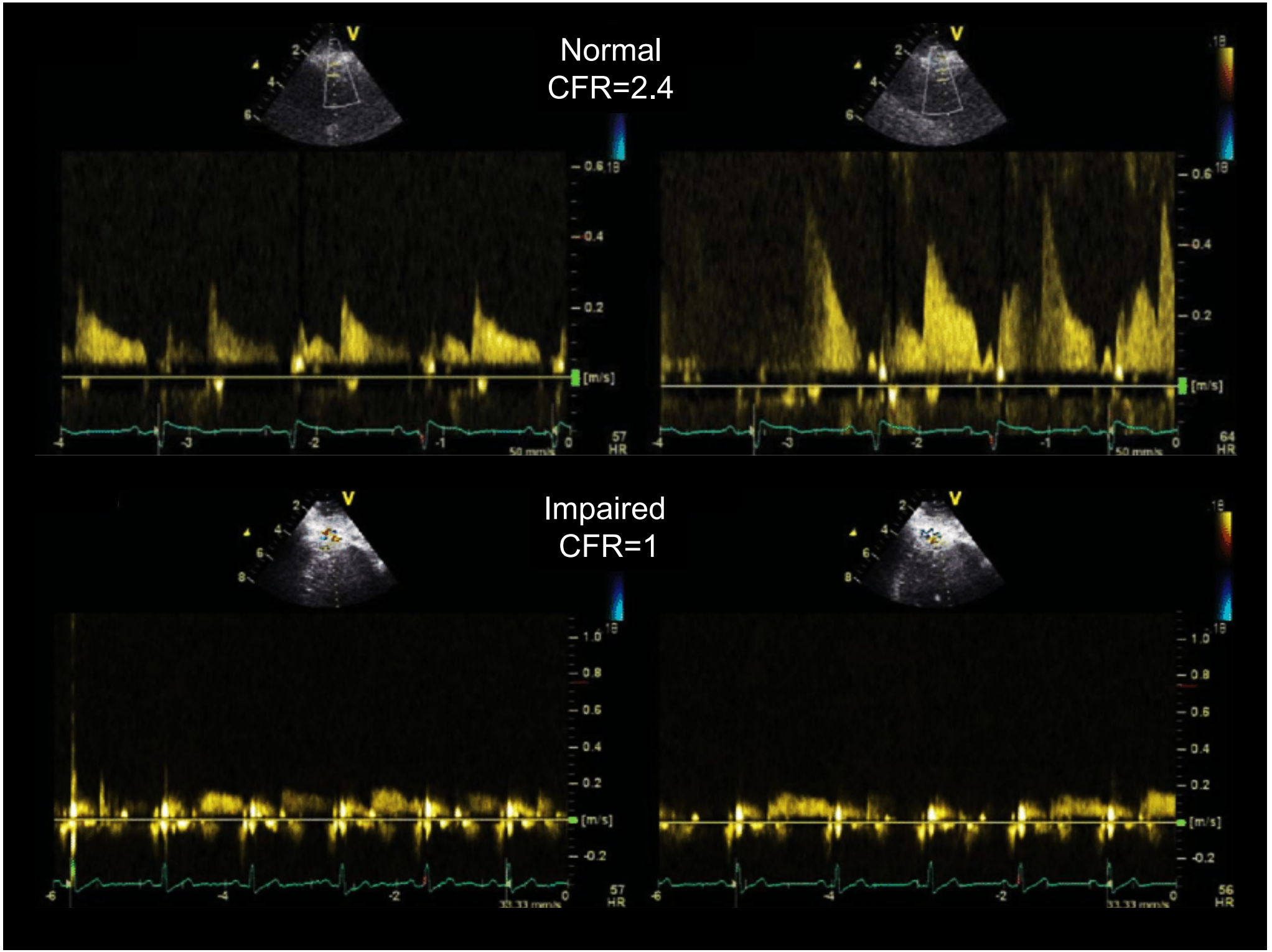
- Adding CFR to regional wall motion allows to have high specificity (regional wall motion) and a high sensitivity (CFR) diagnostic marker

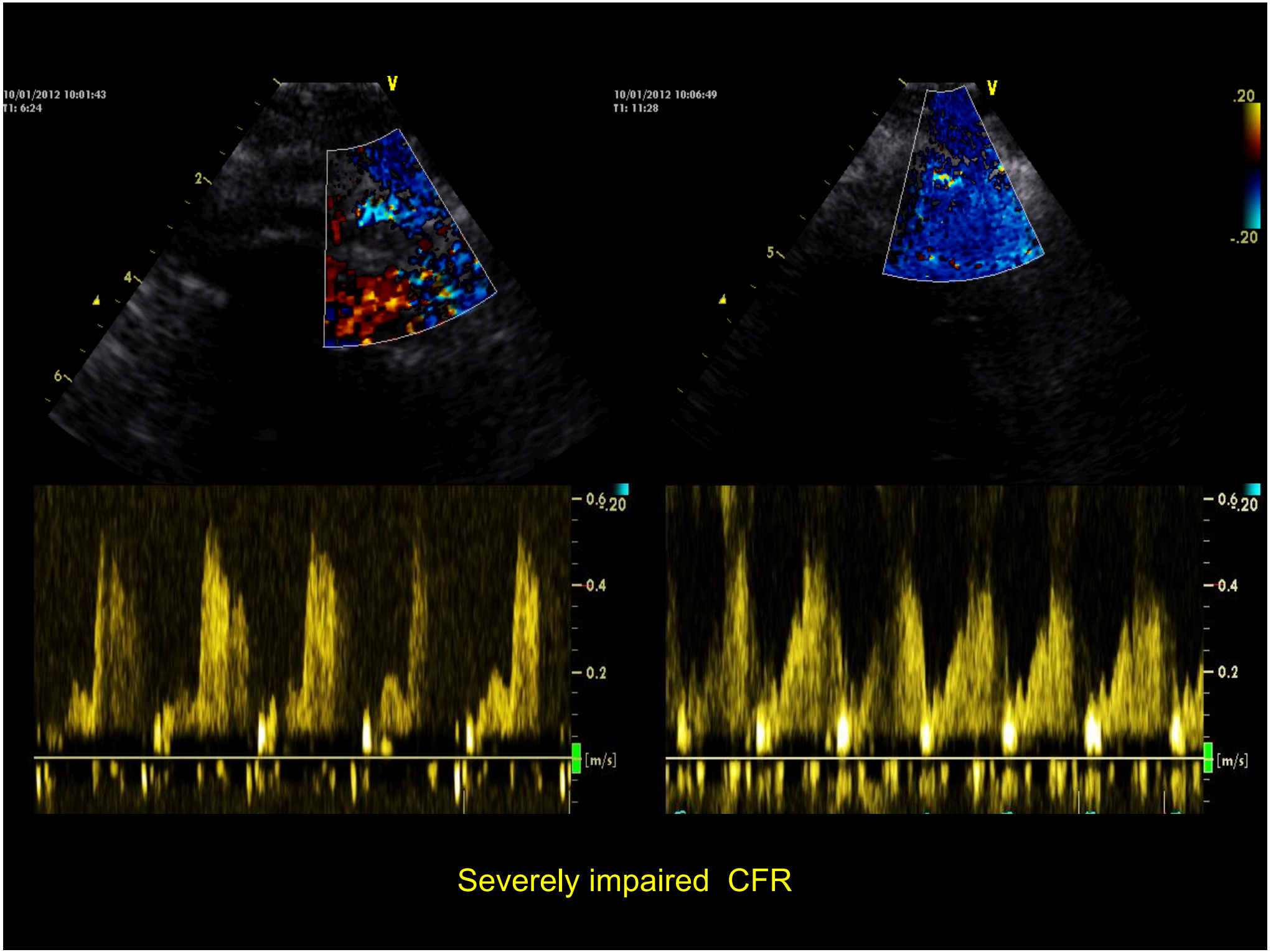
- CFR shifts the balance of stress choice in favour of vasodilators (more robust hyperemic stress and easier to perform with dual imaging than dobutamine or exercise)

