

Integration of Flow Mediated Dilatation Into Clinical Practise.

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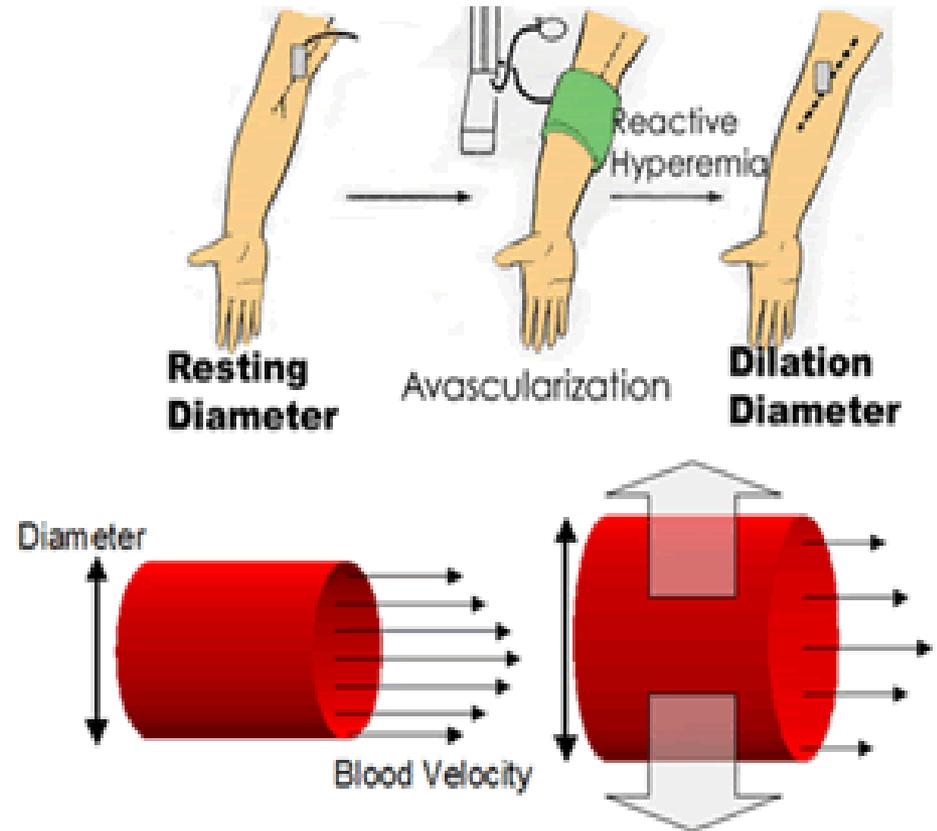
Session Aims.

To review the following:

- What is flow mediated dilatation?
- What does it measure?
- How can we assess flow mediated dilatation?
- How can this be integrated into clinical practise?

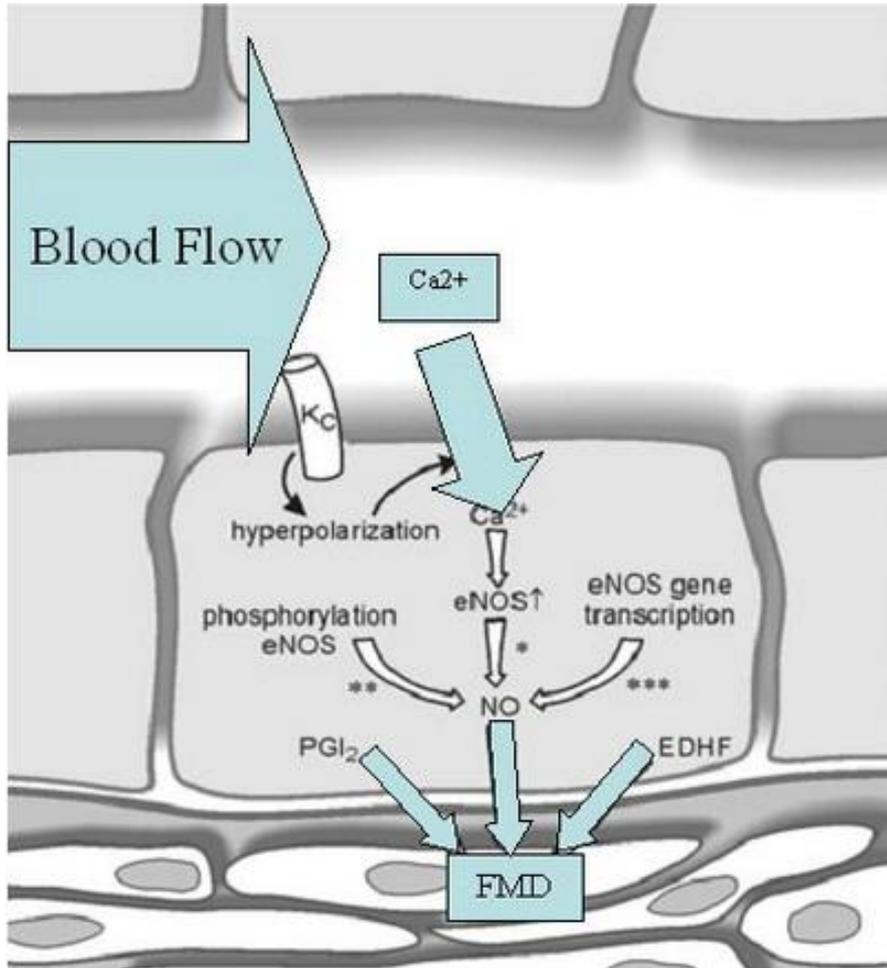
What is Flow Mediated Dilatation?

