1) CARDIOVASCULAR RISK FACTORS TIED TO POOR PREGNANCY OUTCOMES

Abstract

Background
Cardiovascular risk in young adulthood is an important determinant of lifetime cardiovascular disease risk. Women with adverse pregnancy outcomes (APOs) have increased cardiovascular risk, but the relationship of other factors is unknown.

Methods and Results
Among 4471 primiparous women, we related first-trimester atherogenic markers to risk of APO (hypertensive disorders of pregnancy, preterm birth, small for gestational age), gestational diabetes mellitus (GDM) and hypertension (130/80 mm Hg or antihypertensive use) 2 to 7 years after delivery. Women with an APO/GDM (n=1102) had more atherogenic characteristics (obesity [34.2 versus 19.5%], higher blood pressure [systolic blood pressure 112.2 versus 108.4, diastolic blood pressure 69.2 versus 66.6 mm Hg], glucose [5.0 versus 4.8 mmol/L], insulin [77.6 versus 60.1 pmol/L], triglycerides [1.4 versus 1.3 mmol/L], and high-sensitivity C-reactive protein [5.6 versus 4.0 nmol/L], and lower high-density lipoprotein cholesterol [1.8 versus 1.9 mmol/L]; P<0.05) than women without an APO/GDM. They were also more likely to develop hypertension after delivery (32.8% versus 18.1%, P<0.05). Accounting for confounders and factors routinely assessed antepartum, higher glucose (relative risk [RR] 1.03 [95% CI, 1.00–1.06] per 0.6 mmol/L), high-sensitivity C-reactive protein (RR, 1.06 [95% CI, 1.02–1.11] per 2-fold higher), and triglycerides (RR, 1.27 [95% CI, 1.14–1.41] per 2-fold higher) were associated with later hypertension. Higher physical activity was protective (RR, 0.93 [95% CI, 0.87-0.99] per 3 h/week). When evaluated as latent profiles, the nonobese group with higher lipids, high-sensitivity C-reactive protein, and insulin values (6.9% of the cohort) had increased risk of an APO/GDM and later hypertension. Among these factors, 7% to 15% of excess RR was related to APO/GDM.

Conclusions
Individual and combined first-trimester atherogenic characteristics are associated with APO/GDM occurrence and hypertension 2 to 7 years later.

2) BELLY FAT GAIN DURING MENOPAUSE MAY ELEVATE CVD RISK

Abstract

Objectives:
To characterize abdominal visceral adipose tissue (VAT) trajectory relative to the final menstrual period (FMP), and to test whether menopause-related VAT accumulation is associated with greater average, common carotid artery intima-media thickness (cIMT) and/or internal carotid artery intima-media thickness (ICA-IMT).

Methods:
Participants were 362 women (at baseline: age was (mean ± SD) 51.1 ± 2.8 y; 61% White, 39% Black) with no cardiovascular disease from the Study of Women's Health Across the Nation Heart study. Women had up to two measurements of VAT and cIMT over time. Splines revealed a nonlinear trajectory of VAT with two inflection points demarcating three time segments: segment 1: >2 years before FMP; segment 2: 2 years before FMP to FMP; and segment 3: after FMP. Piecewise-linear random-effects models estimated changes in VAT. Random-effects models tested associations of menopause-related VAT with each cIMT measure separately. Estimates were adjusted for age at FMP, body mass index, and sociodemographic, lifestyle, and cardiovascular disease risk factors.

Results:
VAT increased significantly by 8.2% (95% CI: 4.1%-12.5%) and 5.8% (3.7%-7.9%) per year in segments 2 and 3, respectively, with no significant change in VAT within segment 1. VAT predicted greater ICA-IMT in segment 2, such that a 20% greater VAT was associated with a 2.0% (0.8%-3.1%) greater ICA-IMT. VAT was not an independent predictor of ICA-IMT in the other segments or of the other cIMT measures after adjusting for covariates.
Conclusions:
Women experience an accelerated increase in VAT starting 2 years before menopause. This menopause-related increase in VAT is associated with greater risk of subclinical atherosclerosis in the internal carotid artery.

