MHIF Research Highlights: OCTOBER 2018

**Interviewed on KARE 11:**
**Dr. Paul Sorajja**
Small device shows big promise for heart patients
COAPT study using MitraClip

**Interviewed on KDUZ Radio:**
**Dr. Jay Traverse**
CONCERT and SENECA studies for stem cell therapy in HF

**CONGRATULATIONS to MHIF Research Fellow Dr. Peter Tajti!**
for winning the TCT Fellow Case Competition

**FEATURED MHIF STUDIES**
Open for Enrollment and Referrals!

**TRANSCEND** for peripheral artery disease
CONTACT: JoAnne Goldman, 612-863-3973

**ASAP-SVG** for coronary artery disease
CONTACT: Pamela Morley, 612-863-6066

**MINT** for myocardial ischemia & transfusion
CONTACT: Rose Peterson, 612-863-6051

**First Recipient of The Jon DeHaan Foundation Award for Innovation in Cardiology**

**Dr. Kelly Han** is recognized for her outstanding contributions to improving both safety and quality of imaging Congenital Heart Disease in adults, children and infants.

**DISSEMINATING RESEARCH**

Call out to **Dr. John Lesser** and the IIR team, including **Sue Casey**, for work on the PROTECTION VI study

LateBreaker at ESC Congress in August

Published in the European Heart Journal

Study assessed the use of strategies for dose reduction during CCTA as part of a multi-center, international registry
PREVENTION OF HEART DISEASE & STROKE IN WOMEN

Gina P Lundberg MD FACC
Clinical Director, Emory Women’s Heart Center
Associate Professor of Medicine
Emory University School of Medicine
@Gina_Lundberg

DISCLOSURES

• NO DISCLOSURES
OBJECTIVES

• Review Current Guidelines and Important Sex-specific Studies on Heart Disease in Women

• Review AHA/ASA Stroke Prevention Guidelines for Women

• Discuss unique risk factors in Women for CVD
AUDIENCE RESPONSE

• Which is true?
  A- More women die of CVD every year compared to men
  B- Women have more burden of Afib compared to men
  C- Diabetes and HTN are the same risk in women and men
  D- Sex difference and gender differences are the same thing.
Circulation: Cardiovascular Quality and Outcomes

FRONTIERS IN CARDIOVASCULAR OUTCOMES RESEARCH

Sex Differences in Ischemic Heart Disease
Advances, Obstacles, and Next Steps

Niti R. Aggarwal, Hema N. Patel, Laxmi S. Mehta,
Rupa M. Sanghani, Gina P. Lundberg, Sandra J. Lewis,
Marla A. Mendelson, Malissa J. Wood, Annabelle S. Voigtman,
Jennifer H. Mieres
**SEX-BASED DISPARITIES IN OUTCOMES & QUALITY OF CARE**

- Less diagnostic testing or angiography
- Delay in Reperfusion
- Fewer Revascularizations
- Less Pharmacotherapy
- Less Cardiac Rehab referral & completion
- Higher morbidity after MI
- Higher in-hospital mortality with angina, STEMI & ACS
- Higher mortality in younger women (<55yrs)

**TRADITIONAL CVD RISK FACTORS - NOT EQUAL IN WOMEN & MEN**

- **Diabetes mellitus** - 3-7 fold increased risk in women vs 2-3 fold risk in men
- **Tobacco use** - 25% increased risk in women vs men, 3x risk for MI
- **Hypertension** - Higher prevalence in women vs men after age 55
- **Obesity** - Increased risk in women (64%) vs men (46%)
- **Physical inactivity**
  More women are inactive (32.2%) vs men (29.9%)
CVD 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 J 2001;141:735-741
emoryhealthcare.org/womensheart

PATIENT AWARENESS, STIGMA, AND PHYSICIAN AWARENESS AND TRAINING EFFECT CVD CARE IN WOMEN

CENTRAL ILLUSTRATION: Knowledge, Attitudes and Beliefs Regarding Cardiovascular Disease in Women: The Women's Heart Alliance

1. Cardiovascular disease (CVD) is the top cause of death in women in the U.S. - CVD kills more women than all cancers combined.

