Sfide in cardiologia clinica

10/11 marzo 2017
Mantova MaMu, Centro Congressi Mantova Largo di Porta Pradella, 1

Con il patrocinio di:

SESSIONE 3
Cardiopatia ischemica: dai test anatomici e funzionali allo studio della meccanica e della struttura del miocardio
MODERATORI: **A. IZZO, M. PASQUALINI**

15.00
Sospetto clinico di coronaropatia e l'innegabile valore dello Stress-Eco. Ruolo presente e futuro
N. GAIBAZZI

15.20
Uso razionale delle tecniche avanzate ecocardiografiche 2D/3D per lo studio della funzione ventricolare sinistra
D. MELE

15.40
Dolore Toracico: Il Corretto Approccio ed il Valore Incrementale de "Multimodality Imaging" nei Pazienti con Rischio di Malattia Basso-intermedio
G. PONTONE

16.00
Valore incrementale della RMN cardiaca nei pazienti con cardiopatia ischemica
P. MASCI

16.20
Discussione

CLINICAL SCENARIO I

ACUTE CHEST PAIN

Altered Left Ventricular Tissue Velocities, Deformation and Twist in Children and Young Adults with Acute Myocarditis and Normal Ejection Fraction

Nee Scze Khoo, MBChB, Jeffery F. Smallhorn, MD, Joseph Atallah, MD CM, SM, Sachie Kaneko, MD, Andrew S. Mackie, MD, SM, and Ian Paterson, MD, *Edmonton, Alberta, Canada*

(J Am Soc Echocardiogr 2012;25:294-303.)

28 consecutive pts, aged 10 to 45 years

- Prospectively enrolled
- Presenting with new-onset chest pain at rest lasting >30 min
- Two consecutive elevated troponin I measurements
- Normal LV-EF (>50%) on initial echocardiography
- Excluded ischemic heart disease on coronary angio
- CMRI features of myocarditis

64 healthy controls

Altered Left Ventricular Tissue Velocities, Deformation and Twist in Children and Young Adults with Acute Myocarditis and Normal Ejection Fraction

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(J Am Soc Echocardiogr 2012;25:294-303.)

Table 6 Multivariate logistic regression analysis for predictors of acute myocarditis in patients presenting with chest pain (*n* = 28) compared with controls (*n* = 64)

Variable	Odds ratio	95% confidence interval	*P*
Time to peak twist (%)	0.71	0.56–0.79	.004
Peak twist rate (°/sec)	1.11	1.03–1.20	.010
Basal circumferential early diastolic strain rate (s^{-1})	0.01	0.01–0.49	.029
4CH longitudinal strain (%)	2.53	1.19–5.39	.016
Lateral annular E′ (cm/sec)	3.50	1.30–9.42	.013

Table 7 Sensitivity, specificity, and positive and negative predictive values of the five variables identified as independent predictors of myocarditis in the multivariate logistic regression model

Variable	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Time to peak twist (<100%)	73%	89%	76%	88%
Peak twist rate (<100°/sec)	43%	83%	52%	77%
Basal circumferential early diastolic strain rate (<1.35 s^{-1})	63%	81%	61%	83%
4CH longitudinal strain (>−18.5%)	60%	89%	72%	83%
Lateral annular prime; (>−11.5 cm/sec)	50%	84%	58%	79%
Any two variables	93%	91%	82%	97%
Any three variables	67%	98%	95%	86%

SUMMARY – I

Speckle tracking echocardiography may considerably help to evaluate regional LV dysfunction.

In same cases it may help to exclude ischemic heart disease and avoid coronary angio.

This is crucial especially in settings with no easy access to cardiac MRI, which are the vast majority.

CLINICAL SCENARIO II

STABLE ANGINA PECTORIS

Risk stratification by resting echocardiography quantification of ventricular function in SCAD

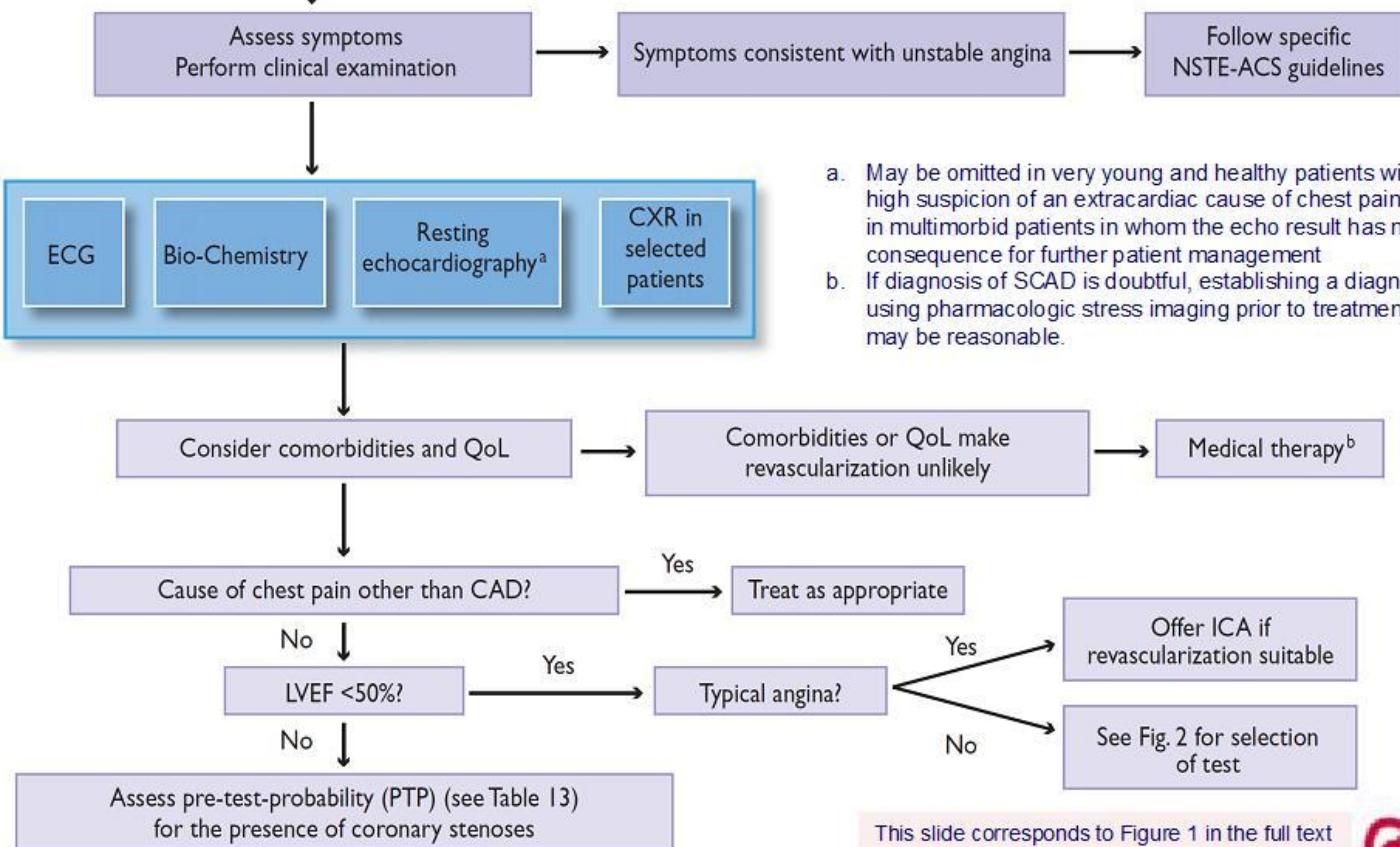
Recommendation	Class	Level
Resting echocardiography is recommended to quantify LV function in all patients with suspected SCAD.	I	C

LV = left ventricular; SCAD = stable coronary artery disease.
This slide corresponds to Table 18 in the full text.

