IMAGING IN WOMEN FOR CARDIOVASCULAR RISK ASSESMENT

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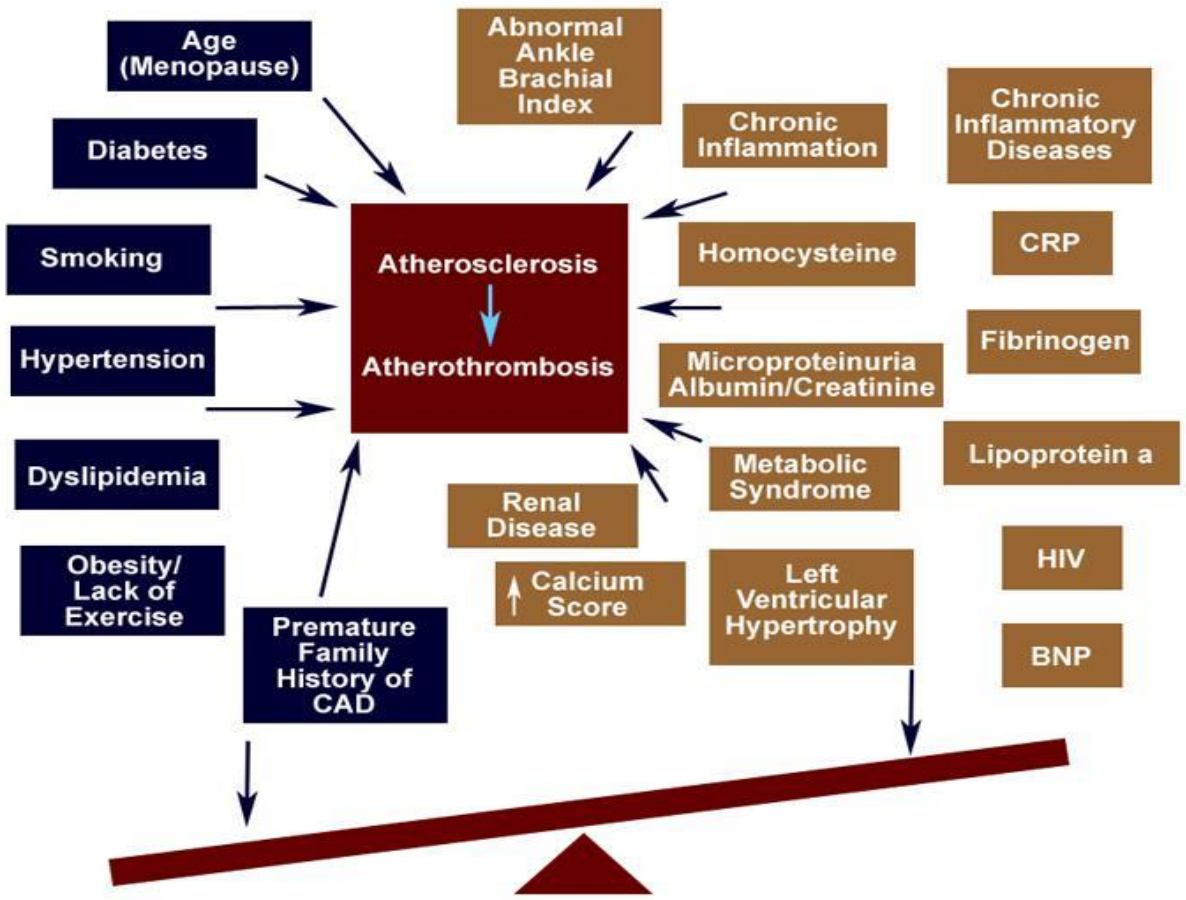


Major Risk Factors for Coronary Artery Disease

- -Age (men ≥ 45 years; women ≥ 55 years)
- -Family history of premature coronary artery disease (CAD in male first-degree relative < 65 years)
- -Hypertension (BP > 140/90 mmHg or on antihypertensive medications)
- -Cigarette Smoking
- -Diabetes
- -Hypercholesterolemia
- -Low HDL cholesterol (< 40 mg/dl)
- -Hypertriglyceridemia (> 200 mg/dl)
- -Obesity

- It is underappreciated that cardiovascular (CV) disease is the number one cause of death in women. In fact, women are more likely to die after a myocardial infarction than men.

- Conventional risk factors such as tobacco use, diabetes, high triglycerides, and low high-density lipoprotein portend a greater risk in women than in men.

- Women are also more likely to suffer from nontraditional CV risk factors, such as systemic autoimmune disorders, and women have unique risk factors such as preeclampsia, gestational diabetes, and pregnancy-induced hypertension, which are unmasked during pregnancy.

- Despite this, most women are unaware of their risk for heart disease, and commonly used clinical risk stratification tools such as the Framingham score underestimate their lifetime risk.

- The identification of women with significant coronary artery disease (CAD) is also complicated by the fact that they often present with atypical symptoms, such as fatigue, sleep disturbances, shortness of breath, indigestion, or anxiety

- Furthermore, the pathophysiology of CAD is somewhat different in women than in men.
- Women have less obstructive CAD and are more likely to have a plaque rupture due to endothelial erosion.
- In fact, in women, angina is often due to microvascular dysfunction rather than significant epicardial coronary stenosis.
- symptomatic women who have *normal* epicardial coronary arteries continue to be at greater risk than their asymptomatic counterparts.

- In addition to the various clinical and pathophysiological obstacles to detecting CAD in women, there are also several challenges related to the most commonly used diagnostic tests.

- Traditional treadmill stress testing is well-known to have a limited sensitivity and specificity for the detection of CAD in women

IMAGING METHODS

ct scan

Mri scan

Pet scan

Spect scan

Ultrasound scan

CARDIAC CT

- consists of an unenhanced CCT for detection and quantification of coronary calcium.

- A contrast enhanced CCT for coronary artery imaging, detection of coronary artery plaques and, to some extent, characterisation of the non-calcified plaques

- Patients are optimally suited if they have a regular heart rate and rhythm, a body mass index below 40 kg/m and a normal renal function.

- The examination is performed following intravenous injection of contrast agent.

- Image quality can be substantially improved by lowering the patient's heart rate to <65 bpm, which is usually achieved by administering β-blockers

- Coronary vasodilatation can be achieved using sublingual nitroglycerin administration.
- With the newest-generation imaging, not only can the heart be imaged in less than one heartbeat but also the radiation can be substantially reduced (~0.7–3 mSv).
- Further reduction in radiation dose can be achieved with iterative reconstruction algorithms

- Calcification in the coronary arteries occurs, with exception of patients with advanced chronic kidney disease, almost exclusively in patients with coronary atherosclerosis.

- Since the amount of coronary calcium roughly correlates to the atherosclerotic plaque extent, detection and quantification of coronary calcium is of interest for patient risk stratification

- coronary calcification is only weakly related to the severity of luminal stenosis.
- In young symptomatic patients, a negative coronary calcium image does not exclude coronary artery stenoses.
- The Agatston score, less frequently volume or mass scores, is used to quantify the amount of calcium. calcification is not related to plaque (in)stability .

Agatston score

- Method of calculation
- The calculation is based on the weighted density score given to the highest attenuation value (HU) multiplied by area of the calcification speck.
- **Density factor:**
- 130-199 HU: 1
- 200-299 HU: 2
- 300-399 HU: 3
- 400+ HU: 4

- Example, if a calcified speck has maximum attenuation value of 400 HU and occupies 8 sq mm area, then its calcium score will be 32.