- CFR adds a quantitative support to the exquisitely qualitative assessment of wall motion analysis

CFR in the echo lab is not a "stand-alone" variable, but provides additional diagnostic and prognostic information




Normal
CFR=2.4
Impaired
CFR=1
[m/s]
HR


10/01/2012 10:01:43
TI: 6:24
10/01/2012 10:06:49
TI: 11:28
.20
-.20
0.6
0.4
0.2
[m/s]
Severely impaired CFR

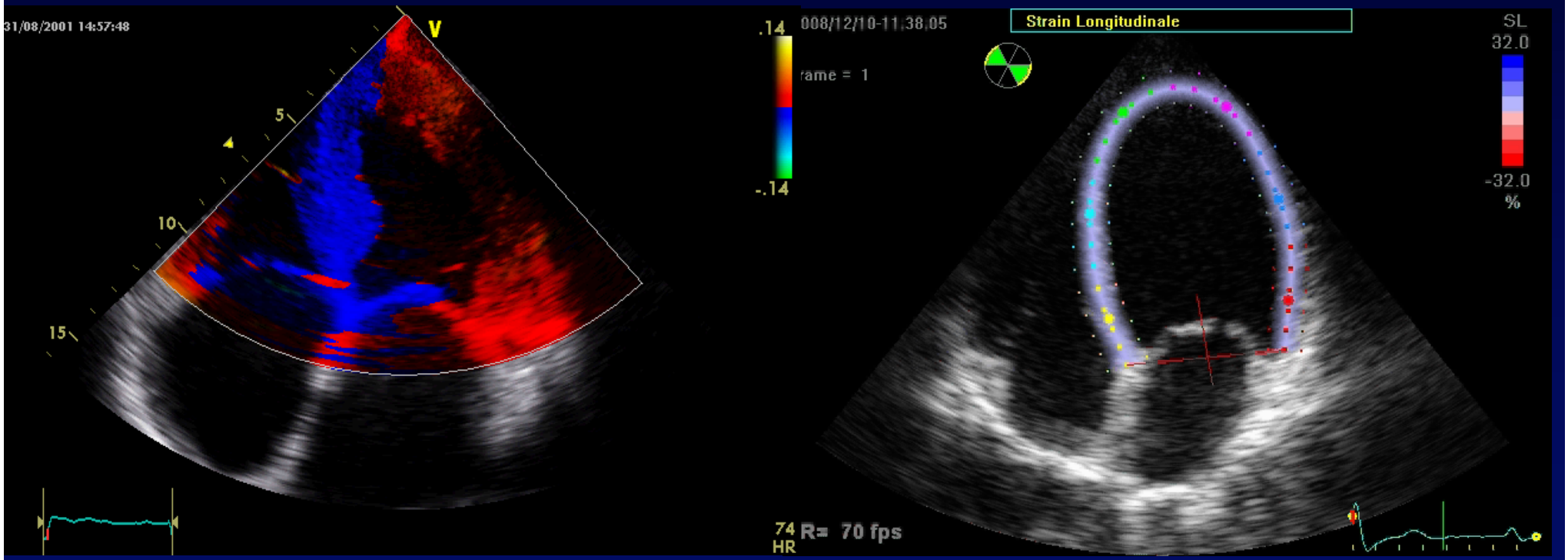
