

Speckle imaging in stress echocardiography

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- Stress echocardiography has been well validated as a sensitive and specific test for the diagnosis of coronary artery disease
- Assessment of myocardial ischemia by echocardiography rests on the detection of systolic wall motion abnormalities, namely, reduced wall thickening.

- Over the past decade, numerous studies have documented its prognostic value in a wide variety of patient populations and have demonstrated the utility of a semi-quantitative, but subjective, approach to interpretation
- This semi-quantitative approach has included assessment of stress-induced changes in wall motion score index, left ventricular end-systolic volume, and ejection fraction, all of which have been shown to be markers of the extent and severity of disease. These markers have been valuable in identifying patients at highest risk of cardiovascular events

- However, there are important limitations:
- Although the reproducibility of the subjective interpretation of stress echocardiograms at a single, high-volume center with experienced readers is very good, the variability of interpretation of stress echocardiography increases if multiple centers are involved or if the interpreter lacks experience
- Second, there are inherent limitations in a technique which relies on the development of stress-induced abnormalities of wall motion and thickening. The extent of coronary disease may be underestimated compared to techniques that involve perfusion or diastolic function, as these abnormalities occur prior to the development of systolic wall motion abnormalities in the ischemic cascade.
- The assessment is semi-quantitative

- Various techniques proposed to improve accuracy of stress echocardiography have included
- peak exercise imaging
- three-dimensional imaging
- myocardial contrast perfusion imaging
- combined stress modalities
- methods to quantify regional wall motion, including acoustic quantification and color kinesis, which involve tracking the blood and myocardial tissue interface

peak exercise imaging

Table 1 Image quality of peak and postexercise views according to the number of clearly visualized segments by view and number of segments obtained from the 16-segment model

	Peak exercise	Postexercise	P value
Apical 4-chamber (%)	5.9 ± 0.7	5.9 ± 0.5	NS
Apical 2-chamber (%)	5.9 ± 0.7	5.9 ± 0.5	NS
Parasernal long-axis (%)	5.1 ± 1.3	5.1 ± 1.1	NS
Parasernal short-axis (%)	5.1 ± 1.1	5.3 ± 1.5	<.001
No. of segments obtained	15.7 ± 1.7	15.9 ± 1.1	<.05
≥13 Segments obtained	18 (3%)	10 (1.7%)	NS
≥10 Segments obtained	8 (1.4%)	4 (0.7%)	NS

NS, Not significant.

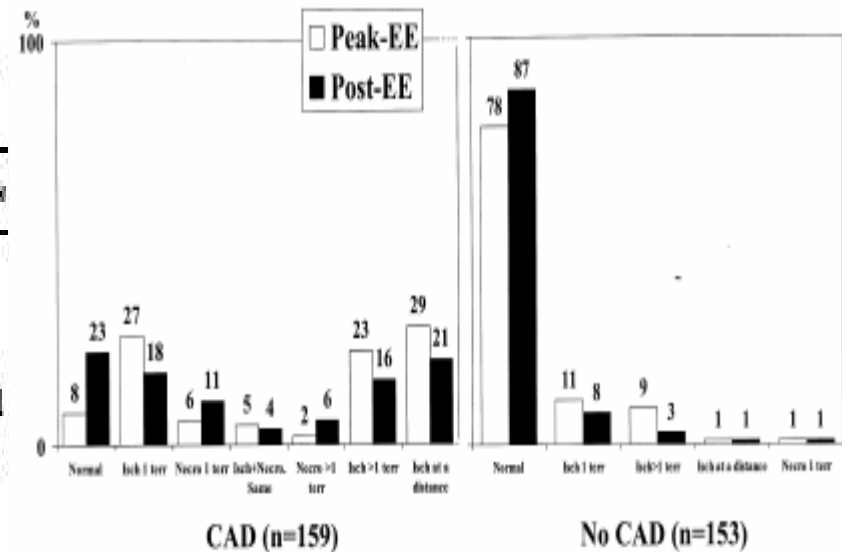


Figure 1 Percentage of patients with and without coronary artery disease having normal results, ischemia in one or more than one territory, necrosis in one or more than one territory, ischemia and necrosis affecting same territory, and ischemia at distance at peak echocardiography and after exercise echocardiography.

Sensitivity 92% vs 77%, p<0.001

Specificity 87% VS 77% P=NS

Peteiro, et a, JASE 2004

myocardial contrast perfusion imaging

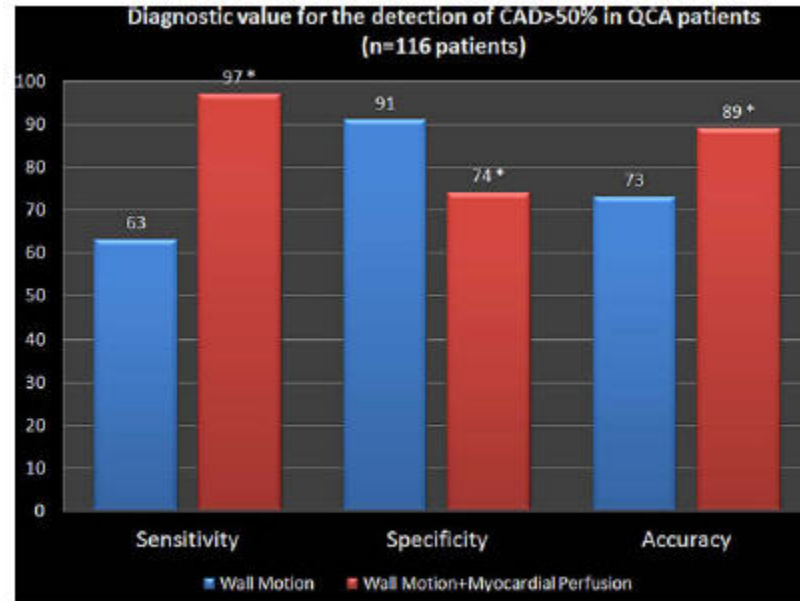


Figure 3 Diagnostic value for WM with and without MPI for detection of CAD > 50% in QCA patients (n = 116). *P < .05 versus WM criteria.

Gaibazzi, et al, JASE 2009

combined stress modalities

- Atropine augmentation in dobutamine stress echocardiography: role and incremental value in a clinical practice setting

