Heart Disease in Women:
Pearls and Pitfalls

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CVD is the leading cause of death in post-menopausal women.[1] The incidence of CVD is declining in men, but increasing in women. This is mostly because of a decrease in MI in younger men, with a concomitant increase in older women. Despite these alarming trends, the magnitude of the problem is still underappreciated. Women are underrepresented in randomized clinical trials and data regarding prevention and treatment of coronary artery disease (CAD) in women is largely extrapolated from populations of men.

Diagnosis of CAD in women

The ability to diagnose CAD in women may be limited by the often atypical presentation, as well as the limitations of noninvasive testing. Currently, the American Heart Association (AHA) guidelines recommend initial evaluation of women with suspected CAD with the exercise treadmill test (ETT).[2] The lower prevalence of CAD, particularly in younger women, higher prevalence of single-vessel disease, lower in exercise capacity and the digoxin-like effects of estrogen are some factors accounting for the lower diagnostic yield of ETT in women compared to men. The addition of cardiac imaging is most helpful in those women whose pretest likelihood of CAD is intermediate. Myocardial Perfusion imaging (nuclear) has been the traditional tool to assess CAD and recently CT angiography is gaining popularity, however they are both associated with significant radiation exposure. Since cancer occurs ≥ 25 years after radiation exposure and breast tissue is highly radiosensitive, clinicians should strive to limit radiation exposure in young women. Stress ECHO has a similar diagnostic yield, without concomitant radiation exposure.

Meet Sarah

Sarah, a 57-year-old retired teacher, presents with recurring right shoulder pain when she goes grocery shopping. She is a known diabetic and recently quit smoking.

She is on a hormone replacement therapy (HRT) and a calcium supplement. Clinical examination and ECG were normal. Exercise treadmill test was positive for exercise induced ischemia. She was found to have mild ischemia with preserved left ventricular function on stress echocardiography.

She was treated with ASA, statin, β-blocker and ACE inhibitor with marked improvement in her symptoms. HRT and calcium supplement were discontinued.

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Table 1

Radiation dose and lifetime attributable risk of cancer from single coronary CT angiography (CTA) scan.

Test	MilliSievert (mSv)	Chest x-ray (CXR) equivalent
CXR PA- Lat	0.04–0.06	1
CTA 64-slice	11.0+4.1	220
Diagnostic angiogram	3-7	100
Nuclear perfusion imaging	6-8	140
Stress echocardiography	0	0
Age (years)	**Women***	**Men***
20	0.7	0.15
40	0.35	0.099
60	0.22	0.081
80	0.075	0.044

* % absolute risk of cancer.

Women presentation with acute coronary syndrome (ACS)

In large cohort studies of MI, women are more likely than men to present without chest pain/discomfort (37% vs. 27%).[3] Typically women develop MI a decade after men. Advancing age is the strongest predictor of MI presenting without chest pain. The differences between men and women are not large enough to warrant sex-specific public health messages regarding the symptoms of ACS. The current public health message suggests that MI may present as sudden onset chest pain, shortness of breath, sweating, nausea, lightheadedness or pain in other areas of the upper body (*e.g.* pain in one or both arms, the back, neck, jaw or stomach).

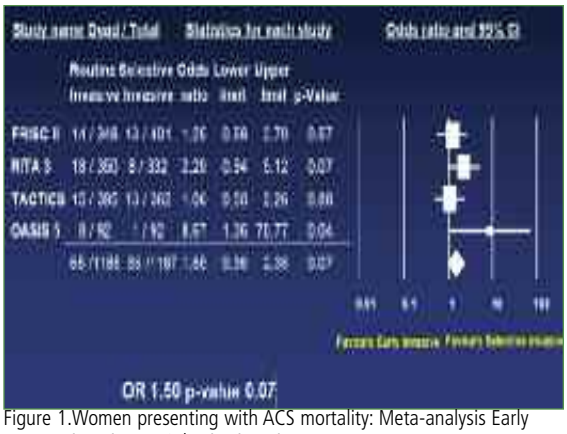

Figure 1.Women presenting with ACS mortality: Meta-analysis Early invasive Vs. Selective invasive strategy

Management of women with ACS

Women have higher in-hospital mortality rates post MI compared with men, however they are not referred as often as men for diagnostic and/or therapeutic procedures. However, unlike the clear benefits found in men for early invasive treatment of non-ST elevation ACS, a recent meta-analysis suggests that this strategy may increase the risk of death in women by up to 50%, possibly because of an increased risk of bleeding. The meta-analysis was based on a small number of patients and much larger trials are needed to properly assess the benefit and risk of invasive strategy.