Stress echocardiography

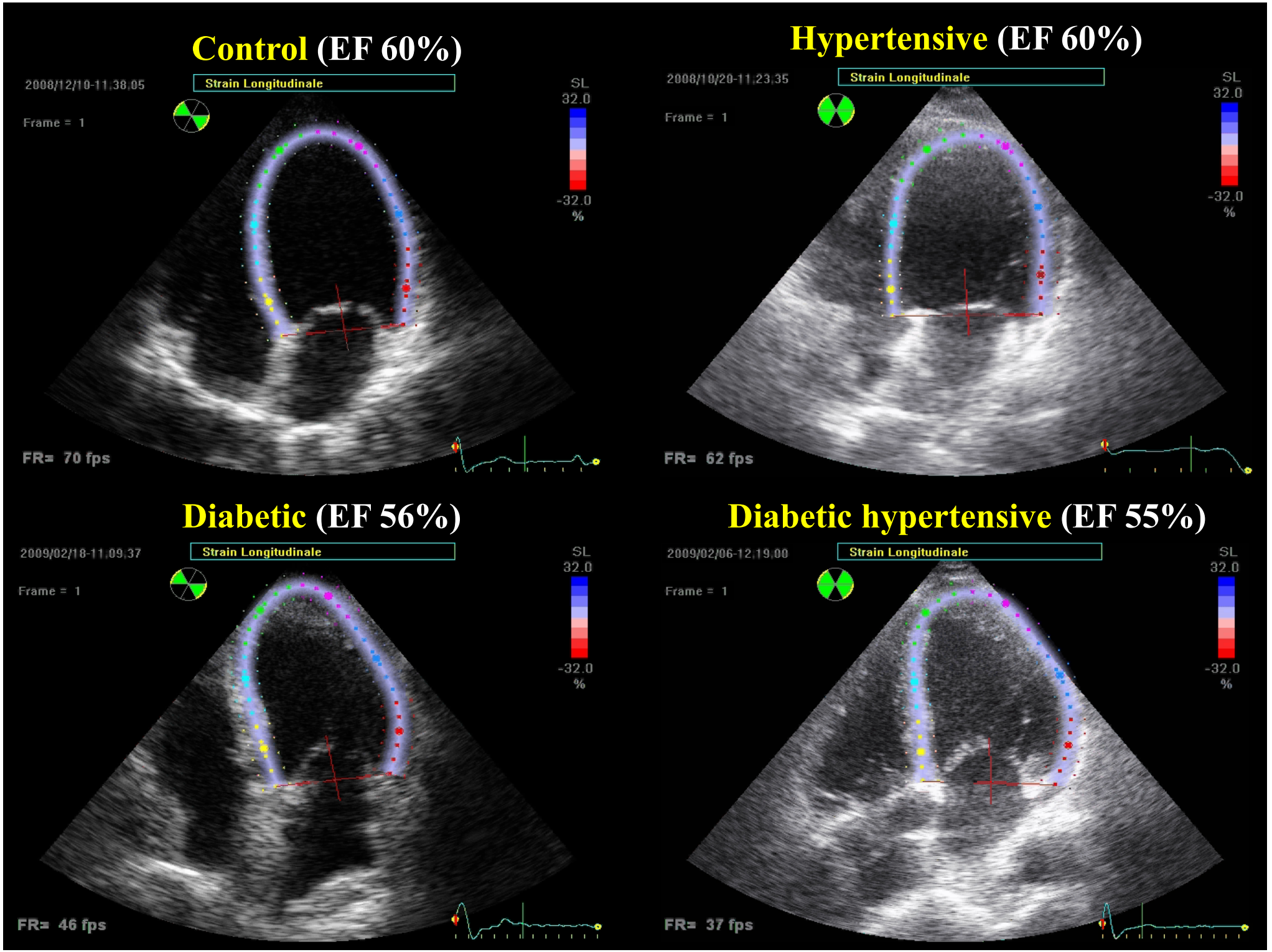
Could we improve sensitivity?

- Noninvasive assessment of coronary flow reserve
- Contrast stress echocardiography
- Application of new technologies to stress echo

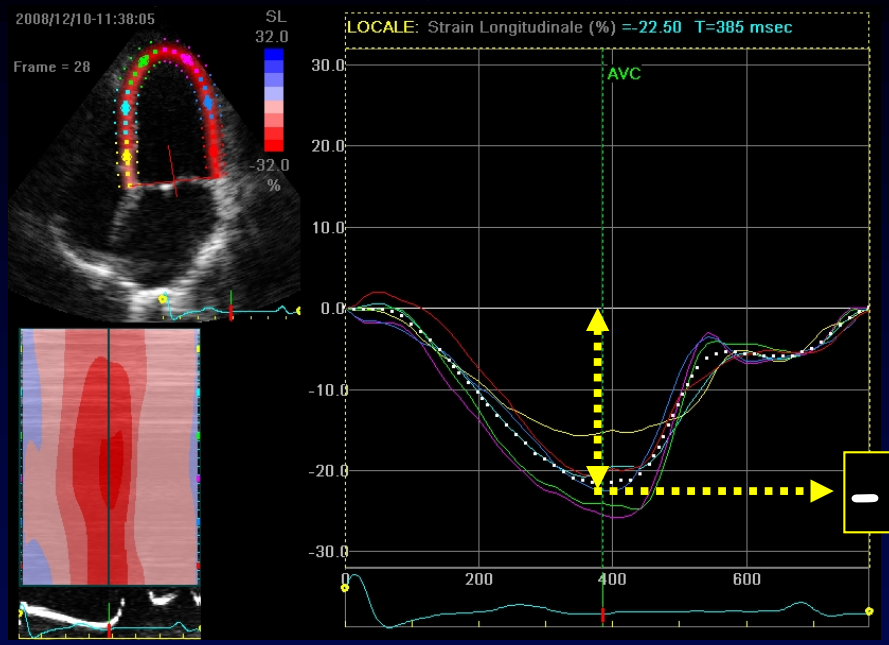
2D strain stress echocardiography

- Angle-independent
- Allows measurement of strain and SR in all geometrical axes