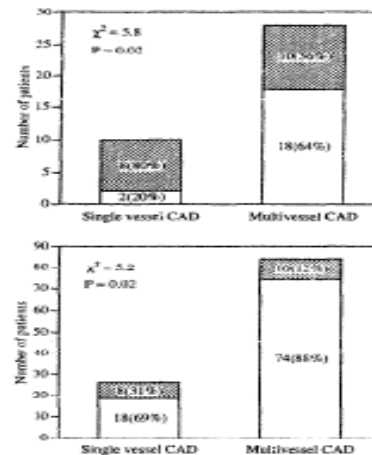
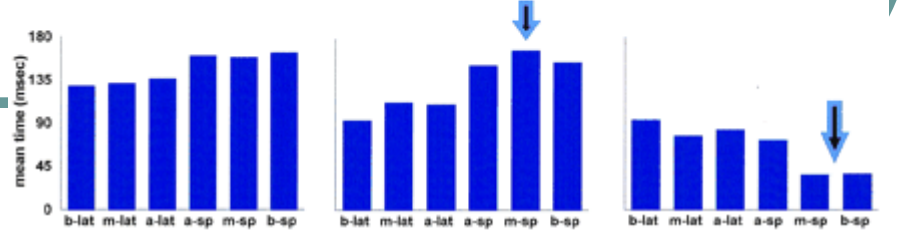
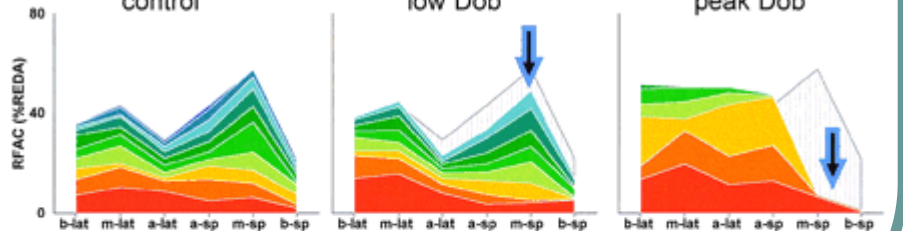
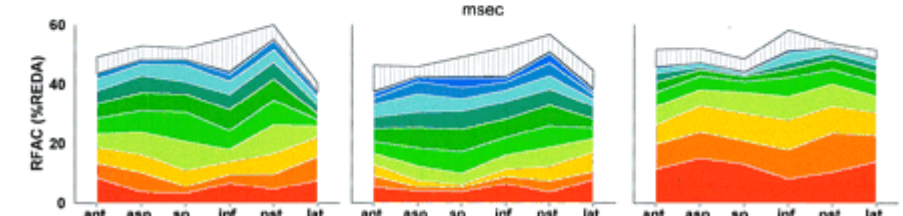
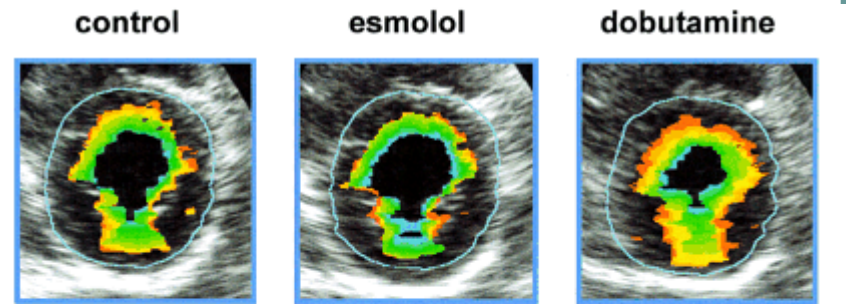
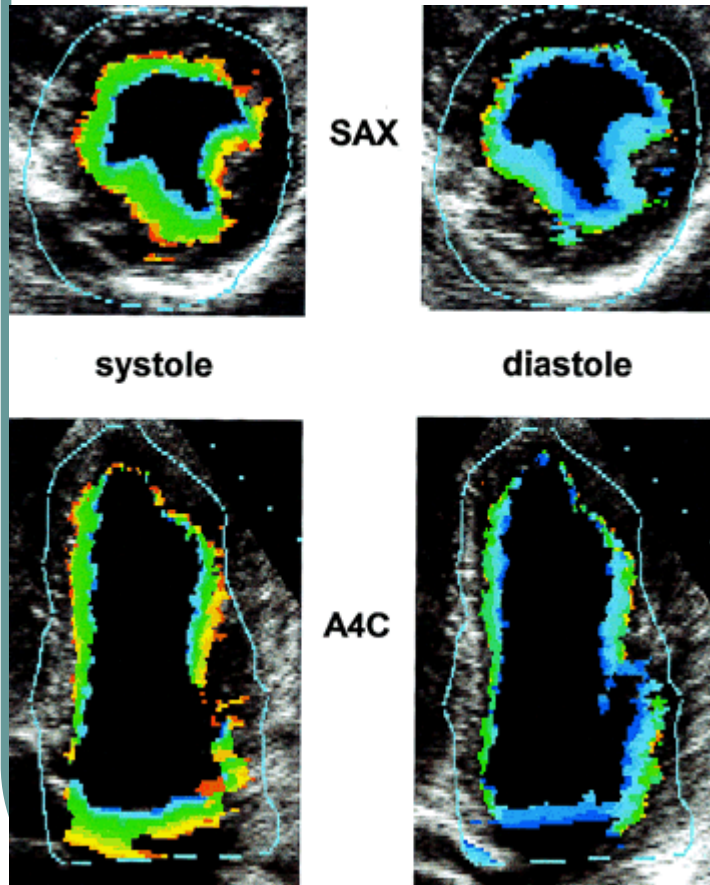


Figure 1. Top. Distribution of angiographic coronary artery disease (CAD) in 38 group II patients with inducible ischemia during dobutamine-atropine stress echocardiography. Ischemia developed after atropine administration in a significantly higher proportion of patients with single-vessel coronary artery disease. **Bottom.** Among the 119 patients with angiographic coronary artery disease and stress-inducible ischemia, atropine was used relatively more frequently in patients with single-vessel coronary artery disease. **Open bars** = ischemia before atropine; **hatched bars** = ischemia after atropine.

color kinesis



Mor Avi, et al circulation 1997

- A quantitative technique would be able to address problems relating to the learning curve, variability between sites, and perhaps even increase the sensitivity of the test by being able to identify smaller areas of ischemia or less ischemic segments.

Tissue Doppler Echocardiography

- High-spatial resolution and high temporal resolution
- does not involve edge detection
- permits quantification of long-axis function, and as this movement is parallel with the direction of subendocardial fibers, abnormal longitudinal function may be more sensitive to ischemia than radial function.
- high temporal resolution and is able to identify temporal dispersion in contraction that may occur with myocardial ischemia.

Regional Diastolic Function by Pulsed Doppler Myocardial Mapping for the Detection of Left Ventricular Ischemia During Pharmacologic Stress Testing

A Comparison With Stress Echocardiography and Perfusion Scintigraphy

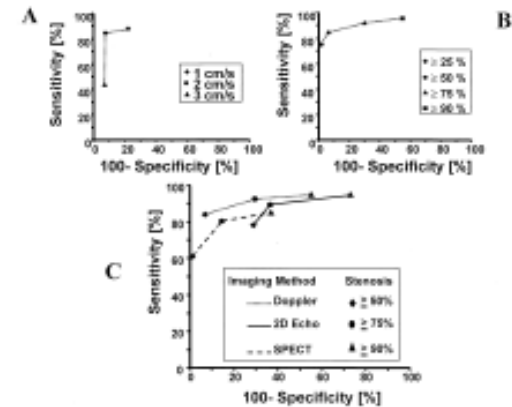
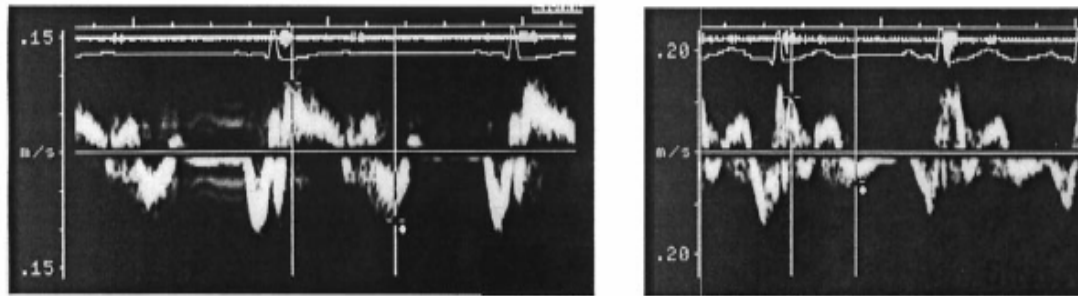
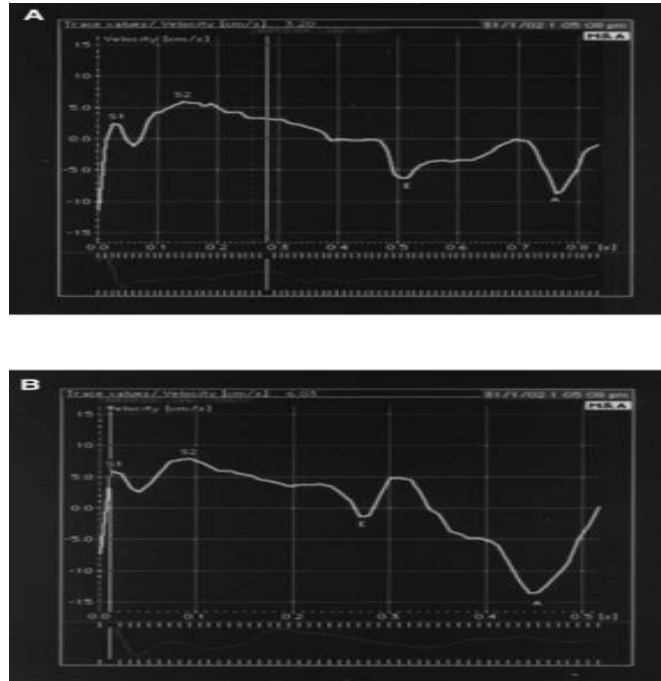


Figure 4. Top: Receiver operating curve (A) for the optimal level of V_e reduction demonstrating clearly that a 2 cm/s decrease has the best level of discrimination. Receiver operating curve (B) for the diagnostic accuracy of stress induced V_e reduction in relation to incremental angiographic luminal narrowing. Optimal discrimination is at $\geq 25\%$ stenosis. Bottom (C): Receiver operating curve comparing the three noninvasive imaging modalities during stress tests each with reference to incremental angiographic luminal narrowing. Pulsed Doppler myocardial mapping has the highest discriminatory power with 0.90 area under the curve (12) as compared with 0.77 in two-dimensional echocardiography and 0.81 in SPECT. A $\geq 50\%$ angiographic stenosis yields the optimal discriminatory power for PMD and stress echocardiography and a $\geq 75\%$ luminal narrowing for SPECT. Doppler = PMD; PMD = pulsed Doppler myocardial mapping; SPECT = perfusion scintigraphy; 2D Echo = two-dimensional echocardiography.