3) RACIAL, ETHNIC, AND SEX DISPARITIES IN PATIENTS WITH STEMI AND CARDIOGENIC SHOCK

Abstract
Objectives
The aim of this study was to evaluate the combined impact of race, ethnicity, and sex on in-hospital outcomes using data from the National Inpatient Sample.

Background
Cardiogenic shock (CS) is a major cause of mortality following ST-segment elevation myocardial infarction (STEMI). Early revascularization reduces mortality in such patients. Mechanical circulatory support (MCS) devices are increasingly used to hemodynamically support patients during revascularization. Little is known about racial, ethnic, and sex disparities in patients with STEMI and CS.

Methods
The National Inpatient Sample was queried from January 2006 to September 2015 for hospitalizations with STEMI and CS. The associations between sex, race, ethnicity, and outcomes were examined using complex-samples multivariate logistic or generalized linear model regressions.

Results
Of 159,339 patients with STEMI and CS, 57,839 (36.3%) were women. In-hospital mortality was higher for all women (range 40% to 45.4%) compared with men (range 30.4% to 34.7%). Women (adjusted odds ratio [aOR]: 1.11; 95% confidence interval [CI]: 1.06 to 1.16; p < 0.001) as well as Black (aOR: 1.18; 95% CI: 1.04 to 1.34; p = 0.011) and Hispanic (aOR: 1.19; 95% CI: 1.06 to 1.33; p = 0.003) men had higher odds of in-hospital mortality compared with White men, with Hispanic women having the highest odds of in-hospital mortality (aOR: 1.46; 95% CI: 1.26 to 1.70; p < 0.001). Women were older (age: 69.8 years vs. 63.2 years), had more comorbidities, and underwent fewer invasive cardiac procedures, including revascularization, right heart catheterization, and MCS.

Conclusions
There are significant racial, ethnic, and sex differences in procedural utilization and clinical outcomes in patients with STEMI and CS. Women are less likely to undergo invasive cardiac procedures, including revascularization and MCS. Women as well as Black and Hispanic patients have a higher likelihood of death compared with White men.

Association of Serum Testosterone and Luteinizing Hormone With Blood Pressure and Risk of Cardiovascular Disease

4) ASSOCIATION OF SERUM TESTOSTERONE AND LUTEINIZING HORMONE WITH BLOOD PRESSURE AND RISK OF CARDIOVASCULAR DISEASE

Abstract

Background
The age-related decline in testosterone levels is thought to be of great importance for male aging and cardiovascular diseases. However, data are controversial on whether abnormal sex hormones are linked to the presence of cardiovascular diseases and it is also uncertain how blood pressure modifies the association between testosterone levels and major cardiovascular diseases.

Methods and Results
This is a multicenter, population-based, cross-sectional study of 62996 men conducted between 2013 and 2016. Basic information and clinical symptoms were obtained by questionnaires. Blood pressure and plasma levels of total testosterone, sex hormone-binding globulin, luteinizing hormone, and free testosterone were determined in men in a multistage random, cluster sampling in 6 provinces of China. There were 5786 Chinese men (mean [SD] age 55.0 [10.1] years) included after exclusion
criteria were applied; 37.2% (2150) of them were diagnosed with hypertension. Total testosterone, free testosterone, and sex hormone–binding globulin were inversely associated with the prevalence of hypertension. Age >65 years or body mass index ≥24 negatively impacted the inverse correlation between testosterone levels and hypertension, whereas smoking and family history of hypertension strengthened the correlation. In participants with grade 2 hypertension, total testosterone was positively associated with the presence of stroke, and luteinizing hormone was also positively correlated with cardiovascular and cerebrovascular diseases.