- **Grading of coronary artery disease. (based on total calcium score)**

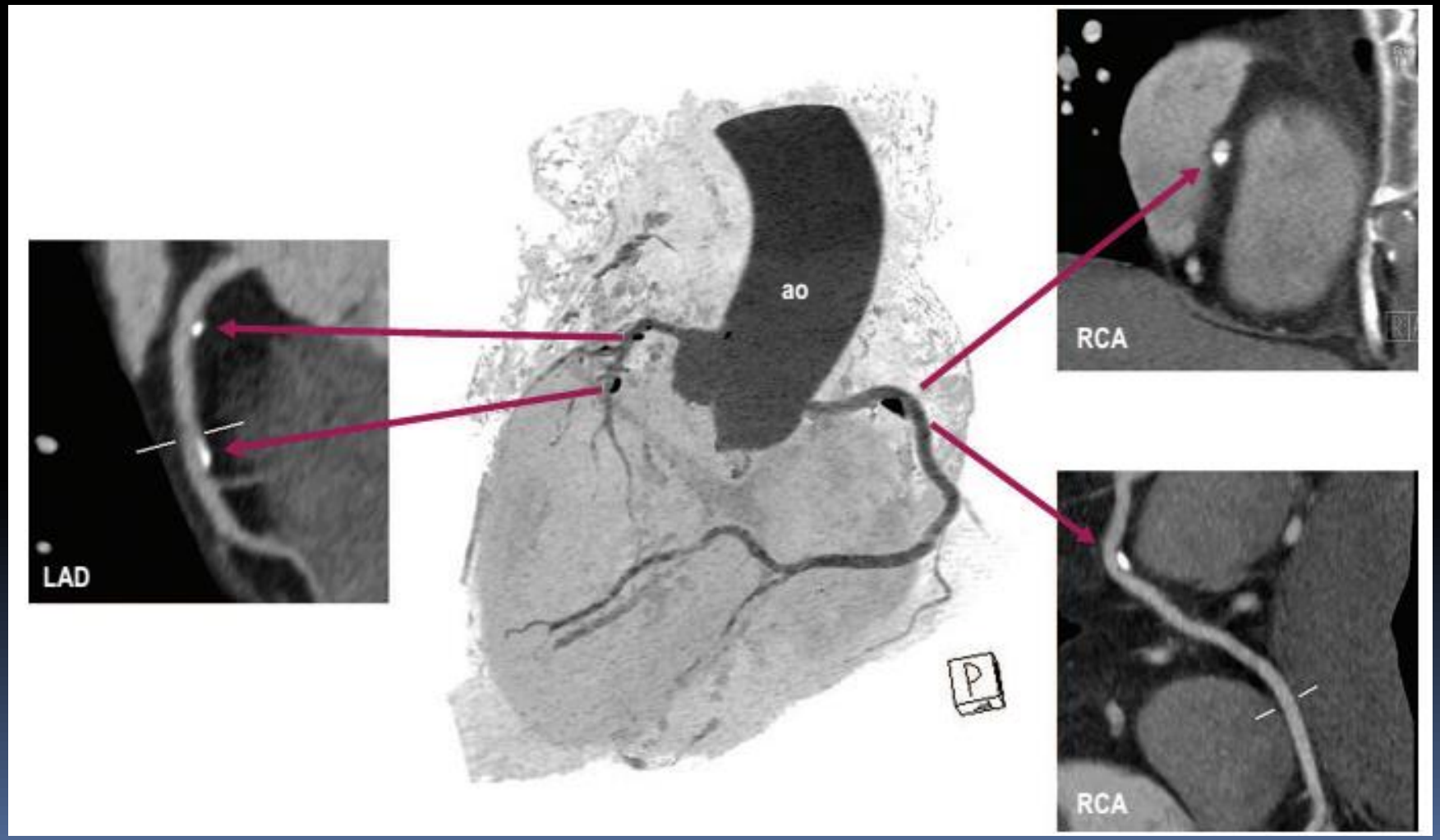
No evidence of CAD: 0 calcium score

- minimal: 1-10
- mild: 11-100
- moderate: 101-400
- severe: >400

Coronary CT angiography

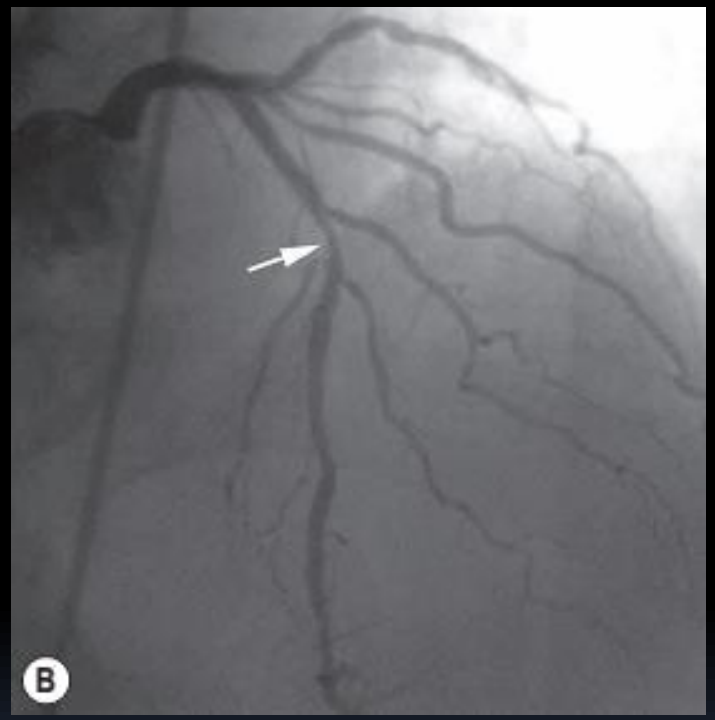
- Coronary CT angiography offers high accuracy for detection and especially for ruling out significant CAD.
- Above a CCS >400, a contrast CT angiography is considered uncertain or inappropriate
- Coronary CT angiography yields promise to determine and to quantify the coronary plaque burden, and to a certain extent to characterise the plaque composition.
- Lipid rich plaques have attenuation values between 11 and 99 HU versus 77–121 HU for fibrous plaques.

Visualisation of calcified non-stenotic plaques by CCT



Patient 1 has normal coronary arteries. Patient 2 has a significant coronary stenosis in the absence of coronary calcifications (arrow). Patient 3 has a large soft plaque (arrowheads) and smaller calcified plaques in the absence of luminal narrowing.

CT Angiography showing right coronary stenosis



Flow-limiting stenosis in mid left anterior descending (LAD) coronary artery

Stress echocardiography

- Stress echocardiography, with exercise or dobutamine pharmacologic stress, can be used to identify stress-induced ischemia.
- By providing information on the presence and location of wall-motion abnormalities related to a decrease in regional myocardial blood flow, the extent and location of ischemia can be defined.
- mean sensitivity of 81% and a specificity of 86%.
- In symptomatic women who are incapable of exercise, dobutamine stress echocardiography reliably detects multivessel disease, with reported sensitivities from 75% to 93% and specificities of 79% to 92%

- Although an abnormal stress echocardiography correlates with a high cardiac event rate in women.
- in the ischemic cascade, perfusion abnormalities detected by SPECT MPI precede the wall-motion abnormalities seen with stress echocardiography.
- acute MI often presents in areas subtended by a less critical stenosis, stress echocardiography may underestimate risk in women with less advanced CAD.
- Therefore, in women, a negative or low-risk stress echocardiography has a higher cardiac death or MI rate compared with a low-risk stress MPI

- Compared with other noninvasive cardiac imaging modalities (eg, SPECT, cardiac CT, coronary artery calcium [CAC]).

- A specific benefit of stress echocardiography for evaluating at-risk women is the absence of radiation exposure.

MYOCARDIAL PERFUSION IMAGING AND SPECT

- SPECT with ECG gating, a nuclear-based technique, provides quantitative information on myocardial perfusion, regional and global left ventricular function, and end-systolic and end-diastolic volumes.
- Traditionally, SPECT MPI has been reported to have challenges that are specific to women.
- Technical limitations in women (including photon attenuation by breast tissue, lower prevalence of epicardial CAD, and small left ventricular chamber size) have accounted with decreased sensitivity and specificity

- Advances in SPECT MPI have led to improvements of the limitations that are specific to women.