- Endothelium-dependent process facilitating the relaxation of an artery in response to increased shear stress.



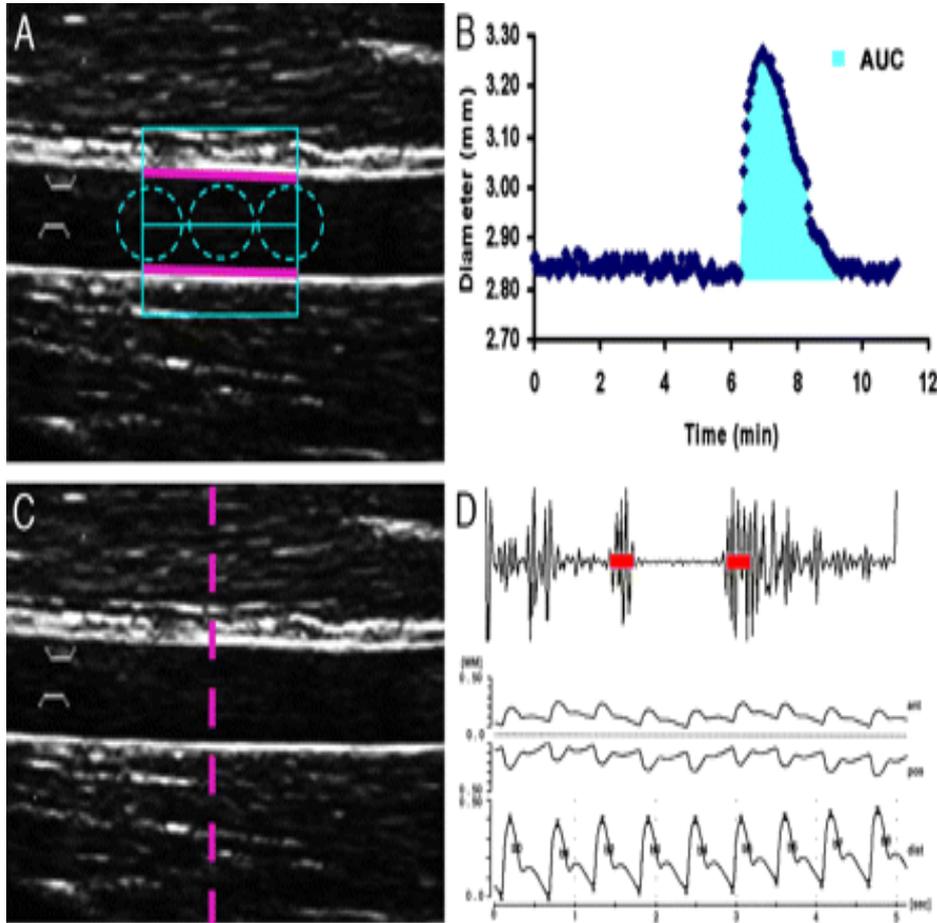
Moens et al, Chest (2005), 127: 2254-2263.

Physiological Process.



