The Men’s Health Center
Comprehensive Compassionate Care
Cardiometabolic Urology: The Future?

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Disclosures

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Why is Men’s Health Critical?

Rationale: THE EDUCATIONAL MISSION

- The standard for most US family medicine residency programs is a one-month rotation encompassing:
  - “Randomly-defined” exposure to various surgical subspecialty fields, which may or may not include urology
  - Widely varying educational goals and objectives

- NO DEFINED MEN’S HEALTH CURRICULUM

Medical students and medicine residents at Brown University have expressed educational concerns regarding:

- Lack of exposure to and training in comprehensive, multi-disciplinary men’s health (we see male patients, but...)
- Lack of adequate training in primary care (office, non-surgical) urology (Sexual health is the portal to men’s health...)
- Lack of adequate training in andrology (What’s this?)

Project Description

- The development of a men’s health curriculum is a novel concept aimed at improving the knowledge base in various subject areas for medical students, family medicine, and internal medicine residents
- Dedicated men’s health center co-led by primary care and urology
- Each clinic session accommodates an average of 12-16 patients on a referral basis
- Allows for re-direction to primary care emphasis
Curriculum

- The development of a men’s health curriculum to include primary care urology is novel and innovative.
- The principal framework is driven by the ACGME competencies of medical knowledge:
  - Patient-centered care
  - Practice-based learning and improvement
  - Systems-based practice
  - Professionalism
  - Inter-professional and communication skills
  - Interdepartmental and Interspecialty Links

Multidisciplinary Outreach
Aims

- Diagnose and treat male sexual dysfunction
  - General sexual dysfunction
  - Sexual dysfunction related to specific disease states
- Evaluate cardiometabolic risks of men with sexual dysfunction
  - Cardiovascular risk stratification
  - Prevention strategies and lifestyle counseling
  - The benefits and risks of male hormonal replacement therapy
- Psychological Evaluation and Therapy

❖ Establish the Miriam/Brown MHC as a national leader in the emerging field of sexual medicine and cardiometabolic health
  - Research
    - Outcomes based
      - Computerized database
    - Industry and NIH support
  - Resident/trainee Education
    - Psychology/Psychiatry
    - Urology
    - Int Medicine/Family Medicine
    - Medical Student
Goals

Offer sexual health services to patient groups not currently served

- After MI or CAD intervention
- Conditions where disease or treatment affects sexual function
  - Post Abdominal/Pelvic Surgical Penile Rehabilitation
  - Non urologic cancer patients eg general oncology: Hodgkins Disease; Colorectal CA
  - Chronic disease states
    - MS, Parkinson’s, COPD, Obesity, DM, Depression
    - OSA and other sleep disorders

Goals

Expand management breadth where services exist

- General male sexual dysfunctions
  - ED
  - Premature Ejaculation
  - Testosterone deficiency
  - Links to Obesity Treatment, Nutrition Education, & Reintroduction of Exercise
- After prostate cancer therapy
  - Penile rehabilitation
  - Urinary Incontinence Pelvic Floor Strengthening/Conditioning PT Specialist
Goals

Expand the evaluation to include underlying risks associated with sexual dysfunction
- Cardiovascular disease (CAD)
- Premature Arterial Aging: Aortic Stiffness Central Arterial Pressure; Pulse Wave Velocity
  - SphygmoCor
  - EndoPat: measure Endothelial Function
- Metabolic syndrome (Individual components)
- Diabetes Mellitus
- Obesity
- Dyslipidemia (Inc TG/ Dec HDL)
- Psychological Evaluation for anxiety, depression, relational disorders esp performance anxiety

MHC: Multidisciplinary Approach

- Psychology
  - John Wincze PhD
    - Elected Member/ Former President
    - International Academy of Sex Research Therapists

- Medicine
  - Martin Miner MD
    - Fellow Sexual Medicine Society of North America
    - Fellow American Academy of Family Practice

- Urology
  - Mark Sigman MD
  - Kathleen Hwang MD
    - Urology/Andrology

- Nutrition
  - Mary Flynn PhD

- Male Pelvic Floor Therapy
  - Christy Cielsa PT
Men’s Health

Why is the relation between ED and CVD important?

