The Link Between ED and CVD

ED: Erectile Dysfunction = Endothelial Dysfunction
André T. Guay, MD, FACP, FASCP

Factors That Cause Endothelial Dysfunction

ED and CVD share common risk factors:
- HTN
- DM
- Obesity
- Hyperlipidemia
- Smoking
Robin Williams: “A man’s two most important organs are his brain and his penis”

Why ED Before CVD?

Why Do We See ED Before CVD?

Table 1  Artery size and atherothrombosis

<table>
<thead>
<tr>
<th>Artery</th>
<th>Diameter (mm)</th>
<th>Circum event</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penile</td>
<td>1–2</td>
<td>ED</td>
</tr>
<tr>
<td>Coronary</td>
<td>3–4</td>
<td>Ischemic heart disease</td>
</tr>
<tr>
<td>Cerebral</td>
<td>6–7</td>
<td>TIA</td>
</tr>
<tr>
<td>Femoral</td>
<td>6–6</td>
<td>Claudication</td>
</tr>
</tbody>
</table>

Pathophysiology of Erectile Dysfunction

Endothelial Cell Activation in Men With ED Without CV Risk Factors and Overt Vascular Damage

- Endothelial cell activation (ECA) is an initiating event in atherosclerosis
- Gr 1: ED but no CV risks
  - Gr 2: ED and DM
  - Gr 3: ED and HTN

Figure 1. Pathophysiology of erectile dysfunction in vascular disease.


Bocchio et al. J Urology 2004; 171: 1601-1604
Endothelial Cell Activation in Men With ED Without CV Risk Factors and Overt Vascular Damage

- ECA factors:
  - P-selectin
  - Intracellular adhesion mol-1
  - Vasc. Cell adhesion mol-1
  - Endothelin-1

- ED is a marker of early endothelial damage—and can represent an earlier indicator of diffuse initial vascular disease

Bocchio et al. J Urology 2004; 171: 1601-1604

Circulating Endothelial Progenitor Cells in Subjects With Erectile Dysfunction


- Patients with ED have a lower number of circulating progenitor cells confirming the existence of endothelial dysfunction

Degree of Metabolic Derangement and ED

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Metabolic Syndrome in Men With Low Testosterone Levels:
Relationship With Cardiovascular Risk Factors and Comorbidities and
with Erectile Dysfunction
García-Cruz et al (Spain) J Sex Med 2013; 10: 2529-2538

N = 2,238 men with T deficiency from multicenters in Spain
N = 1,094 men who had Met Syn assessed

Higher % of Met Syn in men with Erectile Dysfunction

Note high % of Met Syn in many medical co-factors:
DM  HTN  ROH  PVD  Dyslipidemia  Tobacco

The more severe the ED, the higher the % of Met Syn

The more severe the ED, the more components of Met Syn the men had

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Obesity is independently associated with coronary endothelial dysfunction in patients with normal or mildly diseased coronary arteries.

- **N = 397 men**
- **Cor. Vasc. Reactivity Tested**
  - Group I (N=117) - BMI < 25
  - Group II (N=149) - BMI 25-30
  - Group III (N=131) - BMI > 30
  - Adenosine
  - Acetylcholine
  - Nitroglycerine

No difference in:
- Medical risk factors
- Diameter of vessels
- Response to aden./NTG

Diff. to acetylcholine

Indirectly suggests an association between obesity, insulin resistance and end.dys.

Suwaidi, Higano et al (Mayo) J Am Coll Cardiol 2001; 37: 1523

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Insulin resistance as estimated by homeostasis model assessment predicts incident symptomatic cardiovascular disease in Caucasian subjects from the general population: The Bruneck Study


- N=721 men with neg CVD(FU)
- Out of N=1000
- N=118 CVD at F/U
- Insulin Resistance by HOMA predicted incident heart disease
- Insulin Resistance is associated with subsequent CVD independent of all classic and several non-traditional risk factors

Low Grade Inflammation, Obesity and Insulin Resistance in Adolescents


- A differential low grade immune activation is associated with parameters of obesity in adolescents
- IL-6, IL-18, IP-10 and adiponectin (inverse) are associated with Insulin Resistance, and are mainly attributed to obesity
Incidence of Metabolic Syndrome and Insulin Resistance in a Population With Organic Erectile Dysfunction

- Metabolic Syndrome
  - 43% (NCEP ATP III)
  - 24% general population

- Insulin Resistance
  - 79.2% of men with ED
    - 73.3% non-diabetic (n=120)

Correlation with Increasing Severity of Erectile Dysfunction:
- Met Syn...P=0.01
- Ins Res...P=0.01
- FBS>110 g/dL (glucose intolerance)...P=0.01

ED Predicts CVD
Erectile Dysfunction and Subsequent Cardiovascular Disease

- N = 9457...Placebo Group of the Prostate Cancer Prevention Trial
- Time to CV event:
  - 10% chance at 5 years
  - In men with no CV history at baseline

Prediction of Coronary Artery Disease by Erectile Function Status: Evidence-based Medicine

<table>
<thead>
<tr>
<th>Table 2</th>
<th>ED predicts coronary events [16]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group</td>
<td>ED at baseline</td>
</tr>
<tr>
<td></td>
<td>OAD events per 1,000 patient years</td>
</tr>
<tr>
<td>40-49</td>
<td>48.50 (1.35-268.36)</td>
</tr>
<tr>
<td>50-59</td>
<td>27.15 (7.40-69.59)</td>
</tr>
<tr>
<td>60-69</td>
<td>23.03 (11.48-44.13)</td>
</tr>
<tr>
<td>70+</td>
<td>29.82 (19.37-43.75)</td>
</tr>
</tbody>
</table>

Read text illustrates major effect of age and is discussed in the last column. OAD = coronary artery disease; CI = confidence interval; ED = erectile dysfunction

Prediction of Coronary Artery Disease by Erectile Function Status: Evidence-based Medicine

  - N = 36,744 men

  - N = 69,935 men
Treatment

PDE5 Inhibitors Increase Blood Flow

The Effect of Vardenafil on Endothelial Function of Brachial and Cavernous Arteries

- N = 135 men with ED
- N = 30 healthy controls
- Vardenafil 20 mg vs placebo

Flow mediated dilatation is a good measure of endothelial function

PIA = % change in cavernous artery diameter

- More in men with ED than in controls
- More in men with arteriogenic ED

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Conclusions

- The link between ED and CVD is Endothelial Dysfunction
- The severity of ED is associated with increased CV risk factors
- Improving endothelial function by modification of risk factors increases blood flow