CVD IN WOMEN, ISCHEMIA DIAGNOSIS AND MENOPAUSE HORMONE THERAPY

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6TH ANNUAL
HEART IN DIABETES
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Philadelphia, PA
Where the Heart, Kidney and Diabetes Meet in Clinical Practice

EMORY
WOMEN'S HEART CENTER

OBJECTIVES

- Review current knowledge in sex differences in ischemic and non-obstructive CAD
- Describe differences in diagnostic testing for ASCVD in women from men: ETT, Stress imaging testing, CAC
- Examine current recommendations for menopause hormone therapy (MHT)

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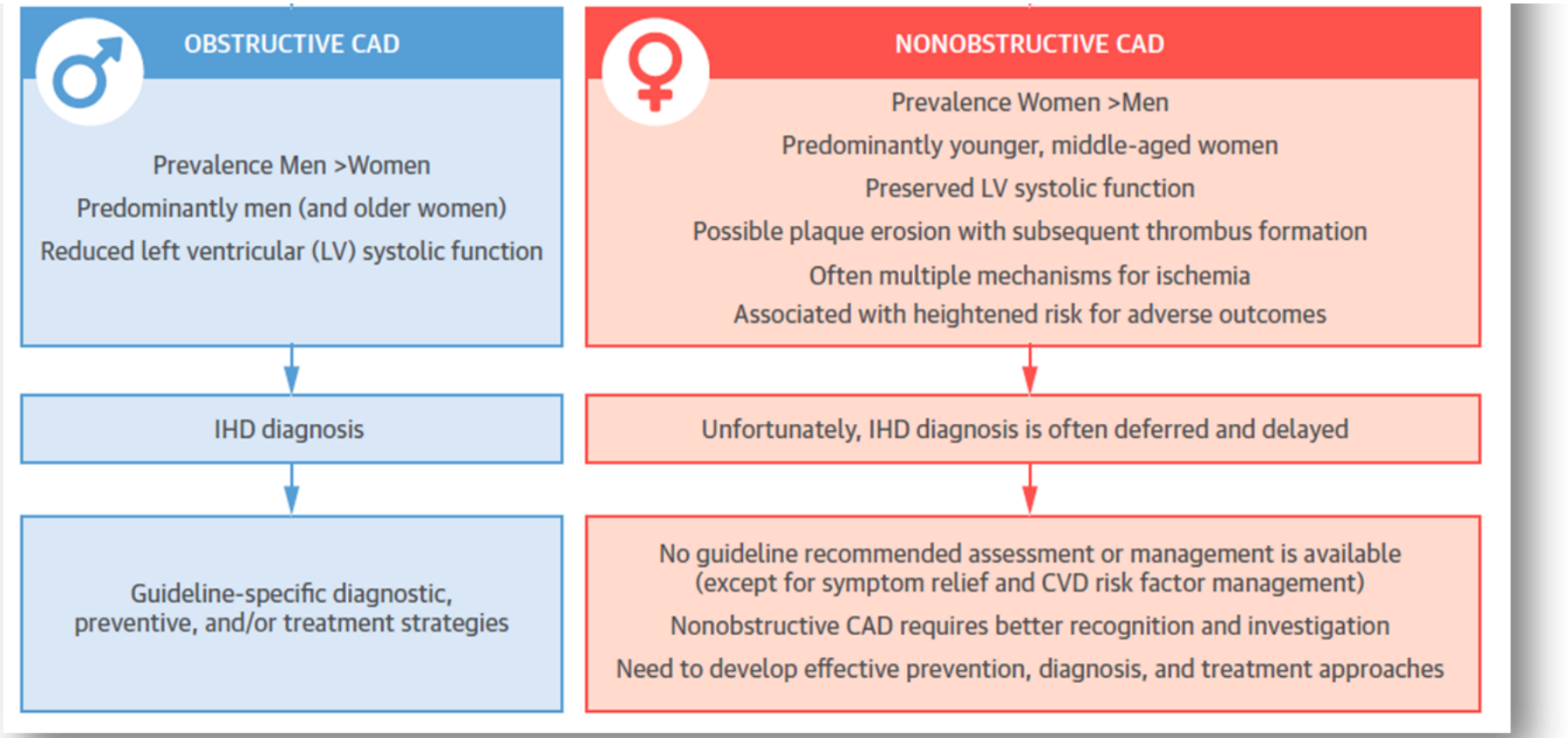
CVD IN WOMEN-
STILL #1 CAUSE OF DEATH IN WOMEN