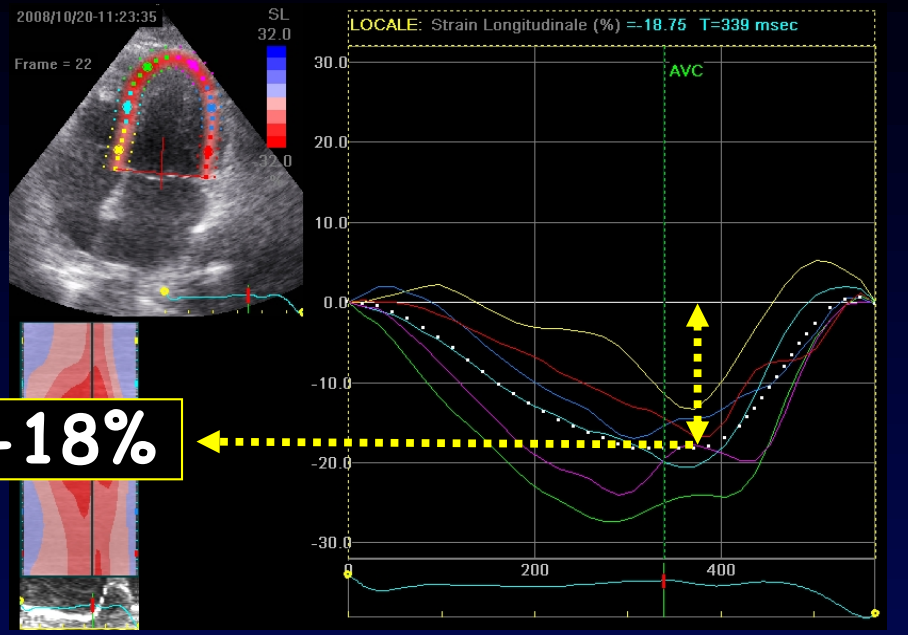

Control (EF 60%)
2008/12/10-11:38:05
Strain Longitudinale
Frame = 1
SL
32.0
-32.0
%
FR= 70 fps
Hypertensive (EF 60%)
2008/10/20-11:23:35
Strain Longitudinale
Frame = 1
SL
32.0
-32.0
%
FR= 62 fps
Diabetic (EF 56%)
2009/02/18-11:09:37
Strain Longitudinale
Frame = 1
SL
32.0
-32.0
%
FR= 46 fps
Diabetic hypertensive (EF 55%)
2009/02/06-12:19:00
Strain Longitudinale
Frame = 1
SL
32.0
-32.0
%
FR= 37 fps

Control (EF 60%)



-22%

Hypertensive (EF 60%)



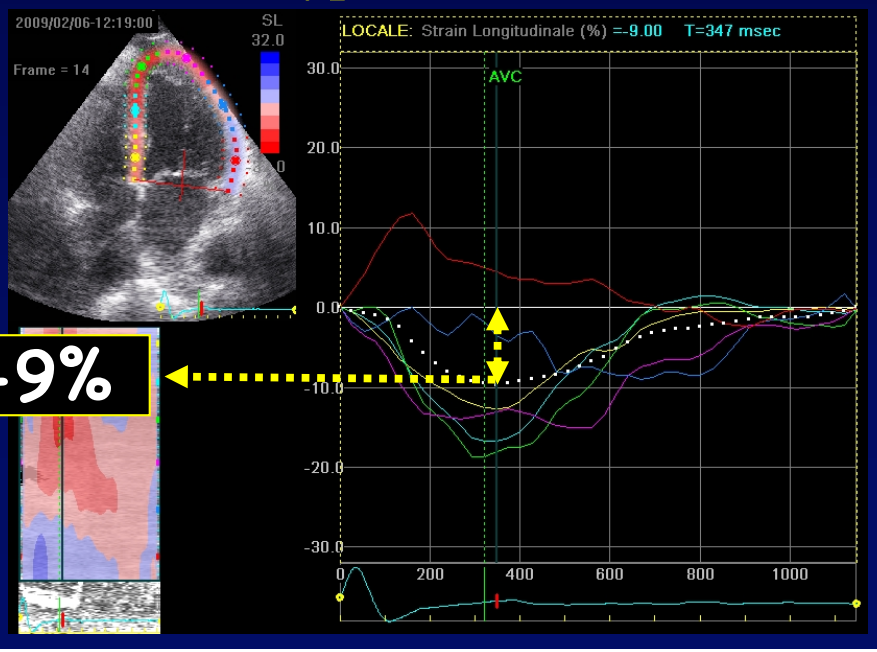
-18%

7.avi

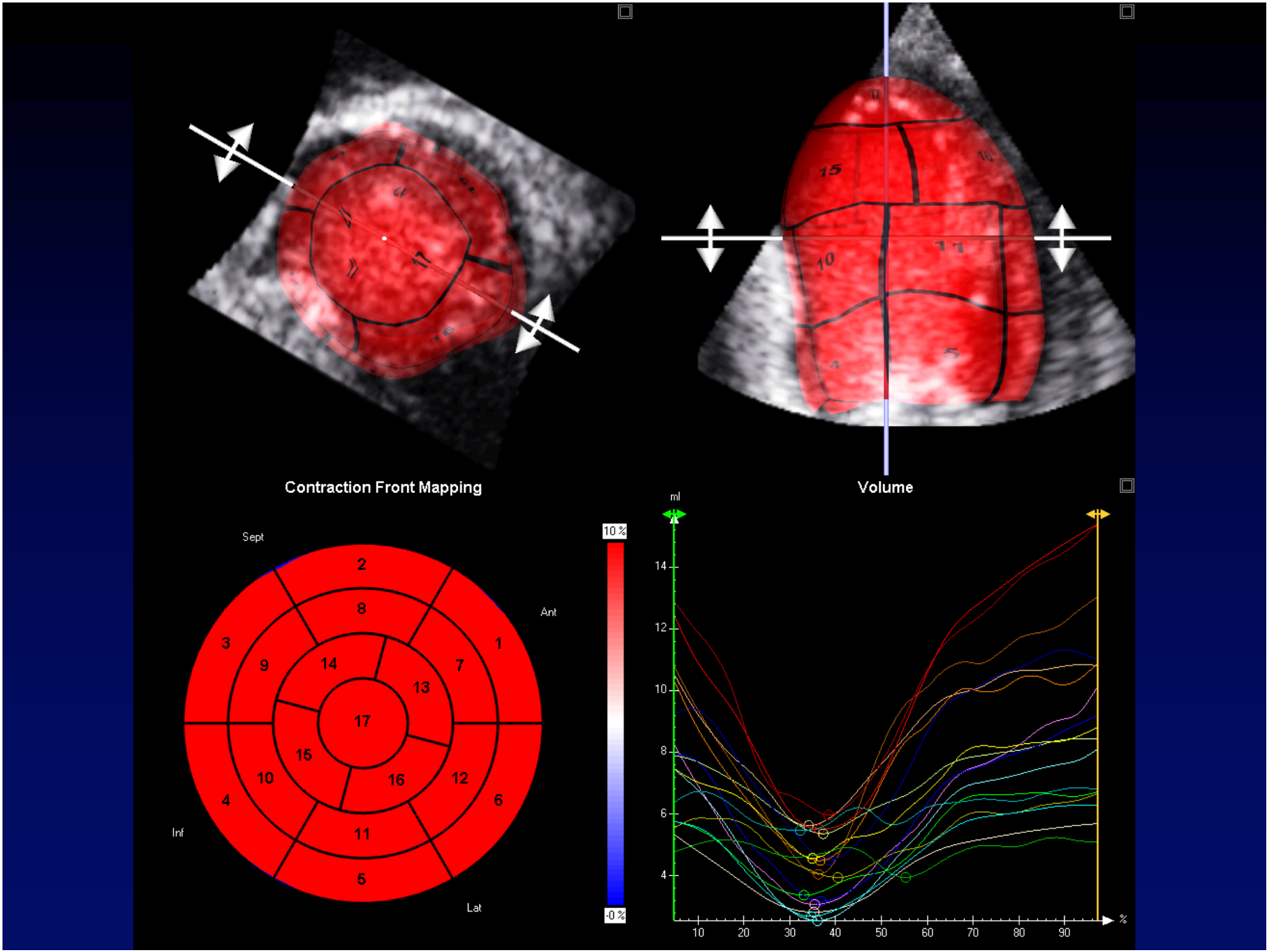
Diabetic (EF 56%)

