1. Sex Differences in the Management and Outcomes of Severe AMI in Patients Presenting With Cardiogenic Shock

OBJECTIVES

The aim of this study was to examine the sex differences in the risk profile, management, and outcomes among patients presenting with acute myocardial infarction cardiogenic shock (AMI-CS).

BACKGROUND

Contemporary clinical data regarding sex differences in the management and outcomes of AMI patients presenting with CS are scarce.

METHODS

Patients admitted with AMI-CS from the National Cardiovascular Data Registry Chest Pain-MI registry between October 2008 to December 2017 were included. Sex differences in baseline characteristics, in-hospital management, and outcomes were compared. Patients ≥65 years of age with available linkage data to Medicare claims were included in the analysis of 1-year outcomes. Multivariable logistic regression and Cox proportional hazards models adjusting for patient and hospital-related covariates were used to estimate sex-specific differences in in-hospital and 1-year outcomes, respectively.

RESULTS

Among 17,195 patients presenting with AMI-CS, 37.3% were women. Women were older, had a higher prevalence of comorbidities, and had worse renal function at presentation. Women were less likely to receive guideline-directed medical therapies within 24 hours and at discharge, undergo diagnostic angiography (85.0% vs 91.1%), or receive mechanical circulatory support (25.4% vs 33.8%). Women had higher risks of in-hospital mortality (adjusted OR: 1.10; 95% CI: 1.02-1.19) and major bleeding (adjusted
OR: 1.23; 95% CI: 1.12-1.34). For patients ≥65 years of age, women did not have a higher risk of all-cause mortality (adjusted HR: 0.98; 95% CI: 0.88-1.09) and mortality or heart failure hospitalization (adjusted HR: 1.01; 95% CI: 0.91-1.12) at 1 year compared with men.

CONCLUSIONS

In this large nationwide analysis of patients with AMI-CS, women were less likely to receive guideline recommended care, including revascularization, and had worse in-hospital outcomes than men. At 1 year, there were no sex differences in the risk of mortality. Efforts are needed to address sex disparities in the initial care of AMI-CS patients.

2. Association of pre-pregnancy cardiovascular risk factor burden with adverse maternal and offspring outcomes

Adverse pregnancy outcomes are associated with long-term risk for cardiometabolic disease in both women and their offspring.\(^1\) Individual cardiovascular risk factors (e.g. obesity and hypertension) present before pregnancy have been associated with higher risk for maternal and neonatal morbidity and mortality;\(^2\) however, the presence of multiple co-occurring risk factors may be associated with greater risk for adverse pregnancy outcomes than any single risk factor alone. Given the rising prevalence of cardiovascular risk factors in women of reproductive age,\(^3,4\) identifying the association between the total burden of pre-pregnancy cardiovascular risk factors and adverse maternal and offspring outcomes can help inform comprehensive prevention strategies that move beyond targeting any single risk factor.

We conducted a cross-sectional analysis of maternal and foetal data from the National Center for Health Statistics (NCHS), which collects data on all live births and foetal deaths (after 20 weeks’ gestation) in the USA. Data are reported to the NCHS by healthcare professionals present at delivery according to a standard protocol that includes a chart review, medical record abstraction, and maternal self-report.\(^5,6\) We pooled individual-level data from births to women aged 15–44 years from 2014 to 2018 to allow for adequate power to examine rare outcomes. Four pre-pregnancy
cardiovascular risk factors were assigned 1 point if present and 0 points if absent, including body mass index (BMI) <18.5 kg/m² or >24.9 kg/m² and smoking by maternal self-report, and hypertension and diabetes ascertained by the medical professional at delivery, to construct a risk factor score ranging from 0 to 4. Pre-pregnancy hypertension and diabetes were defined by diagnosis prior to pregnancy and excluded diagnoses made during pregnancy.\(^6\) In a secondary analysis, we examined all four risk factors individually. We excluded records missing data on any of the pre-pregnancy risk factors or pregnancy outcomes of interest (3.9%). We used modified Poisson regression to estimate relative risks for maternal ICU admission, preterm birth (<37 weeks), low birthweight (<2500 g), and foetal death associated with greater risk factor burden (1, 2, 3, or 4) compared with no risk factors (0). Women with foetal death (0.5%) were included only in the analysis for this outcome. All analyses were adjusted for maternal age at delivery, race/ethnicity, education, receipt of prenatal care, parity, and birth plurality. We conducted a complete case analysis due to low missingness in covariates (3.7%). We completed a sensitivity analysis in nulliparous women to minimize bias related to repeat pregnancies included in the de-identified dataset. This study was exempt from IRB review due to the de-identified, publicly available dataset.