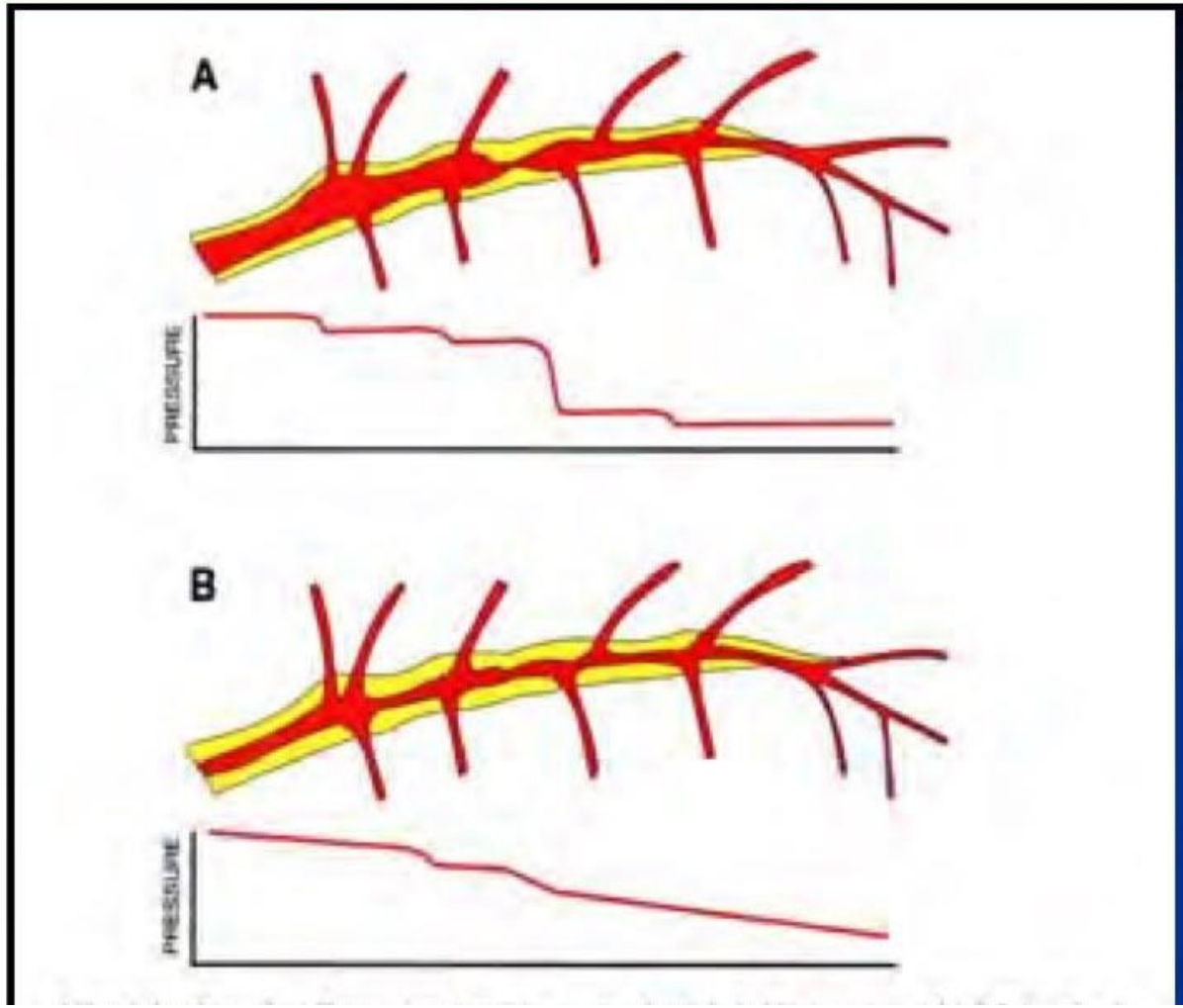
- Women have a higher prevalence of angina
- Women have a lower burden of obstructive CAD
- Women have a poorer prognosis compared to men
- Clinical presentation- chest pain most common but also weakness, dyspnea, nausea, and neck, jaw and back pain