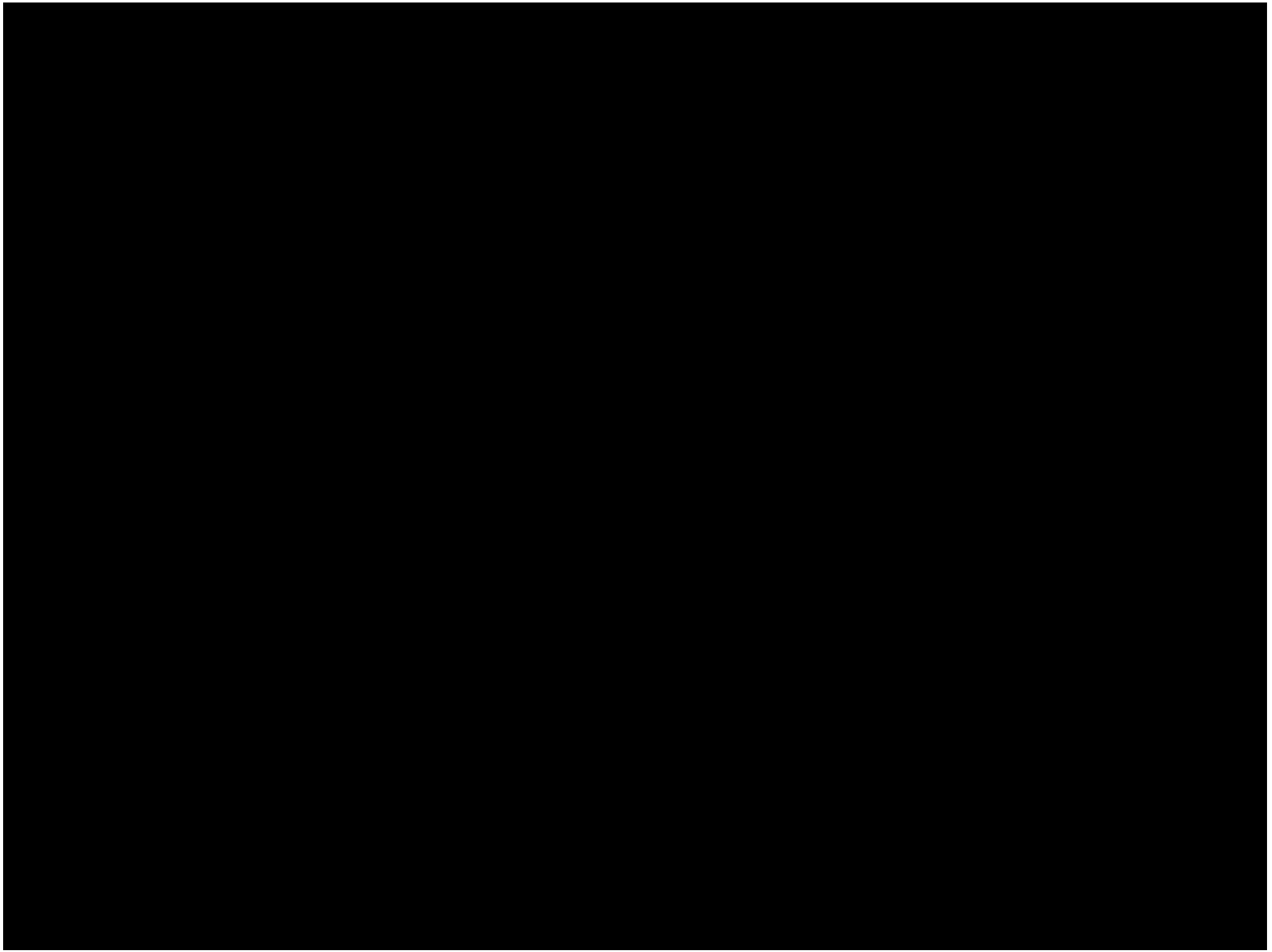
-12%

Diabetic hypertensive (EF 55%)