■ echocardiography with doppler tissue imaging



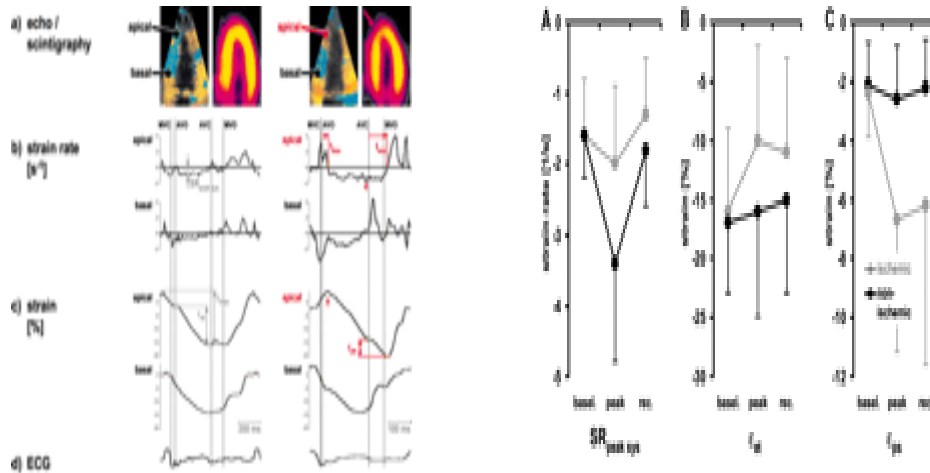
- **Figure 2.** Myocardial velocities obtained from patient with 80% stenosis of right coronary artery. Peak late systolic myocardial velocity (S2) at rest (A) is 6 cm/s and during dobutamine infusion (B) 8 cm/s. Increment in myocardial velocity is 33.3%. A, Late diastolic velocity; E, early diastolic velocity; S1, early systolic velocity.

- Strain is a dimensionless parameter which expresses the deformation of the muscle as a fractional change from its original dimension. SR is the change in strain over time. Tissue Doppler velocities can be used to obtain an estimate of strain rate and from that, of strain. These measurements have been validated both in vitro and in vivo, with interobserver and intraobserver variability of in vivo strain and SR of less than 15% and provide an objective assessment of regional wall motion

- Prior studies have shown that longitudinal strain and SR are very sensitive markers of ischemia
- Acute ischemia induces both early systolic thinning and a delay in the onset of systolic thickening. There is a progressive decrease in the rate and degree of maximal systolic thickening.
- Concomitant with the decrease in maximal systolic thickening, an abnormal ischemia-related relative thickening occurs after aortic valve closure, which has been termed post-systolic thickening (PST). This is actually a result of pathological systolic thinning occurring during acute ischemia, which appears as paradoxical diastolic thickening.
- Strain and SR measurements have also been shown to differentiate between stunned myocardium and ischemic myocardium.

- The strain rate parameters had no major change from base to apex, and had higher diagnostic accuracy compared to conventional wall motion assessment.

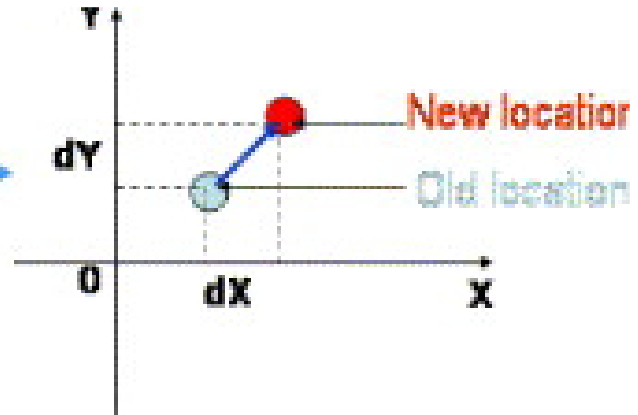
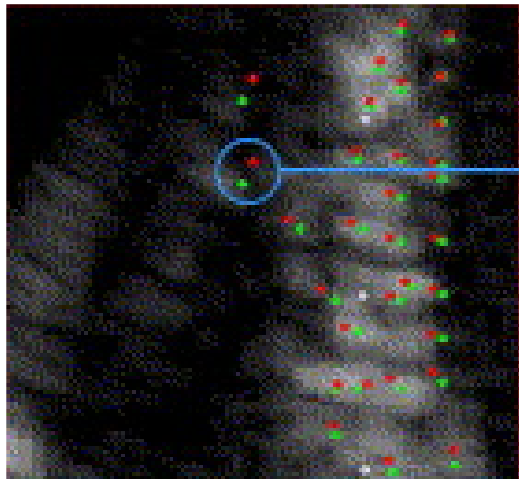
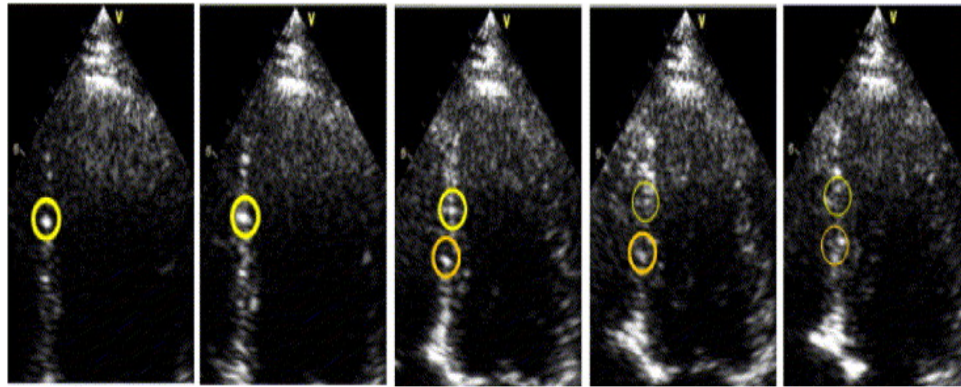
SRI

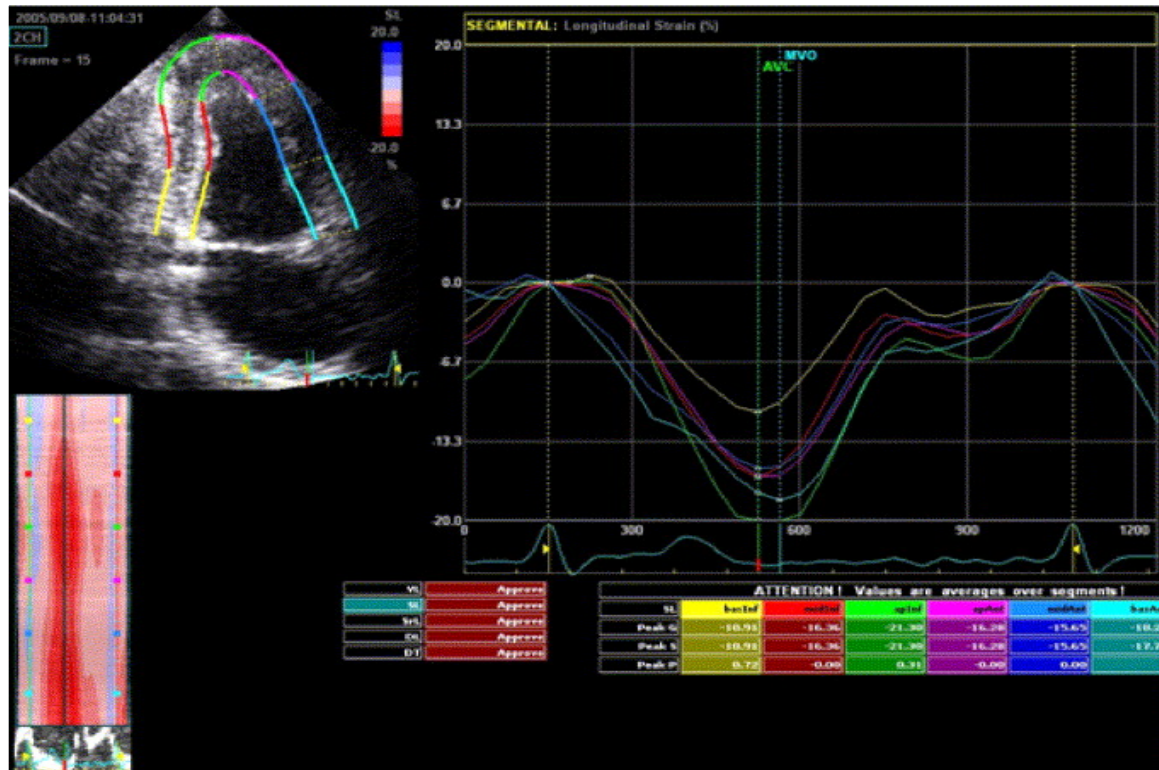


- Strain-rate increase 0.8 ± 1.6 s⁻¹ versus -2.0 ± 1.1 s⁻¹, $P < 0.05$ and strain ($-16 \pm 7\%$ versus $-10 \pm 8\%$, $P < 0.05$) were significantly reduced (both $P < 0.01$) compared with nonischemic. (Postsystolic shortening (PSS) was found in all ischemic segments. The ratio of PSS to maximal segmental deformation was the best quantitative parameter to identify stress-induced ischemia. Compared with conventional readings, SRI curved M-mode assessment improved sensitivity/specificity from 81%/82% to 86%/90%.