WISE investigators, NHLBI WISE study, Am Heart Journal 2001;141:735-741

SEX-SPECIFIC DIFFERENCES IN CAD



WISE investigators, NHLBI WISE study, part II, JACC 2018, 10.1016/j.jacc.2004.12.084



WISE Study

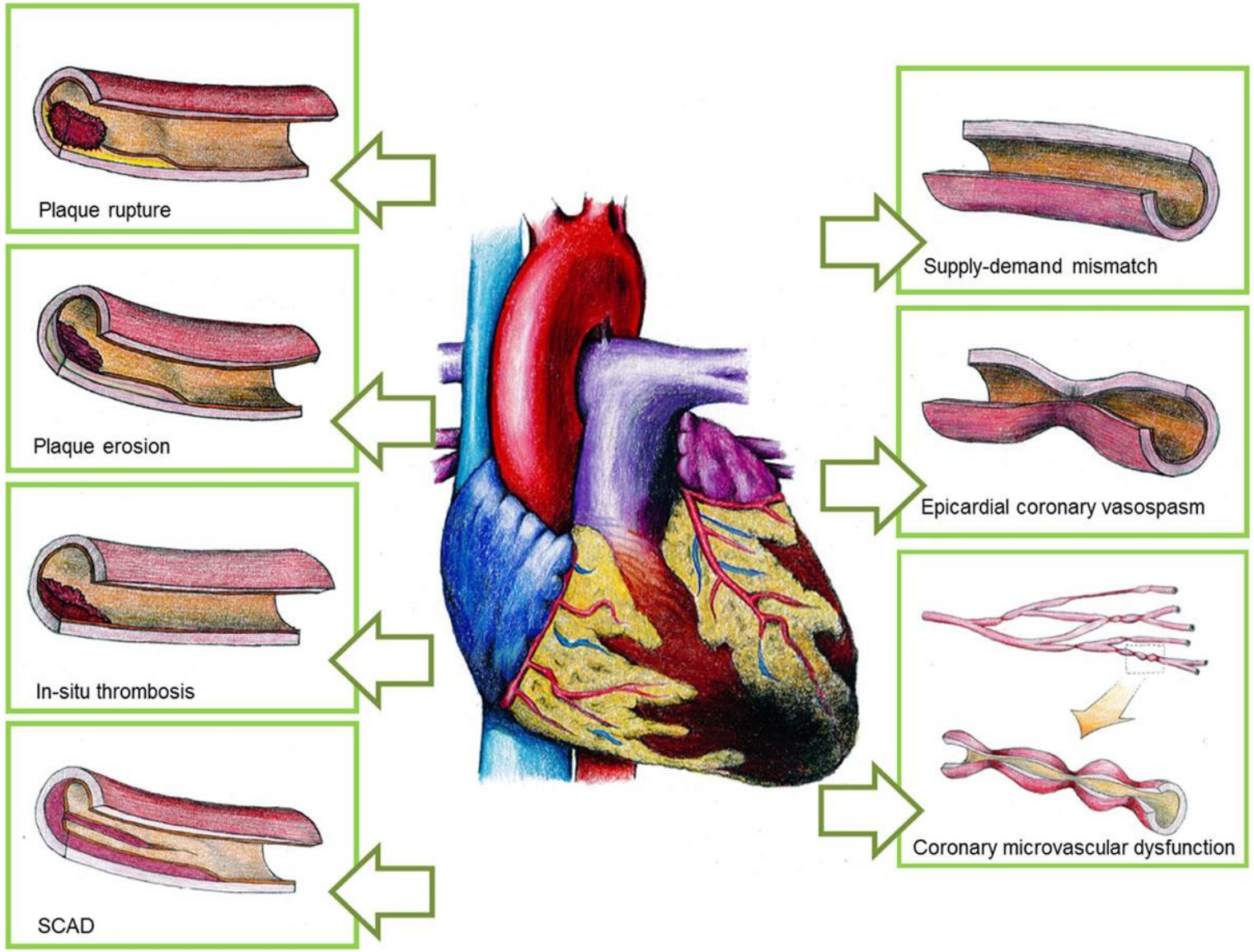
Male pattern fatty plaque:

Beer belly

Female pattern fatty plaque:

Cellulite

WISE investigators, NHLBI WISE study, part II, JACC 2018, 10.1016/j.jacc.2004.12.084


Plaque rupture
Plaque erosion
In-situ thrombosis
SCAD
Supply-demand mismatch
Epicardial coronary vasospasm
Coronary microvascular dysfunction

PLAQUE EROSION VS RUPTURE
WOMEN AND ACUTE MI

- In women older than 50 years, plaque rupture is the most common cause of acute MI
  - Associated with hyperlipidemia
  - Plaque is vulnerable with a thin fibrous cap overlying a necrotic core
- In younger women, plaque erosion is more often responsible for infarction
  - Associated with smoking
  - Estrogen may protect against plaque rupture
  - Eroded plaque is rich in smooth muscle cells and proteoglycans
  - Associated with less obstruction and less calcification (soft plaque)

MICROVASCULAR/ ENDOTHELIAL DYSFUNCTION

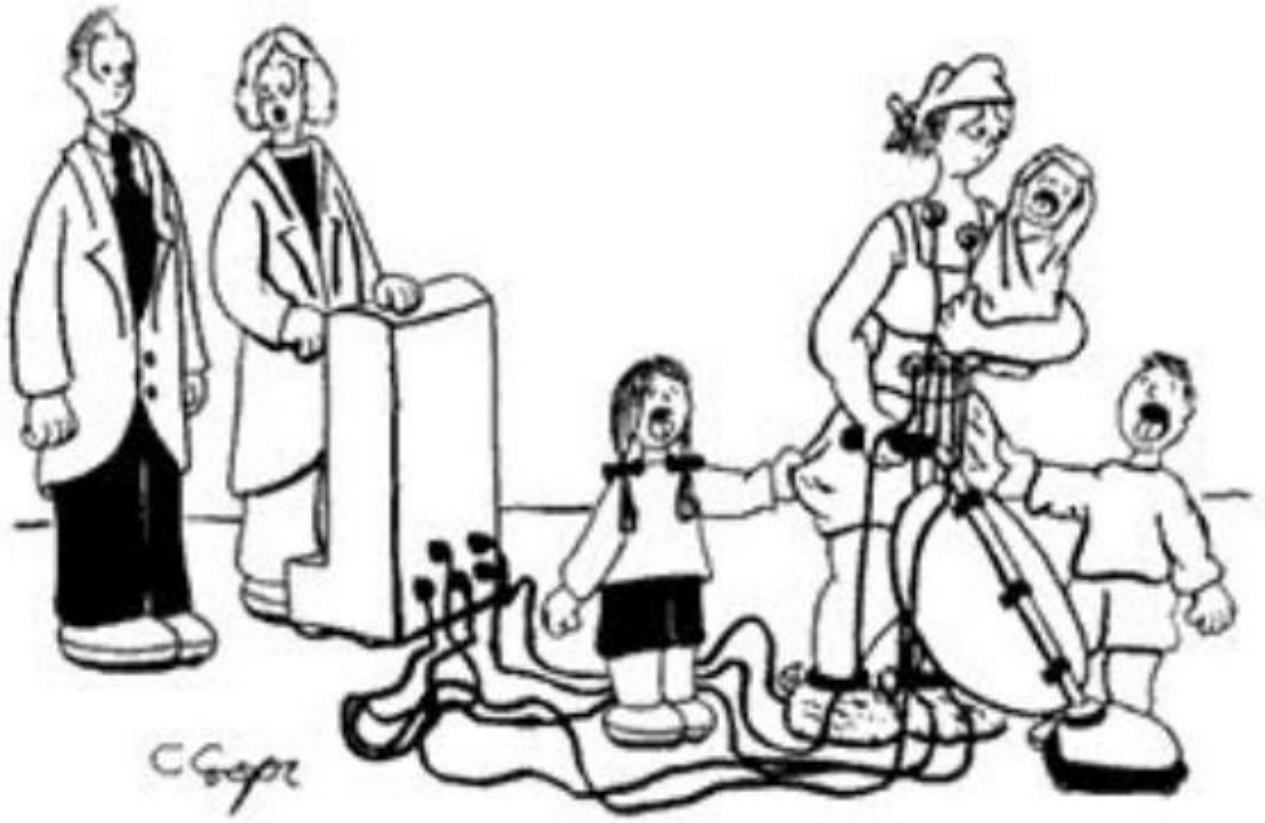
- Defined as limited coronary flow reserve and endothelial dysfunction
- Associated with worse outcome
- Increased rate of cardiac death, stroke and heart failure
- Annual MACE event rate of 2.5% in women