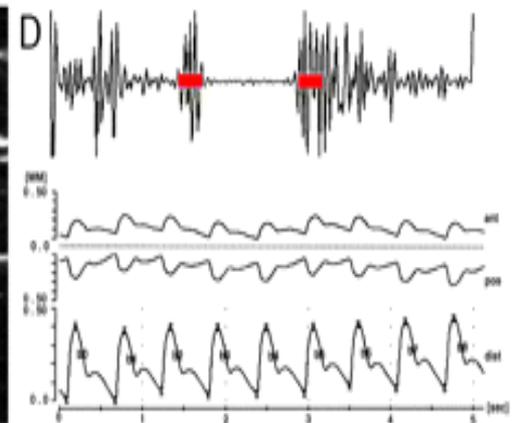
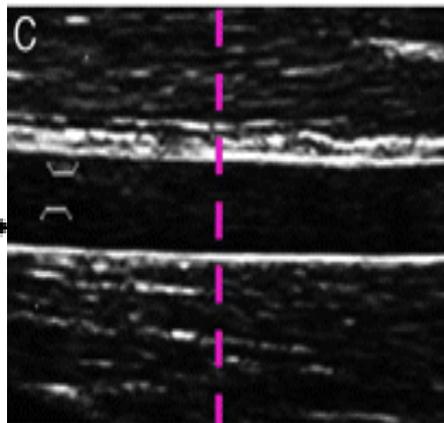
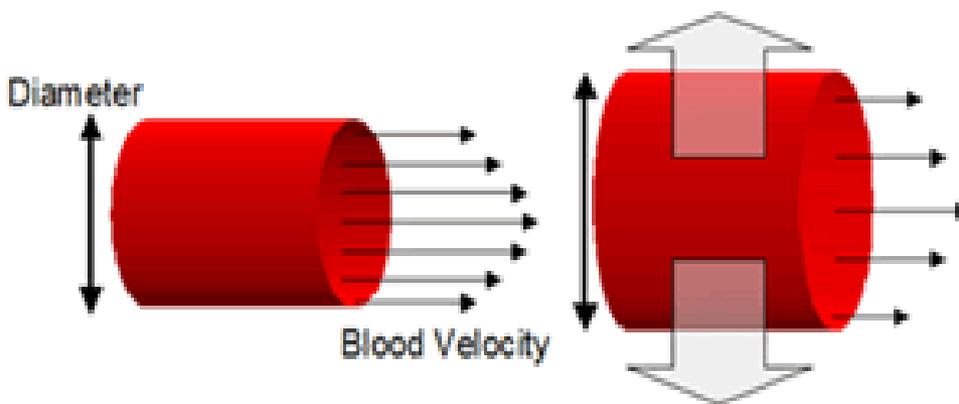
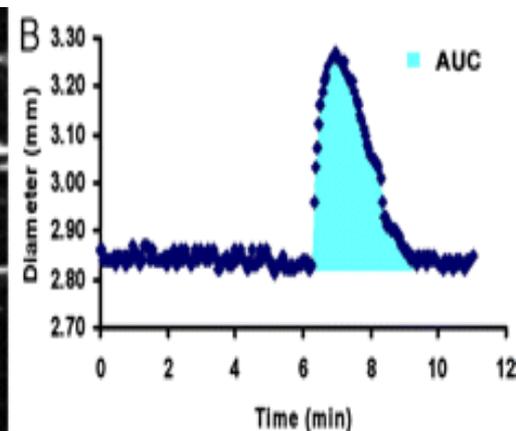
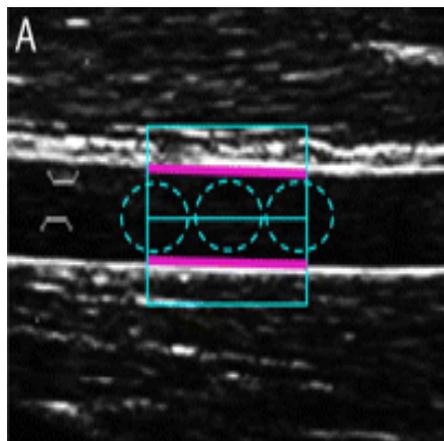
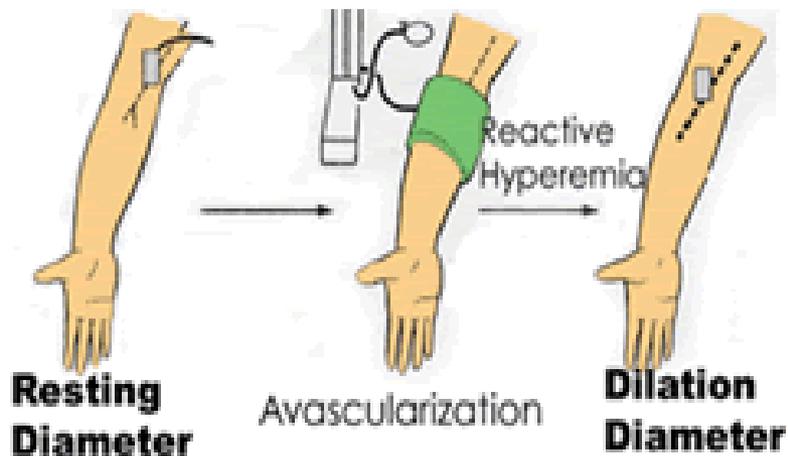
- Vascular endothelium (single cell layer).
- Shear stress = release of vasodilators.
- Nitric oxide, prostaglandins, hyperpolarisation factor.
- Opening of specialised ion channels.
- Ca activated K⁺ channels open to hyperpolarise endothelial cell.
- Increase Ca entry to activate eNOS.
- Subsequent NO generation = FMD.

What are we Measuring?



- Ability of a large conduit artery to dilate in response to a shear stress stimulus that produces a nitric oxide dependent response.
- FMD is a direct marker of nitric oxide bio-availability.

Assessment of FMD: How to do it...



FMD in Clinical Practise.