The number of men with ED will increase from 152 million men in 1995 to 322 million men by 2025.

- North America: 9.1 million
- Europe: 11.9 million
- Asia: 113 million
- South/Central America and Caribbean: 15.6 million
- Africa: 19.3 million
- Oceania: 0.9 million

ED is a remarkably common condition. ED in a substantial majority of men is due to underlying vascular causes. ED is highly prevalent in men with vascular risk factors for CVD.

The Prevalence of ED

Prevalence of ED in Patients With CV Pathologic Conditions or Risks

<table>
<thead>
<tr>
<th>Condition</th>
<th>Estimated Prevalence of ED, %</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 2 diabetes</td>
<td><strong>20–86</strong></td>
<td>Alonso et al, Klein et al, McCulloch et al, Su et al, Yamasaki et al</td>
</tr>
<tr>
<td>Hypertension</td>
<td>27–68</td>
<td>Burchardt et al, Cuellar et al, Jensen et al</td>
</tr>
<tr>
<td>CAD</td>
<td>42–75</td>
<td>Dhabuwala et al, Diokno et al, Kloner et al, Montorsi et al, Solomon et al, Wabrek et al</td>
</tr>
<tr>
<td>Heart failure</td>
<td>75</td>
<td>J aarama et al</td>
</tr>
<tr>
<td>Depression</td>
<td>25–90</td>
<td>Arojo et al</td>
</tr>
<tr>
<td>Obesity</td>
<td>Increased prevalence</td>
<td>Esposito and Giugliano, Esposito et al, Gunduz et al</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>Increased prevalence</td>
<td>Nikoobakhsh et al, Saltman et al, Wei et al</td>
</tr>
<tr>
<td>Smoking</td>
<td>Increased prevalence</td>
<td>Gades et al, Mannino et al, Mione et al</td>
</tr>
<tr>
<td>Medication</td>
<td>Increased prevalence</td>
<td>Derby et al</td>
</tr>
</tbody>
</table>

CAD, coronary artery disease; CV, cardiovascular; ED, erectile dysfunction.
### Risk Factors of ED

#### Traditional
- Age
- High LDL
- Low HDL
- Hypertension
- Diabetes
- Smoking

#### Underlying
- Obesity
- Sedentary lifestyle
- Artherogenic diet

#### Emerging
- Insulin resistance
- Metabolic Syndrome

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### Cardiovascular Disease Risk Stratification in the Asymptomatic Patient

The Framingham Score and National Cholesterol Education Program Adult Treatment Panel are the predominant methods of identifying levels of risk for CHD.

- Typically patients are stratified into 3 categories based on 10-year risk:
  - Low (less than 10%)
  - Intermediate (10-20%)
  - High (>20%)
- Calculations include: age, cholesterol level, HDL cholesterol, BP, smoking and diabetes
- None include ED
Erectile Dysfunction and Subsequent Cardiovascular Disease


Study Population/Design Highlights

- 9,457 men age 55+ randomized to placebo in Prostate Cancer Prevention Trial (PCPT)
  - 8,063 (85%) men with no CVD at study entry
  - 3,816 (47%) with prevalent ED, 2,420 (57%) reported incident ED after 5 y
- Followed for 7 years for development of CVD
  - 255 CVD events
ED and Subsequent Cardiovascular Events

- Incident ED significantly increased the risk of myocardial infarction or angina.
- 2% had CV event 1 year after incident ED.
- 11% had CV event by 5 years after incident ED.
- ED may be considered a harbinger of CV events in some men with an associated risk similar to current smoking, or family history of MI.

<table>
<thead>
<tr>
<th>Covariate</th>
<th>HR (n=4247)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>1.46</td>
<td>.02</td>
</tr>
<tr>
<td>Family hx MI</td>
<td>1.46</td>
<td>.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.34</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Anti-HTN Rx</td>
<td>1.74</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Incident ED</td>
<td>1.46</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>


What about the implications of ED in a broad population Without diabetes and CAD?