Wei J, Mehta PK, Results from WISE, JACC Intervention 2012

MI WITH NON-OBSTRUCTED CORONARY ARTERIES (MINOCA)

- MI with nonobstructive CAD
  - found in 6% of all MIs
  - Median age 58
  - 50% women
  - Possibly due to structural dysfunction, vasospasm, and thrombotic disorders
  - Has guarded prognosis with <u>better</u> 12 mo mortality compared to obstructive CD

Beltrame JF, J Intern Med 2013



"We wanted to make the stress test as realistic as possible."

ETT – FIRST TEST

- Can this woman exercise?
- Do they have an interpretable baseline EKG?
- If YES, do ETT.

- Simple
- Widely available
- Relatively Inexpensive

EVALUATION DURING ETT

- EKG changes – ST segments, arrhythmias
- BP response to exercise/ HTN response
- Assess for symptoms during and after recovery
- METS/exercise time and tolerance – Prognosis
- Arrhythmias- Afib, SVT, VT
- If can’t reach 85% Max PHR: Submax ETT and increased CAD risk

Gulati M et al. Circ 2010

“NEW” STRESS TEST- NO EXERCISE REQUIRED

"That's right! No huffing and puffing for 30 minutes on a treadmill. We've developed a new stress test that is faster and more accurate."

STRESS IMAGING

- Imaging should be reserved for women who have resting ST-segment abnormalities, DM or who are physically unable to exercise.

- If ETT is indeterminate or abnormal, additional diagnostic testing with stress imaging should be performed, and decisions should take into account ongoing symptom burden and degree of abnormalities. Cath vs CTA vs SPECT?

Mieres JH. Circulation 2014;130:350-379.