The strongest predictor of long-term survival is LV function. In patients with SCAD as LVEF declines, mortality increases. In the Coronary Artery Surgery Study (CASS) registry, the 12-year survival rates of patients with EF ≥50%, 35–49% and <35% were 73, 54 and 21%, respectively ($P < 0.0001$).[183] Hence, a patient with an LVEF <50% is already at high risk for CV death (annual mortality >3%), even without accounting for additional event risk factors, such as the extent of ischaemia. As a reduced LVEF <50% confers such an important increase in event risk, it may be important not to miss obstructed vessels causing ischaemia in such patients.[184,185]

Eur Heart J 2013;34:2949–3003. doi:10.1093/eurheartj/eht296

Initial diagnostic management of patients with suspected SCAD (1)

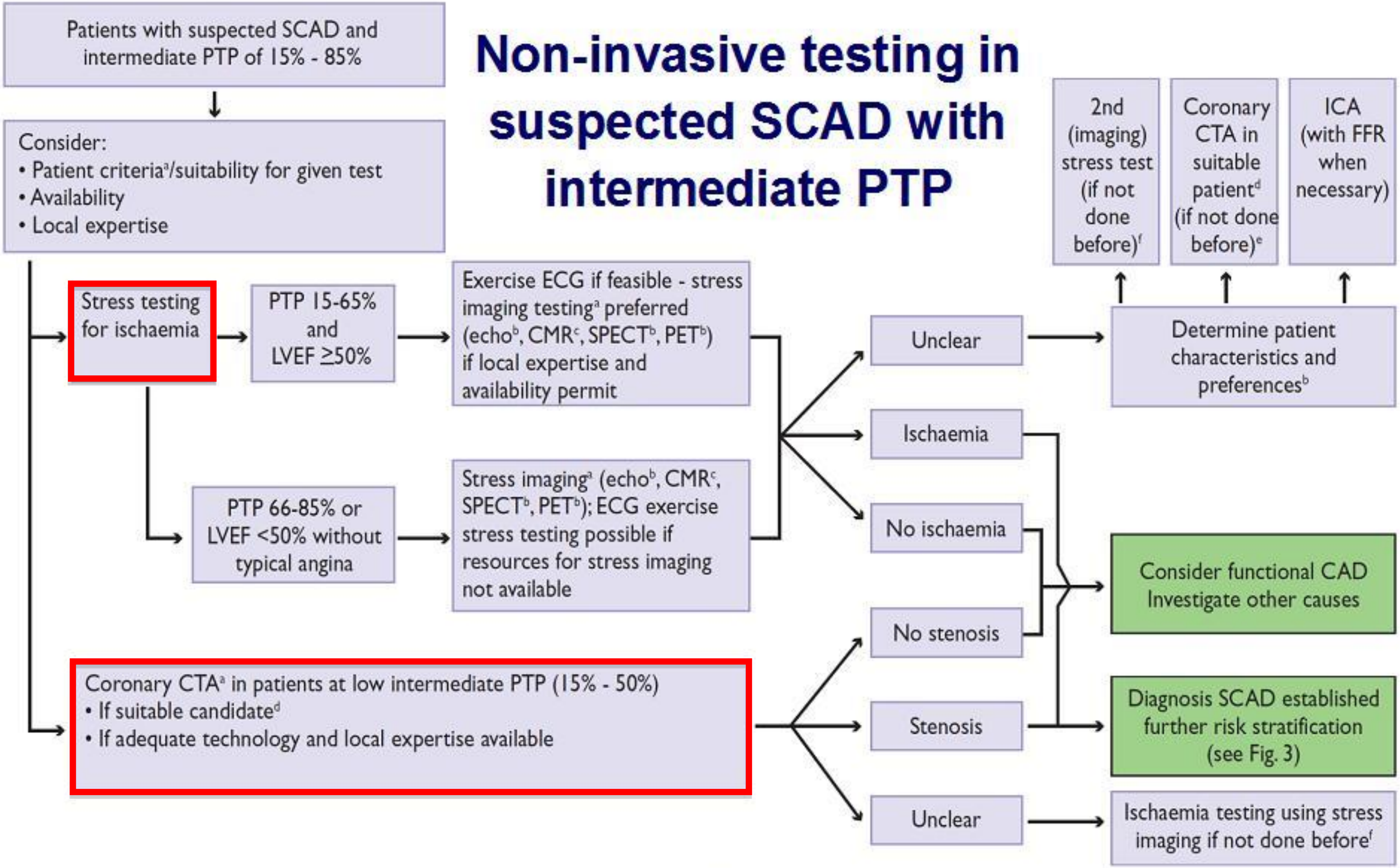


a. May be omitted in very young and healthy patients with a high suspicion of an extracardiac cause of chest pain and in multimorbid patients in whom the echo result has no consequence for further patient management
b. If diagnosis of SCAD is doubtful, establishing a diagnosis using pharmacologic stress imaging prior to treatment may be reasonable.

This slide corresponds to Figure 1 in the full text

[a]May be omitted in very young and healthy patients with a high suspicion of an extracardiac cause of chest pain and in multimorbid patients in whom the echo result has no consequence for further patient management. [b]If diagnosis of SCAD is doubtful, establishing a diagnosis using pharmacological stress imaging prior to treatment may be reasonable.

Non-invasive testing in suspected SCAD with intermediate PTP



a. Consider age of patient versus radiation exposure.
b. In patients unable to exercise use echo or SPECT/PET with pharmacologic stress instead.
c. CMR is only performed using pharmacologic stress.
d. Patient characteristics should make a fully diagnostic coronary CTA scan highly probable (see section 6.2.5.1.2) consider result to be unclear in patients with severe diffuse or focal calcification.
e. Proceed as in lower left coronary CTA box.
f. Proceed as in stress testing for ischaemia box.

This slide corresponds to Figure 2 in the full text.

