Evaluation and control/Follow up of Myocardial Ischemia

THE ROLE OF STRESS ECHOCARDIOGRAPHY

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NO CONFLICTS OF INTEREST
Basic Principle:

Ischemic tissue (pathological) fails to augment function during stress.

T. Marvick
Ischemic cascade

Perfusion abnormalities proceed systolic dysfunction

- Angina
- ECG changes
- Systolic dysfunction
- Diastolic dysfunction
- Hypoperfusion
- Flow maldistribution
- Nuclear, CMR, contrat
- Echo

Time from onset of ischemia
Modalities

- Exercise- stress test
- Pharmacological stress-test: Dobutamine
  Dypiridamole
- Pace-maker stress echo (PM)
Stress-echocardiography

Indications

- Diagnosis of CAD, when exercise ECG is contraindicated, not feasible, uninterpretable, non-diagnostic or with ambiguous results
- Prognosis and risk stratification in patients with established CAD (e.g. after AMI)
- Preoperative risk assessment (non-cardiac surgery)
- LV viability before revascularization
- Evaluation after revascularization (not in the early post-procedural period, with change in symptoms)
- Coronary artery disease of unclear significance of angiography or computed tomography
Pharmacologic Stress-echo

Dynamically: 
- Subend. \( \phi \) supply + adenos Rc
  - Dilation of normal vasc bed (\( \uparrow \)flow x3-5) at the expenses of the bed supplied by stenotic art
  - Side effects: bronchospasm BAV

DOB-atri & Ex
- \( \uparrow \)O\(_2\) demand \( \beta_{1-2}, \alpha \) Rc+ ino-chrono
  - DOB vs Ex: early onset of ischemia & viability
  - No if UA, arrhythm, hyp > 200/120, uncontrolled CHF

Similar accuracy but Dob>sens 1 VD. Decide basing also on side effects
Screening to diagnose CAD

Noninvasive Options

Stress ECG
Stress Echo
Stress MRI
CT scan
PET
Stress MPI

NO RADIATION

Which is the best one?
Pharmacologic stress-protocols

**Dobutamine**
Starting dose 5-10 γ/Kg/m’. Increased by 10 γ/Kg/m’ every 3 min up-to 40 γ/Kg/m’ (20-30).
Atropine in pts not achieving 85% of predicted HR.
Stop beta blockers 48 hrs before.

**Dipyridamole**
0.56 mg/kg over 4 m’, then nothing for 4 m’, followed by 0.28 mg/kg over 2 m’.
Higher dip dose provides higher sens (0.84 mg/kg in 6 min, with atrop). Safety is controversial.
Dobutamine Stress Echo-protocol

- **Dobutamine**
  - 5 mcg/kg/min at 0'
  - 10 mcg/kg/min at 3'
  - 20 mcg/kg/min at 6'
  - 30 mcg/kg/min at 9'
  - 40 mcg/kg/min at 12'
  - 40 mcg/kg/min at 15'

- **Atropine**
  - 1 mg administered at 15'

- **Echocardiography**
  - Throughout the protocol

- **Blood pressure/Electrocardiography**
  - Throughout the protocol
End-points of DSE

Achievement of target HR
Maximal dose of dobut/ atropine
Extensive NWMA
2 mV ↓ST-segment

**Hypertension (BP >240/120 mm Hg)**
↓**SBP >40 mm Hg**

Significant arrhythmias

Intolerable adverse effect of dobut/ atropine
Wall motion changes during stress echo

5-Point scale
1. Normal
2. Mild Hypo
3. Severe Hypo
4. Akinesia
5. Dyskinesia

Ischemia: new or worsened WMA at stress. WMS ≥1 grade in ≥1 segm
ACC/AHA/ACR/ASE/ASNC/HRS/NASCI/RSNA/SAIP/SCAI/ 2008
Key Data Elements and Definitions for Cardiac Imaging

Left Ventricular Segmentation

1. basal anterior  
2. basal anteroseptal  
3. basal inferoseptal  
4. basal inferior  
5. basal inferolateral  
6. basal anterolateral  
7. mid anterior  
8. mid anteroseptal  
9. mid inferoseptal  
10. mid inferior  
11. mid inferolateral  
12. mid anterolateral  
13. apical anterior  
14. apical septal  
15. apical inferior  
16. apical lateral  
17. apex
Δείκτης συστολικής τοιχωματικής πάχυνσης

Άθροισμα της βαθμολογίας (score) των μεμονωμένων τμημάτων της ΑΚ για τον αριθμό των τμημάτων που αξιολογήθηκαν

$$\Delta WMSI = \text{διαφορά μεταξύ WMSI ηρεμίας και WMSI low dose}$$

Παράμετρος εκτίμησης της έκτασης του δυσλειτουργούντος μυοκαρδίου που δείχνει να έχει συστολική εφεδρεία (contractile reserve)

$$> 0.25 \text{ ίσον με πάνω από 4 τμήματα βιώσιμο μυοκάρδιο}$$
Assignment of the 17 Segments on the Echo to Corresponding Coronary Artery