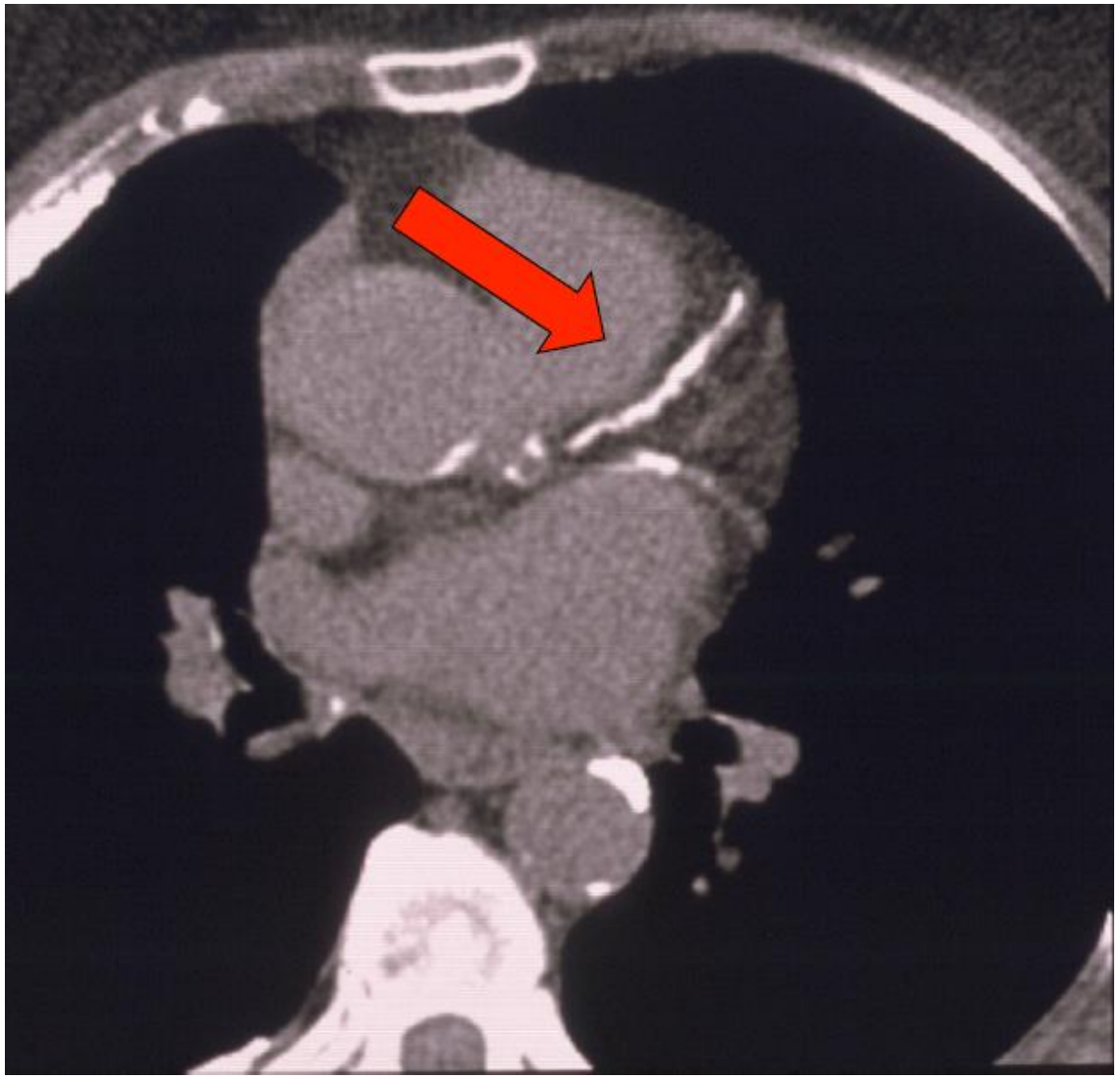
RADIATION CONSIDERATIONS

Average Background Radiation =	3 mSv
Rest-stress SPECT =	**11 mSv**
Rest-stress PET =	3 mSv
CCTA =	**10 mSv**
Coronary Calcium Scan =	2 mSv
Stress Echo/ DSE=	NO Radiation
Cardiac MRI=	NO Radiation

DIAGNOSTIC ACCURACY OF CARDIAC SPECT IN WOMEN IS AFFECTED BY SEX-RELATED FACTORS :

- Higher prevalence of single-vessel obstructive CAD (SPECT) and microvascular dysfunction (PET)
- Smaller left ventricular size- technically difficult
- More breast attenuation (harder for stress echo and SPECT, PET better with large breast/ obesity)