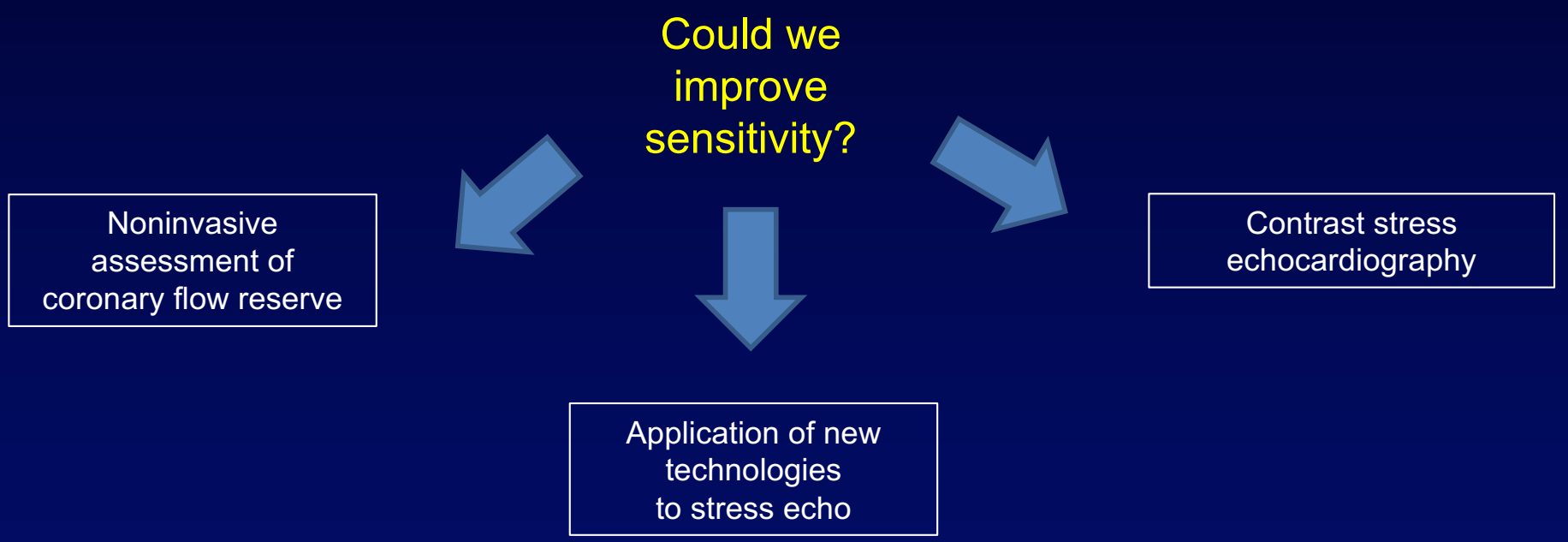


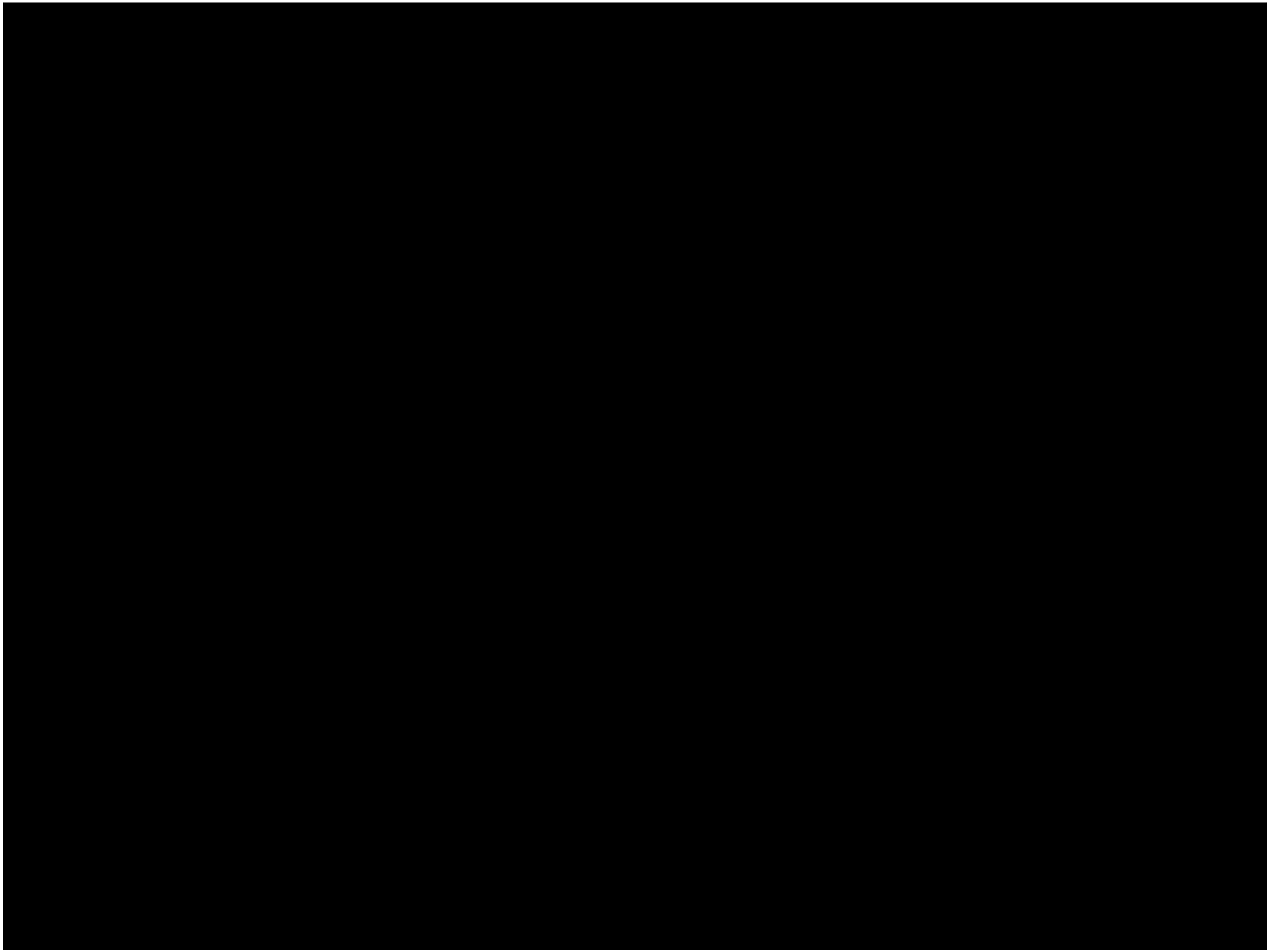
-9%


Contraction Front Mapping
Volume
Sept
Ant
Inf
Lat
2
8
3
1
9
14
7
13
17
15
10
16
12
4
6
11
5
10 %
-0 %
ml
14
12
10
8
6
4
10
20
30
40
50
60
70
80
90
%