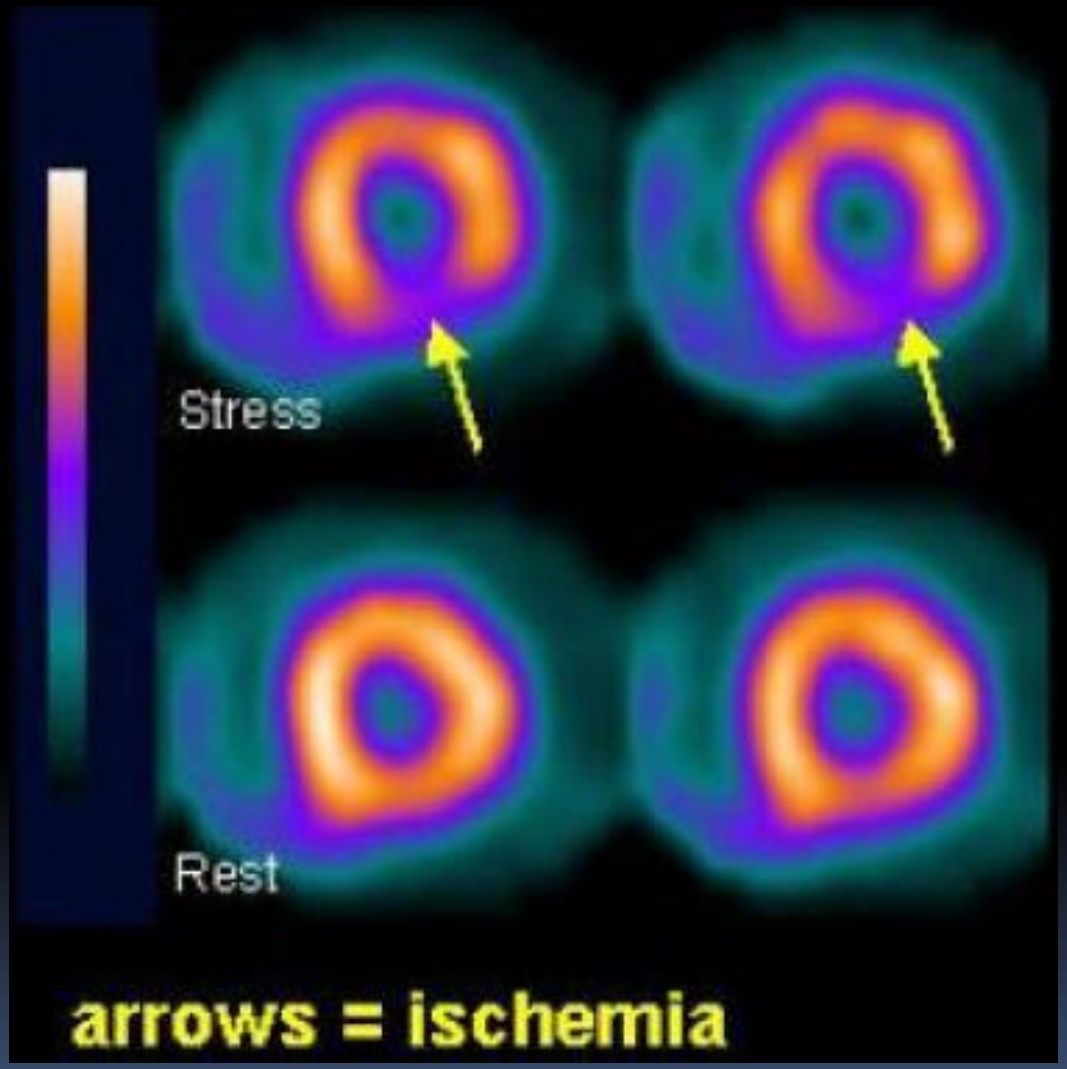
- Contemporary SPECT MPI techniques that include ECG gating, attenuation artifact protocols, and the use of the higher-energy radioisotope technetium have resulted in enhanced diagnostic accuracy for evaluating physiologically significant CAD in women.

- SPECT MPI with pharmacologic stress is extremely useful because at-risk women are generally older and often have decreased exercise capacity when they present with symptoms of IHD.

- Vasodilator stress has been shown to be accurate in detecting physiologically significant CAD in women, with reported sensitivity of 91% and specificity of 86% for detecting a greater than 50% coronary artery stenosis

- SPECT measures the relative myocardial distribution of radionuclides, such as thallium-201 (201Tl), technetium-99m (99mTc) and sestamibi (MIBI).
- Study protocols are specific for the different tracers.
- MIBI SPECT is performed using an injection of tracer during stress and a second injection at rest (or vice versa).
- while 201Tl is injected during stress, and the redistribution of tracer is measured at rest after a delay (e.g. 4 h).
- In regions with impaired myocardial perfusion the number of counts is lower than in the normally perfused myocardium, resulting in a 'defect'.
- Reversible defects (i.e. present on stress but absent at rest) are caused by flow-limiting stenoses and should be differentiated from fixed defects (i.e. present at rest/redistribution at rest) reflecting myocardial scarring.

- The severity of the defect (i.e. reduction in counts) is related to stenosis severity while the extent of the defect is related to the myocardium supplied by the stenotic artery.


Stress
Rest
arrows = ischemia

MPI WITH PET

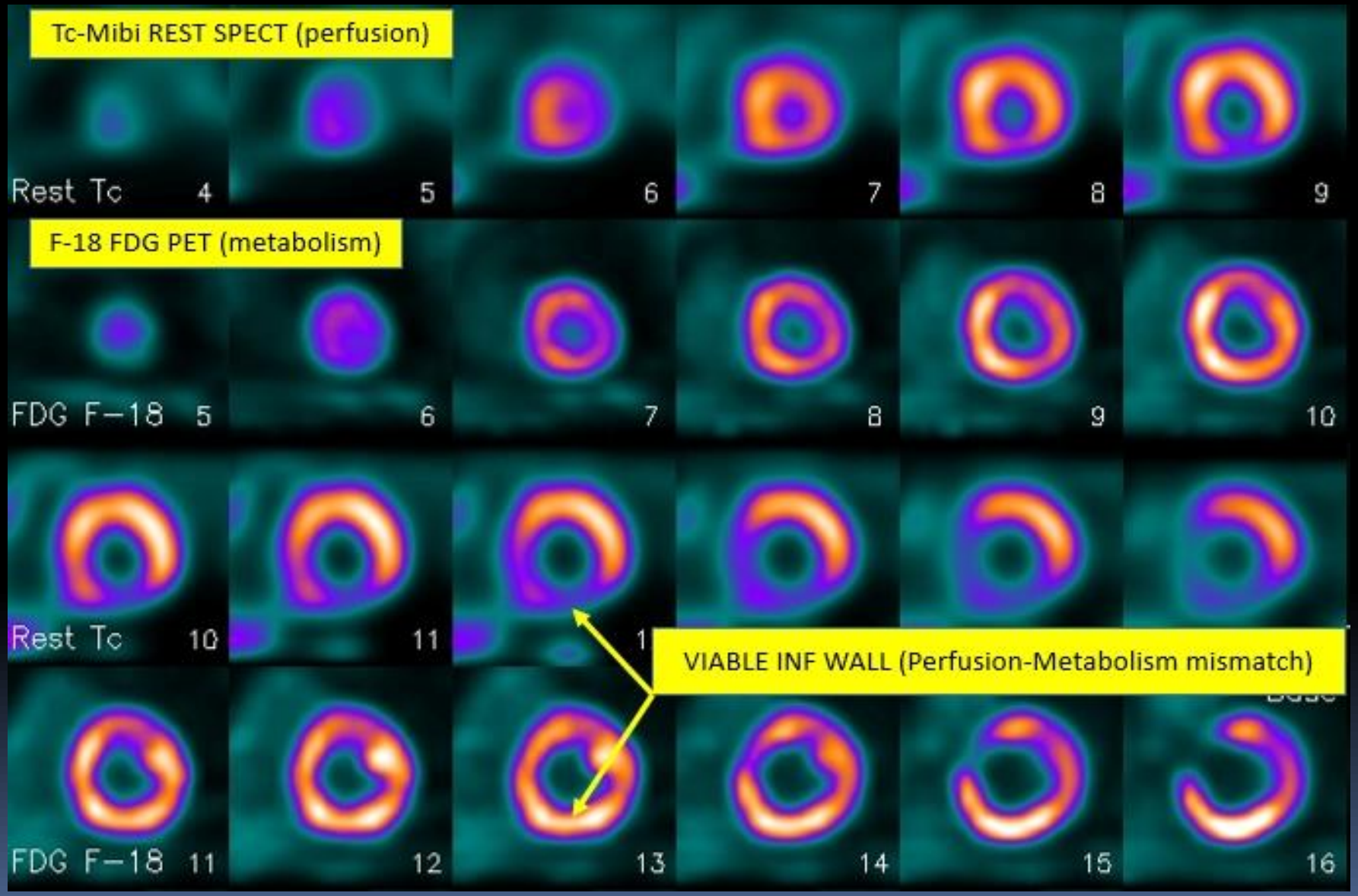
- MPI with PET provides higher spatial resolution than SPECT, and is a powerful noninvasive modality for the diagnosis and risk assessment of CAD.