- **Apical 2 chamber**
  - Apex
  - Inferior
  - Anterior

- **Apical 4 chamber**
  - Apex
  - Septal posterior
  - Lateral

- **Parasternal short axis**
  - Septal
  - Anterior
  - Lateral
  - Inferior
  - Posterior

- **Parasternal long axis**
  - Septal anterior
  - Posterior

Legend:
- LAD
- LCX
- RCA
- Overlap
SE analysis: 17-sgms model
Baseline

Low dose

A2C

Peak

Recovery
If there is any indication for DS MR, it would be in those patient with limited echo windows

E. Nagel, Z Kardiol 1999
DSE in the general population

- Sensitivity: 80%, N 1064
- Specificity: 84%, N 642
- Accuracy: 81%, N 2246

Overall accuracy (weighted mean) of the main studies of the literature (tot 2246 pts)

Dob > sensitive then dyp (1 VD)

Geleijnse et al. JACC 1997
MPS vs. STRESS ECHO

Meta-analysis including 17 studies, 1405 pts, in which MPS was directly compared to Stress echocardiography

Schinkel AFL et al, Eur Heart J 2003
2-fold higher prevalence of LVH in the group with myocardial ischemia, particularly on the concentric LVH group.
Cardiac death+MI in normal DSE

Identification of pts at low risk of cardiac events: avoid risk/cost

When pts with a normal study (with/without previous CAD) require to repeat the test?

- No CAD
- CAD

401 pts normal DSE at rest & peak mean f up 5±1.7y

No difference between pts with/without previous history of CAD.
Low risk of a normal DSE is sustained for the first 3 y. At the second 3 y, the rate is still low but doubled. F-up study after 3 yrs may be required to update the risk status.

Sozzi FB1, Elhendy A, Roelandt JR, van Domburg RT, Schinkel AF, Vourvouri EC, Bax JJ, Rizzello V, Poldermans D. AJC 2003
Stress echo in Hypertension
Hard Cardiac Events (similar total death)

596 pts f.up 3 y mean

Ann. cardiac event rate: Abn. DSE 3.8% vs Normal 1.8%, p <0.05

Clinical variables: age, HF, LVMI
% abnorm sgm peak: incremental to the clinical model for total death: WMSI peak

Sozzi FB, Elhendy A, Rizzello V, van Domburg RT, Kertai M, Vourvouri E, Schinkel AF, Bax JJ, Roelandt JR, Poldermans D, Am J Cardiol 2004
% of hard cardiac events increased proportionally to the extension of ischemia
The prognostic value of pharmacological stress echo is affected by concomitant anti-ischemic therapy at the time of resting.


**Fig. 3** Kaplan-Meier survival curves (considering total mortality as end point) in patients stratified according to presence (DET +) or absence (DET -) of myocardial ischemia at pharmacological stress echocardiography on and off antianginal medical therapy. From [59]
Prognostic implication of stress echocardiography in 6214 hypertensive and 5328 normotensive patients

exercise (n = 4,686), dobutamine (n = 2,524), or dipyridamol (n = 8,332) Stress Echo
Stress echo in diabetic patients
PG in Asymptomatic DM pts with no-history of CAD

SMI:
15% DM pt vs 3% noDM CAD is > advanced at the time of DG (cause of late DG)

161 pts (no previous MI or revasc).
Mean age: 62 yrs.
Median f-up 5 yrs
Ischemia: 45 (28%) pts
Death: 40 pts (25%)
Cardiac events: 25 pts

Predictors of hard cardiac events: age, hypercholest, + ischemia (incremental to clinic.)

Hard cardiac events in DM pts
similar if endpoint is total death

396 pts
Median f-up 3 y

MVA: DSE variable over clinical: RWMA, extension of ischemia at peak

A major RF of CV morb-mort
The presence of rest wall motion abnormalities is an independent predictor of mortality in both groups.

Stress echo in LBBB
Usefulness and limitations of dobutamine–atropine stress echocardiography for the diagnosis of coronary artery disease in patients with left bundle branch block

A multicentre study

M. L. Geleijnse¹, C. Vigna², J. D. Kasprzak³, R. Rambaldi¹, M. P. Salvatori², A. Elhendy¹, J. H. Cornel¹, P. M. Fioretti¹ and J. R. T. C. Roelandt¹


lishes this stress modality as one of the stress tests of choice in left bundle branch block patients with relatively normal rest septal thickening. In patients with abnormal rest septal thickening dobutamine–atropine stress echocardiography may lack good sensitivity for left anterior descending coronary artery disease detection, although the test remains highly specific.
Prevalence and Long-Term Prognosis of Patients with Complete Bundle Branch Block (Right or Left Bundle Branch) with Normal Left Ventricular Ejection Fraction Referred for Stress Echocardiography


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Echocardiography
Patients with LBBB 4.5%/year, RBB 2.5%/year, 1.9%/year

Figure 1. Kaplan–Meier survival curves according to presence of LBBB or RBBB. LBBB = left bundle branch block; RBBB, right bundle branch block.
Patients with abnormal STRESS test and LBBB had more than 2 times greater risk of all-cause mortality.