Of 18 646 512 pregnancies included, mean (SD) maternal age was 28.6 (5.8) years, and 53.6% of women were non-Hispanic White, 14.8% non-Hispanic Black, 23.0% Hispanic, 6.8% non-Hispanic Asian, and 1.9% other race/ethnicity. More than 60% of women had one or more pre-pregnancy cardiovascular risk factors (52.5%, 7.3%, 0.3%, and 0.02% had 1, 2, 3, and 4 risk factors, respectively). Compared with women with no risk factors, women with one or more risk factors had on average lower educational attainment (79.5–85.3% vs. 88.7% graduated high school), less receipt of prenatal care (97.8–98.5% vs. 98.7%), higher prevalence of multiparity (64.4–69.3% vs. 56.9%), and higher prevalence of prior spontaneous or induced pregnancy loss (27.4–46.0% vs. 23.4%) There were consistent and marked graded associations between greater pre-pregnancy risk factor burden and higher risk of adverse maternal and foetal outcomes (Figure 1); for example, the risk ratios (95% CI) of maternal ICU admission (compared to women with no pre-pregnancy risk factors) were 1.12 (1.09, 1.15) for one risk factor, 1.86 (1.78, 1.94) for two risk factors, 4.24 (3.85, 4.68) for three risk factors, and 5.79 (4.07, 8.23) for four risk factors. Individual components of the risk factor score were directly associated with adverse outcomes, with heterogeneity in effect sizes, except for non-ideal BMI, which
was inversely associated with low birthweight (Table 1). Similar patterns were observed in sensitivity analyses in nulliparous women (data not shown).

Figure 1

Relative risk of pre-pregnancy cardiovascular risk factor burden for adverse maternal and offspring outcomes. There were positive and graded associations of greater
cardiovascular risk factor burden, compared with no pre-pregnancy risk factors, for all four outcomes. RR represents relative risk; CI confidence interval.

### Table 1

Relative risk of individual pre-pregnancy cardiovascular risk factors for adverse maternal and offspring outcomes
## Pre-pregnancy Risk Factors and Adverse Outcomes

<table>
<thead>
<tr>
<th>Pre-pregnancy Risk Factor</th>
<th>Maternal ICU Admission</th>
<th>Preterm Birth</th>
<th>Low Birthweight</th>
<th>Foetal Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-ideal BMI</td>
<td>1.04 (1.01, 1.07)</td>
<td>1.08 (1.08, 1.09)</td>
<td>0.94 (0.94, 0.94)</td>
<td>1.39 (1.36, 1.41)</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.23 (1.18, 1.28)</td>
<td>1.28 (1.28, 1.29)</td>
<td>1.64 (1.64, 1.65)</td>
<td>1.59 (1.55, 1.64)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2.84 (2.70, 2.99)</td>
<td>1.92 (1.91, 1.93)</td>
<td>1.98 (1.96, 1.99)</td>
<td>1.92 (1.84, 2.00)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.71 (2.53, 2.90)</td>
<td>2.27 (2.24, 2.29)</td>
<td>1.36 (1.34, 1.38)</td>
<td>2.98 (2.84, 3.13)</td>
</tr>
</tbody>
</table>

*a* Based on modified Poisson regression including all four risk factors coded as 1 if present and 0 if absent. Adjusted for maternal age at delivery, race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, Asian, or Other), education (Less than high school, high school graduate, or any college), receipt of prenatal care (or no prenatal care), parity (nulliparous or multiparous), and birth plurality (singleton or multiple gestation).