- the ability to calculate absolute blood flow in coronary beds, assess wall motion at peak hyperemia with vasodilator stress, and evaluate coronary flow reserve enhances the diagnostic and prognostic accuracy of PET imaging.

- The intrinsic ability of PET to correct for photon attenuation provides enhanced specificity in evaluating IHD as it corrects for attenuation artifacts, such as breast tissue artifact and soft tissue attenuation in obese women.

- Assessment of myocardial perfusion can be performed with nitrogen-13 ammonia, oxygen-15 H_2O, rubidium-82 or carbon-11 acetate.

- Vasodilator stress MPI with PET, using rubidium-82 (Rb-82), offers several advantages for assessing IHD in at-risk obese women who are not capable of maximum exercise stress and in whom soft tissue attenuation can decrease the diagnostic accuracy of SPECT.


Tc-Mibi REST SPECT (perfusion)
Rest Tc 4 5 6 7 8 9
F-18 FDG PET (metabolism)
FDG F-18 5 6 7 8 9 10
Rest Tc 10 11 1
VIABLE INF WALL (Perfusion-Metabolism mismatch)
FDG F-18 11 12 13 14 15 16

CARDIAC MRI

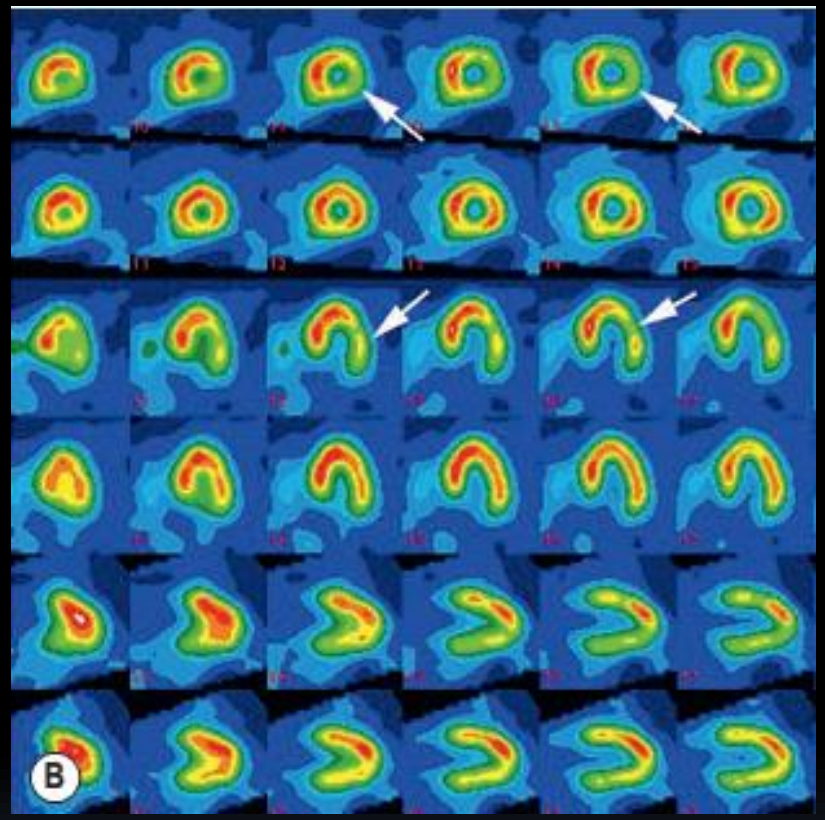
- MRI is emerging as an important imaging modality for assessing CAD in women.

- In addition to the ability to evaluate anatomic obstruction by angiography and blood flow assessment, MR perfusion imaging allows functional assessment of pharmacologic vasodilator-induced ischemia and segmental wall-motion evaluation.

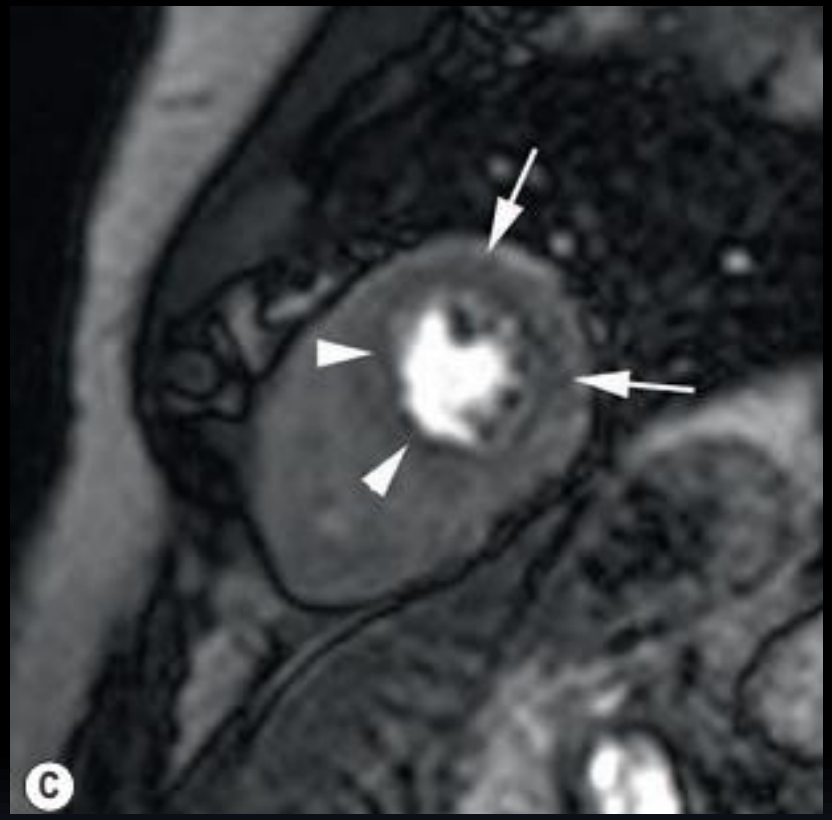
- CMR uses the changes in myocardial signal intensity during the first pass of a bolus of contrast through the heart to assess myocardial perfusion.
- Hypoperfused myocardium appears on CMR as a non- or low-enhancing part of the myocardium (perfusion defect).
- The defect, typically, obeys anatomical borders as well as the boundaries of the coronary artery perfusion territories, and the extent is determined by the position of the stenosis along the coronary artery.