Conclusions

Lower total testosterone could be a promising risk marker for prevalent hypertension. Both low and high levels of testosterone are associated with greater cardiovascular risk. Primary hypogonadism may be a risk marker for major cardiovascular diseases in men with severe hypertension.

Hypertensive Disorders of Pregnancy and Subsequent Risk of Premature Mortality

5) HYPERTENSIVE DISORDERS OF PREGNANCY AND SUBSEQUENT RISK OF PREMATURE MORTALITY

Abstract

Background

Hypertensive disorders of pregnancy (HDPs) are leading causes of maternal and perinatal morbidity and mortality. However, it is uncertain whether HDPs are associated with long-term risk of premature mortality (before age 70 years).

Objectives

The objective of this study was to evaluate whether HDPs were associated with premature mortality.

Methods

Between 1989 and 2017, the authors followed 88,395 parous female nurses participating in the Nurses’ Health Study II. The study focused on gestational hypertension and pre-eclampsia within the term HDPs. Hazard ratios (HRs) and 95% confidence intervals (CIs) for the associations between HDPs and premature mortality were estimated by using Cox proportional hazards models, with adjustment for relevant confounders.

Results

The authors documented that 2,387 women died before age 70 years, including 1,141 cancer deaths and 212 CVD deaths. The occurrence of HDPs, either gestational hypertension or pre-eclampsia, was associated with an HR of 1.31 (95% CI: 1.18 to 1.46) for premature death during follow-up. When specific causes of death were examined, these relations were strongest for CVD-related mortality (HR: 2.26; 95% CI: 1.67 to 3.07). The association between HDPs and all-cause premature death persisted, regardless of the subsequent development of chronic hypertension (HR: 1.20 [95% CI: 1.02 to 1.40] for HDPs only and HR: 2.02 [95% CI: 1.75 to 2.33] for both HDPs and subsequent chronic hypertension).

Conclusions

An occurrence of HDPs, either gestational hypertension or pre-eclampsia, was associated with an increased risk of premature mortality, particularly CVD mortality, even in the absence of chronic hypertension.

6) INFLUENCE OF SEX ON INTRACELLULAR CALCIUM HOMEOSTASIS IN PATIENTS WITH ATRIAL FIBRILLATION

Abstract

Aims

Atrial fibrillation (AF) has been associated with intracellular calcium disturbances in human atrial myocytes, but little is known about the potential influence of sex and we here aimed to address this issue.

Methods and Results

Alterations in calcium regulatory mechanisms were assessed in human atrial myocytes from patients without AF or with long-standing persistent or permanent AF. Patch-clamp measurements revealed that L-type calcium current (I_{Ca}) density was significantly smaller in males with than without AF (-
1.15±0.37 vs. -2.06±0.29 pA/pF) but not in females with AF (1.88±0.40 vs. -2.21±0.30 pA/pF). In contrast, transient inward currents (I_t) were more frequent in females with than without AF (1.92±0.36 vs. 1.10±0.19 events/min) but not in males with AF. Moreover, confocal calcium imaging showed that females with AF had more calcium spark sites than those without AF (9.8±1.8 vs. 2.2±1.9 sites/µm²) and sparks were wider (3.0±0.3 vs. 2.2±0.3 µm) and lasted longer (79±6 vs. 55±8 ms), favoring their fusion into calcium waves that triggers I_ro and afterdepolarizations. This was linked to higher ryanodine receptor phosphorylation at s2808 in women with AF, and inhibition of adenosine A2A or beta-adrenergic receptors that modulate s2808 phosphorylation was able to reduce the higher incidence of I_t in women with AF.

**Conclusion**

Perturbations of the calcium homeostasis in AF is sex-dependent, concurring with increased spontaneous SR calcium release-induced electrical activity in women but not in men, and with diminished I_ca density in men only.