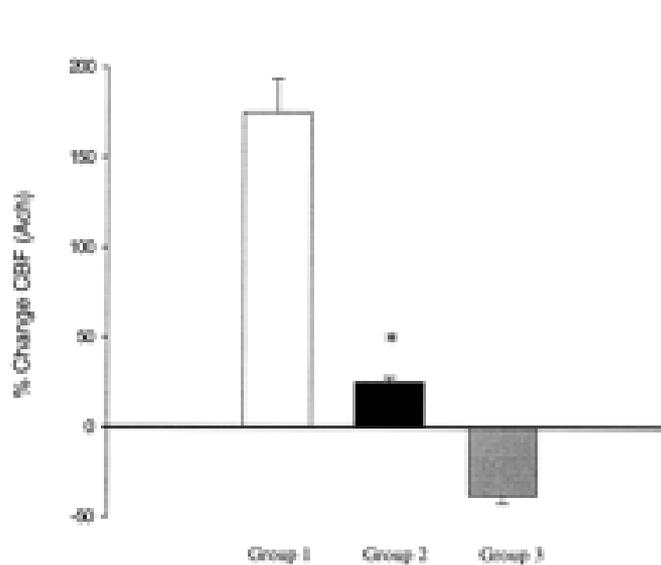
- 4 main applications (in my opinion!).
 1. Research Tool.
 2. Risk Stratification for Cardiovascular Events.
 3. Risk Stratification in Patients with Chest Pain.
 4. Risk Stratification in Chronic Heart Failure.

THE EVIDENCE.....

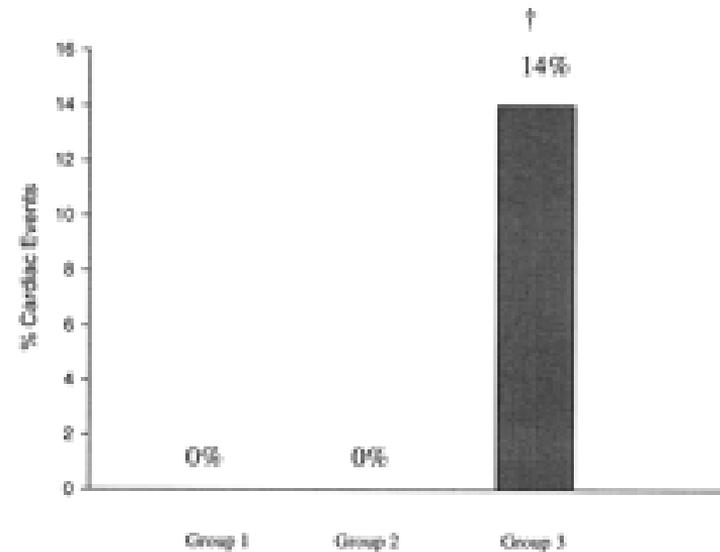
Risk Stratification for Cardiovascular Events.

Long-Term Follow-Up of Patients With Mild Coronary Artery Disease and Endothelial Dysfunction
Jassim Al Suwaidi et al.

•157 patients with mild CAD, divided into response to Ach, normal, mild and severe ED, 14% cardiac events – 28/12 fu.