CORONARY ARTERY CALCIUM SCORING



Coronary Artery Calcification in LAD and LCx arteries

NEW STUDIES SUPPORTING CAC BENEFITS

- CAC better at predicting cardiac events than Framingham 10-yr risk calculator and ETT

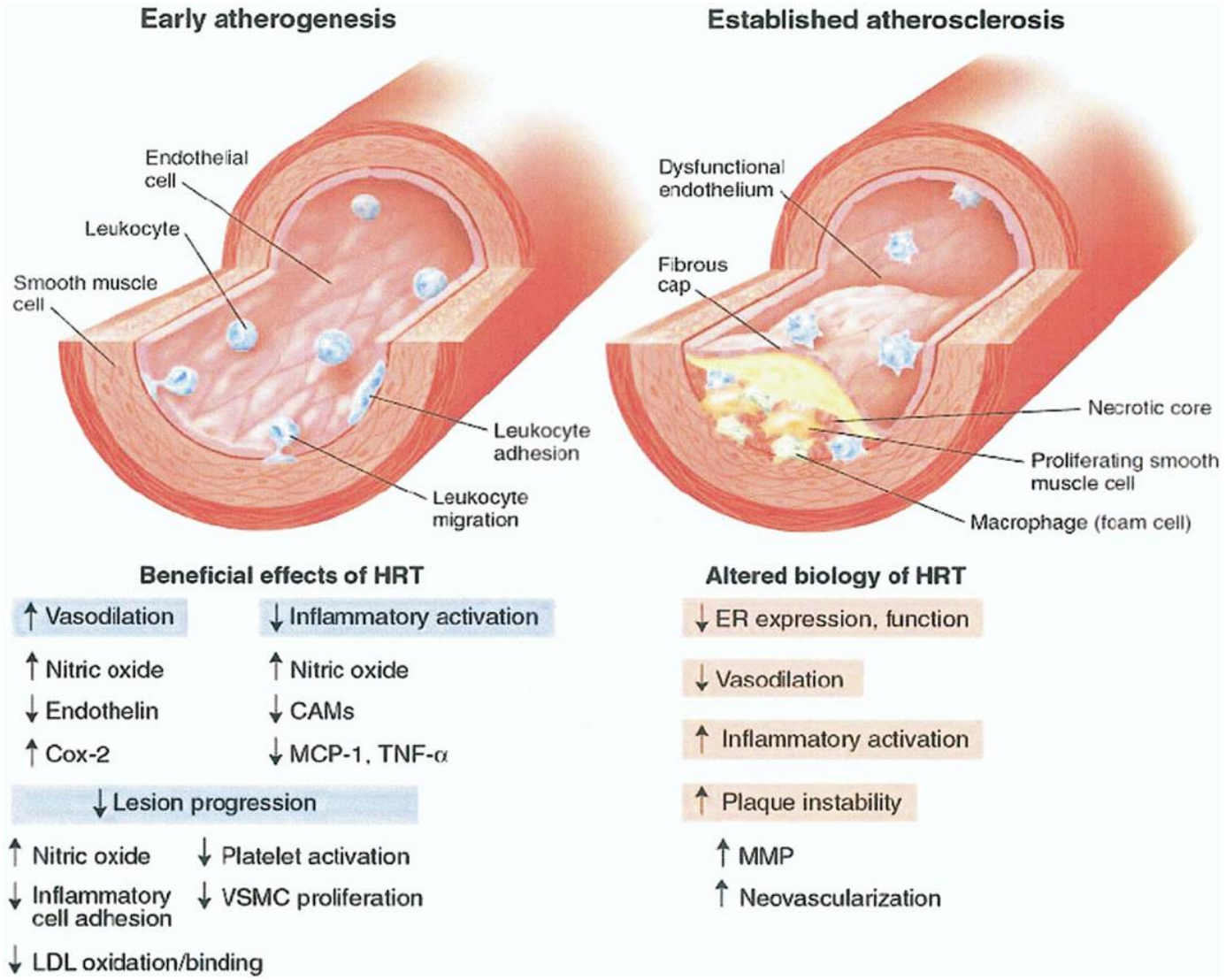
- CAC Score 1-99, 50% more likely to die of heart disease than CAC zero
- CAC Score 100-399, 80% more likely to die of heart disease
- CAC Score >400, 300% more likely to die from heart disease
- CAC percentile over 75% is high risk- important in younger patients