And yet ...

- Only 45% of women knew CVD is #1 killer
- 26% of women find CVD embarrassing, counting risk is solely linked to weight
- Only 40% of routine care includes a heart risk check
- Only 35% of primary care physicians (PCPs) make CVD a top priority
- Only 2% of PCPs and 43% of cardiologists feel well prepared to assess CVD risk

A need to raise awareness of risk and symptoms of heart disease
A need to de-stigmatize the disease risk by countering stereotypes with facts
A need to invest in women's CVD research and physician education/training


emoryhealthcare.org/womensheart
RECOMMENDATIONS FOR PREVENTION OF HEART DISEASE IN ALL WOMEN

• HTN control-
  – ideal 120/80 and max 130/80
• DM control
• Lipid control
• Lifestyle- Diet and Physical activity
• Smoking Cessation
• Obesity- BMI<25 ideal

RECOMMENDATIONS FOR PREVENTION OF HEART DISEASE

• Evaluation after pregnancy complication-
  Gest DM, HTN, Preeclampsia, Eclampsia
• Evaluation of CVD risks in Rheumatic/ Autoimmune disorders
• Close observation after Breast Cancer, Chemotherapy, Radiation
• Close observation with Depression/Stress, domestic violence, trauma, etc
ACC/AHA POOLED COHORT RISK EQUATION

http://tools.cardiosource.org/ASCVD-Risk-Estimator/

emoryhealthcare.org/womensheart

PRIMARY PREVENTION FOR CVD IN WOMEN

• Aspirin controversies
• Statin controversies

emoryhealthcare.org/womensheart
USPSTF 2018 ASPIRIN FOR PRIMARY PREVENTION

- **Adults 50-59** with ASCVD risk >10% for 10 years - Grade B recommendation
- **Adults 60-69** with ASCVD risk >10% for 10 years - Grade C
- Adults under 50 and over 70 - Insufficient evidence

STATINS RECOMMENDATIONS

**ACC/ AHA 2013 Recommendations: Four Statin Benefit Groups**

1. Individuals with clinical ASCVD
2. Individuals with primary elevations of LDL-C ≥190 mg/dL
3. Individuals 40 to 75 years of age with diabetes and LDL-C 70 to 189 mg/dL without clinical ASCVD
4. Individuals without clinical ASCVD or diabetes who are 40 to 75 years of age and have LDL-C 70 to 189 mg/dL and an estimated 10-year ASCVD risk of ≥7.5%. This requires a clinician-patient discussion.
LIKELIHOOD OF RECEIVING EVIDENCE-BASED TREATMENT BY SEX

<table>
<thead>
<tr>
<th>Treatment</th>
<th>OR</th>
<th>95% CI</th>
<th>P value</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reperfusion treatment</td>
<td>0.64</td>
<td>0.59 to 0.69</td>
<td>&lt;0.001</td>
<td>48112</td>
</tr>
<tr>
<td>Beta blocker at discharge</td>
<td>0.91</td>
<td>0.86 to 0.96</td>
<td>&lt;0.001</td>
<td>48109</td>
</tr>
<tr>
<td>ACEi/ARB at discharge</td>
<td>0.85</td>
<td>0.82 to 0.89</td>
<td>&lt;0.001</td>
<td>48109</td>
</tr>
<tr>
<td>Aspirin</td>
<td>0.95</td>
<td>0.90 to 1.00</td>
<td>0.075</td>
<td>48109</td>
</tr>
<tr>
<td>Statins at discharge</td>
<td>0.81</td>
<td>0.77 to 0.86</td>
<td>&lt;0.001</td>
<td>48109</td>
</tr>
<tr>
<td>Other antiplatelet</td>
<td>0.82</td>
<td>0.77 to 0.86</td>
<td>&lt;0.001</td>
<td>24602</td>
</tr>
<tr>
<td>Nitrites</td>
<td>1.09</td>
<td>1.04 to 1.14</td>
<td>&lt;0.001</td>
<td>48109</td>
</tr>
</tbody>
</table>