- A major limitation of current TDE and TDSE is that peak amplitudes, and to some extent phase (timing), of velocity and strain variables are influenced by the angle of the incident ultrasound beam with the myocardial wall. This restricts imaging to the apical projections wherein the operator attempts to align the myocardial wall parallel to the ultrasound beam; however, this is not always possible.
- the complex 3-dimensional deformation of the heart during the cardiac cycle may not be adequately captured by investigating velocity and strain only in the longitudinal direction. This limitation may impact the ability of this method to accurately detect inducible ischemia.

- Non-Doppler, two dimensional (2D) speckle image processing is a newer technique for obtaining strain and strain rate measurements. It is based on automatic tracking of natural acoustic markers. These markers are stable acoustic speckles (that result from ultrasound wave backscatter), that are statistically equally distributed throughout the myocardium.
- Current available software allows spatial and temporal image processing with recognition and selection of such elements on ultrasound image. The geometric position of these speckles changes from frame to frame with the surrounding tissue motion. The geometric shift of each speckle represents local tissue movement
- By tracking these speckles, 2 dimensional tissue velocity, strain and strain rate can be calculated



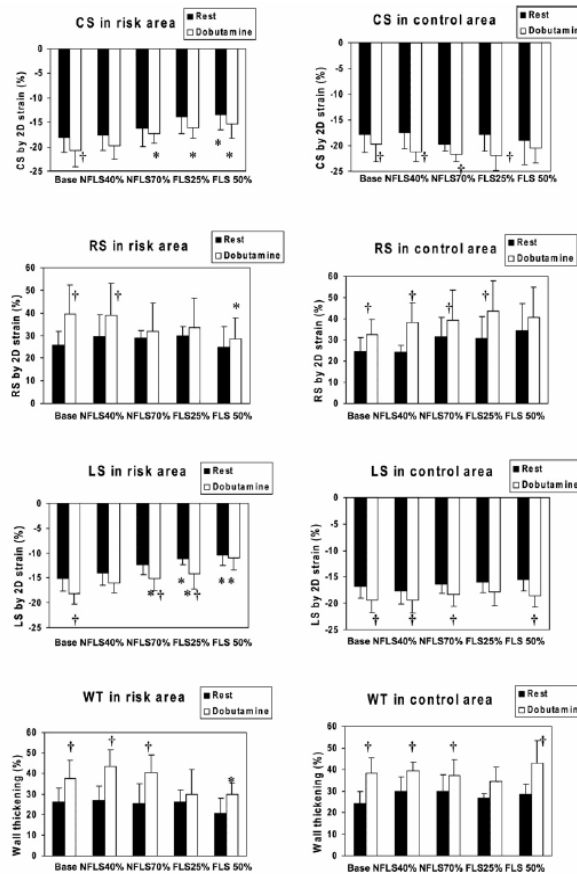


- Non-Doppler 2D strain imaging is simple to perform. It requires only one cardiac cycle to be acquired; further processing and interpretation can be done after image data acquisition. Since it is not based on tissue Doppler measurements, images are easier to obtain as they are angle independent - it is not necessary for the main motion vector to be parallel to the beam.
- The currently available software allows a bull's eye strain map to be created, which may be an important tool in localizing ischemic changes.

- The clinical application of non-Doppler 2D strain imaging has been studied. It has been shown that 2D strain correlates well with tissue-Doppler derived strain parameters and accurately identifies infarcted myocardial segments
- 2D strain has also been used to calculate global longitudinal strain, which has been shown to be an important indicator of left ventricular systolic function

2D strain during stress echocardiography

- Reant et al assessed 2D strain for detection of ischemia during dobutamine stress echocardiography in open chest pigs. They measured peak systolic longitudinal, radial and circumferential strain at rest and during dobutamine infusion at various degrees of coronary artery stenosis. They found that circumferential and longitudinal strains are decreased at rest in presence of flow limiting stenosis and during dobutamine in non flow limiting stenosis. Radial strain was decreased in the presence of severe flow limiting stenosis during dobutamine



Myocardial Strains Measured by 2D Strain in RA and CA at Rest and During Dobutamine Stress

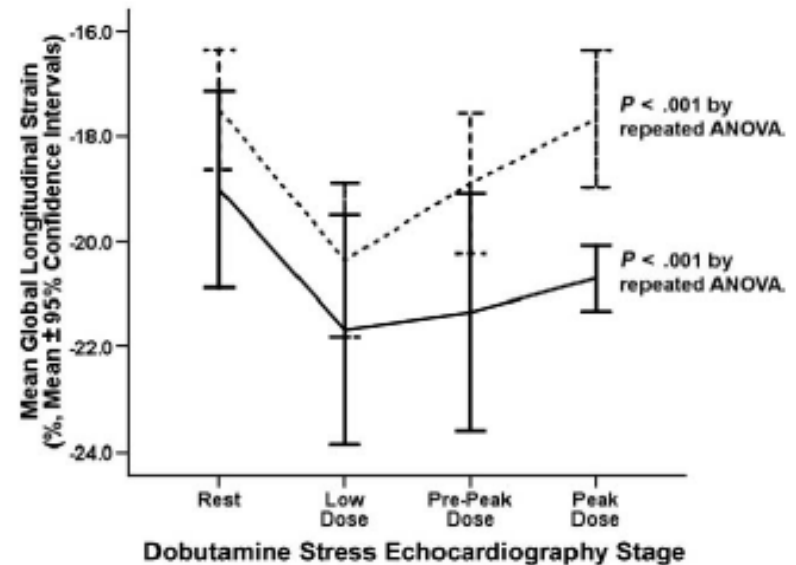
Incremental value of 2-dimensional speckle tracking strain imaging to wall motion analysis for detection of coronary artery disease in patients undergoing dobutamine stress echocardiography

Table II. Two-dimensional strain parameters during dobutamine stress echocardiography in the derivation study population

Variable	CAD (-) (n = 14)	CAD (+) (n = 48)	P*
Mean global longitudinal strain (%)			
Rest	-19.1 ± 2.9	-16.3 ± 2.4	.001
Peak stress	-21.7 ± 3.0	-15.7 ± 2.9	<.001
Global circumferential strain (%)			
Rest	-20.3 ± 3.5	-19.9 ± 4.1	.75
Peak stress	-25.2 ± 5.7	-19.1 ± 5.6	.005
Mean radial strain (%)			
Rest	46.0 ± 14.7	41.6 ± 12.9	.34
Peak stress	52.4 ± 14.0	38.1 ± 14.0	.008

CAD (-), No significant CAD; CAD (+), significant CAD.

*P values by unpaired Student *t* test between CAD (-) and CAD (+).



Values of global longitudinal strain at each dobutamine stress echocardiography stage

	Rest	Low Dose	Pre-Peak Dose	Peak Dose
— No significant CAD	-19.0 ± 2.8	-21.7 ± 3.3*	-21.3 ± 2.9*†	-20.7 ± 0.8†
--- Significant CAD	-17.5 ± 2.4	-20.4 ± 3.1*	-18.9 ± 2.8*	-17.7 ± 2.7

Mean global longitudinal strain for patients with and without significant CAD at 4 different stages of dobutamine stress echocardiography. **P* < .05 versus corresponding mean global longitudinal strain at rest with Bonferroni correction (within group); †*P* < .05 between mean global longitudinal strain at corresponding dobutamine stress echocardiography stage (between group).