A



B

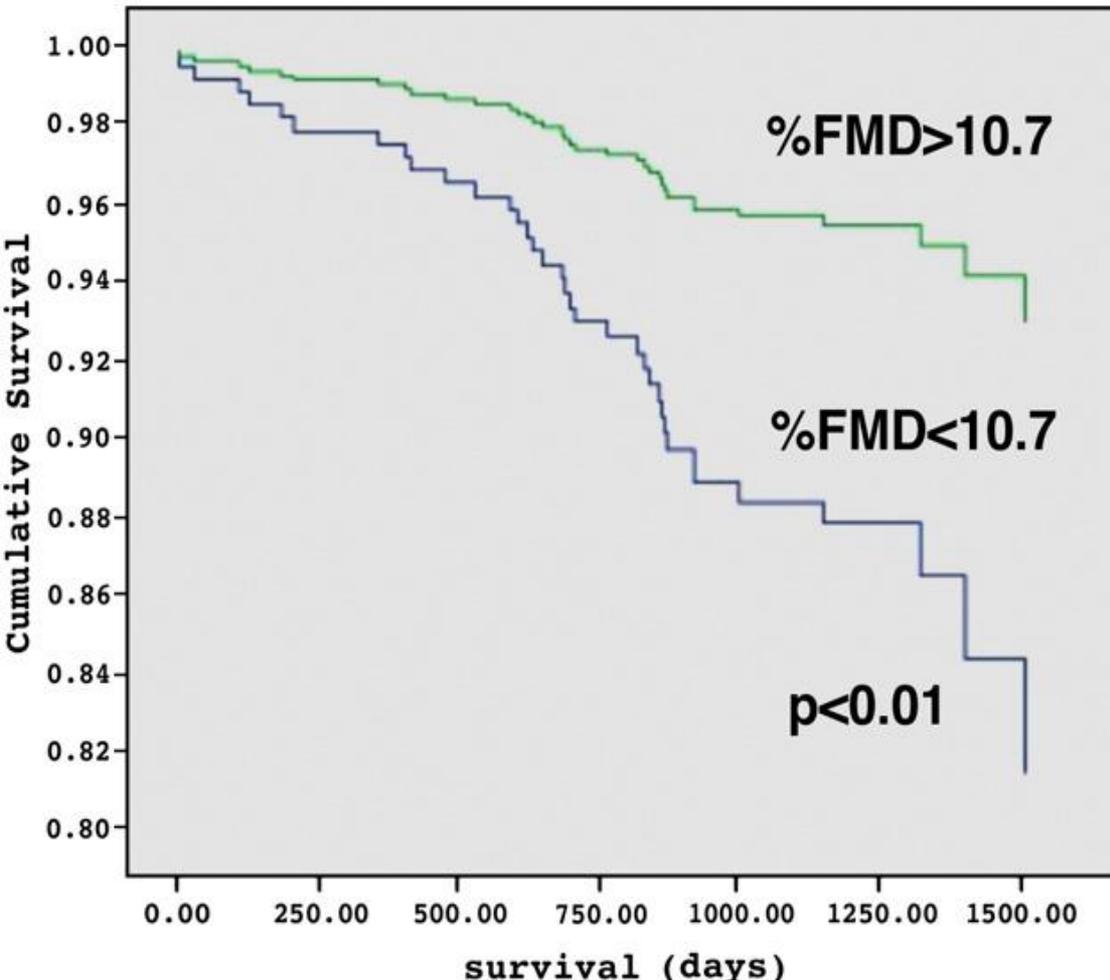
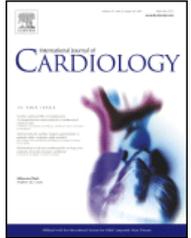
Circulation 2000;101:948-954

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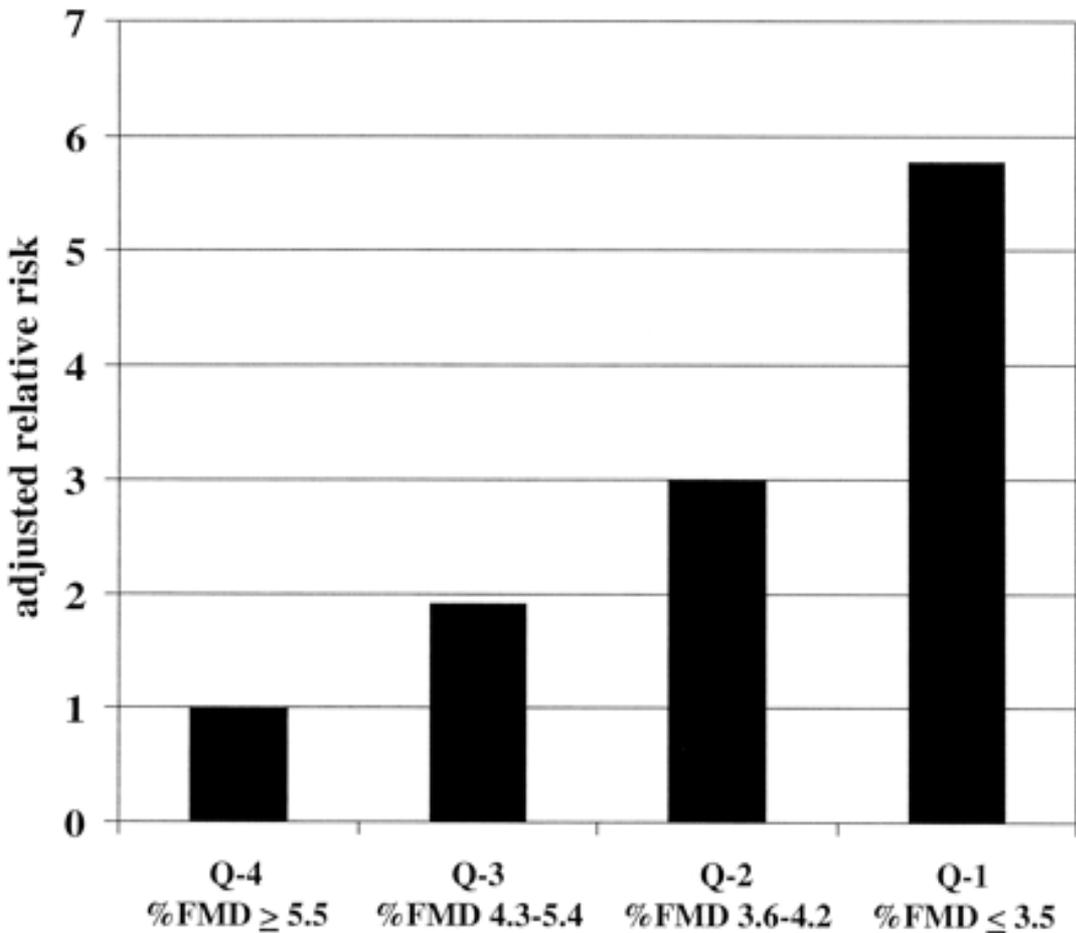
Risk Stratification cont....