MORE COMMON IN WOMEN

- Thrombus formation on a ruptured or eroded plaque
- Coronary vasospasm
- Spontaneous coronary artery dissection
- Stress-related (Takotsubo) cardiomyopathy
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 calcification

CENTRAL ILLUSTRATION: Features of Pregnancy-Associated Spontaneous Coronary Artery Dissection

<table>
<thead>
<tr>
<th>Spontaneous Coronary Artery Dissection (SCAD)</th>
<th>Pregnancy-associated SCAD (P-SCAD)</th>
<th>Recommended areas of P-SCAD research</th>
</tr>
</thead>
<tbody>
<tr>
<td>A coronary artery hematoma + tear limits coronary blood flow to the myocardium</td>
<td>Frequently occurs in first month postpartum (majority of these within first week after delivery)</td>
<td>Hemodynamic stressors</td>
</tr>
<tr>
<td></td>
<td>P-SCAD presentation often severe:</td>
<td>Hormonal fluctuations</td>
</tr>
<tr>
<td></td>
<td>- ST-segment elevation myocardial infarction</td>
<td>Oxytocin release in breastfeeding mothers</td>
</tr>
<tr>
<td></td>
<td>- Reduced left ventricular function</td>
<td>Older, multiparous mothers</td>
</tr>
<tr>
<td></td>
<td>- Left main and/or multivessel SCAD</td>
<td>Relationship to:</td>
</tr>
<tr>
<td></td>
<td>Compared to non-pregnancy-associated SCAD:</td>
<td>- Eclampsia</td>
</tr>
<tr>
<td></td>
<td>- P-SCAD has a higher risk presentation</td>
<td>- Pre-eclampsia</td>
</tr>
<tr>
<td></td>
<td>- P-SCAD patients are older at time of first childbirth and more frequently have history of multiple pregnancies</td>
<td>- Peripartum cardiomyopathy</td>
</tr>
<tr>
<td></td>
<td>- P-SCAD patients have fewer extraordinary vascular abnormalities</td>
<td>- Fibromuscular dysplasia and other extracoronary vascular abnormalities</td>
</tr>
</tbody>
</table>

PREGNANCY SCAD & NON-PREG SCAD

<table>
<thead>
<tr>
<th></th>
<th>P-SCAD -54</th>
<th>NP-SCAD -269</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presentation</td>
<td>STEMI- 57%</td>
<td>STEMI- 36%</td>
</tr>
<tr>
<td></td>
<td>EF&lt;35% 26%</td>
<td>EF&lt;35% 10%</td>
</tr>
<tr>
<td>Assoc with FMD</td>
<td>42%</td>
<td>64%</td>
</tr>
<tr>
<td>Pregnancy Hx</td>
<td>Multiparous-91%</td>
<td>76%</td>
</tr>
<tr>
<td></td>
<td>Infertility tx-28%</td>
<td>16%</td>
</tr>
<tr>
<td></td>
<td>Pre-eclampsia-11%</td>
<td>6%</td>
</tr>
<tr>
<td>LM SCAD</td>
<td>24%</td>
<td>5%</td>
</tr>
<tr>
<td>Multivessel SCAD</td>
<td>33%</td>
<td>14%</td>
</tr>
<tr>
<td>Age</td>
<td>35 yrs</td>
<td>47 yrs</td>
</tr>
<tr>
<td>Race</td>
<td>89% Caucasian</td>
<td>97 Caucasian</td>
</tr>
</tbody>
</table>

MI WITH NO OBSTRUCTED CORONARY ARTERIES (MINOCA)

- MI with nonobstructive CAD
  - found in 6% of all MIs
  - Median age 55
  - 40% women
  - Possibly due to structural dysfunction, vasospasm, and thrombotic disorders
  - Has guarded prognosis with better 12 mo mortality compared to obstructive CD
**TAKOTSUBO/ STRESS CM IN WOMEN**