Table IV. Sensitivities, specificities, and accuracies of different analysis methodologies during peak dobutamine stress echocardiography in detecting significant CAD

Variable	Sensitivity (%)	Specificity (%)	Accuracy (%)
Mean radial strain	78.3	57.1	70.3
Global circumferential strain	73.9	78.6	75.7
Mean global longitudinal strain	84.2	87.5	85.2
Expert wall motion analysis	76.0	92.9	82.1
Combination mean radial strain and expert wall motion analysis	95.7	57.1	81.1
Combination global circumferential strain and expert wall motion analysis	82.6	78.6	81.1
Combination mean global longitudinal strain and expert wall motion analysis	100	87.5	96.3

- Although there has been a focus on assessment of systolic abnormalities, ischemia also affects diastole.
- Akin to global systolic dysfunction, regional diastolic dysfunction could exist in the absence of global diastolic dysfunction and that a certain critical mass of regional diastolic dysfunction resulted in global diastolic dysfunction
- Liang et al reported altered diastolic strain rates in the setting of ischemia at rest
- diastolic strain rates seemed more specific and a combination of diastolic and systolic mechanics provided the highest accuracy for prediction of CAD

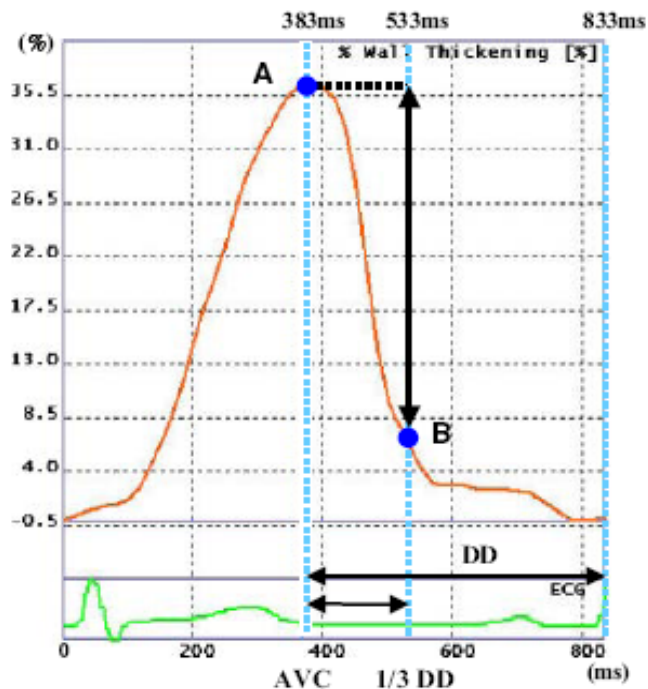


Figure 1 Transverse Strain Curve and SI-DI of Normal Control

Both strain values at aortic valve closure (A) and at one-third of diastole duration (B) were measured. The strain imaging diastolic index (SI-DI) was calculated as: $(A - B)/A \times 100\%$. 1/3 DD = one-third of diastole duration; AVC = aortic valve closure; DD = diastole duration.

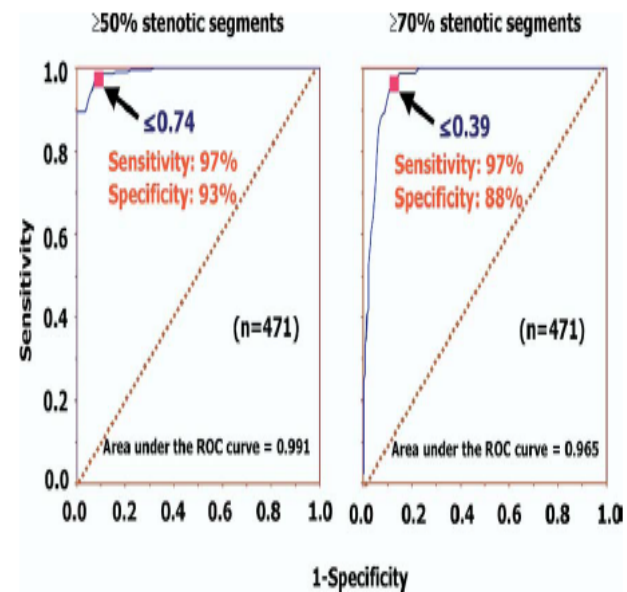


Figure 4 Sensitivity and Specificity of SI-DI Ratio 5 Min After Treadmill Exercise for $\geq 50\%$ and $\geq 70\%$ Stenotic Segments

Sensitivity and specificity of the strain imaging diastolic index (SI-DI) ratio 5 min after treadmill exercise for the detection of $\geq 50\%$ and $\geq 70\%$ coronary stenosis. Sensitivity and specificity were derived from the receiver-operator characteristic (ROC) curve.

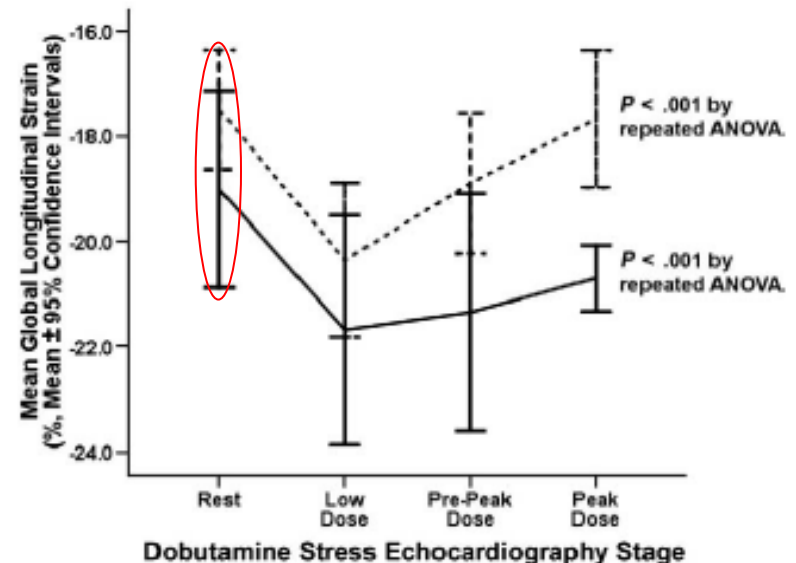
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Mean global longitudinal strain for patients with and without significant CAD at 4 different stages of dobutamine stress echocardiography. **P* < .05 versus corresponding mean global longitudinal strain at rest with Bonferroni correction (within group); †*P* < .05 between mean global longitudinal strain at corresponding dobutamine stress echocardiography stage (between group).

Rest studies

Hsin-Yueh Liang,	Stable AP, Cath	SR+S Segmental	SRs+SRe	93%/93%
Jin-Oh Choi,	Stable +UA AP, Cath	LS, Global+segmental	LS-Basal segments	79%/79% High risk
Gaetano Nucifora,	Asympt Risk factors MSCT	Global S, SR	GLOBAL	83%-77%