A Population-Based, Longitudinal Study of Erectile Dysfunction and Future Coronary Artery Disease

Incidence of Coronary Artery Disease with Respect to Age and ED Status

- Overall new incident CAD developed in 156/1402 (11%) of men, followed from 1996-2005.
  - 14.7% MI
  - 78.8% angiographic
  - 6.4% sudden death
- Association between ED and incident CAD declined with increasing age.
- ED presence in men > 70 years old was of no prognostic significance.
- Men with ED at age 40 had an 80% higher risk for subsequent CAD over 9 years.


Can we use ED as a means of detecting cardiovascular disease?

Can we use ED as a means of preventing cardiovascular disease?
Time interval between ED onset and CAD
ED Prevalence and Time of Onset in 300 Consecutive Men With Acute Chest Pain and CAD

◆ In 67% of 300 pts, symptoms of ED had started before the symptoms of CAD (mean 39 months) – retrospective study
◆ Mean age, 62.5 y ED prevalence, 49% (147/300)


Clinical spectrum of coronary artery disease

The Endothelium: A Living Organ

ED May Be a Sign of Endothelial Damage: Part 1

Poor lifestyle choices increase oxidative stress in endothelial cells, causing early injury

- Poor lifestyle choices increase oxidative stress in endothelial cells, causing early injury.
- Cigarette smoking
- Obesity
- High-fat meals
- Sedentory behavior
- Psychological stress

Impaired NO production

ED May Be a Sign of Endothelial Damage: Part 2

ED may occur with the early endothelial cell damage before other serious diseases are manifest1-3

Endothelial cell: Early endothelial damage
Vascular damage

Anxiety/Depression4
Hyperlipidemia5-7
Visceral Obesity10,11
Diabetes5,6,9

Early endothelial dysfunction may lead to atherosclerosis and vascular remodeling10,11


ED and Probability of Future CAD

- 10-y coronary risk according to presence and severity of ED
- 2561 men with no history of CAD
- IIEF5 to assess prevalence and severity of ED
- Moderate to severe ED, but not mild ED, associated with considerably increased risk for CAD within 10 y
- These data could serve as basis for preventing life-threatening events in men with ED through risk factor management and lifestyle modification

Severe ED IIEF: 5-7 n=56
Moderate ED IIEF: 8-16 n=94
Mild ED IIEF: 17-21 n=499
No ED IIEF: 22-25 n=1213

10-Year CAD risk, % (Mean, 95% CI)

Why ED occurs before other vascular diseases?

- The small diameter of the cavernosal arteries.
- The penis is a vascular organ, sensitive to changes in oxidative stress and NO levels.
- The high content of endothelium and smooth muscle on a per gram tissue basis (compared to other organs).

Atherosclerosis in Coronary Vessels  Atherosclerosis in Penile Arteries

Conclusions

- ED and CHD frequently coexist, especially in older men (> 70)
- ED may occur in the absence of coronary symptoms ie. ED precedes coronary ischemia perhaps even more so in younger men (<60)
- ED may precede a CAD event by years (ave 2-5)
- Aggressive CVD risk reduction should be considered for all men with organic ED and no cardiac symptoms

Conclusion

“These data could serve as a basis for preventing life-threatening events by risk factor management and lifestyle modification in men with ED”

Ponholzer A et al  *Eur Urol* 2005;48:512-8
Testosterone Therapy: Where Have We Been, Where Are We Going?

Survival of Treated Versus Untreated Testosterone-Deficient Men in VA Population

- 1031 Men aged > 40 yrs, Testosterone < 250 ng/dL
- Mortality: 10.3% treated, 20.7% untreated (p<0.0001)

VA. US Department of Veterans Affairs.
Shores MM et al. J Clin Endocrinol Metab. 2012 Apr 11 [Epub ahead of print]
TRT Improves Survival in Men With T2DM

• Six year follow-up study
  • N=587
• Effect of baseline T and TRT on all-cause mortality in hypogonadal men with T2DM
  • Low T predicts increased mortality by hazard ratio of ~2.0 (20% vs 10%)

Muraleedharan V, Jones H et al. Early Online 2012 Diabetes Care

TRT Improves Survival in Men with T2DM—results

✦ Mortality rate was significantly higher in patients with low TT without TRT compared to patients with normal TT
✦ Low TT patients with TRT had lower mortality rate