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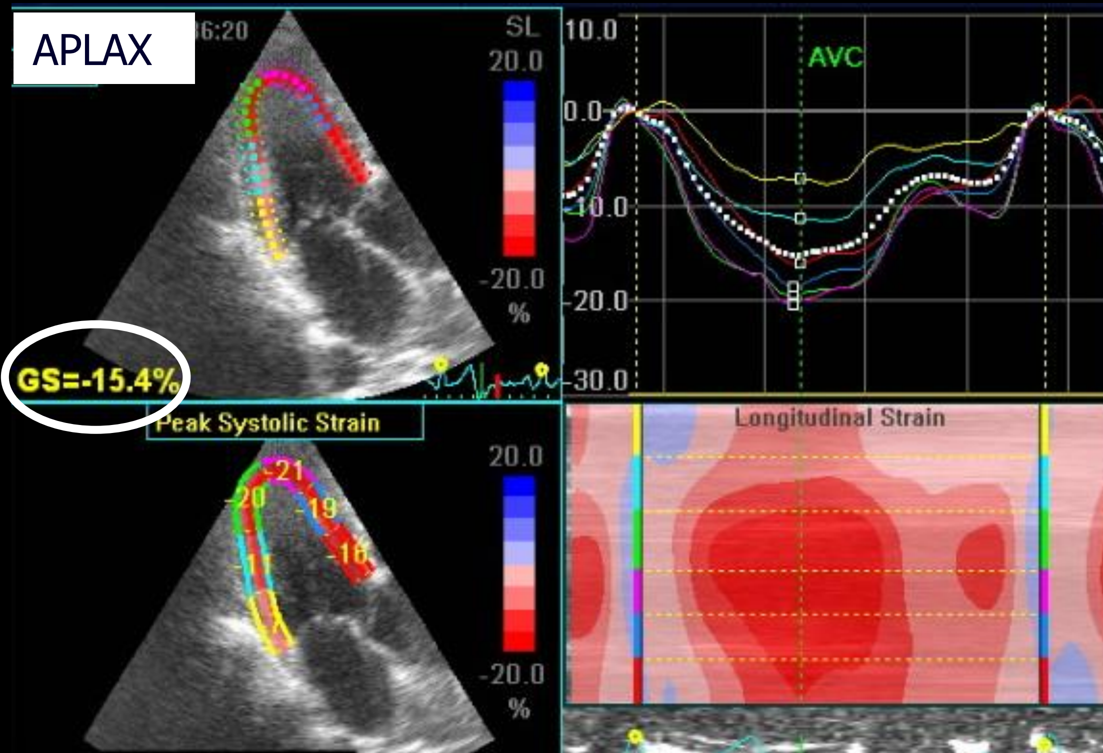
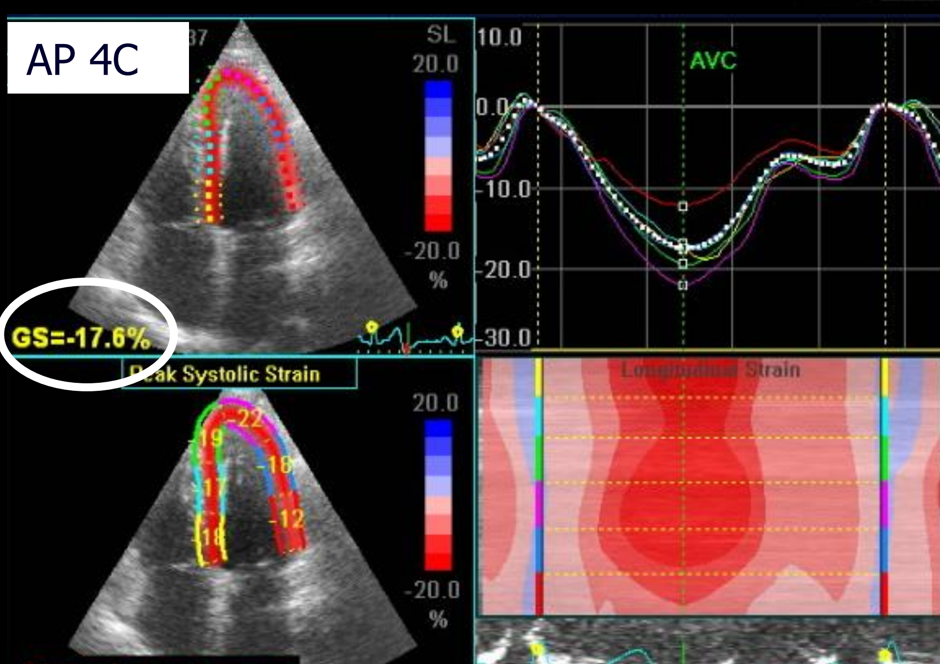
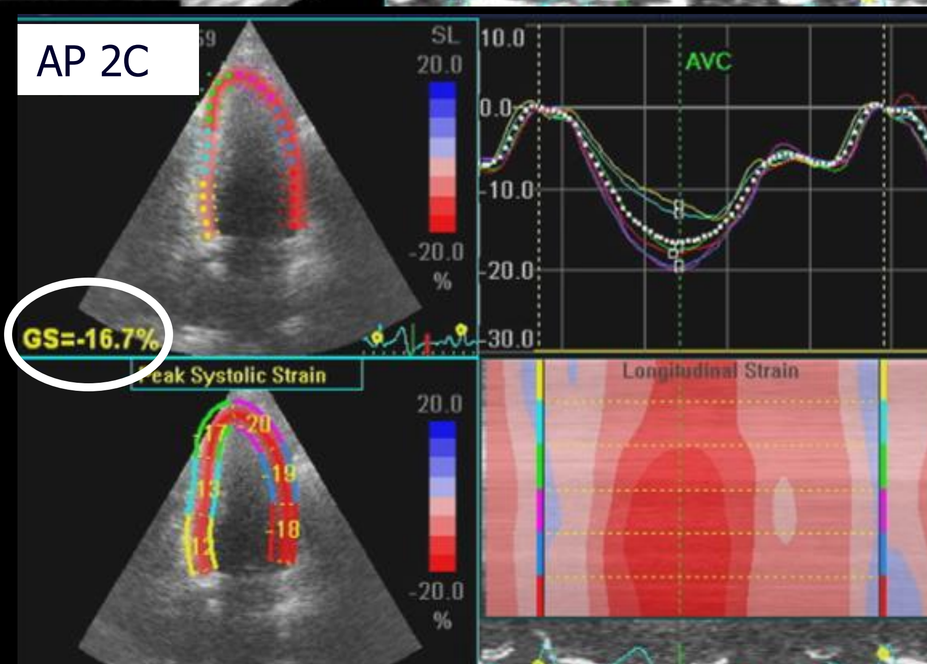
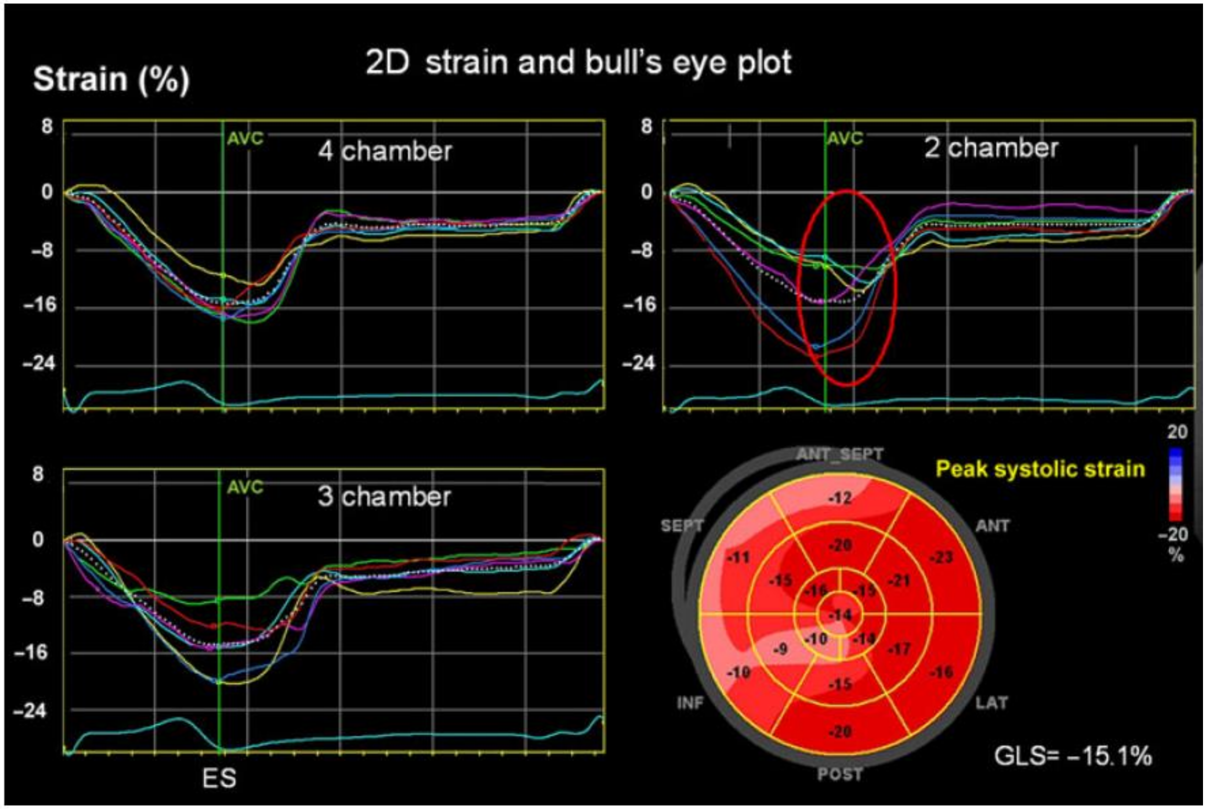
Would resting deformation imaging help?

GLOBAL LONGITUDINAL STRAIN (GLS)



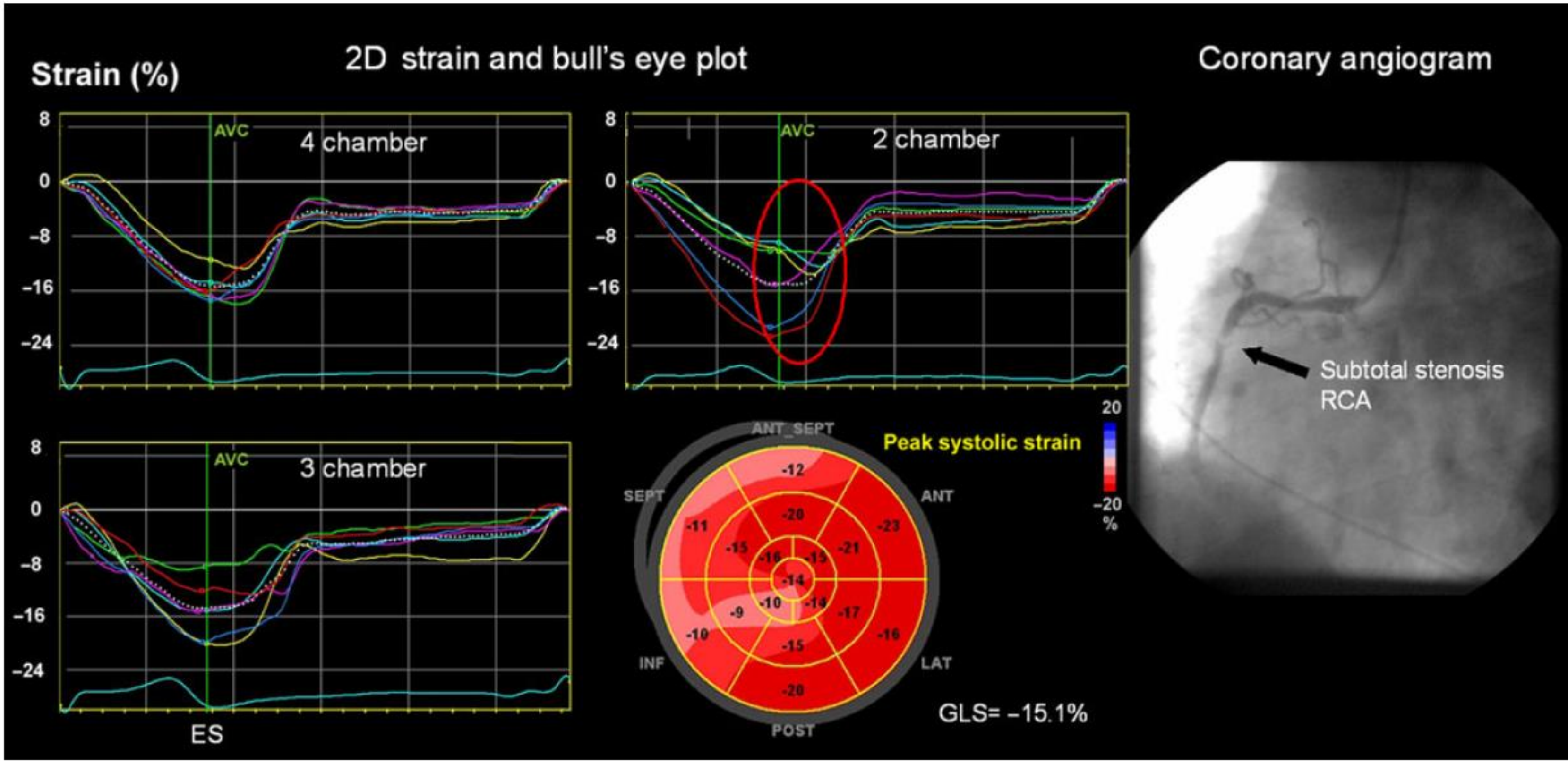






Strain imaging in patient with atypical symptoms, no chest pain and no signs of ischaemia in electrocardiogram. Each trace represents one LV segment. Possible inferior wall hypokinesia on grey scale imaging. Strain imaging showed moderately reduced systolic shortening and marked post-systolic shortening in the inferior wall (red circle).