- Mainly affects postmenopausal women
- Generally after extreme emotional or exertional trigger
- ACS with no obstructive CAD & effects multiple artery territories

**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
PREVENTION OF STROKE IN WOMEN

AUDIENCE RESPONSE

• Which is true?
  A- Women with migraine with aura have higher risk of stroke.
  B- Men with Afib have higher risk of stroke compared to women.
  C- HTN risk is the same risk for stroke in black women compared to white women.
  D- Gestational HTN does not increase lifetime risk for CVD.
SCOPE OF THE PROBLEM

- 200K more disabled women than men after stroke
- Women are more likely to be living alone & widowed before stroke
- Women are more often institutionalized after stroke & have poorer recovery
- Nearly half of stroke survivors have residual deficits 6 mo after strokes

Stroke is the 5th leading cause of death for men but 3rd leading cause of death for women
- Stroke occurrence in women in 2014-4.1 Million
- Stroke deaths in women in 2014-77,632
PREVALENCE OF STROKE


NHANES indicates National Health and Nutrition Examination Survey.

Source: National Center for Health Statistics and National Heart, Lung, and Blood Institute.

FIRST STROKE PREVENTION GUIDELINES FOR WOMEN- 2014

Guidelines for the Prevention of Stroke in Women
A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists.

Endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons

Cheryl Bushnell, MD, MHS, FAHA, Chair; Louise D. McCullough, MD, PhD, FAHA, Vice-Chair;
Issam A. Asad, MD, MSc; Monique V. Chireau, MD, MPH, FAHA; Wende N. Fedder, DNP, RN, FAHA;
Karen L. Furie, MD, MPH, FAHA; Virginia J. Howard, PhD, MSPH, FAHA;
Judith H. Lichtman, PhD, MPH; Lynda D. Lisabeth, PhD, MPH, FAHA;
Ileana L. Piña, MD, MPH, FAHA; Mathew J. Reeves, PhD, DVM, FAHA;
Kathryn M. Rexrode, MD, MPH; Gustavo Saposnik, MD, MSc, FAHA;
Vincenta Singh, MD, FAHA; Amyitis Towfighi, MD; Viola Vaccarino, MD, PhD;
Matthew R. Walters, MD, MBCiB, MSc; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, Council on Epidemiology and Prevention, and Council for High Blood Pressure Research
KEY POINTS: UPDATE ON 2014 AHA/ASA GUIDELINE FOR PREVENTION OF STROKE IN WOMEN

- Women experience more prevalent stroke, more death from stroke and more disability from stroke
- HTN worse with age & race in women
- Afib associated with higher risk of stroke, cardiac events, and mortality in women
Women with DM have higher risk of stroke compared to men with DM
Evidence lacking for stroke risk and abnormal lipids (TC, LDL, HDL, TG)
Migraine is more common in women & migraine with aura assoc with ischemic stroke
Estrogen-containing OCP may increase risk of stroke in migraine with aura

HTN & STROKE IN WOMEN
WHI showed older women (mean age 63) with preHTN had a 93% increased risk of stroke compared to normotensive women
Early & sustained treatment of HTN is critical
Meta-analysis of 31 large RCTs showed treatment of HTN in women >55 yrs was assoc with a 38% risk reduction in fatal & nonfatal cerebrovascular events
MENTAL DISTRESS AS A RISK FACTOR OF STROKE
JACKSON C, CIRCULATION: CV QUALITY AND OUTCOMES JOURNAL

• Anxiety, depression and other mental distress was associated with an increased risk of heart attack and stroke among adults ages 45 or older, even after factoring for lifestyle behaviors and disease history.
• The associations were slightly stronger for stroke among women than men.
• The risk of a heart attack was higher than expected among men ages 45 to 79 with high levels of mental distress.