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ASA and women

Both women and men benefit similarly from the favorable effect of β-blockers, ACE inhibitors and statins. The role of ASA has been questioned. Secondary prevention trials show similar reduction in stroke and MI when compared to men. The effect of ASA for primary prevention was studied in the Women's Health Study. The result suggested benefit against stroke but not MI in the overall group. However, the Framingham risk score was < 5% in 85% of the participants. There was a significant reduction in MI in women ≥ 65-years-of-age that was similar to the previously reported benefit in men. Of note, > 30% of events occurred in the ≥ 65 year age group despite being only 10% of the total group. There is no evidence to suggest that women respond differently to ASA than men and the anticipated benefits are higher when used in high-risk women. The current guideline from the AHA recommends ASA prophylaxis for women with a Framingham risk score ≥ 10% as well as for secondary prevention.

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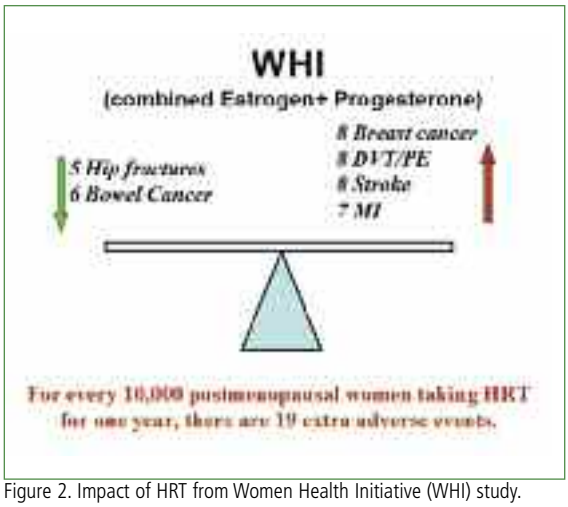

Figure 2. Impact of HRT from Women Health Initiative (WHI) study.

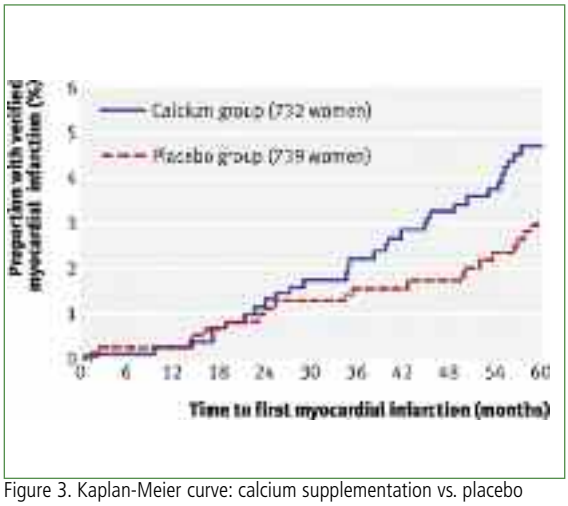

Figure 3. Kaplan-Meier curve: calcium supplementation vs. placebo

Hormonal replacement therapy (HRT)

The Women's Health Initiative (WHI) study demonstrated a higher risk of CVD and breast cancer in women taking HRT (Figure 2). Recently published three year follow-up data suggests that the CVD risk returns to baseline after discontinuation of HRT, however women remain at increased risk of breast cancer.[4] On the basis of the available evidence, HRT should not be prescribed to post-menopausal women of any age for primary or secondary prevention of CAD. In women taking HRT for menopausal symptoms, it should be used for the shortest

period of time necessary (one to two years). HRT should be discontinued if an acute CAD event occurs and should not be resumed.

Calcium supplements

A recently published study from New Zealand randomized 1,471 post-menopausal women to receive calcium supplement (1 g q.d.) or placebo with five years mean follow-up and suggested that calcium use is associated with an increase in MI rates (relative risk 1.49) possibly by accelerating vascular calcification.[5] Until further evidence emerges, the benefits of calcium supplements in elderly women should be weighted against the potential increased risk of CAD events. In younger patients, calcium supplement is reasonable, but it may be sensible to use smaller doses (*e.g.* 500 mg q.d.). Other large trials of calcium supplementation have shown a trend toward increased CV events although this is not consistent.

Take-home message

1. CVD is the leading cause of death in women
2. Differences in ACS presentation do not warrant changes or sex-specific public health messages
3. ETT is the recommended initial evaluation modality
4. Stress echocardiography has a similar diagnostic yield without the radiation exposure associated with nuclear perfusion imaging or CTA
5. ASA is recommended for women at high risk of developing CVD and for secondary prevention
6. Women should not receive HRT at any age for primary or secondary prevention of coronary heart disease (CHD) and should be stopped as soon as possible
7. Calcium supplementation is potentially associated with increased CV event rates

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