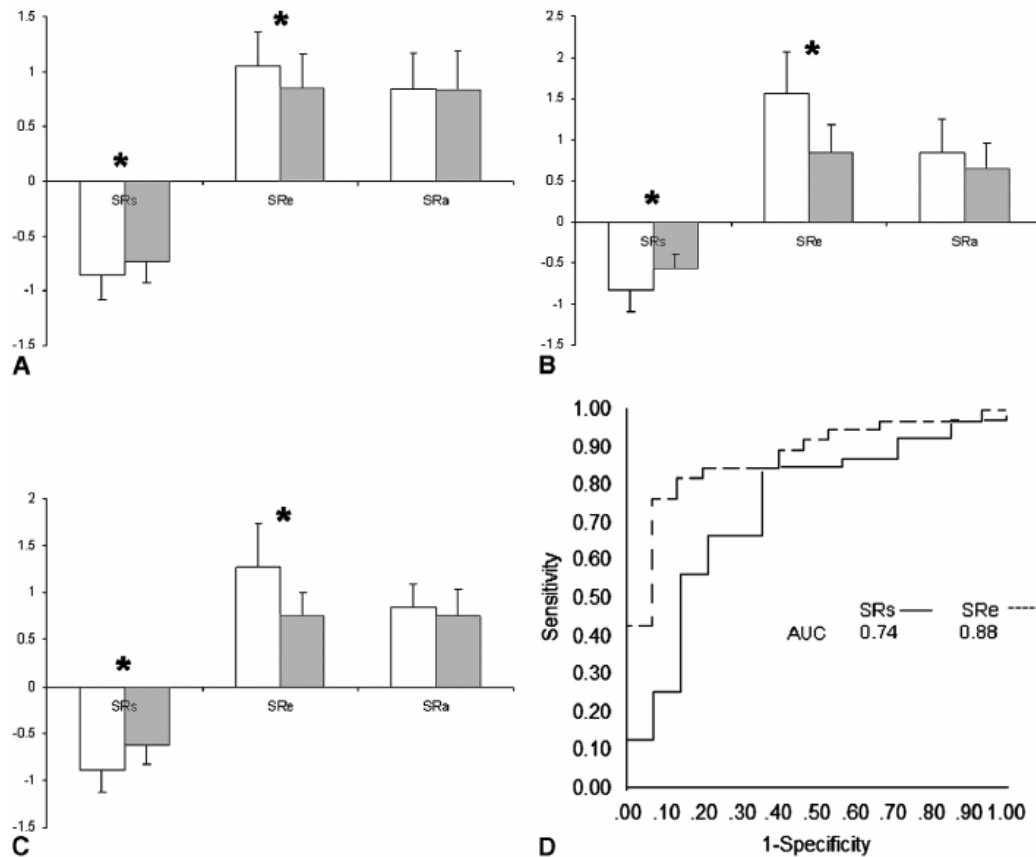


Figure 2. Deformation variables for normal and ischemic (shaded bars) segments in territories of the (A) left coronary, (B) circumflex, and (C) right coronary arteries. *p < 0.05. (D) Receiver-operating characteristic curves for SRs and SRe. AUC = area under the curve.

ROC curve analysis for the detection of high-risk CAD

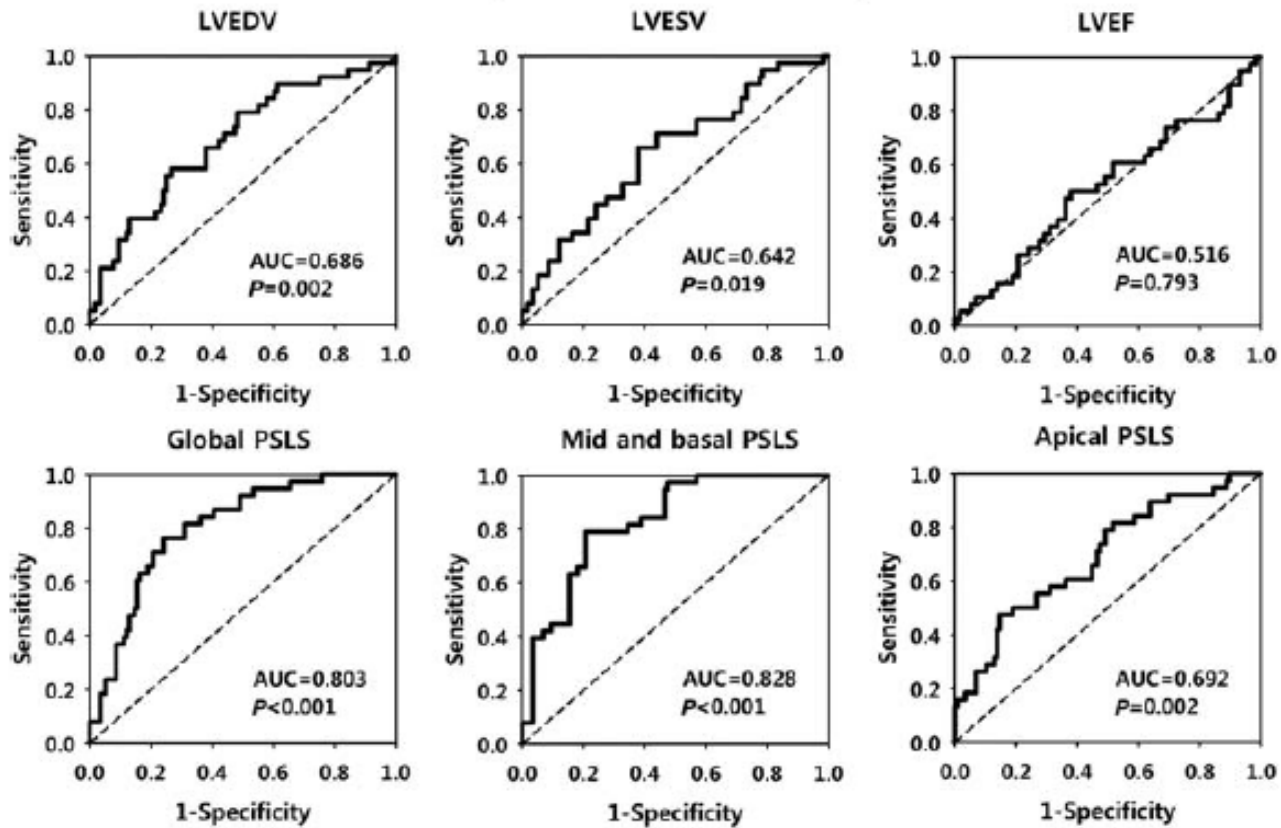
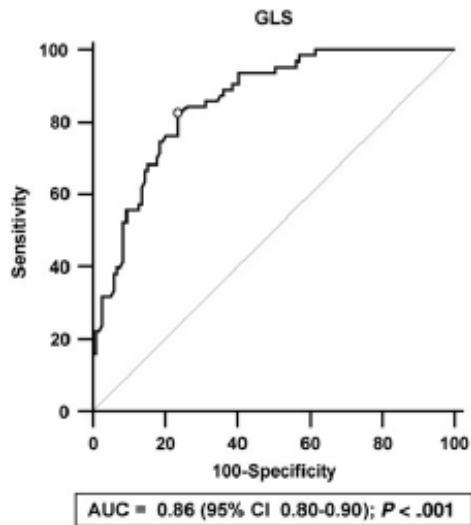


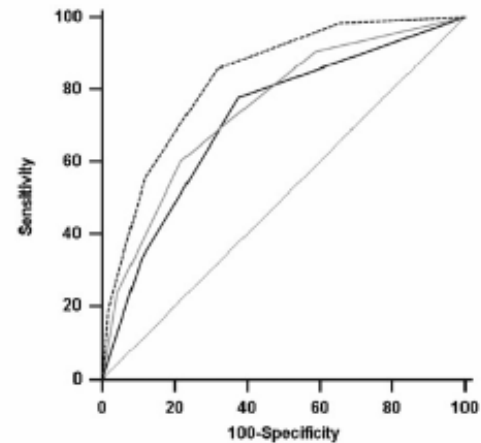
Figure 3



Accuracy of GLS to detect obstructive CAD. Receiver-operator characteristic curve, testing the accuracy of GLS to detect obstructive CAD. $GLS \geq -17.4\%$ provided the highest sensitivity (83%) and specificity (77%) for identification of patients with obstructive CAD (positive likelihood ratio 3.51, negative likelihood ratio 0.23). AUC indicates area under the curve.

Relation between CAD and LV diastolic dysfunction

Figure 4



Model 1 (Duke Clinical Score)

AUC = 0.72 (95% CI 0.65-0.78); $P < .001$

Model 2 (Duke Clinical Score + diastolic dysfunction)