BMI, body mass index; CI, confidence interval; RR, relative risk.

In this analysis of nationwide data, we found that pre-pregnancy cardiovascular risk factors are highly prevalent, and there are consistent and graded associations between greater risk factor burden and key adverse maternal and offspring outcomes. Although
individual risk factors were generally associated with these outcomes, the cumulative risk factor burden was associated with higher risk than any single risk factor; compared to women with no pre-pregnancy risk factors, those with all four risk factors (3242 women) had approximately 5.8-fold higher risk for ICU admission, 3.9-fold for preterm birth, 2.8-fold for low birthweight, and 8.7-fold for foetal death. Limitations of this analysis include the potential for misclassification of pre-pregnancy risk factor status such as bias related to self-report of BMI, inability to characterize risk factor control and its potential to modify associations with adverse pregnancy outcomes, lack of available data on lifestyle factors, and absence of linkage with maternal mortality. However, the NCHS Birth Data Files represent the most robust and comprehensive surveillance dataset, which captures all pregnancies in the USA resulting in a live birth or foetal death. While the primary sample included repeat pregnancies, data from nulliparous women demonstrated similar findings.

The association between risk factor counting and cardiovascular and non-cardiovascular outcomes has been examined extensively outside of pregnancy. Our data extend prior findings by validating the importance of the pre-pregnancy cardiovascular risk factor profile for risks of several key adverse maternal and offspring outcomes, which are known to influence the risk of subsequent cardiovascular disease. Future studies should seek to incorporate measures of cholesterol and lifestyle factors, as well as important non-modifiable risk factors such as family history of cardiovascular disease, which has been associated with pregnancy loss and may warrant increased attention to optimizing pre-pregnancy cardiovascular health. Assessment of cardiovascular risk factors on the individual level could be applied before pregnancy, when prevention may have a greater benefit than during pregnancy when the time period to intervene is limited.

3. The need for better cardiac rehabilitation for women

We read with interest the article by Kringeland et al., on stage 1 hypertension, sex, and acute coronary syndromes (ACS) during midlife. It was interesting to note that 42% of
the female subjects had isolated diastolic hypertension compared to only 24% of the male subjects. Furthermore, after adjusting for diabetes, smoking, body mass index, cholesterol, and physical activity, stage 1 hypertension was associated with a higher risk of ACS in women than in men.

This research continues to add to the previous studies that highlighted the higher prevalence of cardiovascular diseases in women. A recent article by Núñez et al. indicated that women with known or suspected coronary artery disease are at a higher risk of new-onset heart failure (HF). The study involved 5899 HF-free patients. Cardiac magnetic resonance was used to assess the ischemic burden and left ventricular ejection fraction (LVEF). A follow-up after 4.5...

4. Pregnant Women With Mild Hypertension Benefit From Antihypertensive Therapy

Among women with chronic mild hypertension during pregnancy, using antihypertensive therapy to reduce blood pressure to below 140/90 mm Hg reduced the risk of adverse pregnancy outcomes, according to research presented at the American College of Cardiology 2022 Scientific Sessions, which took place here and online from April 2 to 4.

“Chronic hypertension affects upwards of 2% of pregnancies in the United States,” said lead author Alan Tita, MD, PhD, of the University of Alabama at Birmingham Heersink School of Medicine, during his presentation of the data. “It is rising due to older age at childbirth and obesity. Blacks are disproportionately affected. Chronic hypertension causes several maternal and fetal complications, including death, preeclampsia, ... babies that are small for gestational age (SGA) based on their birth weight, preterm birth, and cardiovascular morbidities. The American College of Obstetricians and Gynecologists classifies chronic hypertension in pregnancy into two groups: severe, with blood pressures of at least 160/110 mm Hg, and mild or non-severe, with blood pressures below that threshold.” He noted, however, that this definition of non-severe
disease encompasses ACC/American Heart Association stage 2 hypertension. The risks and benefits of antihypertensive therapy among pregnant patients remain unclear.