**Translational Perspective**

Statistical analysis taking into account confounding effects of concurrent disease, risk factors and treatments revealed differential sex-dependent alterations of the calcium homeostasis in AF. The analysis suggests that suppression of calcium release-induced membrane depolarizations with adenosine receptor antagonists may be efficient in women with AF only while therapies aiming to restore L-type calcium current may be more efficient in males with AF.

**7) PREGNANCY-ASSOCIATED STROKE MORTALITY INCREASED AMONG BLACK WOMEN**

In-hospital mortality due to pregnancy-associated stroke (PAS) was elevated among Black women, according to study findings presented at the International Stroke Conference, held remotely from March 17 to 19 2021.

Study researchers from the Cleveland Clinic analyzed data collected between 2002 and 2017 in the United States by the Nationwide Inpatient Sample. Pregnant and postpartum women (N=38,797,752) were assessed for instance of PAS and associated mortality on the basis of race. Within the study cohort, 21.9% were Black and 0.03% (n=10,959) had PAS. Despite the fact that Black women made up about a fifth of the entire cohort, more than a third of the women who had a PAS event (41.3%; n=4521) were Black. Stratified by race, the in-hospital mortality rates from PAS were 7.8% among Black women and 5.0% among White women (P <.001).

Stratified by age and race, compared with White women of the same ages, Black women who were between 18 and 24 years old had elevated mortality (adjusted odds ratio [aOR], 2.10; 95% CI, 1.88-2.35; P <.001). The risk for mortality increased for those who were 25 to 29 years old (aOR, 2.75; 95% CI, 2.46-3.07; P <.001) and 30 to 34 years old (aOR, 3.94; 95% CI, 3.50-4.43; P <.001). At ages 35 to 40 years, risk for in-hospital mortality from PAS among Black women began to decrease (aOR, 3.73; 95% CI, 3.25-4.29; P <.001). Risk was lowest among Black women who were greater than 40 years old (aOR, 1.27; 95% CI, 1.08-1.51; P =.005).

Socioeconomic status appeared to be a significant contributing factor to mortality among Black women. Black women in the lowest income quartile had lower risk (aOR, 1.91; 95% CI, 1.74-2.10) than those in the highest quartile (aOR, 2.38; 95% CI, 2.02-2.80) compared with their White counterparts.

These findings indicated increased risk for PAS and associated in-hospital mortality in Black women compared with White women. Age and socioeconomic features were contributing factors to the patterns observed. Study researchers added, "[t]argeted interventions are needed to minimize these observed racial differences."

**Reference**


PTSD Increases the Risk of Incident Ischemic Heart Disease in Women Veterans
In this study of almost 400,000 women veterans, the authors identify posttraumatic stress disorder (PTSD) as significantly associated with an increased risk of developing incident ischemic heart disease, particularly among women veterans younger than 40 years of age at baseline. We learn that women veterans are younger and more racially and ethnically diverse than their male peers, and they have an increased prevalence of traditional cardiovascular risk factors and mental health disorders compared with civilian women and male veterans.\(^1\)

Of concern is that cardiovascular mortality has increased in recent years among young women in the community, erasing the progress of prior years. Young women of racial and ethnic minorities are most adversely impacted.

Psychosocial issues, particularly depression, preferentially disadvantage women, with psychological factors and emotional stress also predictive of early-onset myocardial infarction, particularly in younger women.\(^2,3\) Mental stress has been documented to induce changes of myocardial ischemia in young patients with recent myocardial infarction. Yet psychosocial risk factors are not included as risk enhancers in the 2019 ACC/AHA Guideline for Primary Prevention of Cardiovascular Disease.\(^4\)

PTSD is associated with a number of behavioral risk factors for ischemic heart disease, including unhealthy diet, obesity, smoking, and physical inactivity; additionally, disruptions in a number of neuroendocrine pathways could lead to deleterious effects on the immune, metabolic, and cardiovascular systems. Further, PTSD is often coexistent with other psychiatric conditions that impart increased ischemic heart disease risk. The authors advocate for a more intense study of PTSD in women veterans. My call to action would be to concomitantly evaluate PTSD in community women, particularly those of younger age and racial and ethnic minorities, a vulnerable population. The resultant data should determine whether psychosocial risk factors, including depression, stress, and PTSD, would warrant listing as risk enhancers for the prevention of ischemic heart disease.