- compared to SPECT, CMR enables visualisation of smaller, subendocardially located, perfusion defects.
- Moreover, CMR is not hampered by soft-tissue and attenuation artefacts.
- Similar to PET, absolute myocardial blood flow can be quantified with myocardial perfusion CMR.

- In analogy to stress echocardiography, stress function studies can be performed safely in an MR environment.
- Dobutamine, a β-agonist, increases oxygen consumption by increasing myocardial contractility and heart rate.
- A stepwise dose increment of dobutamine allows for the evaluation of the myocardial response at each stress level



MIBI SPECT shows reversible perfusion defect in lateral LV wall



Stress perfusion CMR shows extensive stress-induced perfusion defect in lateral LV wall and subendocardial perfusion defect in anterior LV wall and septum

Carotid Intima Media Thickness

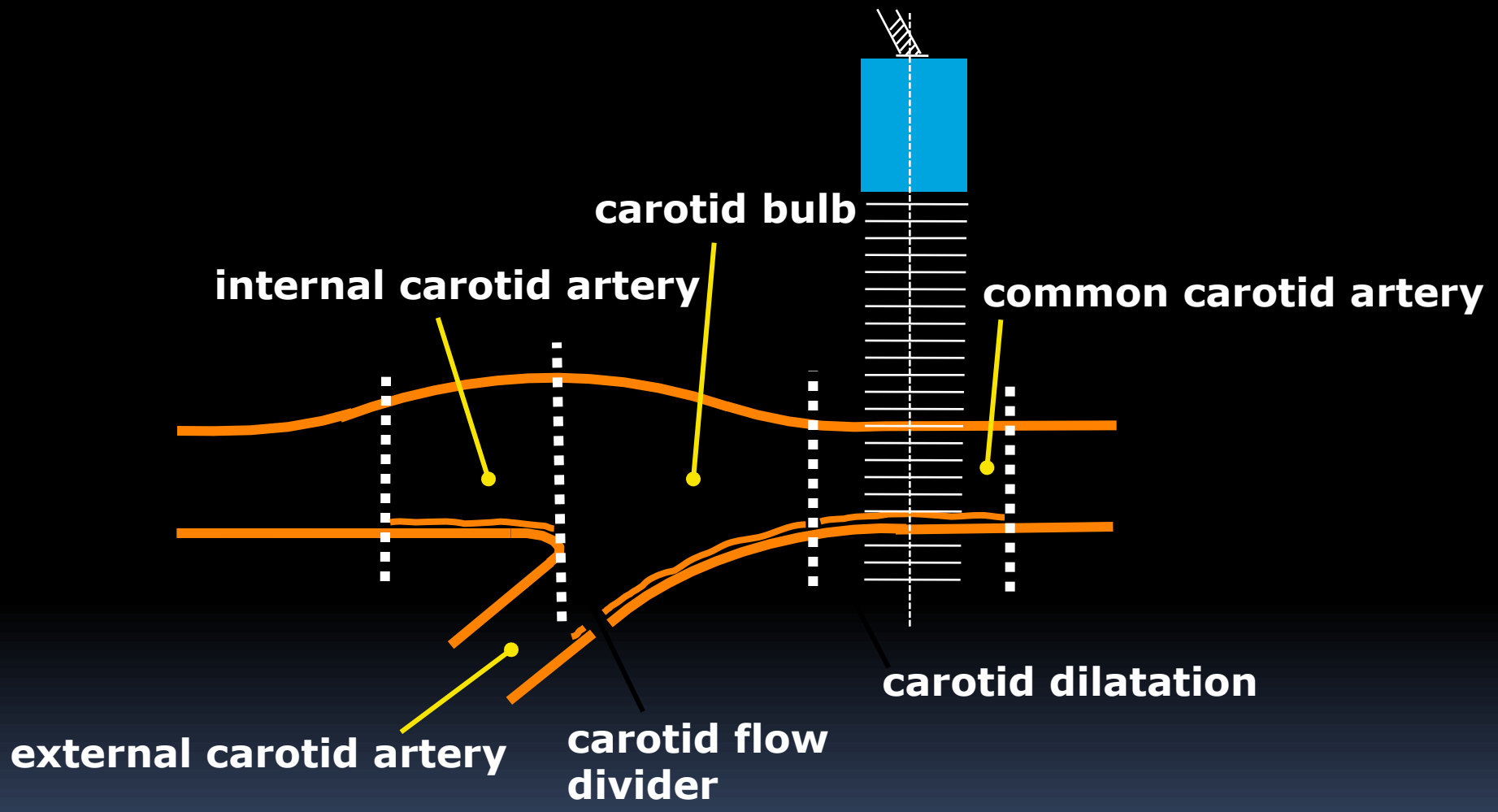
RECOMMENDATIONS

- **AHA Prevention V (Greenland et al., Circ. 2000) persons at intermediate risk may be suitable for screening by noninvasive tests, including ABI and carotid US, for those over age 50 years.**

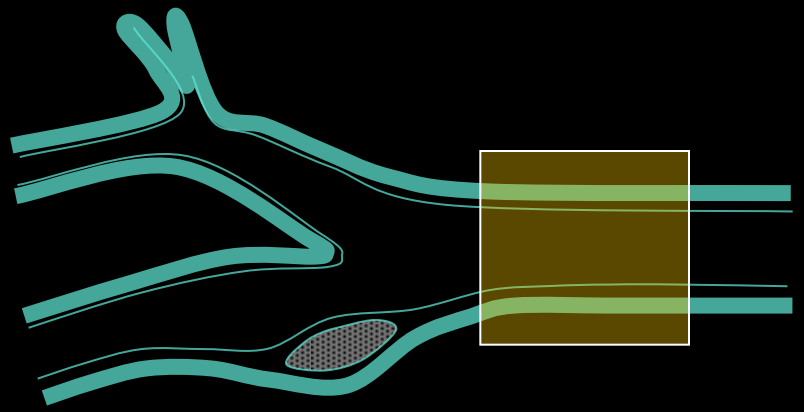
- **Task force 4, 34th Bethesda Conference (Wilson et al., JACC 2003; 41: 1898-1905) patients at intermediate risk for total CHD event possibly warrant further risk stratification by noninvasive tests to assess atherosclerotic burden.**