For the open-label, multicenter CHAP trial, 2404 women with mild chronic hypertension and a singleton pregnancy < 23 weeks’ gestation were randomized, stratified by center, to either treatment with a first-line antihypertensive for pregnancy to a blood pressure goal < 140/90 mm Hg (n = 1208) or to no treatment unless blood pressure was ≥ 160/105 mm Hg (n = 1200). The main antihypertensive agents used were labetalol or nifedipine ER. Others (methyldopa, amlodipine) were accepted, but these were not provided through the study.

The centrally adjudicated primary outcome was a composite of preeclampsia with severe features, preterm birth < 35 weeks, abruption, and neonatal/fetal death. The safety outcome was SGA (birth weight < 10th percentile). Secondary outcomes included preterm birth (< 37 weeks) and preeclampsia. Patients were followed up through 6 weeks postpartum.

The two groups of patients were similar at baseline. At enrollment, 56% were on antihypertensives. Overall, 48% were black, 28% were white non-Hispanic, and 20% were Hispanic. In addition, 16% were diabetic, and their mean body mass index was 37.6 kg/m².

The primary outcome incidence was lower in the treatment group, at 30.2% versus 37.0%, for a relative risk of 0.82 (95% confidence interval 0.74–0.92, P < .001). Also lower with active therapy were the incidence of severe preeclampsia (23.3% vs 29.1%, relative risk 0.80, 95% confidence interval 0.70–0.92) and indicated preterm birth < 35 weeks (12.2% vs 16.7%, relative risk 0.73, 95% confidence interval 0.60–0.89). The number needed to treat to prevent one of these events was 14.7. There were no significant differences between the two groups with respect to abruption or fetal/neonatal death, nor were there notable differences observed in subgroup analyses.

The safety outcome was similar for both groups, at 11.2% versus 10.4%, P = .76.

A composite maternal morbidity outcome that included death, heart failure, stroke, myocardial infarction/angina, pulmonary edema, intensive care unit admission, encephalopathy, and acute kidney injury was similar for both groups. However, rates of
any preeclampsia (24.4% vs 31.1%), worsening chronic hypertension (10.9% vs 13.0%), and severe hypertension (36.1% vs 44.3%) were all lower in the intervention arm.

Rates of multiple neonatal outcomes, evaluated as a composite and individually, did not differ between the two groups, with the exception of preterm birth (27.5% vs 31.4%) and low birthweight < 2500 g (19.2% vs 23.1%), which were lower in the intervention arm.

“CHAP supports treatment of chronic hypertension in pregnancy to a blood pressure goal of < 140/90 mm Hg, especially continuing established antihypertensive therapy,” concluded Dr. Tita. “Long-term studies will further clarify these treatment effects.”

5. Treatment for Mild Chronic Hypertension During Pregnancy

Treatment of non-severe chronic hypertension in pregnancy

The standard of care before a 2022 RCT has been to only treat severely elevated blood pressures for chronic hypertension in pregnancy. Some have been concerned that the treatment of non-severely elevated blood pressures could lead to hypoperfusion of the placenta, which puts the fetus at risk for fetal growth restriction (FGR) or stillbirth.

A 2018 Cochrane Review found that the treatment of non-severe chronic hypertension decreased the risk of developing severe hypertension (RR, 0.49; 95% CI, 0.40–0.60; 20 RCTs; 2558 women); however, it did not decrease the risk of preeclampsia (aRR, 0.92; 95% CI, 0.75–1.14; 23 RCTs; 2851 women), fetal or neonatal death (aRR 0.72; 95% CI, 0.50–1.04; 29 RCTs; 2265 women), or preterm birth at <37 weeks of gestation (aRR, 0.96; 95% CI, 0.83–1.12; 15 RCTs; 2141 women). In addition to no significant increase in fetal or neonatal death, there was no increase in the delivery of small for gestational age (SGA) babies (aRR 0.96; 95% CI, 0.78–1.18; 21 RCTs; 2686 babies).