References

8) RISK STRATIFICATION AND MANAGEMENT OF WOMEN WITH CARDIOMYOPATHY/HEART FAILURE PLANNING PREGNANCY OR PRESENTING DURING/AFTER PREGNANCY

Abstract
This position paper focusses on the pathophysiology, diagnosis and management of women diagnosed with a cardiomyopathy, or at risk of heart failure (HF), who are planning to conceive or present with (de novo or previously unknown) HF during or after pregnancy. This includes the heterogeneous group of heart muscle diseases such as hypertrophic, dilated, arrhythmogenic right ventricular and non-classified cardiomyopathies, left ventricular non-compaction, peripartum cardiomyopathy, Takotsubo syndrome, adult congenital heart disease with HF, and patients with right HF. Also, patients with a history of chemo-/radiotherapy for cancer or haematological malignancies need specific pre-, during and post-pregnancy assessment and counselling. We summarize the current knowledge about pathophysiological mechanisms, including gene mutations, clinical presentation, diagnosis, and medical and device management, as well as risk stratification. Women with a known diagnosis of a cardiomyopathy will often require continuation of drug therapy, which has the potential to exert negative effects on the foetus. This position paper assists in balancing benefits and detrimental effects.

Introduction
The number of women with heart disease who become pregnant is increasing, thereby contributing to a significant morbidity or mortality due to heart failure (HF), peripartum thromboembolic events and...
arrhythmias.\textsuperscript{1} Due to advances in genetic testing, there are also more men and women known to have a mutation associated with a cardiomyopathy and HF\textsuperscript{2} seeking pre-conception counselling. Also, patients with a history of cardiotoxic therapies (e.g. for malignant conditions), but without HF before pregnancy, need specific advice and risk stratification. Clear guidelines/directions how to counsel those patients before, during or after pregnancy are lacking.

The aetiology of cardiomyopathies occurring de novo, in association with pregnancy, is diverse (Graphical Abstract). Cardiomyopathies are neither very rare nor common, but they are important as they may cause severe complications, contributing substantially to maternal morbidity and mortality during pregnancy, in the immediate peripartum period and up to several months thereafter. Women with these heterogeneous forms of cardiomyopathies also commonly have arrhythmias which need specific management, including device therapy. Very little information and few recommendations have been published in this important field.

Women with a known diagnosis of a cardiomyopathy or presenting with (de novo) HF during/after pregnancy, will often require continuation of medical therapy, which has the potential to exert a negative effect on the foetus, meaning that adequate and appropriate treatment is vital. Accurate information on the foetal effect of medication is crucial to weigh the advantages of treating the mother against the possible long-lasting negative effects on the child.

Hypertensive HF, an important and prevalent complication during pregnancy, is not covered by this position paper. During pregnancy hypertensive emergencies with increased risk for the foetus can develop, including pulmonary oedema at lower levels of blood pressure compared with non-gravid women. Treatment of hypertension can prevent the progression to HF and decrease the risk of maternal and foetal complications.\textsuperscript{1}

This position paper refers to other recently published papers,\textsuperscript{1-3} but will fill important gaps in knowledge and is, therefore, a much-needed reference for cardiologists, specialist physicians, obstetricians, neonatologists, anaesthetists, intensivists, cardiothoracic surgeons, genetic counsellors and others.

9) COVID-19 VACCINE RESPONSE IN PREGNANT AND LACTATING WOMEN

Abstract
Background: Pregnant and lactating women were excluded from initial COVID-19 vaccine trials; thus, data to guide vaccine decision-making are lacking.