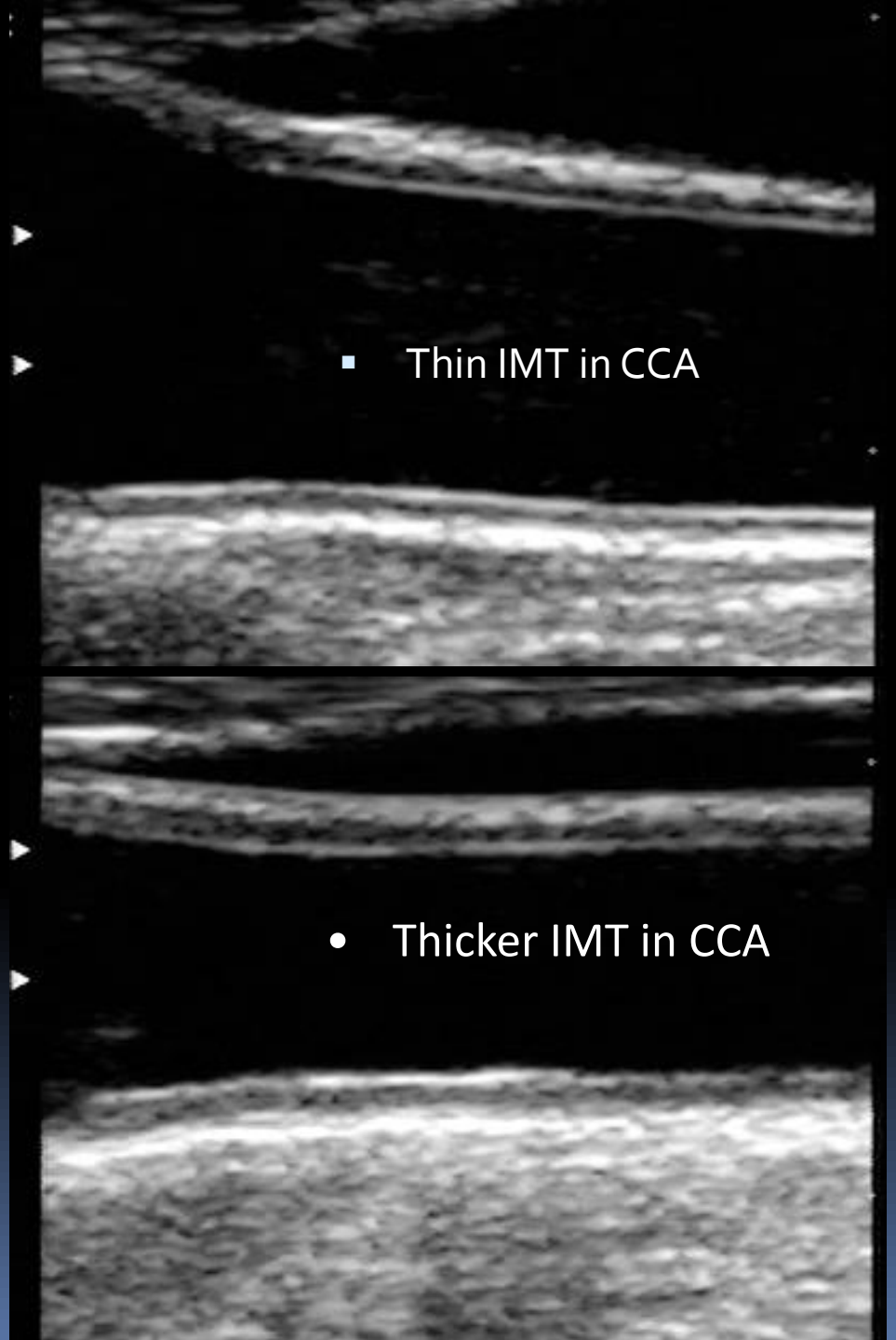
- **ACCF/AHA 2007 clinical expert consensus document on coronary artery scoring by CT on global risk assessment (Greenland et al. J Am Coll Cardiol 2007) stated it reasonable to obtain CAC in asymptomatic patients with intermediate CHD risk, based on possibility of reclassification to a higher risk status and altered medical management.**

Ultrasound measurement of CIMT



CIMT

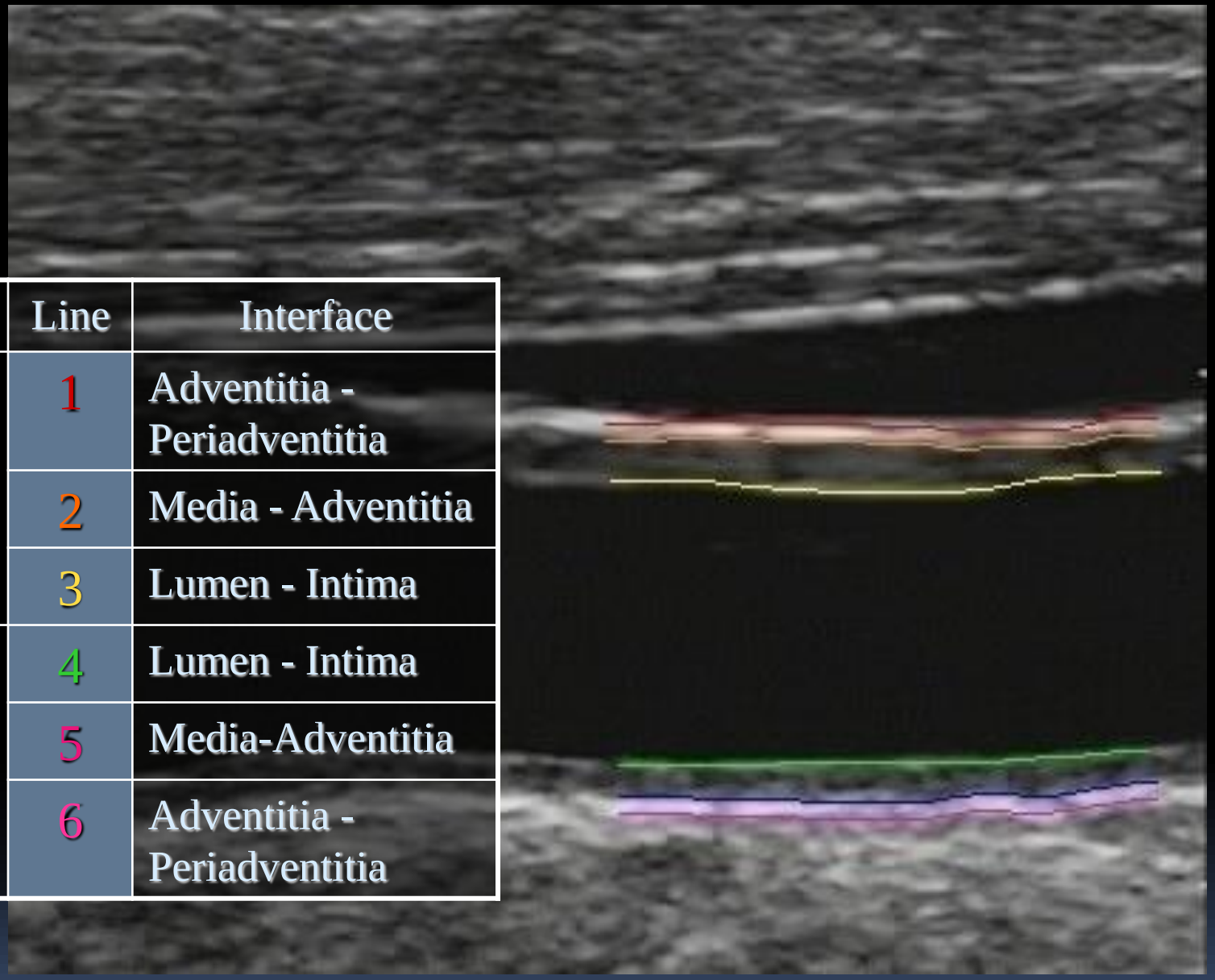




- Thin IMT in CCA

- Thicker IMT in CCA

Wall	Line	Interface
Near Wall	1	Adventitia - Periadventitia
	2	Media - Adventitia
	3	Lumen - Intima
Far Wall	4	Lumen - Intima
	5	Media-Adventitia
	6	Adventitia - Periadventitia



Near and Far Wall Identification

IMT Definition of Plaque

- a focal structure that encroaches into the arterial lumen of at least 0.5 mm or 50% of the surrounding IMT value.

or

- a thickness > 1.5 mm as measured from the media-adventia interface to the intima-lumen interface