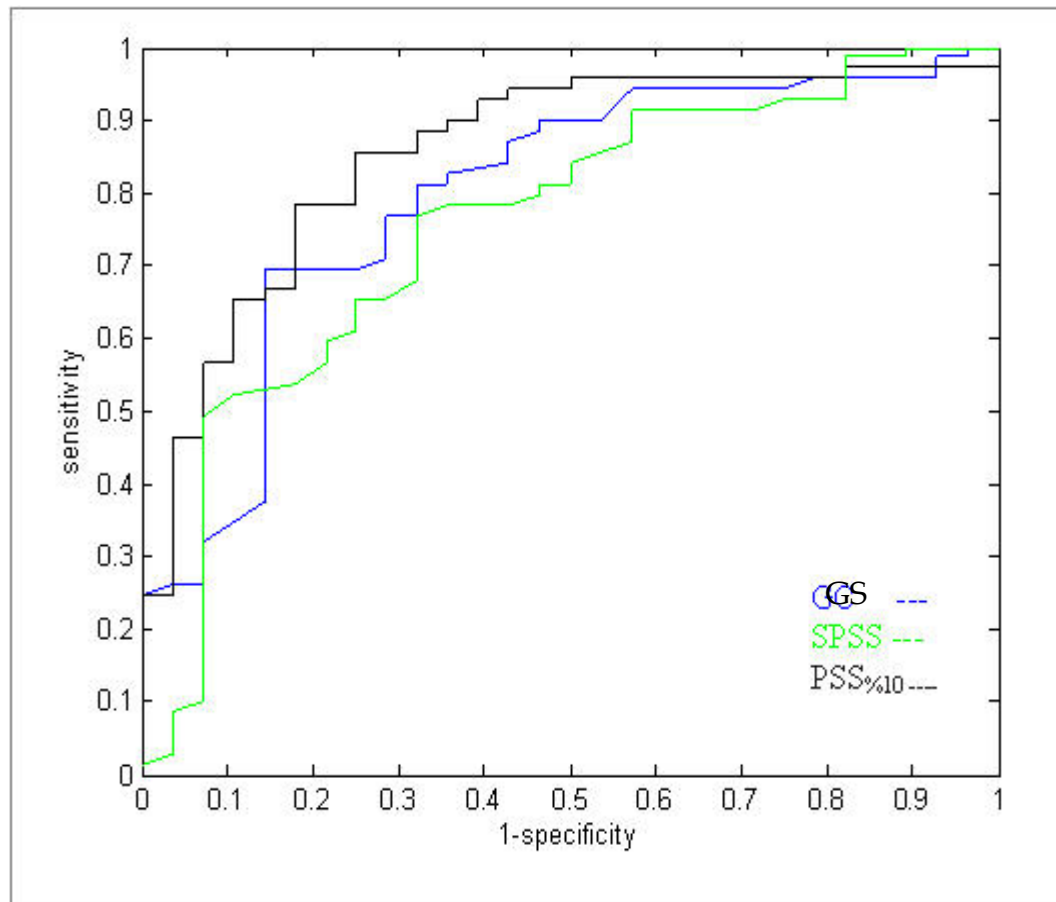
AUC = 0.75 (95% CI 0.68-0.81); $P < .001$
($P = .25$ vs. Model 1)

Model 3 (Duke Clinical Score + diastolic dysfunction + $GLS \geq -17.4\%$)

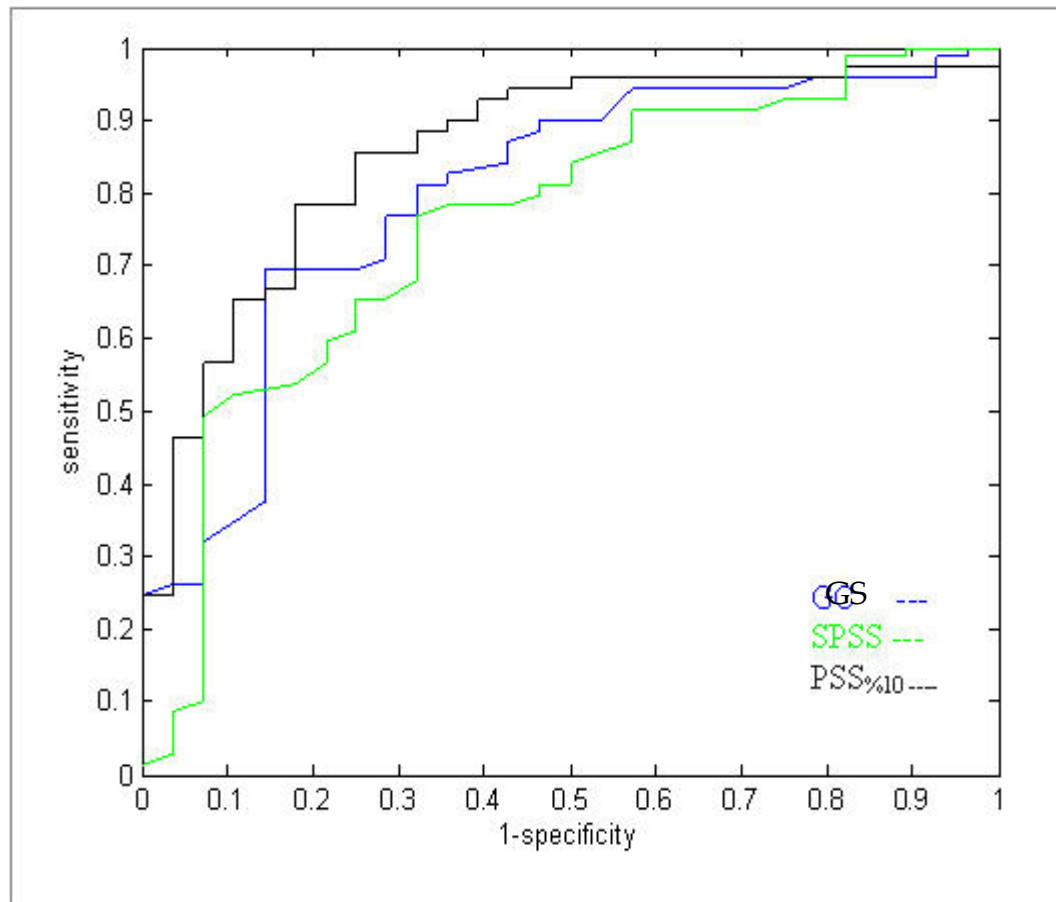
AUC = 0.83 (95% CI 0.77-0.88); $P < .001$
($P < .001$ vs. Model 1 and Model 2)

Incremental value of GLS. Receiver-operator characteristic curves testing the potential incremental value of diastolic dysfunction and $GLS \geq -17.4\%$ over the Duke Clinical Score to detect obstructive CAD. AUC indicates area under the curve.

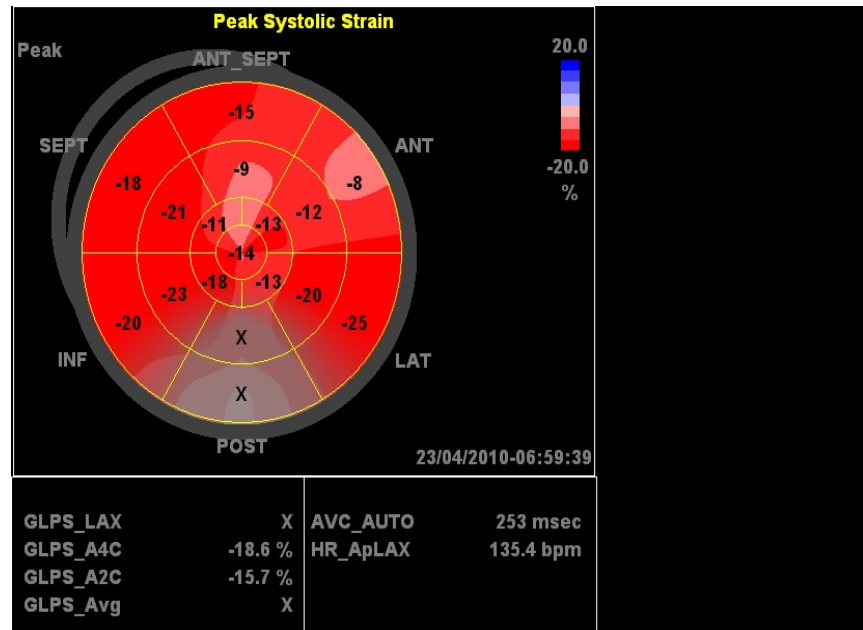
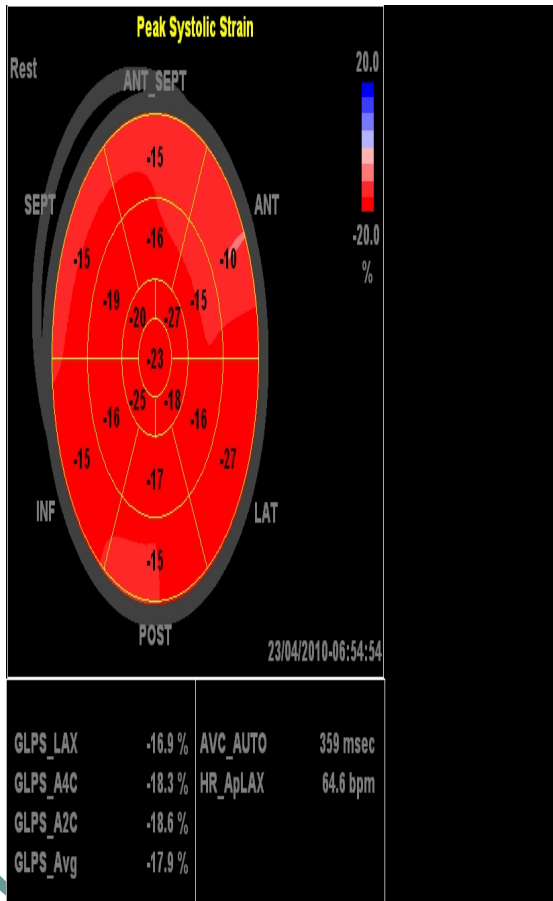
ROC curves of Global strain, SPSS and PSS%10