- CAC zero generally associated with negative SPECT-MPI study
- Power of Zero after age 65

LIFETIME OF ASCVD RISK

Timing Hypothesis

- Timing Hypothesis: The beneficial effects of MHT in preventing atherosclerosis occur only when the therapy is initiated EARLY before advanced atherosclerosis develops.
- Predicts that MHT is NOT beneficial when given to older women, because the underlying biologic characteristics of the vessel wall and vascular response to MRT are altered in older, more atherosclerotic vessels.



Ouyang et al. J Am Coll Cardiol. 2006 May 2;47(9):1741-53

High Risk/ Avoid MHT

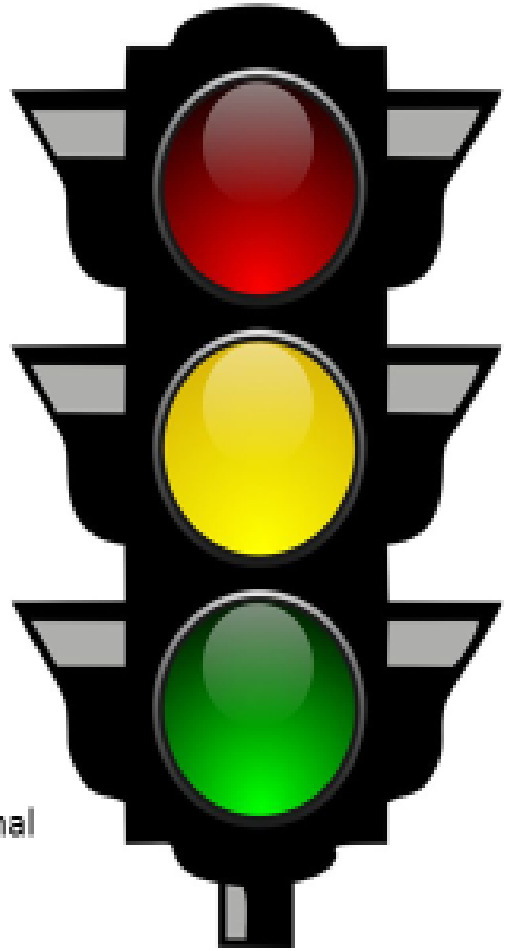
- Known ASCVD/ CAD/ PAD
- Known venous thrombosis or pulmonary embolism
- Known Stroke/TIA or MI
- Known Clotting Disorder
- Known Breast Cancer
- ASCVD Risk≥7.5%

Definite Risk/ Caution with MHT

- Known Diabetes
- Smoking
- Uncontrolled HTN
- Obesity/ Sedentary/ Limited mobility
- SLE/ RA/ Migraine with aura
- High TG or uncontrolled cholesterol
- ASCVD Risk ≥5.0-7.4%

Low Risk/ Acceptable for MHT

- Recent menopause, normal weight, normal blood pressure, active female
- ASCVD Risk <5%



High Risk/ Avoid MHT

- Oral combination MHT for more than 10 years or after age 65
- Unopposed estrogen in women with an intact uterus

Definite Risk/ Caution with MHT

- Oral combination MHT for more than 5 years or after age 65

Low Risk/ Acceptable for MHT

- MHT at early onset of Menopause for less than 5 years duration
- Low dose transdermal E2 patch
- Vaginal creams, estradiol rings, tablets, & inserts

Thank you to HiD Program Committee and special thanks to

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