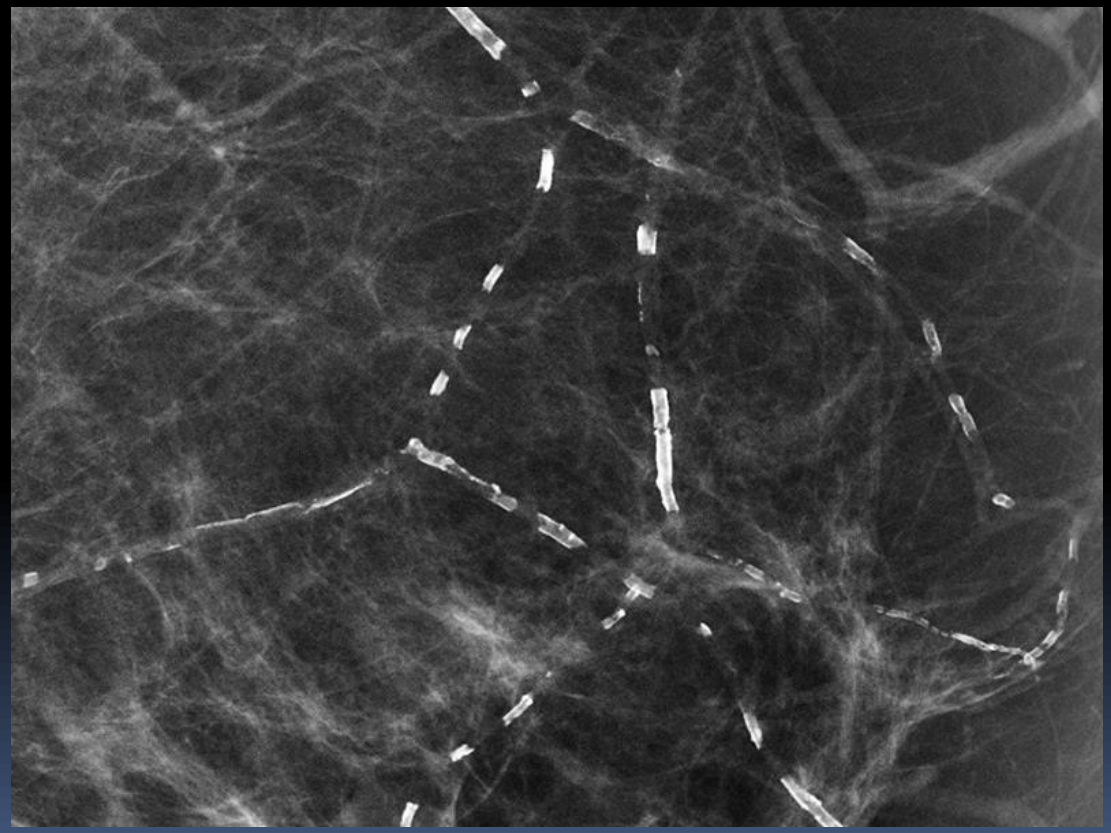
Mannheim Carotid Intima-Media Thickness Consensus (2004-2006). *Cerebrovasc Dis* 2007;23:75-80

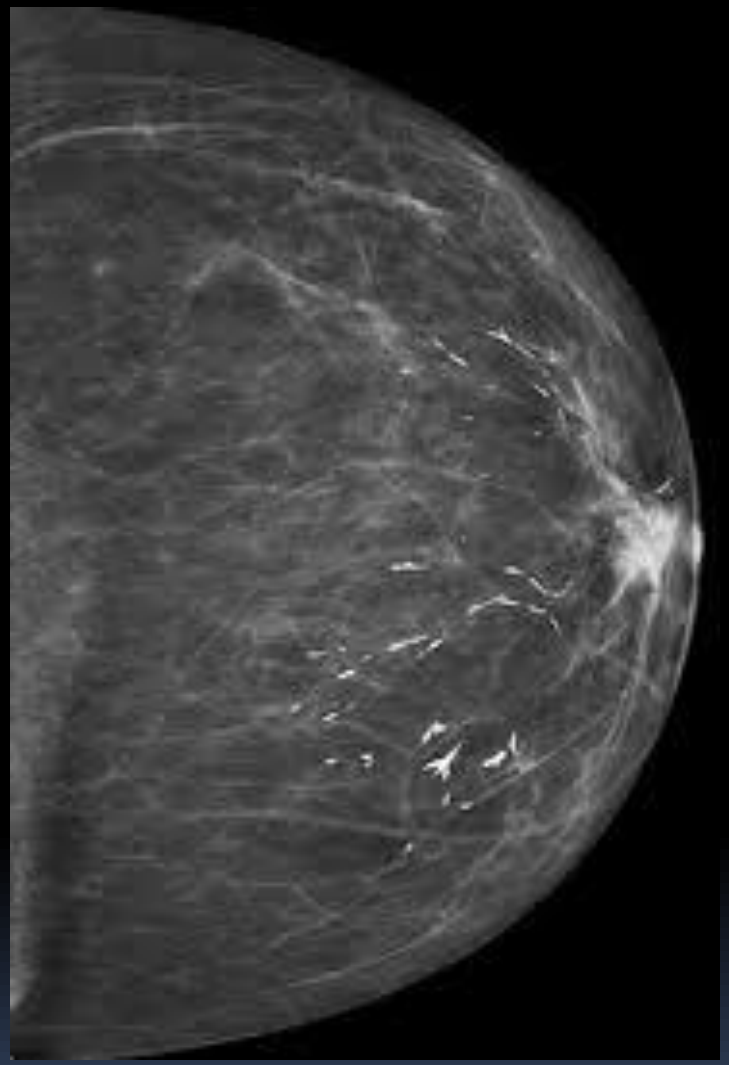
Consensus statement from the American Society of Echocardiography CIMT Task Force

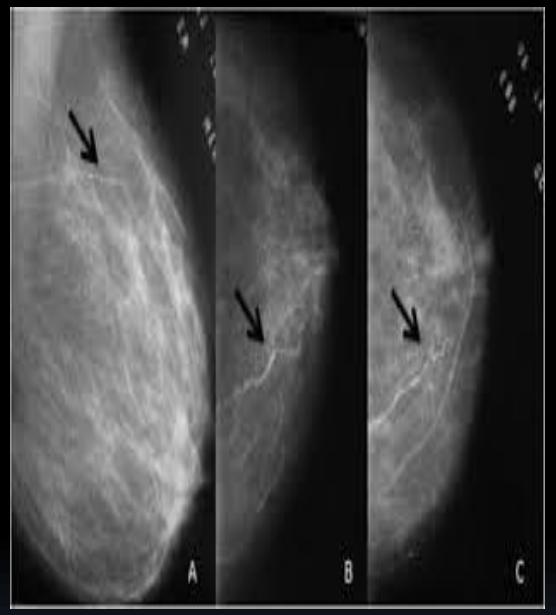
- CIMT measurements of far wall CCA only
- Scan extracranial carotid arteries (CCA, bulb, ICA) for presence of focal plaque
- Presence of plaque or far wall CCA CIMT greater or equal to the 75th percentile for the patient's age, sex, and race/ethnicity are indicative of increased CVD risk and may signify the need for more aggressive risk reductions
- Serial studies of CIMT to address progression or regression are not recommended

Stein JH et al. J American Society of Echocardiography 2008;21:93-111

Breast Arterial Calcification on Mammography IDs Atherosclerotic CVD Risk






A
B
C

- Mammographically-detected breast arterial calcifications (BAC) are considered to be an incidental finding without clinical importance.

- The proposed putative mechanism by which medial calcification may increase CVD risk is increased arterial stiffness.