2022 RCT supporting treatment of mild chronic hypertension in pregnancy

Overall, 2408 women with a singleton pregnancy and mildly elevated blood pressure before 23 weeks of gestation from 61 sites in the US were randomized to pharmacologic treatment for blood pressure >140 mm Hg systolic or >90 mm Hg diastolic or to pharmacologic treatment only for blood pressure >160 mm Hg systolic or >105 mm Hg diastolic. The primary outcome was a composite of preeclampsia with severe features,
induction at <35 weeks gestation for medical reasons, placental abruption, fetal death, or neonatal death. The secondary outcomes included composites of preeclampsia, preterm birth, and serious maternal or neonatal complications. The safety was evaluated by monitoring for small for gestational age (<10 percentile and <5 percentile) babies at birth.3

The primary outcome was statistically lower in the group treated for non-severe chronic hypertension in pregnancy than in the severely elevated blood pressure group (30.2% vs 37.0%; aRR, 0.82; NNT, 14–15). Secondary outcomes of preeclampsia and preterm birth were also significantly lower in the non-severe chronic hypertension group: preeclampsia (24.4% vs 31.1%; RR, 0.79) and preterm birth (27.5% vs 31.4%; RR, 0.87). Safety was demonstrated with no significant difference in SGA babies with cut off <10% (11.2% vs 10.4%; aRR, 1.04; P = 0.76) or <5% (5.1% vs 5.5%; RR, 0.92).3

**American College of Obstetricians and Gynecologists (ACOG) practice advisory**

In response to the 2022 RCT, The ACOG issued a practice advisory: “based on these findings, the ACOG recommends utilizing 140/90 mm Hg as the threshold for initiation or titration of medical therapy for chronic hypertension in pregnancy rather than the previously recommended threshold of 160/110.”1 However, the ACOG advisory points out that a target blood pressure lower limit is not established and there may be a blood pressure below which the risk of FGR increases. Additionally, because of the increased FGR risk with chronic hypertension regardless of treatment, a third trimester growth ultrasound is recommended.1 The 2022 RCT is seen as superior to previous studies because of the large number of patients diagnosed with chronic hypertension on medications at the start of the trial, the large number enrolled in early pregnancy, and the racial and ethnic diversity of the study participants.1

**Summary**

A 2022 RCT demonstrates improved outcomes with a good safety profile when pharmacologic treatment is used for non-severe chronic hypertension in pregnancy. This counters a 2018 Cochrane Review which included over 20 RCTs and over 2000 women for each of the outcomes evaluated and ACOG’s previous clinical guidance. Due to the quality of the 2022 RCT, The ACOG now recommends treating non-severe hypertension in pregnancy with a blood pressure goal of <140/90 mm Hg.
Infertility is a predictor of increased risk for heart failure with preserved ejection fraction (HFpEF) later in life, according to an analysis of over 38,000 postmenopausal women followed for a median of 15 years.

Those with a history of infertility had a 16% greater risk of developing any heart failure compared with women without infertility (P = 0.006), but among the HF subtypes, only the association with HFpEF was significant (P = 0.002). Examination of established CV risk factors, including 10-year atherosclerotic cardiovascular disease (ASCVD) score and infertility-related risk factors, did not help explain the association.

“We actually don’t know very much about the long-term health effects of infertility, despite how common a condition it is,” said Emily S. Lau, MD, MPH (Massachusetts General Hospital, Boston), the study’s lead author. “There’s a lot of social stigma associated with infertility. Plus, it’s just not an exposure variable that many people have rigorously tried to ascertain when they design studies.”

In the paper, published Monday in the Journal of the American College of Cardiology, Lau and colleagues drew on the wealth of sex-specific data from the Women’s Health Initiative (WHI), which enrolled over 160,000 women in the 1990s. The WHI was a pioneering effort, gathering information related to pregnancy, menstrual cycles, and menopause decades before those factors began to be recognized as important in the long-term health consequences of women, said Lau. This latest research, she added, complements evidence linking other reproductive factors, including preeclampsia, nulliparity, and shorter reproduction duration, to an increased risk of HF in women.