Smiseth et al, Eur Heart J 2016



Strain imaging in patient with atypical symptoms, no chest pain and no signs of ischaemia in electrocardiogram. Each trace represents one LV segment. Possible inferior wall hypokinesia on grey scale imaging. Strain imaging showed moderately reduced systolic shortening and marked post-systolic shortening in the inferior wall (red circle). The patient was referred for angiography which revealed a subtotal stenosis of the right coronary artery (right panel) and was successfully treated with percutaneous coronary intervention. ES = end systole.

Smiseth et al, Eur Heart J 2016

Myocardial Strain Analysis by 2-Dimensional Speckle Tracking Echocardiography Improves Diagnostics of Coronary Artery Stenosis in Stable Angina Pectoris

Biering-Sorensen et al, Circ Cardiovasc Imaging 2014

Table 3. Echocardiographic Measures

	Patients Without Significant CAD	Patients With Significant CAD	*P* Value
n	186	107	
LVEF, %	59±5	58±4	0.08
GLS 18 segments, %	−18.9±2.6†	−17.3±2.6†	<0.001*†
GLS 12 segments, %	−18.8±2.6†	−17.1±2.5†	<0.001*†

*Echocardiographic measures predicting CAD after adjustment for baseline characteristics (age, sex, diabetes mellitus, and angina type).

†Measures predicting CAD after adjustment for baseline characteristics (age, sex, diabetes mellitus, and angina type), conventional echocardiographic measures (LVMI, E/A ratio, DT, and e′), and Duke score.

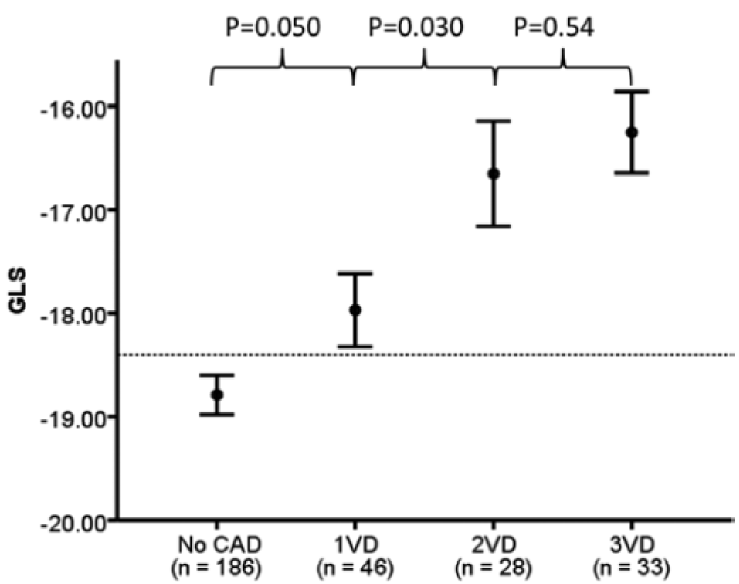
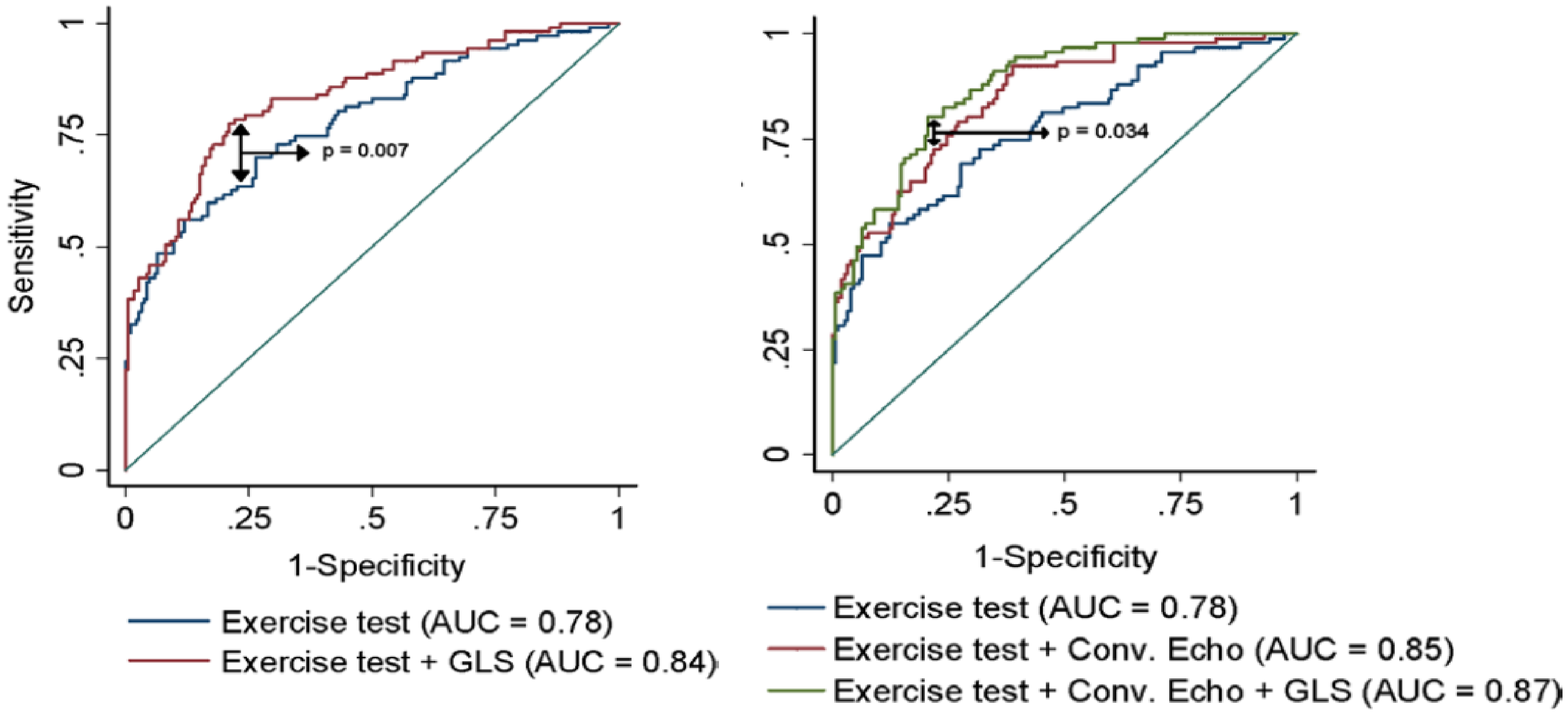


Figure 3. Global longitudinal peak systolic strain (GLS) and severity of coronary artery disease (CAD). Mean GLS for patients stratified according to no CAD, 1-vessel disease (VD), 2VD, and 3VD. Dotted line indicates the cutoff of −18.4%. Error bars represent SEs.

Myocardial Strain Analysis by 2-Dimensional Speckle Tracking Echocardiography Improves Diagnostics of Coronary Artery Stenosis in Stable Angina Pectoris

Biering-Sorensen et al, Circ Cardiovasc Imaging 2014



Detection of Obstructive Coronary Artery Disease Using Peak Systolic Global Longitudinal Strain Derived by Two-Dimensional Speckle-Tracking: A Systematic Review and Meta-Analysis

Liou et al, JASE 2016

Table 4 Summary of diagnostic performance for GLS and strain values

GLS	DOR	Sensitivity (%)	Specificity (%)	PLR	NLR	AUC	GLS, CAD (%)	GLS, no CAD (%)
Overall	8.5	74.4	72.1	2.9	0.35	0.8	−16.5	−19.7
Severe CAD	7.1	73.9	68.3	2.7	0.38	0.75	−16.8	−19.2
Normal LVEF	7.8	74.2	69.8	2.7	0.37	0.8	−16.9	−19.5
No prior IHD/CAD/MI	8.0	75.1	69.9	2.7	0.36	0.80	−16.3	−18.9
GLS (16 segments)	8.5	70.2	75.8	2.9	0.38	0.78	−16.9	−19.3

IHD, Ischemic heart disease; *MI*, myocardial infarction.

CONCLUSIONS

Current evidence supports the use of GLS by speckle-tracking to aid the detection of moderate to severe obstructive CAD in symptomatic patients with intermediate pretest probability.