Objectives: To evaluate the immunogenicity and reactogenicity of COVID-19 mRNA vaccination in pregnant and lactating women compared to: (1) non-pregnant controls and (2) natural COVID-19 infection in pregnancy.

Study Design: 131 reproductive-age vaccine recipients (84 pregnant, 31 lactating, and 16 non-pregnant) were enrolled in a prospective cohort study at two academic medical centers. Titers of SARS-CoV-2 Spike and RBD IgG, IgA and IgM were quantified in participant sera (N=131) and breastmilk (N=31) at baseline, second vaccine dose, 2-6 weeks post second vaccine, and at delivery by Luminex. Umbilical cord sera (N=10) titers were assessed at delivery. Titers were compared to those of pregnant women 4-12 weeks from natural infection (N=37) by ELISA. A pseudovirus neutralization assay was used to quantify neutralizing antibody titers for the subset of women who delivered during the study period. Post-vaccination symptoms were assessed via questionnaire. Kruskal-Wallis tests and a mixed effects model, with correction for multiple comparisons, were used to assess differences between groups.

Results: Vaccine-induced antibody titers were equivalent in pregnant and lactating compared to non-pregnant women [median [IQR] 3.59 [4.68-5.89] pregnant, 5.74 [5.06-6.22] lactating, 5.62 [4.77-5.98] non-pregnant, p = 0.24]. All titers were significantly higher than those induced by SARS-CoV-2 infection during pregnancy (p < 0.0001). Vaccine-generated antibodies were 109 present in all umbilical cord blood and breastmilk samples. Neutralizing antibody titers were lower in umbilical cord compared to maternal sera, although this finding did not achieve statistical significance [median [IQR] 104.7 [61.2-188.2] maternal sera, 52.3 [11.7-69.6] cord sera, p=0.05]. The second vaccine dose (boost dose) increased SARS-CoV-2-specific IgG, but not IgA, in maternal blood and breastmilk. No differences were noted in reactogenicity across the groups.

Conclusions: COVID-19 mRNA vaccines generated robust humoral immunity in pregnant and lactating women, with immunogenicity and reactogenicity similar to that observed in non pregnant women. Vaccine-induced immune responses were significantly greater than the response to natural
infection. Immune transfer to neonates occurred via placenta and breast milk. KEYWORDS: Antibodies; breastfeeding; breastmilk; cord blood; COVID-19 vaccine; maternal immunity, mRNA; neonatal immunity; pregnancy

INTRODUCTION More than 73,600 infections and 80 maternal deaths have occurred in pregnant women in the United States alone as of March 1, 2021. SARS-CoV-2 infection is more severe in pregnant women compared to their non-pregnant counterparts, with an increased risk of hospital admission, ICU stay, and death. Despite their higher risk, pregnant and lactating women were not included in any initial coronavirus disease 19 (COVID-19) vaccine trials, although the first vaccine trial began in pregnant women in February of 2021 (Pfizer/BioNTech, ClinicalTrials.gov Identifier: NCT04754594). The COVID-19 pandemic has given rise to hundreds of vaccine platforms in development to fight SARS-CoV-2. However, few of these platforms have been tested or are specifically designed to elicit immunity in vulnerable populations, including pregnant women. Pregnant women have long been left out of therapeutic and vaccine research, reportedly due to heightened safety concerns in this population. Although the American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal- Fetal Medicine (SMFM) encouraged the Food and Drug Administration (FDA) to include pregnant women in the COVID-19 vaccine emergency use authorization (EUA) due to the risk of increased disease severity in this population, evidence about vaccine immunogenicity to guide patient decision-making and provider counseling is lacking. Specifically, given the novelty of the first emergency approved COVID-19 vaccines, both of which utilize mRNA to deliver SARS-CoV-2 Spike to educate the immune system, it remains unclear whether this novel vaccine approach will drive immunity in the context of pregnancy, and whether antibodies will be transferred efficiently to neonates via the cord and breast milk. Here, vaccine-induced immunity was profiled in vaccinated pregnant, lactating and non-pregnant controls compared to women infected with SARS-CoV-2 during pregnancy.