To TCTMD, Lau said the findings are a bit surprising since the hypothesis initially was that heart failure with reduced ejection fraction (HFrEF) would be more common in women with infertility, driven by ischemic heart disease. In the paper, she and her
colleagues say it appears that the mechanisms mediating HF risk in infertility are independent of ASCVD risk.

Writing in an accompanying editorial, Ersilia M. DeFilippis, MD (Columbia University Irving Medical Center, New York, NY), adds that the lack of an association with traditional CVD risk provides more justification for sex-specific risk scores that “incorporate reproductive factors, such as history of preeclampsia, gestational hypertension, and infertility, that can incur risk independent of traditional cardiovascular risk factors.”

**No Mediators for Infertility/HF Association**

In the WHI data set, 38,528 postmenopausal women (mean age 63.7 years; 33% Black; 15% Hispanic) had adjudicated HF outcomes. Among them, 14% had a history of infertility. Women with versus without infertility were more likely to be former or current smokers and to have a history of irregular menses, thyroid disease, and early menopause (≤ 45 years).

Over the 15-year follow-up period, 2,373 women developed incident HF, including 807 cases of HFrEF and 1,133 of HFpEF. The increased risk of HF in the group with infertility remained consistent after adjustment for race/ethnicity and exclusion of women who never became pregnant. Looking at causes of infertility, slightly more women with a history of infertility attributable to hormones or ovulation developed incident HF compared with those who did not, but the differences were not statistically significant.

When the researchers analyzed the association of infertility with traditional CV risk factors, they found body mass index, white race, and smoking status were independently associated with having infertility. Both former and current smoking were associated with a nearly 1.2-fold higher odds of infertility compared with never smoking. No association was seen between systolic blood pressure, hypertension treatment, diabetes, or hyperlipidemia and having infertility.

In exploratory analyses, having irregular menses was not associated with future risk of overall HF or HF subtypes. Thyroid disease was associated with future risk of overall HF (HR 1.11; 95% CI 1.01-1.22) but not incident HFpEF or HFrEF. Early menopause was
associated with future risk of overall HF (HR 1.11; 95% CI 1.02-1.21) and HFrEF (HR 1.17; 95% CI 1.01-1.35), but not HFpEF.

“However, further adjustment for these infertility-related risk factors did not attenuate the association between infertility and incident HF, which argues that they do not mediate the association between infertility and HF,” Lau and colleagues write.

**Emphasis on Better History-Taking**

DeFilippis notes that the WHI data differ from an analysis of women in the Framingham Heart Study, in which infertility was associated with increased odds of obesity and diabetes, higher serum triglycerides, and decreased HDL-cholesterol levels.

According to Lau, while studies such as this help investigators see potential links between a woman’s reproductive risk factors and subsequent heart disease risk, in clinical practice physicians are not asking questions about infertility, pregnancy, and menopause.

“It’s important for both physicians and for patients to bring these topics to the table,” she said. “As doctors, we would never think twice about asking about high blood pressure, family history of heart disease, hypertension, etc. We need to also be asking about a woman’s reproductive history . . . because we’re still trying to parse together these links and history-taking is a fundamental tool.”

DeFilippis adds that history-taking in young women of reproductive age should include “an assessment of traditional cardiovascular risk factors but also inquire about age of menarche, difficulty conceiving, number of pregnancies and any adverse pregnancy outcomes, breastfeeding, and timing of menopause.

Furthermore, this risk assessment should be an iterative process as new information about a woman’s reproductive health becomes available,” she writes.
7. Peripartum Cardiomyopathy Management: 5 Things to Know

Most treatment strategies for PPCM are based on those for cardiomyopathies in the general, nonpregnant population.

Although there have been many advances in medical therapy for chronic systolic HF in the past decade (eg, angiotensin receptor-neprilysin inhibitors, sodium-glucose cotransporter 2 inhibitors, ivabradine), these therapies have not been studied extensively in pregnant and lactating patients. Treatments for HF, including beta-blockers, loop diuretics, hydralazine, nitrates, and digoxin, remain the standard of care for the management of PPCM. In the postpartum period, enalapril, captopril, and spironolactone are compatible with breastfeeding.