SUMMARY – II

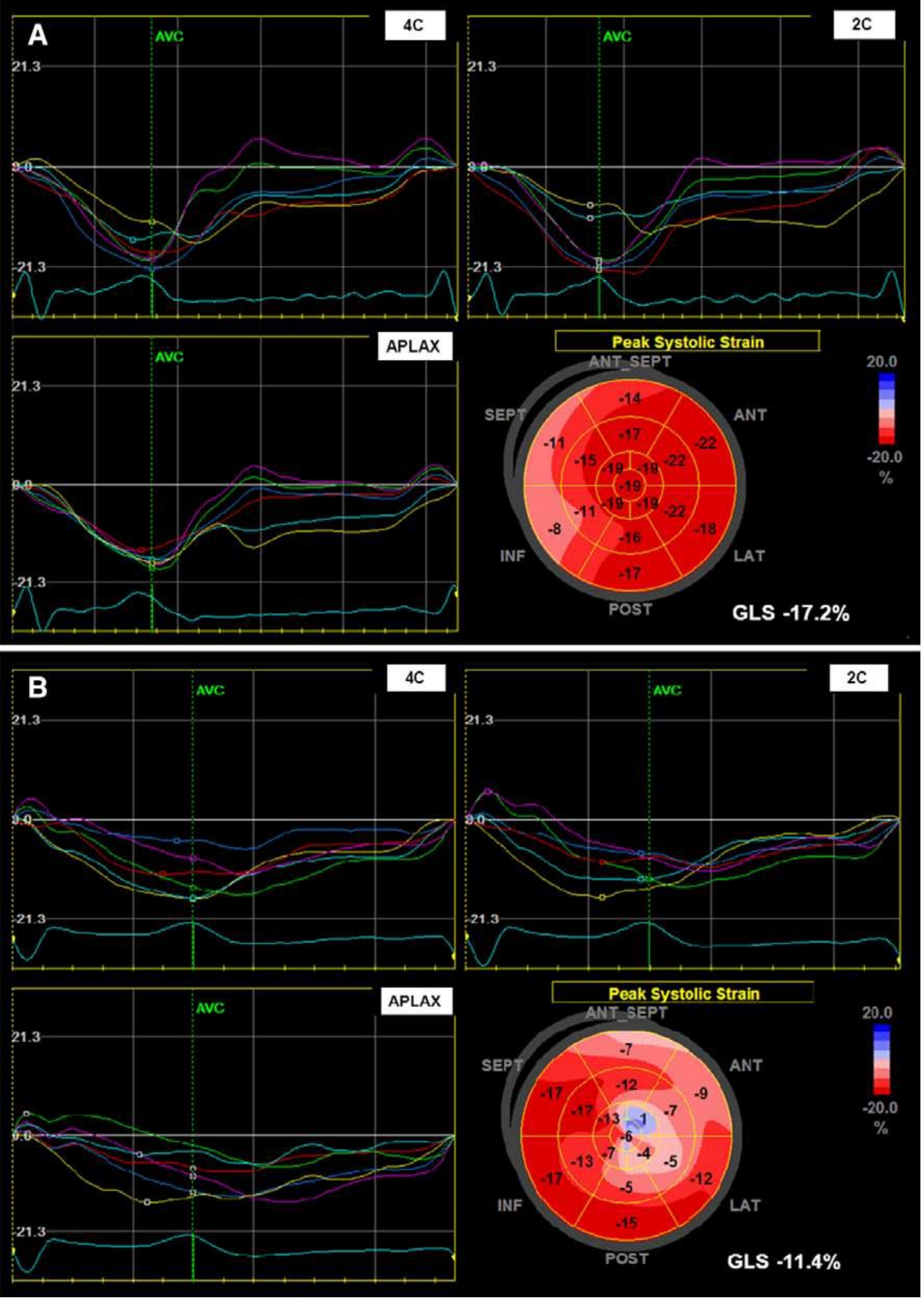
- Speckle tracking echocardiography improves diagnostic of coronary artery stenosis in stable angina pectoris patients with normal EF.

- GLS may complement existing diagnostic algorithms.

- This approach may be particularly helpful if there is no expertise for stress testing, except for exercise ECG.

CLINICAL SCENARIO III

POST-INFARCT REMODELING AND OUTCOME



Association Between Left Ventricular Global Longitudinal Strain and Adverse Left Ventricular Dilatation After ST-Segment–Elevation Myocardial Infarction

Joyce et al, Circ Cardiovasc Img 2014

A patient with acute inferior myocardial infarction. LVGLS was abnormal at −17.2% but remained below (more negative) the cutoff threshold of −15.0%. During the course of 3- and 6-month follow-up, LV end-diastolic volume (EDV) did not increase significantly (134, 139, and 152 mL, respectively).

A patient with acute anterior myocardial infarction. LVGLS was significantly impaired (less negative) at −11.4%. During the course of follow-up, LVEDV increased from 93 mL at baseline to 118 mL at 3 months and 129 mL at 6 months, representing a 39% increase overall.

Prediction of Left Ventricular Remodeling after a Myocardial Infarction: Role of Myocardial Deformation: A Systematic Review and Meta-Analysis

Huttin et al, PlosOne 2016

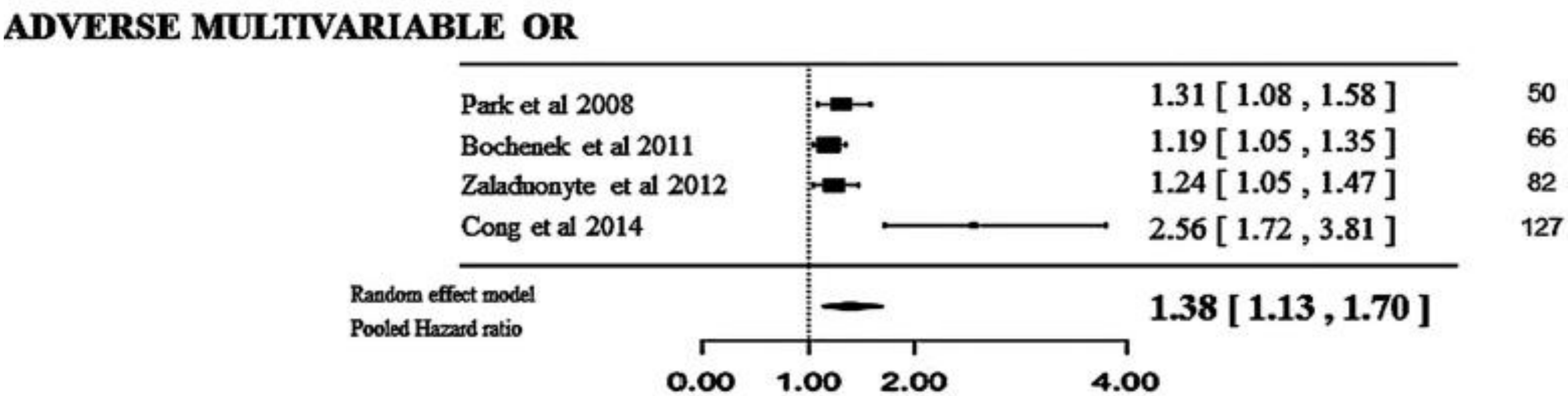


Fig 2. Forest Plot. Pooled Odds Ratios (OR) for the association of global left ventricular peak systolic longitudinal (GLS) strain evaluated in acute phase of STEMI and left ventricular remodeling at follow-up.

Predictive cut-off: -12.8% to -10.2%

for each 1% decrease in 2D GLS (a 1% GLS decrease in absolute value of 2D GLS), the odds were increased by 27% to 38%.

XStrain 4D analysis predicts left ventricular remodeling in patients with recent non-ST-segment elevation myocardial infarction

Antonello D'Andrea [a,*], Donato Mele [b], Eustachio Agricola [c], Enrica Pezzullo [a], Matteo Cameli [d], Andrea Rossi [e], Roberta Esposito [f], Giuseppina Novo [g], Sergio Mondillo [d], Roberta Montisci [h], Sabina Gallina [i], Eduardo Bossone [j], Maurizio Galderisi [f], On behalf of Working Group on Echocardiography of the Italian Society of Cardiology

International Journal of Cardiology 206 (2016) 107–109

Table 1
Demographic and clinical characteristics of the study population (n = 75).

Variable	Remodeled (n = 32)	Non-remodeled (n = 43)	P value
Age (years)	62.2 ± 9.3	61.2 ± 8.3	NS
Male/female	23/9	30/13	NS
Body surface area (m^2)	1.87 ± 0.12	1.88 ± 0.15	NS
Heart rate (b/m)	67.4 ± 10.9	63.4 ± 10.9	NS
Systolic blood pressure (mm Hg)	128.5 ± 22.4	131.5 ± 27.4	NS
Diastolic blood pressure (mm Hg)	88.5 ± 12.3	85.5 ± 11.5	NS
Diabetes mellitus (%)	41.5	25.5	< 0.001
Smoker (%)	44.2	46.2	NS
Systemic hypertension (%)	25.5	27.7	NS
Hypercholesterolemia (%)	56.5	53.6	NS
STEMI/NSTEMI	13/15	18/22	NS
Killip class > I (%)	22.2	19.2	NS
Time from ACS to PCI (days)	7.5 ± 9.3	7.1 ± 8.6	NS
Culprit coronary artery undergoing PCI			
LAD (%)	45.3	42.4	NS
RCA (%)	32.5	33.3	NS
LCX (%)	22.2	24.3	NS
Pharmacological therapy			
ACE-inhibitors/ARB (%)	76.6	77.9	NS
Beta-blockers (%)	72.2	74.8	NS
Statins (%)	88.3	90.3	NS
Aspirin (%)	98.2	98.5	NS
Clopidogrel or prasugrel or ticagrelor (%)	97.4	97.8	NS

ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blockers; LAD: left anterior descending; RCA: right coronary artery; LCX: left circumflex.