10) FEMALE SEX, WORK CULTURE BIGGEST CONTRIBUTORS TO PHYSICIAN BURNOUT

Abstract

Importance Electronic health records (EHRs) are considered a potentially significant contributor to clinician burnout.

Objective To describe the association of EHR usage, sex, and work culture with burnout for 3 types of clinicians at an academic medical institution.

Design, Setting, and Participants This cross-sectional study of 1310 clinicians at a large tertiary care academic medical center analyzed EHR usage metrics for the month of April 2019 with results from a well-being survey from May 2019. Participants included attending physicians, advanced practice providers (APPs), and house staff from various specialties. Data were analyzed between March 2020 and February 2021.

Exposures Clinician demographic characteristics, EHR metadata, and an institution-wide survey.

Main Outcomes and Measures Study metrics included clinician demographic data, burnout score, well-being measures, and EHR usage metadata.

Results Of the 1310 clinicians analyzed, 542 (41.4%) were men (mean [SD] age, 47.3 [11.6] years; 448 [82.7%] White clinicians, 52 [9.6%] Asian clinicians, and 21 [3.9%] Black clinicians) and 768 (58.6%) were women (mean [SD] age, 42.6 [10.3] years; 573 [74.6%] White clinicians, 105 [13.7%] Asian clinicians, and 50 [6.5%] Black clinicians). Women reported more burnout (survey score ≥50: women, 423 [52.0%] vs men, 258 [47.6%]; P=.008) overall. No significant differences in EHR usage were found by sex for multiple metrics of time in the EHR, metrics of volume of clinical encounters, or differences in products of clinical care. Multivariate analysis of burnout revealed that work culture domains were significantly associated with self-reported results for commitment (odds ratio [OR], 0.542; 95% CI, 0.427-0.688; P<.001) and work-life balance (OR, 0.643; 95% CI, 0.559-0.739; P<.001). Clinician sex significantly contributed to burnout, with women having a greater likelihood of burnout compared with men (OR, 1.33; 95% CI, 1.01-1.75; P=.04). An increased number of days spent using the EHR system was associated with less likelihood of burnout (OR, 0.966; 95% CI, 0.937-0.996; P=.03). Overall, EHR metrics accounted for 1.3% of model variance (P=.001) compared with work culture accounting for 17.6% of variance (P<.001).
Conclusions and Relevance In this cross-sectional study, sex-based differences in EHR usage and burnout were found in clinicians. These results also suggest that local work culture factors may contribute more to burnout than metrics of EHR usage.

Introduction

Recognition of burnout among health care clinicians has increased over the past 10 years, the same timeframe over which electronic health records (EHRs) have been rapidly adopted. The negative effects of burnout extend beyond the well-being of clinicians themselves to include clear correlations with increased errors and poorer outcomes for their patients. Health care worker burnout has become a significant focus of research with specific attention to the EHR as a contributing factor. Differentiating the potential contribution of the EHR to clinician burnout provides opportunities for better interventions.

Changes in care processes introduced with the EHR include increased time spent completing clinical work, especially after scheduled work hours. In their 2017 study, Arndt et al demonstrated with time-and-motion studies of clinical care and EHR usage metrics that clinicians spend 5.9 hours in the EHR out of an 11.4-hour day. Another study found that physicians spend an average 1 to 2 hours in the EHR after hours per scheduled day.