8. Relationship Between Age at Menopause and Incident Heart Failure and Effect of Obesity

BACKGROUND

The mechanisms linking menopausal age and heart failure (HF) incidence are controversial. We investigated for heterogeneity by obesity on the relationship between menopausal age and HF incidence.

METHODS AND RESULTS

Using postmenopausal women who attended the Atherosclerosis Risk in Communities Study Visit 4, we estimated hazard ratios of incident HF associated with menopausal age using Cox proportional hazards models, testing for effect modification by obesity and adjusting for HF risk factors. Women were categorized by menopausal age: <45 years, 45 to 49 years, 50 to 54 years, and ≥55 years. Among 4441 postmenopausal women, aged 63.5±5.5 years, there were 903 incident HF events over a mean follow-up of 16.5 years. The attributable risk of generalized and central obesity for HF incidence was greatest among women who experienced menopause at age ≥55 years: 11.09/1000 person-years and 7.38/1000 person-years, respectively. There were significant interactions of menopausal age with body mass index and waist circumference for HF incidence, P_interaction 0.02 and 0.001, respectively. The hazard ratios of incident HF for a
SD increase in body mass index was elevated in women with menopausal age <45 years [1.39 (1.05-1.84)]; 45-49 years [1.33, (1.06-1.67)]; and ≥55 years [2.02, (1.41-2.89)]. The hazard ratio of incident HF for a SD increase in waist circumference was elevated only in women with menopausal age ≥55 years [2.93, (1.85-4.65)].

CONCLUSIONS

As obesity worsened, the risk of developing HF became significantly greater when compared with women with lower body mass index and waist circumference, particularly among those who had experienced menopause at age ≥55 years.

9. Mediterranean Diet Linked to Lower Risk for Preeclampsia

Pregnant women who had a higher adherence to a Mediterranean-style diet had a lower risk of preeclampsia, according to the results of a new study. "As an observational study, it obviously has limitations that need to be considered, but these results build on other evidence that Mediterranean diet reduces cardiovascular risk and extends those findings to pregnancy as preeclampsia is a cardiovascular outcome," senior author Noel Mueller, PhD

10. Digital Gamification Intervention to Improve Postpartum Exercise

Study Questions:

Can a digital health intervention improve physical activity in postpartum women with hypertensive disorders of pregnancy?

Methods:

A randomized clinical trial design was used to examine a digital intervention to promote physical activity among postpartum women. The intervention duration was 12 weeks, conducted between October 2019–June 2020, at the University of Pennsylvania. All participants received a wearable activity tracker, established a baseline step count,
selected a step goal greater than baseline, and were randomly assigned to control or intervention. Participants in the intervention arm were placed on virtual teams and enrolled in a game with points and levels for daily step goal achievement and informed by principles of behavioral economics. Participants in the control arm received daily feedback on goal attainment. The primary outcome was a change in mean daily step count from baseline to 12-week follow-up.

Results:

A total of 127 participants were randomized (63 in the intervention group) and were enrolled a mean of 7.9 weeks postpartum. The mean age was 32.3 (SD 5.6) years, 70 (55.1%) were Black, and 52 (41.9%) had Medicaid insurance. The mean (SD) baseline step count was similar in the control and intervention arms (6,042 [2,270] vs. 6,175 [1,920] steps, respectively). After adjustment for baseline steps and calendar month, participants in the intervention arm had a significantly greater increase in mean daily steps from baseline compared with the control arm (647 steps; 95% confidence interval [CI], 169-1,124 steps; p = 0.009). Compared with the control arm, participants in the intervention arm achieved their step goals on a greater proportion of participant-days during the intervention period (0.47 vs. 0.38; adjusted difference, 0.11; 95% CI, 0.04-0.19; p = 0.003). By the end of the follow-up, 24 participants (37.5%) in the control arm and 20 participants (31.7%) in the intervention arm had stopped syncing step count data for >6 days. Participants in the control arm were more likely to stop syncing data earlier in the study compared with the intervention arm.