- studies have reported associations of BAC presence with older age , diabetes, body mass index , hypertension , albuminuria [61], triglycerides, homocysteine , and hs-CRP

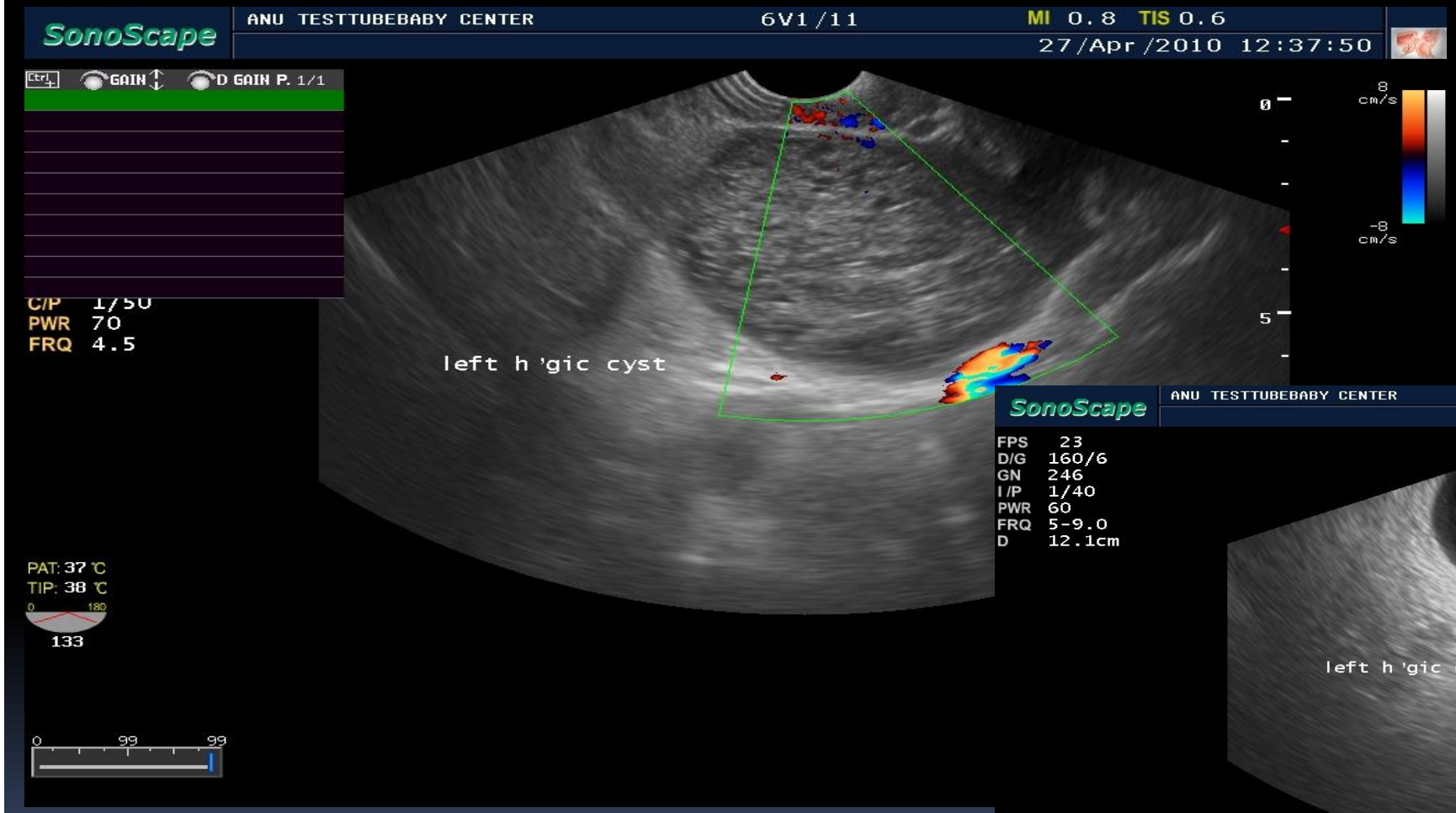
- BAC quantity is associated with an increased risk of CVD events.

- if a woman is found to have BAC, particularly highly elevated BAC mass, it should trigger an investigation of cardiovascular risk factor profile (diabetes, hypertension, lipid profile, inflammatory status) and this woman should be treated more aggressively if 1 or more of these risk factors are found to be present (in a similar fashion proposed for CAC.

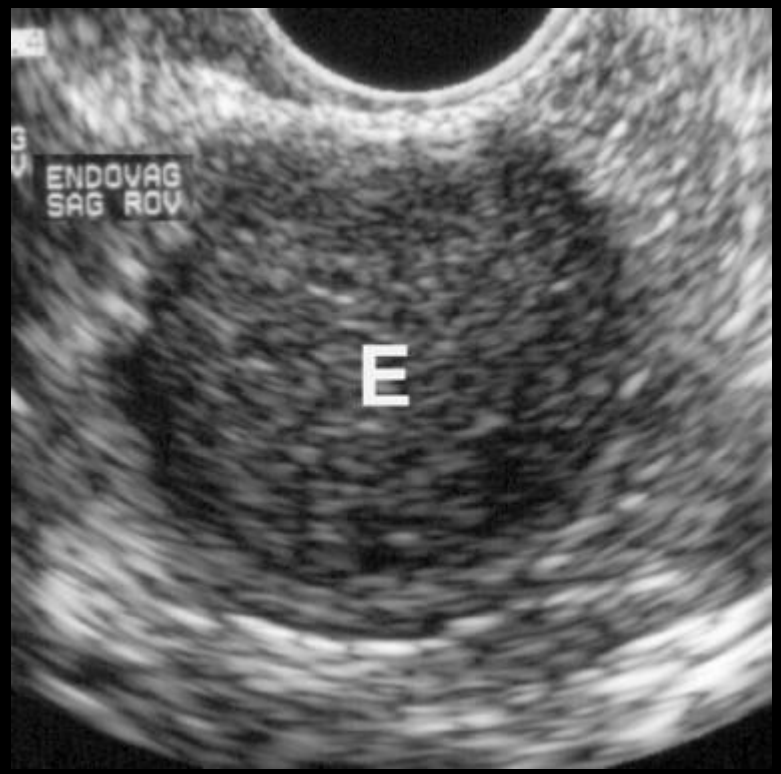
Women with endometriosis at higher risk for heart disease

- Women with endometriosis – especially those 40 or younger – may have a higher risk of heart disease.
- During 20 years of follow-up, researchers found that compared to women without endometriosis, women with the condition were.
- 1.35 times more likely to need surgery or stenting to open blocked arteries.
- 1.52 times more likely to have a heart attack.
- 1.91 times more likely to develop angina (chest pain).
- Moreover, women age 40 or younger with endometriosis were three times as likely to develop heart attack, chest pain or need treatment for blocked arteries, compared to women without endometriosis in the same age group

Haemorrhagic cyst



Bilateral endometriosis



Endovaginal ultrasound scan of an endometrioma

T1-weighted magnetic resonance image of an endometrioma

PREVENTION

Diet

- Eat healthy fats, having a low carb, low sugar diet, and eating healthy proteins such as fish.

Stay active

- The American Heart Association recommends at least 30 minutes of moderate to rigorous physical activity per day.

Maintain a healthy weight

- Losing weight can decrease chronic inflammation, which is one of the key issues with both endometriosis and cardiovascular disease.

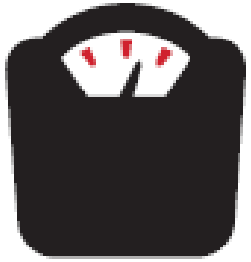
Quit or don't start smoking

- Smoking is the No. 1 individual risk factor for dying in America, according to a recent report from the Institute for Health Metrics and Evaluation at the University of Washington.

Recognize the symptoms

- Heart disease and stroke cause 1 in 3 women's deaths each year, according to the American Heart Association. Routine medical exams where blood pressure and cholesterol are checked are all important for young women. Diabetes is also a risk factor for heart disease.

Tips to reduce your risk for heart disease.



Maintain a Healthy Weight

Make Healthy Food Choices

Stay Active

Stop Smoking

Know Your Diabetes ABCs Talk to your health care team about how to manage your A1C, blood pressure, and cholesterol. This will help lower your chances of having a heart attack, a stroke, or other diabetes problems.


Thank You!