Erectile Dysfunction and Cardiovascular Disease Advances and Detection of Subclinical CVD

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I have no relevant financial relationships with commercial interests to disclose.
AGENDA

- Case 1 Presentation
- Vascular ED: Clinical Significance
- Role of ED in CAD Risk Assessment
- Workup of Men with Vasculogenic ED
- Means to detect subclinical CAD in men with vasculogenic ED
- New Guideline for work-up of Vasculogenic ED
CASE: 54 YO MALE WITH ED: WHAT IS VASCULOGENIC ED?

- 54 yo male BMI: 31.2 kg/m², BP135/85, HR 84R
- WC 109 cm (42.9 in) ED of 2 yr dur (grad worse).
- ED: primarily in the domain of an inability to sustain erections during intercourse; fails to reach orgasm.
- onset was gradual, rarely awakens with morning erections.
- absence of nocturnal erections for 4 yrs.
- As he and his wife proceed to make love, he admits to increasing anxiety about his performance. He thought his ED was primarily related to stress.
- Masturbatory erections are not firm
CASE: 54 YO MALE WITH ED:

- He no HX CVD; no SX CAD
- His diet: Eats white bread and likes carbohydrates
- He drinks 3 sugar-sweetened beverages/day
- Does not exercise.
- Four yrs ago, his 10-yr risk of CHD using Framingham:
  Risk Score was “low” <10% 10 yr. risk of MI
CASE: 54 YO MALE WITH ED:

- Father has HTN; Mo & Fa elevated cholesterol. No hx Premature CAD; 2 of Father’s siblings had prostate cancer.
- GU exam is normal; mod visceral adiposity (WC 42 in); mildly buried penis
- Testes normal vol bilat. His penile exam
  - NL stretched length of 6”, circumcised, good turgor
- He has no hernias. He has NL femoral pulses without auscultated bruits, NL dorsalis and posterior tibial pulses in each extremity.
CASE: 54 YO MALE WITH ED

- He is on no meds
- Hct of 42%.
- BUN/Cr are 18/1.1. His FBS is 112, TT 320ng/dL
- Lipids: TC 210; TG 210; HDL 39mg/dl, LDL 112. HgBA1c is 5.8%
- His EKG is normal with the exception of a small 1st degree heart block.
- Vascular ED was confirmed by doppler u/s
  - Peak Systolic flow is < 30 cm/s and he has elevated diastolic flow of > 7 cm/sec = venous leak
VASCULAR ED: CLINICAL SIGNIFICANCE
Vascular ED: powerful marker of incr CVD risk beyond traditional risk factors

Detection of vascular ED should trigger CVD risk assessment/reassessment for subclinical CAD

No guidelines exist for w/u vascular ED

In patients with vascular ED considered at intermediate or high CVD risk, coronary artery calcium (CAC) may be particularly valuable for further assessment

30 men with ED and no other clinical cardiovascular disease vs. 27 age-matched controls without ED

<table>
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<tr>
<th>Lab Results</th>
<th>NI Subjects (27)</th>
<th>ED Patients (30)</th>
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<tbody>
<tr>
<td>Tot Chol (mg/dl)</td>
<td>193.1 ± 8.6</td>
<td>203.6 ± 7.6</td>
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<tr>
<td>Trigly (mg/dl)</td>
<td>130.7 ± 18.4</td>
<td>115 ± 11.5</td>
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<tr>
<td>HDL-C (mg/dl)</td>
<td>47.9 ± 3.9</td>
<td>47.7 ± 2.4</td>
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<tr>
<td>LDL-C (mg/dl)</td>
<td>118.5 ± 7.0</td>
<td>128.2 ± 6.8</td>
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<tr>
<td>Glucose (mg/dl)</td>
<td>92.9 ± 2.1</td>
<td>90.0 ± 1.6</td>
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<tr>
<td>Lipo a (mg/dl)</td>
<td>24.3 ± 10.3</td>
<td>22.4 ± 3.7</td>
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<tr>
<td>Homocys (mg/dl)</td>
<td>9.2 ± 0.3</td>
<td>8.9 ± 0.5</td>
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Figure 1. Brachial artery flow-mediated vasodilation (FMV) was significantly reduced in erectile dysfunction patients (circles) versus normal control subjects (squares) over the whole time period (p=0.014). The difference was also significant when comparing the percent dilation from baseline to 60s after cuff release (p=0.05).

Figure 2. The vasodilator response to 0.4 mg sublingual nitroglycerin (NTG) was significantly impaired in erectile dysfunction (ED) patients versus normal control subjects (13.0 1.4% vs. 17.8 1.4%, p 0.02).
THE PLACE OF ED IN CAD RISK ASSESSMENT
The patient is reluctant to start pharmacotherapy for lipids (Statin) or undergo further testing.