LV negative remodeling was defined as lack of improvement of LV function (at least 5% of LV EF), with increase in LV ESV of greater than or equal than 15% during the follow-up.

In a stepwise forward multiple logistic regression analysis, after adjusting for potential determinants, diabetes mellitus [odds ratio (OR) 2.1, 95% confidence interval (CI) 1.5–3.1, $P < 005$], peak of troponin I after PCI (OR 1.31, 95% CI 1.12-1.58, $P < 0.005$), GLS at baseline (OR: 4.5; 95% CI: 3.1–5.5; $p < 0.0001$), and the lack of GLS improvement after PCI (OR: 1.33, 95% CI: 1.15–1.77; $P < 0.01$) were powerful independent predictors of negative LV remodeling at follow-up. At the ROC curve analysis a GLS value ≤ 12% predicts negative LV remodeling at follow up with a sensitivity and a specificity of 84.7% and 88.8% respectively (AUC: 0.91; 95% C.I. 0.80–0.95; $p < 0.0001$).

Prediction of All-Cause Mortality and Heart Failure Admissions From Global Left Ventricular Longitudinal Strain in Patients With Acute Myocardial Infarction and Preserved Left Ventricular Ejection Fraction

Ersboll et al, JACC 2013

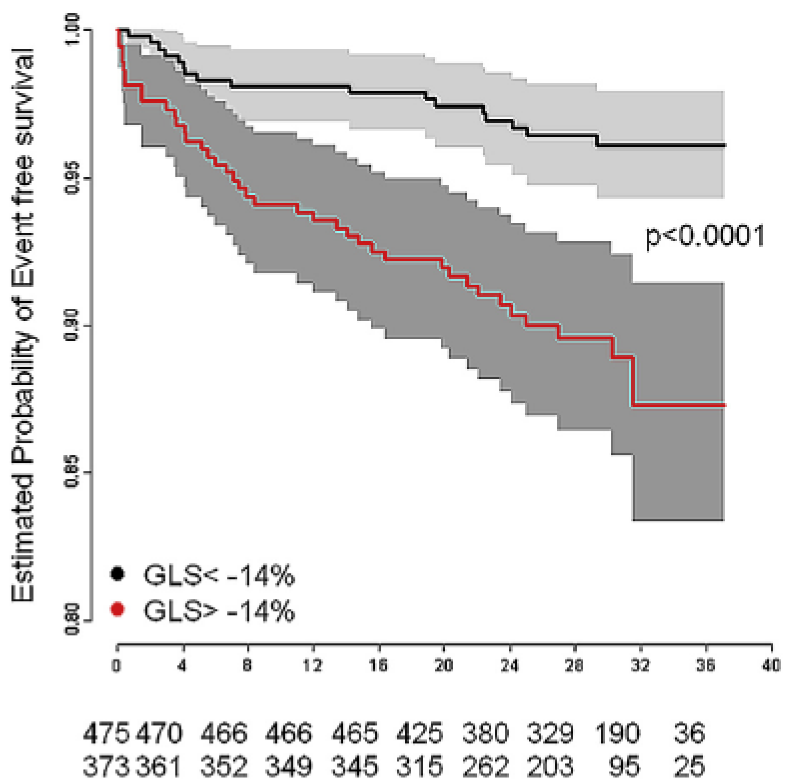


Figure 1 **Kaplan-Meier Curve Showing Freedom From the Combined Endpoint in 848 Patients With LVEFs >40% After Myocardial Infarction**

Patients with global longitudinal strain (GLS) $> -14\%$ ($n = 373$) had increased risk for the combined endpoint of all-cause mortality and heart failure admission ($p < 0.001$). Time indicates months after echocardiography in relation to the myocardial infarction.

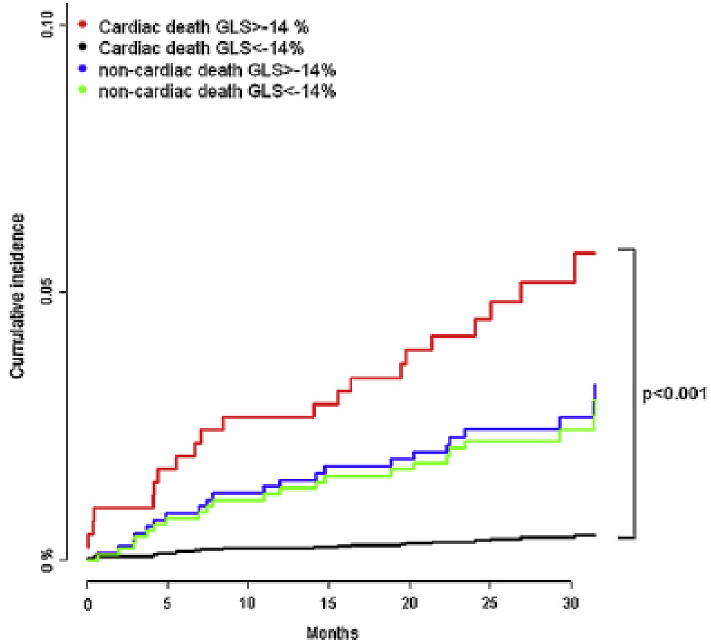


Figure 2 **Cumulative Incidence Curve for Cardiac Death With Adjustment for Competing Risk**

The red and black curves depict cardiac death stratified according to global longitudinal strain (GLS) $>-14\%$ ($p < 0.001$). The blue and green curves show death from other causes stratified according to GLS $>-14\%$, with no significant prognostic value of GLS.

SUMMARY – III

- Early evaluation of LV GLS after acute myocardial infarction treated with pPCI could be helpful to predict adverse LV remodeling and outcome in pts with preserved EF.

- Preliminary data show the capacity to predict reverse LV remodeling after STEMI and LV remodeling in general after NSTEMI.

CLINICAL SCENARIO IV

TREATMENT (ICD, CRT)

Strain Echocardiography Improves Risk Prediction of Ventricular Arrhythmias After Myocardial Infarction

Haugaa et al, JACC Jmg 2013

Table 3. **Cox Regression Analysis for Ventricular Arrhythmias in 569 Patients After Myocardial Infarction**

	Univariate		Multivariate	
	HR (95% CI)	p Value	HR (95% CI)	p Value
Age, per yr	1.0 (1.0–1.1)	0.06		
LVEDV, per 10-ml increase	1.2 (1.0–1.3)	0.03		
LVESV, per 10-ml increase	1.3 (1.1–1.5)	<0.001		
LVEF, per 5% decrease	1.4 (1.1–1.7)	0.004	1.2 (0.9–1.5)	0.26
GLS, per 1% increase	1.2 (1.1–1.4)	<0.001	1.0 (0.8–1.2)	0.79
Mechanical dispersion, per 10-ms increase	1.8 (1.4–2.2)	<0.001	1.7 (1.2–2.5)	<0.01
PSSI, per 1%	1.1 (1.0–1.1)	<0.001		

CI = confidence interval; HR = hazard ratio; other abbreviations as in Tables 1 and 2.

Multicenter study
569 pts >40 days after acute MI

Mechanical dispersion predicted VA also in pts with EF>35% and NSTEMI

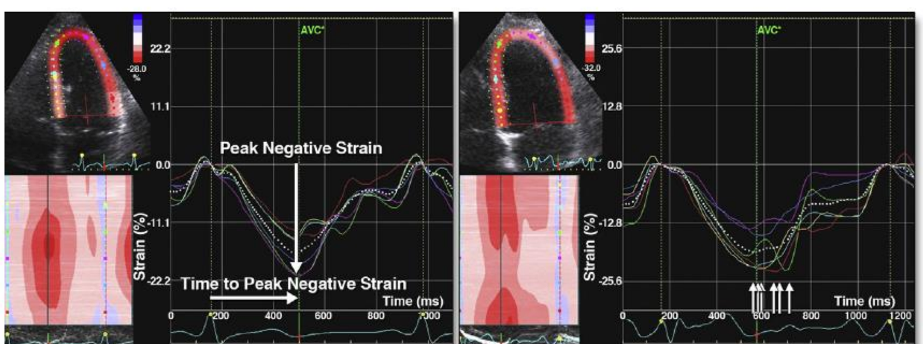
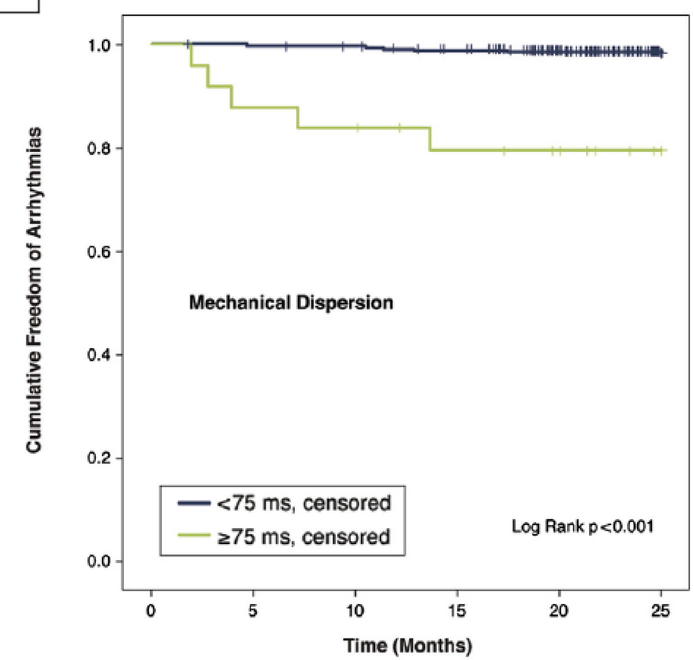