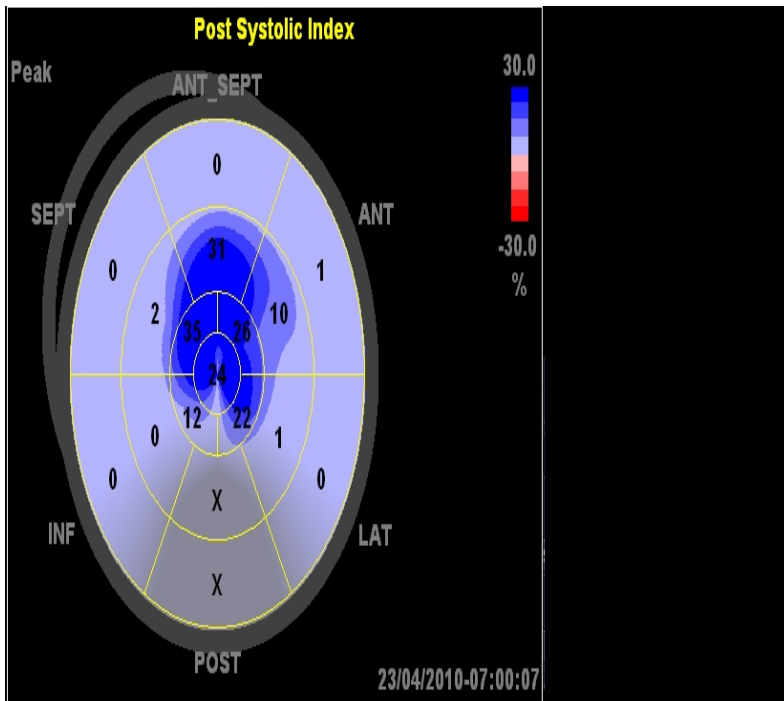


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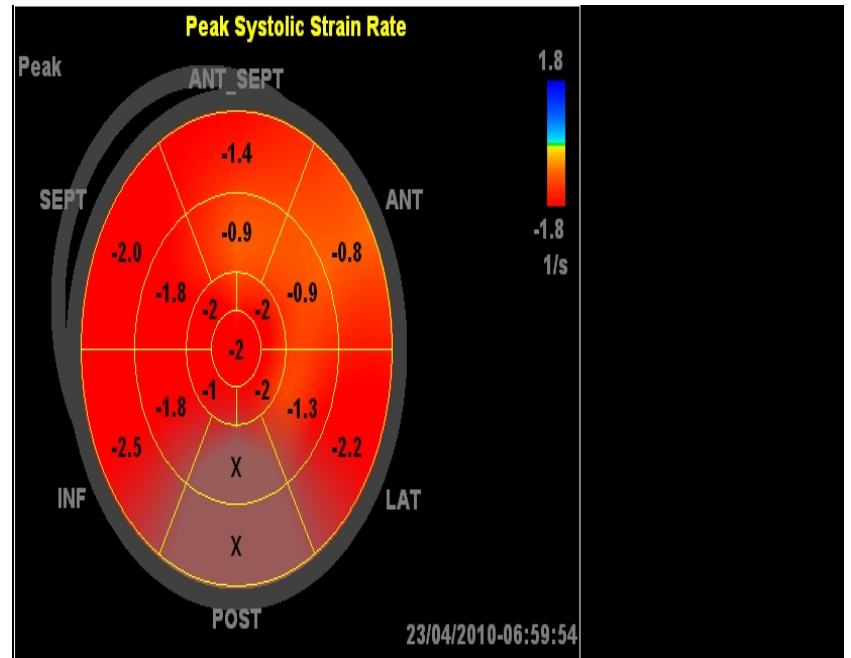


- Rest changes
- Peak exercise systolic and diastolic changes
- Recovery





GLPS_LAX	X	AVC_AUTO	253 msec
GLPS_A4C	-18.6 %	HR_ApLAX	135.4 bpm
GLPS_A2C	-15.7 %		
GLPS_Avg	X		



GLPS_LAX	X	AVC_AUTO	253 msec
GLPS_A4C	-18.6 %	HR_ApLAX	135.4 bpm
GLPS_A2C	-15.7 %		
GLPS_Avg	X		

High Resolution Speckle Tracking Dobutamine Stress Echocardiography Reveals Heterogeneous Responses in Different Myocardial Layers: Implication for Viability Assessments

Assami Rösner, MD, Ole Jakob How, PhD, Erling Aarsæther, MD, Thor Allan Stenberg, Thomas Andreasen, Timofei V. Kondratiev, MD, PhD, Terje S. Larsen, PhD, and Truls Myrnes, MD, PhD, *Tromsø, Norway*

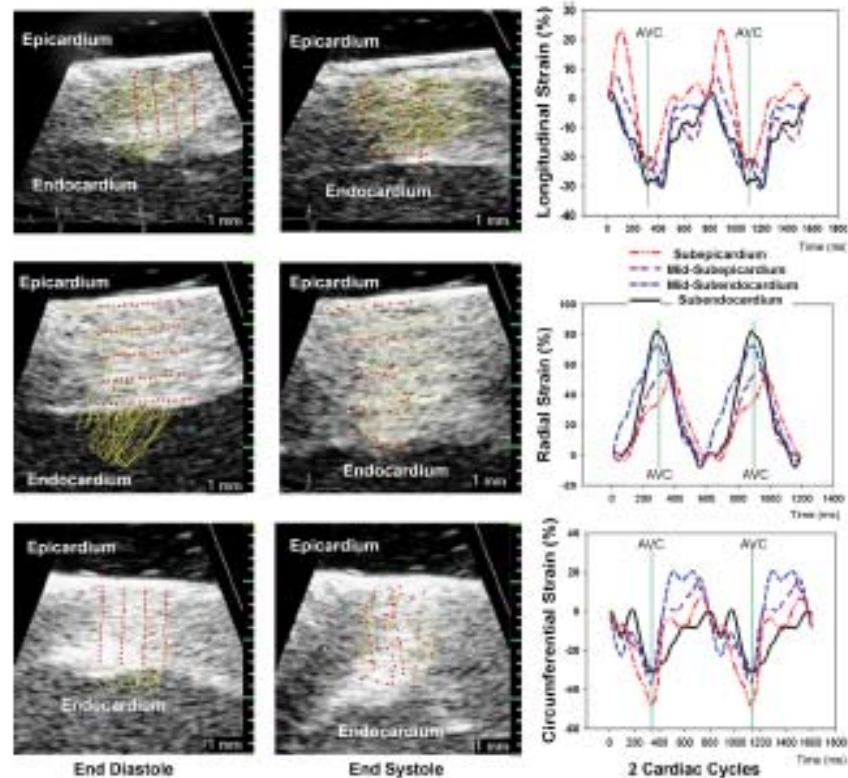


Figure 1. Two-dimensional images scanned epicardially on the anterior wall in resting condition, first at end-diastole and then at end-systole. Longitudinal and radial strains are shown in long-axis projections, whereas circumferential strain is derived from a short-axis projection. The probe was directly positioned on the epicardium of the depicted myocardial segment. Red points depict the PCCs placed at end-diastole to track speckles throughout a cardiac cycle. The maximal displacement of the same points depicts strain gain at end-systole (middle column). Yellow lines in all frames correspond to the displacement of PCCs (red points) throughout one cardiac cycle. The right column depicts two heart cycles with longitudinal, radial, and circumferential strain curves of 41 layers, calculated from the displacement of points from frame to frame. The curves start with the time point after the first mitral valve closure (corresponding to electrocardiographic maximum R), and aortic valve closure (AVC) marks the time point of the end of ET.

Results: Dobutamine stress at constant coronary stenosis increased flow in all layers. ET strain increased predominantly in the midmyocardial layers in the longitudinal and circumferential directions, whereas subendocardial strain did not improve in either direction.

Conclusion: Dobutamine stress influences ET strain differently in the various axes and layers of the myocardium and only partially in correspondence to tissue flow. Longitudinal and circumferential functional reserve opens the potential for the specific detection of midsubendocardial viable tissue by high-resolution STE. (J Am Soc Echocardiogr 2010;23:439-447.)

2D strain in stress echo