Muraleedharan V, Jones H et al. Diabetes Care 2012
Testosterone Therapy Effects on Diabetes TIMES2 Study

Study Design
- A 12-month, multicenter, prospective, randomized, double-blind, placebo-controlled study

Population
- 220 hypogonadal men with T2DM and MetS

Results
- **Significantly improved:**
  - Insulin resistance in all patients by 15.2% at 6 months; 16.4% at 12 months
  - HDL -0.049 mmol/L and LDL cholesterol -0.210 mmol/L, lipoprotein a -0.31 mmol/L in selected groups
  - Erectile Function increase of 4.8 on IIEF-5


Testosterone Therapy

- In late 1980s, rarely used and almost not at all in urology
- Reserved for men with unequivocal or severe testosterone deficiencies
  - Absent testes
  - Pituitary/hypothalamic tumors or resection
  - Genetic abnormalities, eg, Klinefelter syndrome
- Not recognized as useful in otherwise healthy men with sexual or other symptoms
Current Status of Testosterone Therapy

- Growing awareness of benefits for men who are symptomatic and testosterone-deficient
  - ED
  - Diminished libido
  - Chronic fatigue
  - Poor bone mineral density
  - Decreased sense of vitality and well-being
- Ongoing debate about usefulness for mid-life blues or male menopause

Conclusions

- A relationship exists between TD and MetS and its individual components; similar cross-sectional studies have demonstrated an association between TD and T2DM
- Prospective studies have demonstrated that a low T at baseline can predict the development of T2DM
- Visceral adiposity induces hypogonadotrophic hypogonadism
Conclusions

◆ TRT appears to improve insulin sensitivity and potentially glycemic control in TD men with T2DM

◆ Men with erectile dysfunction, diminished desire, impaired orgasmic function, and metabolic diseases including MetS and T2DM should be screened for TD and treated with TRT

◆ The issue of TRT in preventing CVD needs further study.

New Topics of T Repletion:

◆ Emerging data that testosterone therapy may no longer be contraindicated for men with localized prostate cancer

◆ Testosterone therapy may provide benefits for voiding despite conventional belief that higher testosterone levels cause BPH growth

◆ T and Bone Health in Men

◆ Testosterone may improve insulin resistance, ameliorate early type 2 DM, improve CVD and all cause mortality

Provocative, no consensus
Will be fascinating to see what we learn in next 5-10 years
The Future

- Testosterone therapy for general health and longevity?
- Several publications showing associations between low testosterone and atherosclerosis, risk of diabetes and metabolic syndrome, and increased mortality
- Causal relationship versus mere association?

Barriers to Success of Men’s Health Center

- Unclear boundaries and newly recognized fears regarding cardiometabolic risk screening crossing specialties and increasing costs (PCP vs ED spec; Inc $ testing)
- Ensure receptivity and lack of threat to referring providers—Refer back to PCP with faxed evaluation and non-threatening evidence-based recommendations
- Must “vette” cardiometabolic workup with local and national preventative cardiologists: the workup must be evidence-based, cost-effective, and individualized to each patient
- Establishing a computerized data base from the start
- Engaging both community and academic providers as well as allowing self-referral
- Ensure timely access
- Ensure cross-specialty patient discussions at weekly meeting
What is the offer to our patients?

- A relevant issue: the value of a holistic approach to their health including sexual medicine
- It is 180° different from sports-page penile injection clinic (Boston Medical)
- It is a coherent message: everything is linked and all should be taken into account
- Patients are investing in quality of life
- One-stop Shopping: Links to Exercise; Diet; Preventative Medicine

Who are our patients-clients? Why a Men’s Health Center?

- Men above 35 y.o
- Worried about their health
- Want to improve their global performance
- Want to prevent age-related problems
- Want to be active and healthy

A very large segment of the male population
Future Long-term Goals of Men’s Health Center:

- Incorporate Female Sexual Dysfunction and Partners for therapy beyond couples counseling
- Develop referral algorithms/links for other specialties: oncology; cardiology; pulmonary (COPD & OSA)
- Establish the service of Male Bone Health
- Publish outcomes research