Discussion included a decision on trial of oral PDE5 therapy and 3 mo. Lifestyle intervention.
Lifestyle intervention:
- Heart-healthy diet; avoid sugar-sweetened beverages; emphasize whole grains
- Regular physical activity of moderate intensity 4-5x/wk.
- Sustained weight loss

F/U & reassessment 3 mo later.
- Anthropomorphic measurements unchanged
- Labs essentially unchanged
- Pt admits to low adherence to lifestyle recommendations
Current CVD prevention guidelines recommend men > 40 yo or older undergo CVD risk assessment 1,2

Same guidelines recommend that risk should be reassessed every 4 to 6 years in non high-risk individuals 1

These recommendations are often neglected 3

When ED symptoms prompt a urologic or PCP visit, these men might otherwise be “invisible” to the medical system

This encounter provides an opportunity for assessing and reassessing CVD risk, especially with a vascular component of ED

CASE: 54 YO MALE WITH ED
CARDIOVASCULAR DISEASE RISK ASSESSMENT

- Am College of Cardiology/Am Heart Assn 2013
  Pooled Cohort Equations:
  7.2% 10-year risk of MI/CVA
- Low risk of stroke; MI < 5%
- Intermediate risk: > 5% < 7.5%
- High risk: > 7.5%

- Will likely favor the use of more potent statin therapy in 20 million Americans

WORKUP OF MEN WITH VASCULOGENIC ED
All men with largely vasculogenic ED should undergo a thorough medical assessment, including **waist circumference, testosterone, fasting lipids, fasting glucose and blood pressure measurement**.

Following assessment, patients should be stratified according to the risk of future cardiovascular events.

Low and high risk patients should have clear management protocols.

What about the “intermediate risk” patient with vascular ED?
The detection of subclinical CVD:

- If.... ED is a better marker for CVD in younger middle-aged men and ED reclassifies ~7%-10% of men in FRS 5-20%, i.e. intermediate CVD risk¹
- Then...which test will have the greatest potential to detect subclinical CVD?

CVD cardiovascular disease; ED erectile dysfunction.
CONTINUUM OF ATHEROSCLEROSIS PROPAGATION PRIOR TO A CHD EVENT

The Top 4 Tell us Who Might Have CAD

“Funnel”

Genetics
Environment
Risk Factors
Biomarkers

Subclinical Atherosclerosis

CAC Tells Us Who Has Subclinical CAD

Overt CAD
Coronary artery calcium provide superior discrimination and risk reclassification compared with other risk markers.

Comparison of Novel Risk Markers for Improvement in Cardiovascular Risk Assessment in Intermediate-Risk Individuals

CONCLUSIONS REGARDING CAC AND DETECTION OF SUBCLINICAL CVD

- We now have modern, head-to-head data
- CAC >>> Biomarkers
- CAC > cIMT in most patients
- In general, cIMT > ABI in asymptomatic patients
- Consider cIMT in young people (<40 yr)
We recommend considering/discussing a coronary artery calcium score for men with vascular ED not already stratified at high risk by scores.

At present it is self-pay: cost to patient ranges from $100-$250.

CAC of zero is “gatekeeper” of further testing.

**CAC AND SUBCLINICAL ATHEROSCLEROSIS: SUMMARY**

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<th>Assessment of CAC appears to be most predictive in the intermediate-risk group</th>
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<td>Emerging data suggest individuals in the low-risk group who benefit from CAC screening, are those with a family history of premature CAD (First degree &lt;55yo)</td>
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<td>What about a role of CAC in the younger male [40-60yo] with vasculogenic ED? This needs further study</td>
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<td>ED may identify high-risk individuals who harbor advanced subclinical atherosclerosis presently considered low or intermediate risk</td>
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<td>Further research needed regarding addition of CAC to ED in FRS/SCORE/ and new 2013 AHA/ACC CV Risk Calculators in NRI and prediction of all ASCVD events</td>
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Recommendation for the Evaluation and Management of CVS risk in men with ED and no known CVD: PRINCETON III 2012

Vasculogenic erectile dysfunction patient with no known cardiovascular disease

Initial Risk Stratification (Framingham Risk Score)

Low risk

Intermediate Risk

Exercise Stress Testing

Normal

Consider carotid intima thickness, ankle-brachial index, or coronary artery calcium scoring

Normal

Risk factor management, consider emerging prognostic markers (e.g. testosterone)

Abnormal

Risk factor management, refer to cardiologist

High risk
Pt agrees to undergo coronary artery calcium testing.

**CAC score is 140 Agatston Units (>95\textsuperscript{th} percentile for subjects of the same age, sex, and race/ethnicity)**
Figure  Modified algorithm for cardiovascular risk assessment and management in asymptomatic men aged ≥40 years without known cardiovascular disease. Modified from Miner et al.33 * Using the American College of Cardiology/American Heart Association 2013 10-Year-Risk Cardiovascular Risk Calculator based on the American College of Cardiology/American Heart Association 2013 Pooled Cohort Equations. CAC = Coronary artery calcium; CVD = cardiovascular disease; ED = erectile dysfunction.
Refer to Cardiologist (Primary Prevention)

Intensive lifestyle intervention including motivational/behavior intervention

After careful explanation of his CVS risk and CAC score, patient and clinician agree on the need for treatment with high-intensity statin

Stress Echo completed (Neg): Obstr. Dz.

Cardiology does NMR Lipid particle testing

LpA2/ApoB levels: markers which can serve as an indicator for more aggressive treatment which can be changed to slow/halt progression of atherosclerosis

Follow-up with Prev Cardiologist Q6mo
YOU CAN’T THROW A HABIT OUT OF THE WINDOW, YOU HAVE TO COAX IT DOWNSTAIRS ONE STEP AT A TIME!

--Mark Twain