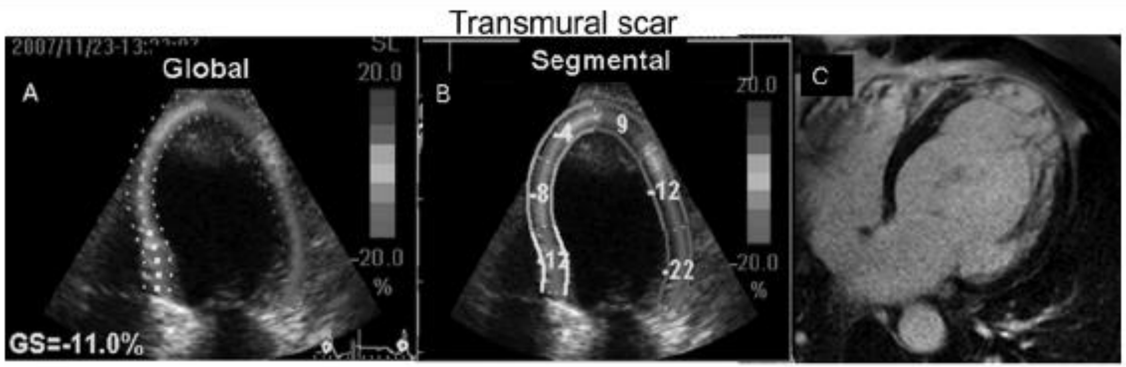
Figure 1. **Strain Curves in Patients After MI**

Strain curves from the apical 4-chamber view in a patient after myocardial infarction (MI) without arrhythmic events during follow-up **(left)** and a patient after MI who died of ventricular fibrillation during follow-up **(right)**. White vertical arrows indicate the timing of peak negative strain. The patient who died of ventricular fibrillation showed a more dispersed contraction pattern. The dispersion is also shown in the color-coded images below the 2-dimensional 4-chamber views. The patient who died of ventricular fibrillation **(right)** showed a more inhomogenous color coding compared with the survivor **(left)**.



Effects of global longitudinal strain and total scar burden on response to CRT in patients with ischaemic dilated cardiomyopathy

D'Andrea A et al. *Eur J Heart F 2009; 11: 58-67*



Average Global longitudinal strain (GLS) correlates closely with MRI total scar burden (r=0.64, P<0.001).

GLS and radial intraventricular dyssynchrony were powerful independent determinants of response to CRT.

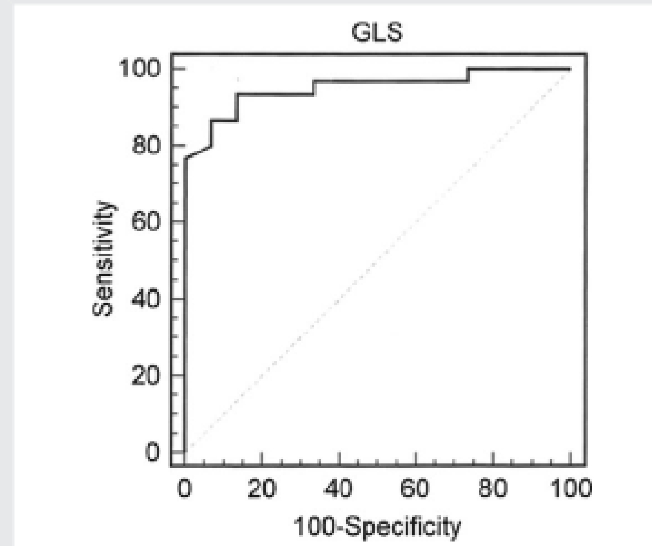
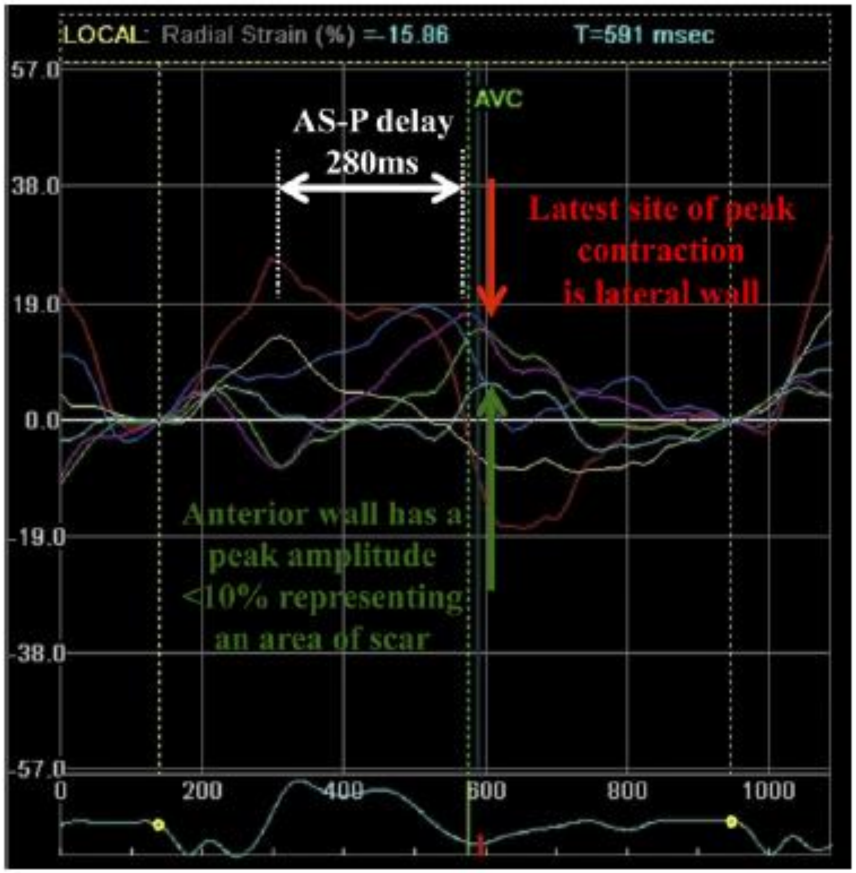


Figure 4 Interactive plots diagrams (receiver-operating characteristic curve analyses) of global longitudinal strain (GLS) in dilated cardiomyopathy patients. A GLS $<12\%$ showed a sensitivity and a specificity, respectively, of 84.7% and 88.8% [area under curve 0.88; 95% CI 0.80–0.95; $P < 0.0001$) to predict response to cardiac resynchronization therapy.