**Figure 2.** Adjusted survival curves according to presence of LBBB and results of stress echocardiogram. LBBB = left bundle branch block.
LV viability before revascularization
Viable myocardium

• A chronic, reversible left ventricular dysfunction due to coronary artery disease.

• Inotropic stimulation causes a transient change in regional and global left ventricular dysfunction.

• In chronic LV dysfunction recovery occurs after revascularization.

Viable dyssynergic myocardium

- **Myocardial stunning**: postischemic myocardial dysfunction with (nearly) normal myocardial flow.
- **Myocardial hibernation**: a compensatory state that allows myocardium to survive a state of chronic ischemia. Myocardial function is depressed, flow is normal or moderately reduced, but flow reserve is reduced.
- Repeated episodes of stunning result in hibernating myocardium.
Viable dysfunctional myocardium

- Membrane integrity: thallium-201 SPECT
- Metabolic activity: FDG PET / SPECT
- Contractile function: stress echo

Contractile response to dobutamine predicts recovery in patients with LV dysfunction after CABG.

N=61 patients
Before revascularisation, 3 months and 14 months after

Cornel et al. JACC 1998;31:1002.
Prognostic value of the amount of viable myocardium assessed by low-dose DSE prior to revascularization

- 133 patients, mean EF 34 ± 5%.
- Quantification amount of viability by DSE.

<table>
<thead>
<tr>
<th>Group</th>
<th>No. segments</th>
<th>EF %</th>
<th>EF %</th>
</tr>
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<tbody>
<tr>
<td>Group I</td>
<td>6 or more</td>
<td>35±5</td>
<td>47±6*</td>
</tr>
<tr>
<td>Group II</td>
<td>2-5</td>
<td>34±4</td>
<td>40±5*</td>
</tr>
<tr>
<td>Group III</td>
<td>&lt; 2</td>
<td>36±4</td>
<td>37±6</td>
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Meluzín et al. JACC 1998;32:912
Prognostic value of dysfunctional myocardium

Meluzin et al. JACC 1998;32:912
Myocardial viability during DSE predicts survival in patients with CAD and severe LV dysfunction

<table>
<thead>
<tr>
<th></th>
<th>No</th>
<th>Viable</th>
<th>Revasc.</th>
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<tbody>
<tr>
<td>I</td>
<td>85</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>II</td>
<td>119</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>III</td>
<td>30</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>IV</td>
<td>84</td>
<td>no</td>
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</tr>
</tbody>
</table>

Follow-up: 18±10 months.

N=318 pts

*Afridi et al. JACC 1998;32:921*
Time Course of Functional Recovery of Stunned and Hibernating Segments After Surgical Revascularization

Bax; Circulation 2001;104:1-314-I-318
In-Hospital and Long-Term prognostic value of viable myocardium detected by DSE early after acute myocardial infarction

DSE 1st week and 3 months post MI

Viability means instability

\[ p = 0.026 \]
\[ \chi^2 = 4.95 \]

Prediction of reversible dysfunction by DSE after acute myocardial infarction in 155 patients

Biphasic correlates with the AMI responsible cor. Artery

DSE 1 week post MI
Stress echo 2020: the international stress echo study in ischemic and non-ischemic heart disease
A= Asynergy (ischemic vs non-ischemic heart)

B= B lines (wet vs dry lung)

C= contractile reserve (LVCR) weak vs strong heart) based on Force. (cut off>2)

D=Doppler flowmetry, coronary flow velocity reserve (CFVR) –targeting microcirculation (cut off>2)

\[
\text{SBP} \\
\text{Force (mmHg)} = \text{ESV} \\
\text{LVCR} = \frac{\text{Force stress}}{\text{Force rest}}
\]
Coronary flow reserve during stress echo predicts mortality
Sicar R, Cordigiani L, Cardiovascular Ultrasound 2017

**Fig. 7** Mortality rates in patients with known or suspected coronary artery disease separated on the basis of presence (+) or absence (−) of ischemia at stress echocardiography (SE) and coronary flow reserve (CFR) of left anterior descending artery >2 or ≤2. From [145]
Coronary flow reserve during stress echo predicts mortality

Sicar R, Cordigiani L, Cardiovascular Ultrasound 2017

Fig. 9 Hard event rates in unselected patients (left upper panel), hypertensives patients (right upper panel), diabetic patients (left lower panel), and patients with left bundle branch block (LBBB) (right lower panel) with normal or near normal coronary arteries separated on the basis of coronary flow reserve (CFR) values. From [147, 149–151]
Conclusion: Advantages of SE

• Higher feasibility and accuracy than exercise EKG
• Quantification and localization of abnormalities
• Lower cost, wider availability, no irradiation, immediate results
• Evaluation of LV function, LVH, valve structures
• Incremental value in prediction of total mortality
• Higher specificity for ischemia and viability
• Preoperative risk assessment
Disadvantages/Pitfalls of SE interpretation

• Poor or suboptimal imaging Quality (4-10%) (use contrast)
• Subjective analysis without quantification

New protocol ABCD (force, CFVR) might improve it in the future

• Adequate experience is required
• Lower sensitivity than SPECT
ΕΥΧΑΡΙΣΤΩ ΠΟΛΥ!