Conclusions:

In this trial, the investigators concluded that a digital health intervention using remote monitoring, gamification, and social incentives among postpartum individuals at elevated cardiovascular risk significantly increased physical activity throughout 12 weeks.

Perspective:

Women with hypertensive disorders during pregnancy are at increased risk for cardiovascular disease later in life. Therefore, healthy lifestyle behavior is important to
initiate in this group. This study suggests that a digital health intervention with gamification can promote physical activity. However, further study is required to reduce disengagement and promote the long-term sustainability of physical activity behaviors.

11. **No sex-related differences in infarct size, no-reflow, and protection by ischaemic pre-conditioning in Göttingen minipigs**

**Aims**
Female sex has been proposed to be cardioprotective per se. Studies with myocardial ischaemia/reperfusion and infarct size as endpoint have demonstrated cardioprotection in female, castrated male, and male pigs. These studies are difficult to compare, given the different pig strains, models, durations of ischaemia, and methods of infarct size quantification. The few studies using both female and male pigs reported no differences in infarct size and cardioprotection. We, therefore, prospectively compared infarct size in Göttingen minipigs undergoing ischaemia/reperfusion (I/R) without and with ischaemic pre-conditioning (IPC) between female, castrated male, and male pigs.

**Methods and results**
In a prospective, randomized approach, 28 Göttingen open-chest, anaesthetized minipigs underwent 60 min ischaemia by distal left anterior descending artery (LAD) occlusion and 180 min reperfusion without and with IPC by three cycles of 5 min LAD occlusion/10 min reperfusion. Infarct size with I/R was not different between female, castrated male, and male pigs (45 ± 8 vs. 45 ± 13 vs. 41 ± 9% area at risk), as was the reduction in infarct size with IPC (25 ± 11 vs. 30 ± 8 vs. 19 ± 10% area at risk). In addition, the area of no-reflow was not different between female, castrated male, and male pigs with I/R (57 ± 13 vs. 35 ± 7 vs. 47 ± 26% infarct size) or IPC (4 ± 10 vs. 12 ± 20 vs. 0 ± 0% infarct size). Phosphorylation of signal transducer and activator of transcription 3 was increased at 10 min reperfusion by IPC but not by I/R to the same extent in female, castrated male, and male pigs (198 ± 30 vs. 230 ± 165 vs. 179 ± 107% of baseline).

**Conclusion**
Our data do not support the notion of sex- or castration-related differences in infarct size, coronary microvascular injury, and cardioprotection by IPC.
12. **Preeclampsia is associated with increased Neurodevelopmental Disorders in children with Congenital Heart Disease**

**Aims**

Our primary aim was to examine whether exposure to preeclampsia increases the risk of neurodevelopmental disorders in children born with congenital heart disease (CHD). Our secondary aim was to evaluate if CHD and preeclampsia may act in synergy and potentiate this risk.

**Method and Results**

Using population-based registries, we included all Danish children born with CHD between 1994 to 2017. Non singletons and children born with a syndrome were excluded. Neurodevelopmental disorders including attention deficit/hyperactivity disorder (ADHD), autism spectrum disorders and tic disorders were identified with the use of the ICD-10 codes DF80-98. Using Cox proportional hazard regression we estimated the risk of neurodevelopmental disorders in children with CHD exposed to preeclampsia compared to those with CHD not exposed to preeclampsia. The population consisted of 11,449 children born with CHD. Children exposed to preeclampsia had an increased risk of neurodevelopmental disorders, HR: 1.84 (95% CI: 1.39; 2.42).

Further, a comparison cohort of 113,713 children with no CHD diagnoses were included. Using cumulative incidence analyses with death as competing risk we compared the risk of neurodevelopmental disorders if exposed to preeclampsia amongst children with CHD and children without CHD. Exposure to preeclampsia drastically increased the cumulative incidence of neurodevelopmental disorders in children born with CHD.

**Conclusion**

Exposure to preeclampsia is associated with increased risk of neurodevelopmental disorders in children born with CHD. CHD and preeclampsia may act in synergy and potentiate this effect. Clinicians should therefore be especially attentive to neurodevelopmental problems in this vulnerable subgroup.