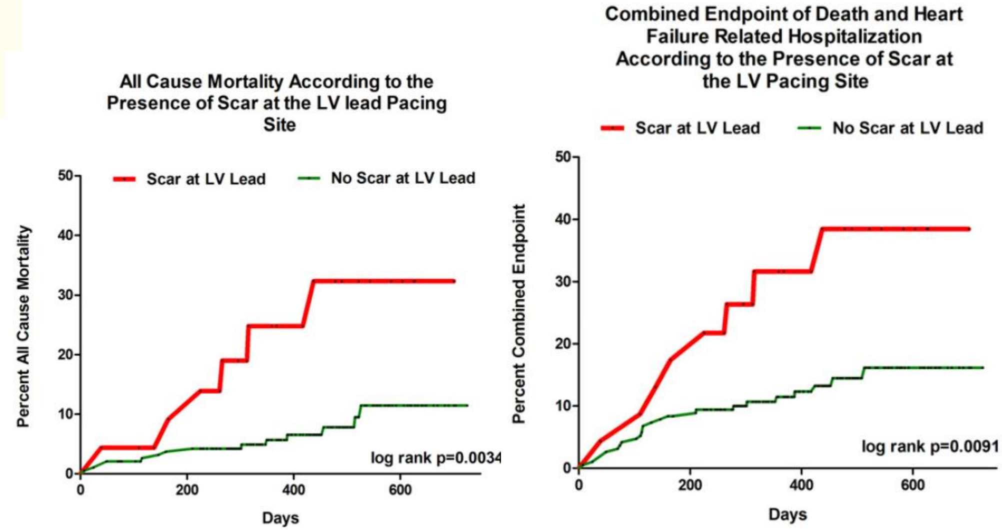
Targeted Left Ventricular Lead Placement to Guide Cardiac Resynchronization Therapy

The TARGET Study: A Randomized, Controlled Trial

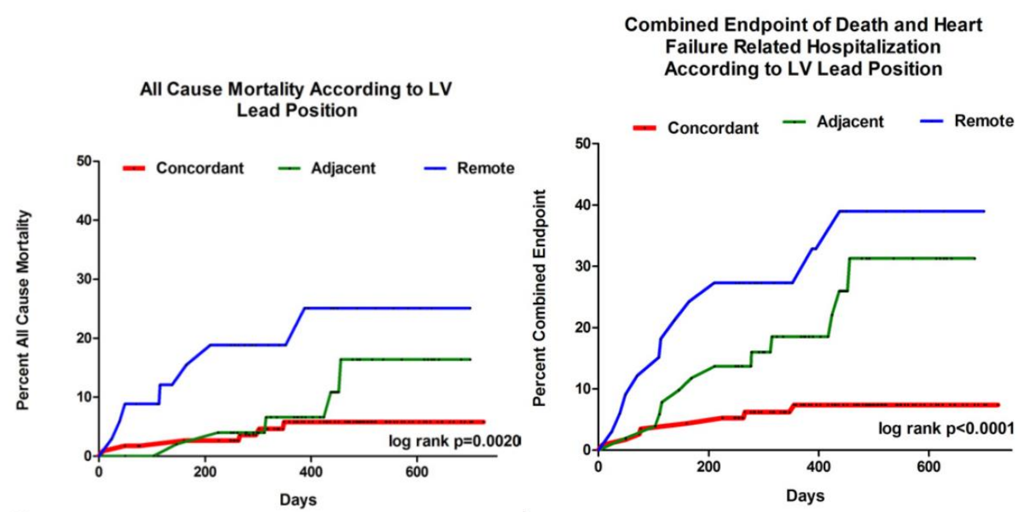
Khan FZ et al., J Am Coll Cardiol 2012;59:1509–18



Effect of Scar



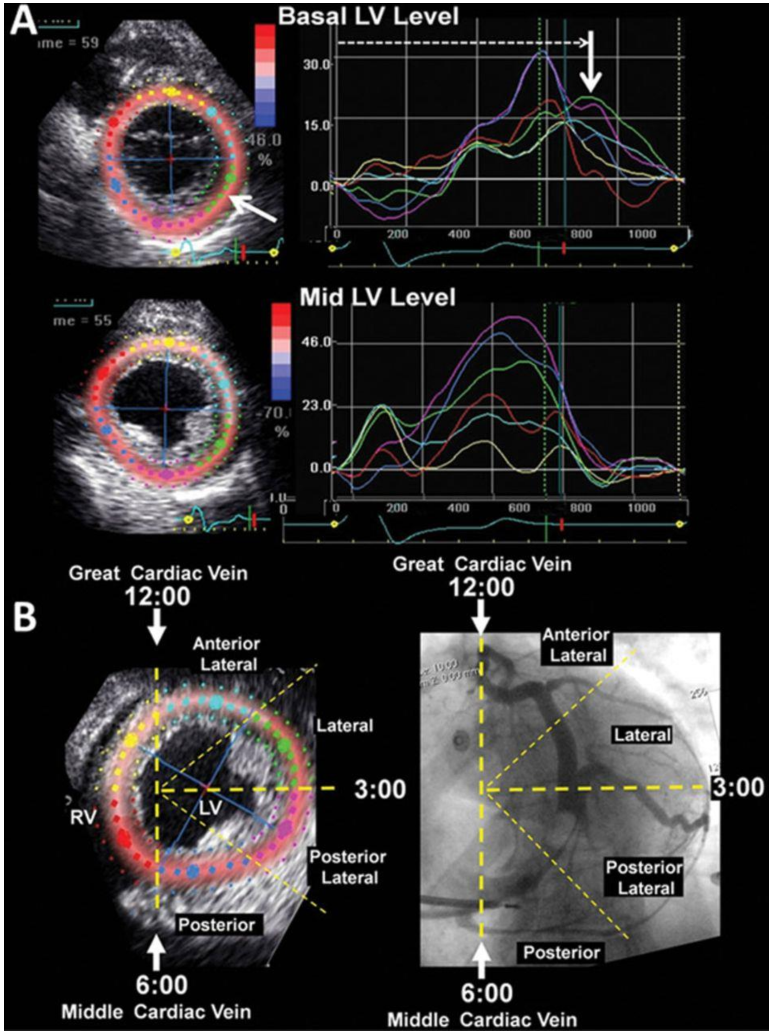
Effect of LV Lead Position



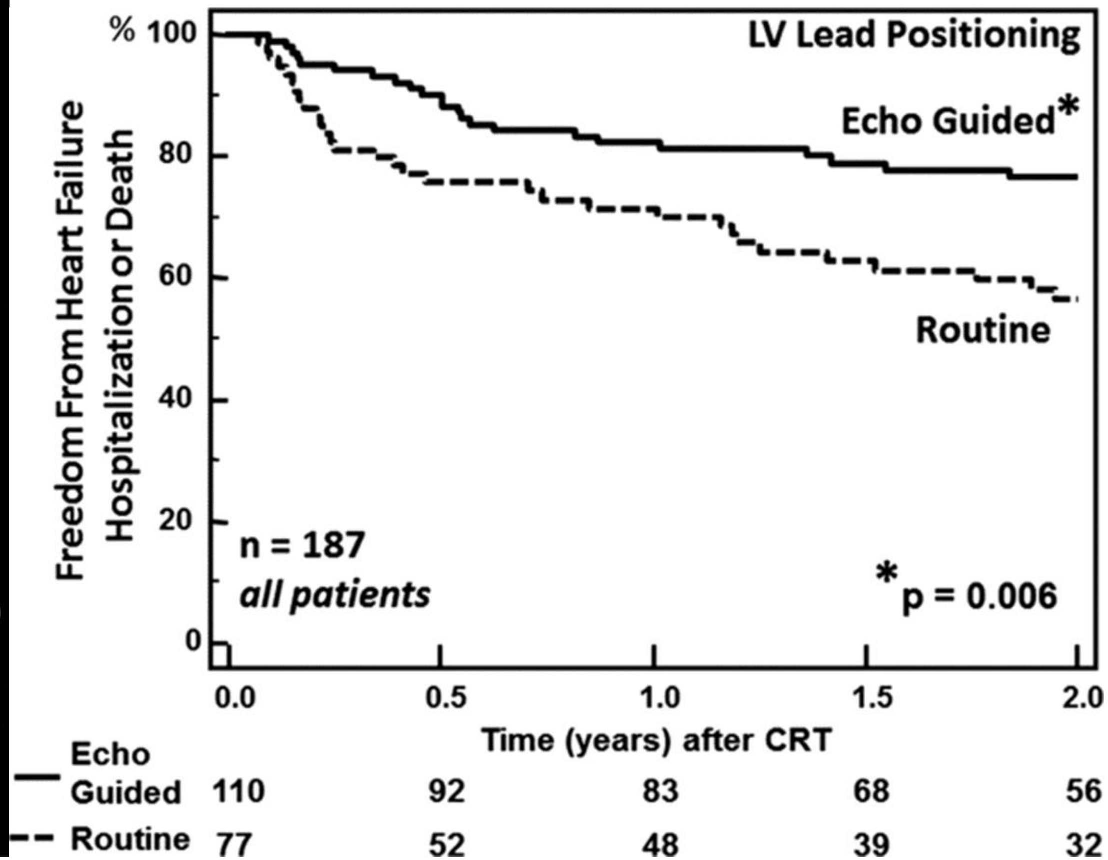
Echocardiography-Guided Left Ventricular Lead Placement for Cardiac Resynchronization Therapy

Results of the Speckle Tracking Assisted Resynchronization Therapy for Electrode Region Trial

Saba S et al. Circ Heart Fail. 2013;6:427-434



STARTER: prospective, double-blind, randomized controlled trial



CONCLUSIONS

1. Strain imaging has additive value in several clinical scenarios of the ischemic heart disease, through the evaluation of global and regional LV function, and should be used as a complementary tool to LV-EF, especially when LV-EF is preserved.

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2. Acute chest pain, stable angina pectoris, prediction of post-infarct LV remodeling & CRT may benefit of strain imaging in current clinical practice. Rifinement of the ICD indication is a future challenging task.

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2. Acute chest pain, stable angina pectoris, prediction of post-infarct LV remodeling & CRT may benefit of strain imaging in current clinical practice. Rifinement of the ICD indication is a future challenging task.

3. Use of strain imaging is helpful especially if access to other cardiac imaging techniques is difficult.