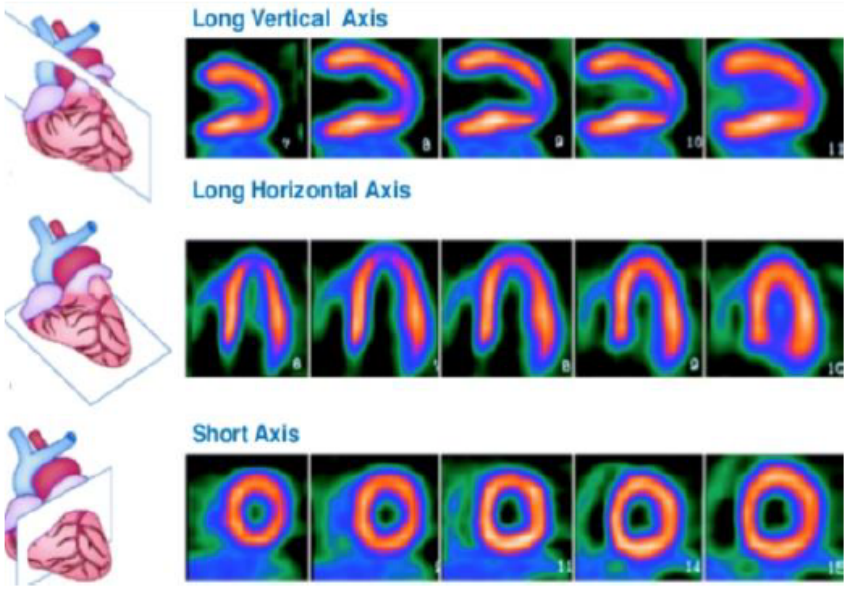


Stress echocardiography





SPECT Nuclear Myocardial Perfusion Scan



Advantages

- Can be used in patients with moderate to high pre-test probability
- Perfusion and function
- Can localize disease
- Can risk stratify
- Pharmacologic stress may be performed
- Higher sensitivity than stress echo (flow heterogeneity)

Limitations

- Relatively expensive
- Decreased specificity (attenuation artifact)
- Radiation exposure

	Compares perfusion Rest	vs	Stress
Normal	N		N
Ischemia	N		Abn
Scar	Abn		Abn

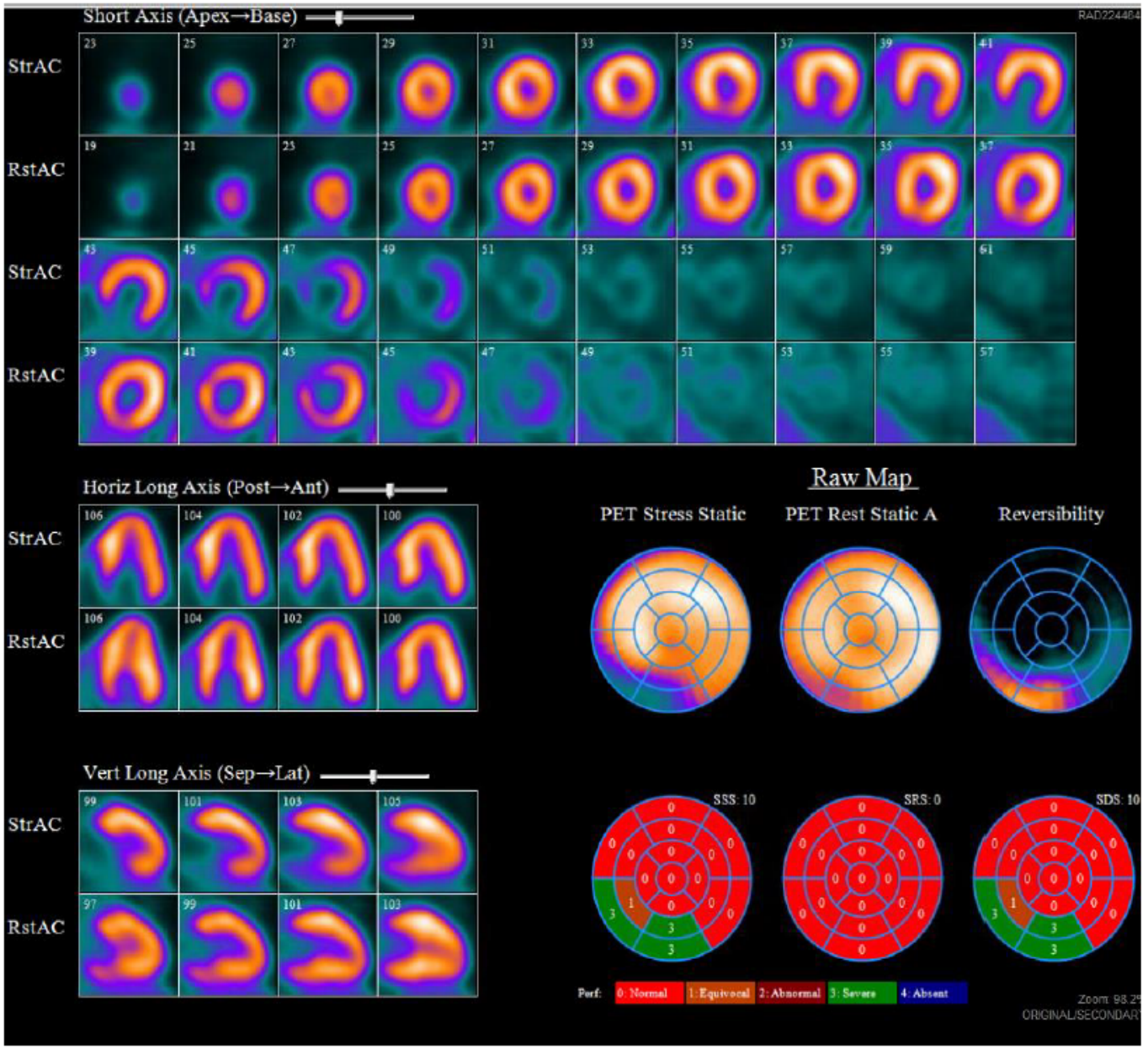
Nuclear Myocardial Perfusion Scan

Radiation:

www.scai.org
The Society for Cardiovascular Angiography and Interventions

Echo/EKG	None
Chest X ray (for comparison)	0.1 mSv
Coronary Angiogram	7 mSv (~15 PCI)
Cardiac CT Angiography	10-16 mSv
Nuclear Stress: SPECT - Tc-99 PET - 82 Rubidium	10-12 mSv
Nuclear Stress – Thallium	17 -29 mSv