Shechter et al (2009). Int J of Cardiol, 134: 52-58.



- 435 healthy subjects.
- Median FMD of 10.7%
- Almost 3 year follow-up.
- Participants with below median FMD significantly more prone to CV endpoints 11.8% versus 4.7 % ($p < 0.007$).

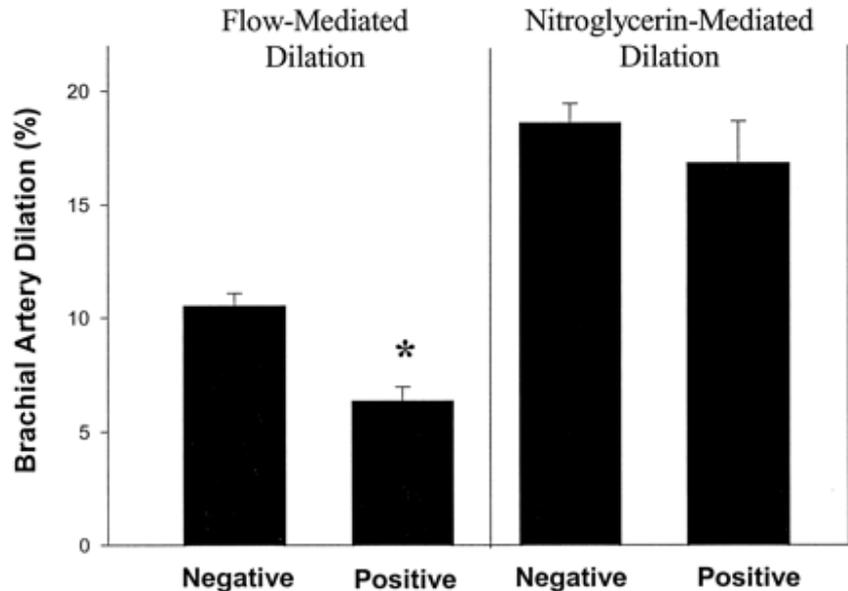
Risk Stratification for Hypertension.



- Relative risk of developing hypertension in relation to the percent of flow-mediated dilation (FMD) quartiles.
- 952 Post menopausal healthy females – 112 developed HTN.
- Almost 4 yr follow-up.
- FMD of brachial artery.
- Each 1 unit less FMD = 16% adjusted risk of developing HTN.

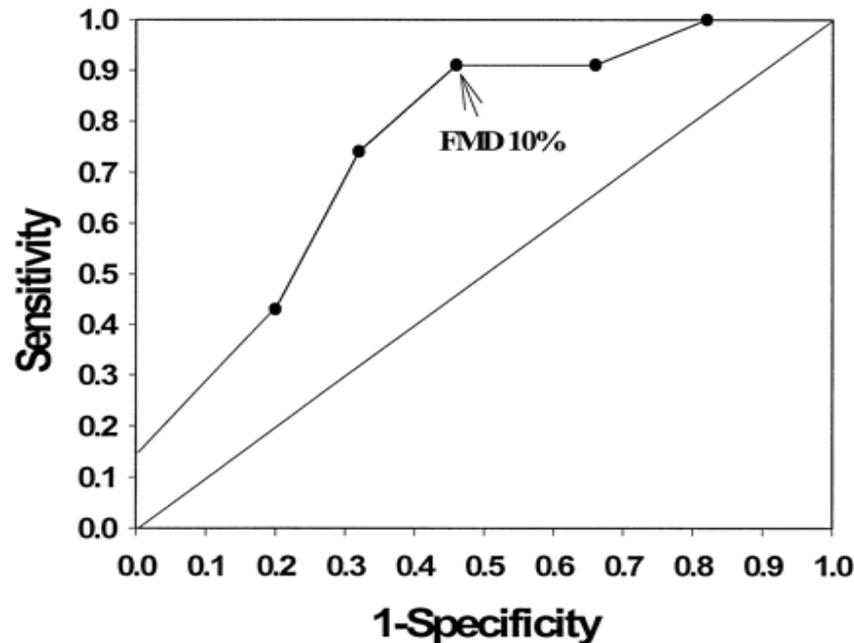
Rossi et al JACC (2004), 44: 1636-1640.

Risk Stratification in Patients with Chest Pain.