ASPIRIN FOR PREVENTION OF STROKE

• Aspirin therapy can be useful in women > 65 years of age (81 mg daily or 100 mg every other day)
• if BP is controlled & benefit for ischemic stroke & MI prevention is likely to outweigh risk of GI bleed & hemorrhagic stroke
• may be reasonable for women <65 years of age for ischemic stroke prevention
STROKE & PREGNANCY

• Pregnancy-related HTN is the leading cause of both hemorrhagic & ischemic stroke in pregnant & post partum women
• Stroke is not common during pregnancy
• Risk for stroke is higher in pregnant women (34 per 100K) vs nonpregnant women (21 per 100K)
• Highest risk in the 3rd trimester & post partum
RISK FACTORS FOR PREGNANCY-INDUCED HTN

- Obesity
- Chronic HTN
- Gestational HTN
- First time pregnancy
- Multiple pregnancy
- Pre-existing vascular disease
- Personal or family hx of preeclampsia
- Collagen (connective tissue) vascular disease

CLASS I RECOMMENDATIONS

- Women with chronic primary or secondary hypertension, or previous pregnancy-related hypertension, should take low dose aspirin from the 12th week of gestation until delivery
- Calcium supplementation (of at least 1g/d, orally) should be considered for women with low dietary intake of calcium (<600 mg/d) to prevent preeclampsia
CLASS I RECOMMENDATIONS

Severe hypertension in pregnancy should be treated with safe & effective antihypertensive medications such as methyl dopa, labetalol and nifedipine, with consideration of maternal & fetal side effects.

RECOMMENDATIONS: TREATMENT OF HTN POSTPARTUM

Because of the increased risk of future HTN & stroke 1-30 years after delivery in women with a history of preeclampsia it is reasonable to:

(1) consider evaluating all women starting 6 mo to 1 year postpartum and those who are past childbearing age for a HX of preeclampsia/eclampsia, and document their history is a CVD risk factor

(2) evaluate and treat for CVD risk factors including hypertension, obesity, smoking & dyslipidemia.
GROUPS AT HIGHER RISK OF STROKE WITH ORAL CONTRACEPTIVES

- Older women
- Tobacco users
- Hypertension
- Diabetes
- Obesity
- Hypercholesterolemia
- Prothrombotic mutations/ factors

MENOPAUSAL & POSTMENOPAUSAL HORMONE THERAPY RECOMMENDATIONS

- Hormone therapy (conjugated equine estrogen) with or without medroxyprogesterone) should not be used for primary or secondary prevention of stroke in postmenopausal women
  – Class III LOE A

- Selective estrogen receptor modulators, such as raloxifene, tamoxifen, or tibolone, should not be used for primary prevention of stroke
  – Class III LOE A
STROKE RISK HIGHER IN WOMEN
WITH AFIB & PRIOR CVD

ATRIAL FIB RECOMMENDATIONS

- Most common arrhythmia
- Modifiable stroke risk factor
- AF increases stroke risk (4-5 fold)
- AF stroke associates with higher death and disability
- Stroke risk from AF increases with age
  - 1.5% for persons 50-59 years
  - 25% for persons 80 years or older
ATRIAL FIB RECOMMENDATIONS

- Non-Hispanic whites have the highest prevalence of AF compared to Blacks, Hispanic whites, Asians or other ethnic groups
- 60% of AF patients over age 75 are women

ATRIAL FIB RECOMMENDATIONS

- Female sex is an independent predictor of stroke in patients with AF
- CHADS2-VASc score:
  CHF, HTN, Age>65, DM, Stroke,
  Vascular disease, Age>75, Female Sex

Score>2 is high risk for Stroke
SUMMARY

• CVD continues to be the leading cause of death for women in the US (CHD is #1, Stroke is #5)
• Women need aggressive CVD risk reduction for prevention of heart disease & stroke and guideline directed therapy
• Women have unique risk factors (pregnancy complications, hormones, inflammation, stress, depression, etc) for BOTH heart disease & stroke
Thanks so much to all my mentors, teachers & to the Emory Women’s Heart Center faculty.

Q&A