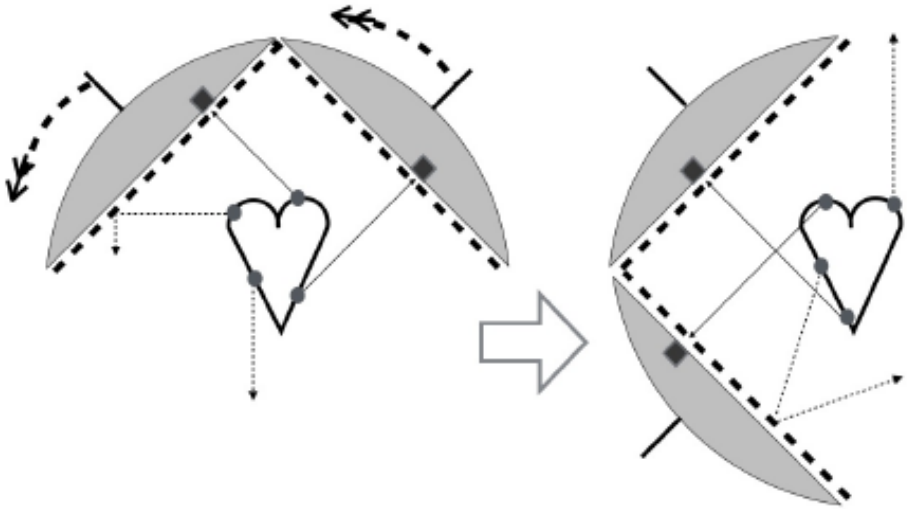
Mark DB et al, JACC, 2010:55;2663-2699

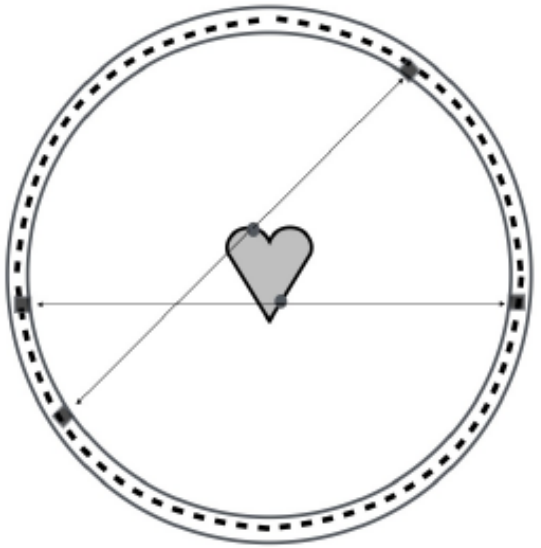


Large-sized area of severely decreased uptake in the inferoseptal wall. This defect is almost fully reversible on rest images, EF 44%.

SPECT

PET





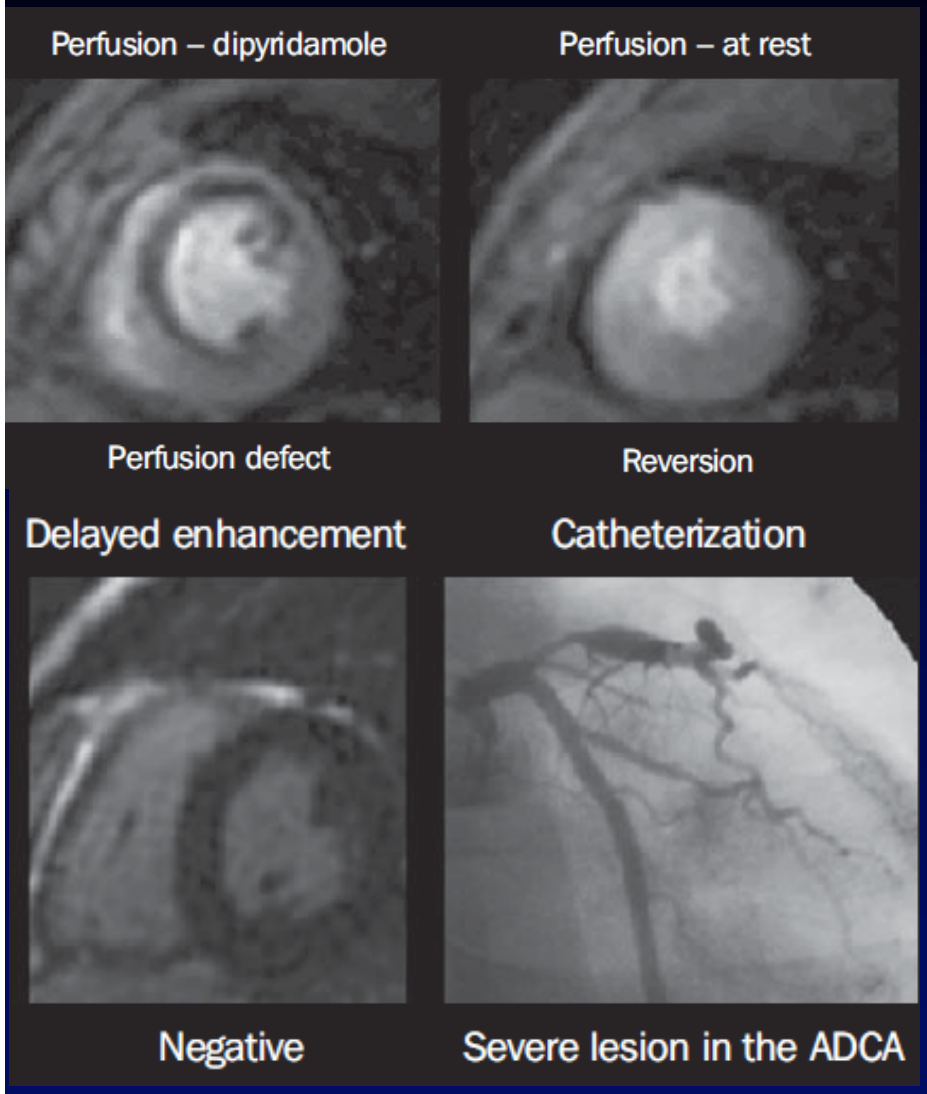
Technetium-99

13N- ammonium
Rubidium 82

18-Fluorodeoxyglucose

Higher spatial resolution
Higher sensitivity for CAD detection, particularly in women and obese

Stress CMR



Allows assessment of myocardial perfusion and pattern of delayed enhancement. Cine CMRI allows for the same type of analysis of segmental contractility than echocardiography

Conclusions

- Keep a Bayesian approach in the diagnosis of myocardial ischemia
- Updated Diamond/Forrester score or CAD Consortium scores
- Focus on patients with pretest probability in the range 15-85%
- Choose between an «anatomic» or «functional» test
- If a functional test is indicated, strictly consider advantages and disadvantages to selecting the most appropriate stress test. For stress echo, sensitivity can be increased by CFR, 2D-strain, and contrast agents.