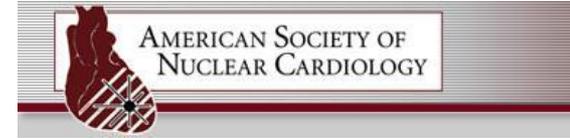
Kuvin et al (2001),

Journal of the American College of Cardiology
38: 1843



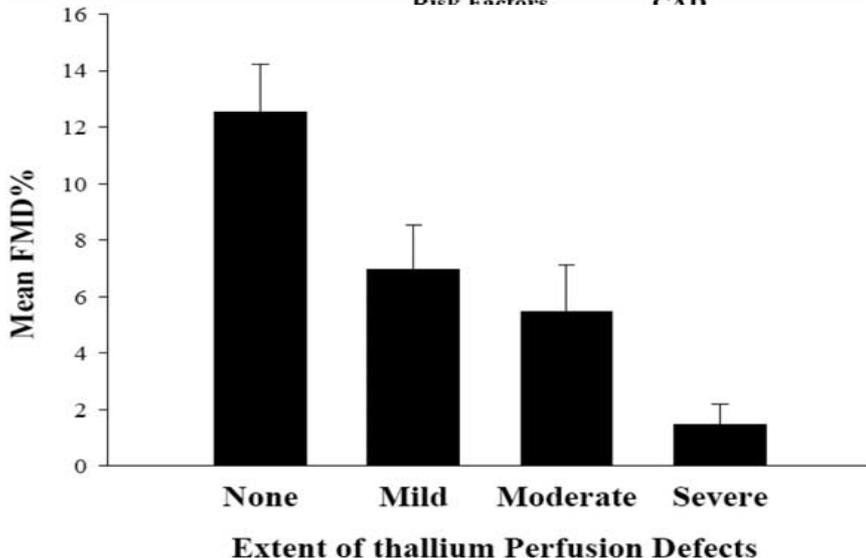
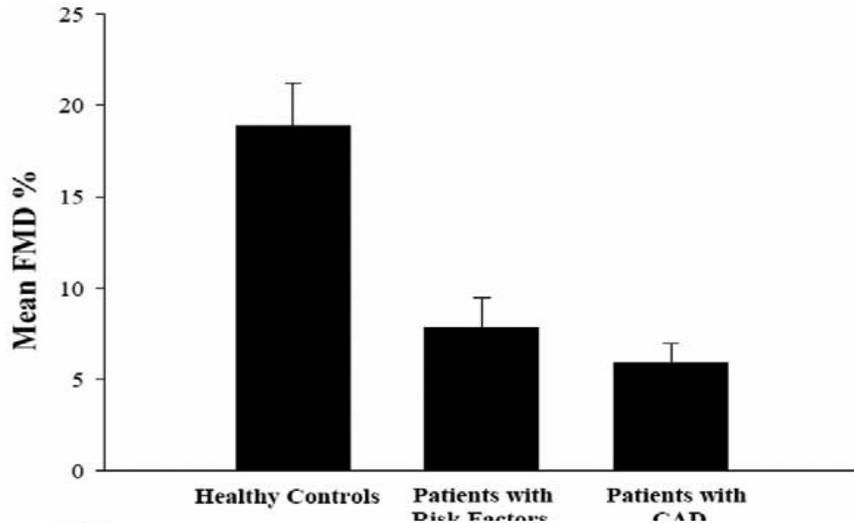
- 94 subjects underwent clinically relevant myocardial perfusion imaging and FMD.
- Subjects with CAD on perfusion had significantly lower FMD%.
- FMD% highly predictive for CAD – odds ratio of 1.32 for each % decrease in FMD.
- 21/23 subjects with positive perfusion had FMD% < 10 (sensitivity of 91%).
- 2 subjects with positive perfusion had FMD > 10% (negative predictive value of 95%).
- FMD < 10% significantly shorter exercise tolerance.

Risk Stratification in Patients with Chest Pain.



Wu et al (2005).

Journal of Nuclear Cardiology, 12: 538.

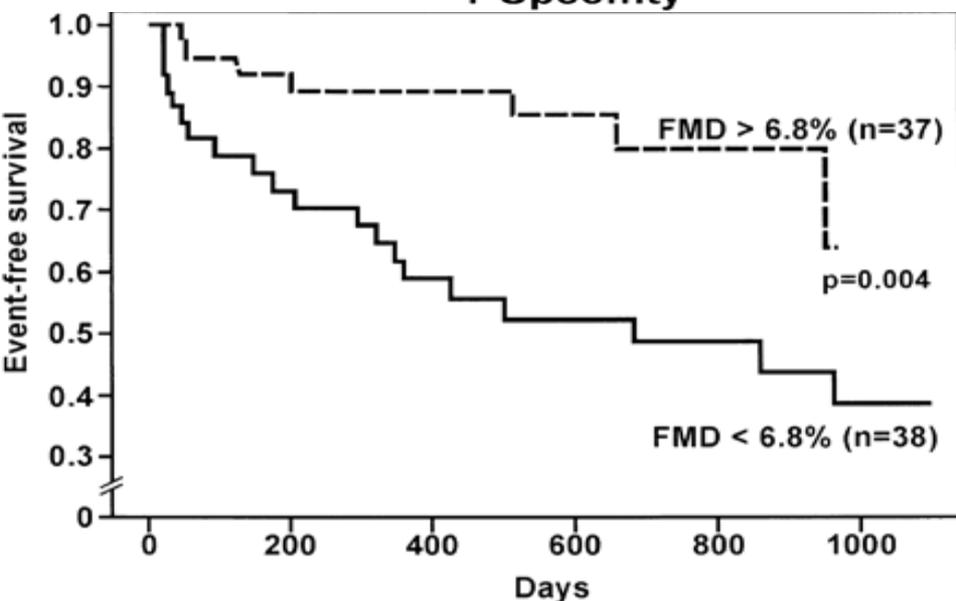
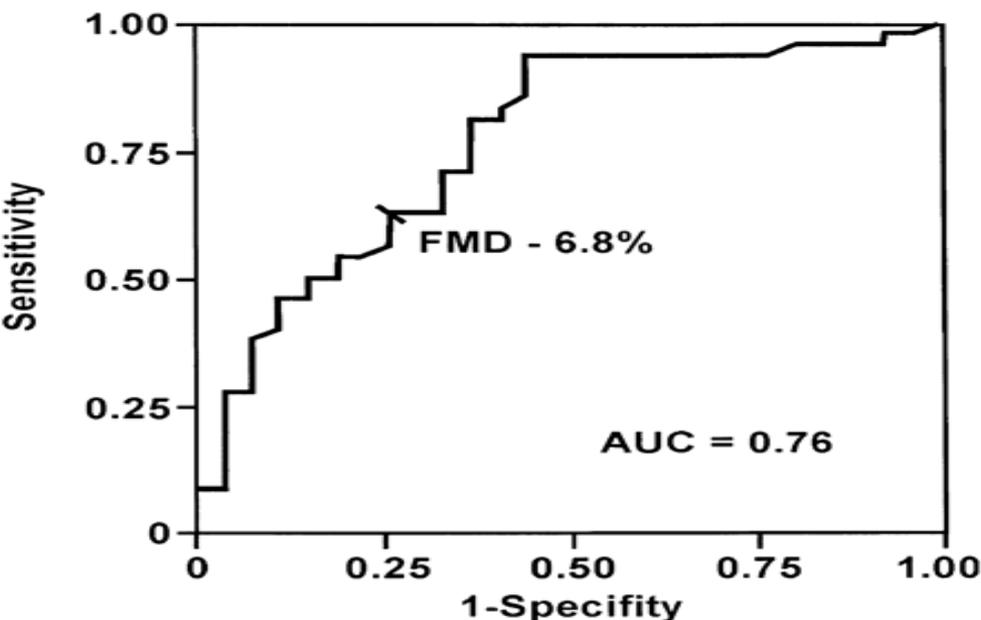


- 55 patients with chest pain referred for SPECT and 11 controls.
- Main outcome was %FMD and number of perfusion defects on SPECT.
- Significant correlation between number of perfusion defects and lower FMD%.
- FMD of <7.5% was 72.5 sensitive and 73.1 specific for predicting thallium defects.
- FMD strongest predictor of scintigraphic CAD – following risk factor adjustment.

Risk Stratification in Patients with CHF.



*Meyer et al (2005),
Journal of the American College of Cardiology
46 (6): 1011.*



- 75 patients with CHF and LVEF% $\leq 30\%$
- Brachial artery FMD%, neurohormonal, haemodynamic and clinical variables measured.
- Analysed for prediction of increased severity CHF or death.
- 3 yr follow-up (28% increased severity, 8% death).
- Univariate analysis risk factors were logBNP, FMD and mean BP.
- Significantly more patients with FMD $\leq 6.8\%$ (mean) met end points than FMD% $> 6.8\%$.

Variability and Reproducibility.

- Normal healthy FMD% response is 7-10.
- CV disease less or absent response.
- Framingham Study:
 - Mean reactivity responses of 3.3% females and 2.4% males with known CV disease.
- Poor reproducibility unless strict guidelines and techniques are followed.
 - *Correti et al (2002). Guidelines for the Assessment of Endothelial Dependent FMD of the Brachial Artery. J. American College of Cardiol, 39: 257.*

Conclusion.

- Clinically FMD can be used for risk stratification
 - Predict future CV events,
 - CAD in patients with chest pain,
 - Prognosis in CHF.
- Can be used as a research tool
 - E.g. to assess effectiveness of an intervention.
- Cost Effective technique.. BUT...
 - Only reproducible with skilled operator.
 - Need correct equipment and lab conditions.
 - Does not give detailed data (e.g. CAD plaque type, length, anatomy etc).
 - Although non-invasive is still fairly uncomfortable in some patients.

Thanks for Listening.
Any questions?