Variations by sex in clinical care and usage of the EHR are also becoming more apparent. A 2020 study demonstrated that female primary care clinicians spent more time with their patients at the point of clinical care, and a 2017 study found that female hospitalists' patients experience lower mortality and fewer readmissions. Differences in EHR usage by sex have identified that female clinicians spend more time in the EHR overall. It has also been shown that female clinicians have more burnout than their male counterparts. These differences across clinical care, patient outcomes, burnout, and EHR usage are described primarily for attending physicians. There is limited literature to evaluate the sex differences for alternate clinician groups.

Much of the literature on clinician burnout is in the form of surveys of burnout and perceived burdens of the EHR. EHR usage logs provide quantifiable data demonstrating clinician time and volume of activities in the EHR and provides an opportunity to differentiate usage patterns between user groups. Time-and-motion studies of clinical care and EHR usage metadata have validated the correlation of these metrics as a good proxy of clinician activities. Nevertheless, a recent systematic analysis of EHR metrics found a need for these studies to better define EHR metrics in standard methodologically transparent formats. The purpose of this study was to describe clinician burnout using clinician demographic characteristics, EHR usage, and surveys of local work culture.

Methods

This cross-sectional study included 3 types of clinicians using EHR usage metadata metrics and an institutional survey of burnout, wellness, and work satisfaction. This study was reviewed by the Duke University institutional review board and deemed exempt from informed consent requirements because data were deidentified.

Participants and Data Source

Clinicians included in the study practice in primarily outpatient settings in an academic tertiary health care system. We collected data for clinicians who had participated in an institution-wide employee engagement and work culture survey in mid-May 2019 (19,396 individuals with a response rate of 72.3%). Participants were restricted to 3 types of clinicians: attending physicians, advanced practice providers (APPs), and house staff with at least 1 day of outpatient appointments for the month of April 2019 and who had complete burnout survey responses. Of these, 1,848 individuals had EHR usage metadata for the study period of April 2019 and 1,310 met our inclusion/exclusion criteria (Figure 1).

We used EHR usage metadata from our vendor's EHR usage report (called Signal [Epic]). EHR usage metrics are derived from a user's interactions with the EHR that are captured in the User Action Log (UAL) Lite. The UAL calculates active time in EHR activity based on keyboard clicks or any mouse movements. After 5 seconds of inactivity, attribution of active time capture ceases. Time in the system during scheduled hours is measured as 30 minutes before the first patient and 30 minutes after the last patient. The Signal report divides time in the EHR to time spent within scheduled hours, time outside of scheduled hours, and time on nonscheduled days without appointments.

We chose EHR usage data for the study period of April 2019 for its temporal correlation with the May 2019 wellness/burnout survey. We used metrics for total time in the EHR and volume of EHR usage
for clinical activities of patient encounters, in-basket messages, and documentation. We evaluated 9 EHR metrics directly and derived an additional 7 metrics to enable evaluations across all clinicians (eTable 1 in the Supplement includes operational definitions and EHR metric). The calculated EHR metrics include total ambulatory encounters (15 metrics), total in-basket messages received (109 metrics), and proportional metric of time spent in the EHR (after hours/total hours). For the purposes of consolidating discussion of nonscheduled time, after hours henceforth refers to a summation measure of time spent working in EHR after work hours on scheduled days plus time spent working on nonscheduled days.

Well-being Survey Data

An organizational employee work culture survey was administered to the entire health system in mid-May 2019 and received responses from 19,396 individuals (72.3%). This survey is administered periodically for our health system by a third-party vendor to maintain respondent anonymity.28 EHR usage metadata was linked to the institutional survey using unique user identification, respondent identifiers were removed, and data returned for further analysis. The demographic variable for sex (male or female) was self-identified at the beginning of employment.

The survey includes a 5-item derivative of the Maslach Burnout Inventory emotional exhaustion domain (henceforth burnout).29-34 While the Maslach Burnout Inventory is the gold standard for burnout measurement, a meta-analysis found that the other 2 domains of burnout, depersonalization and personal accomplishment, consistently produced smaller coefficient α estimates than emotional exhaustion.35 In addition, emotional exhaustion is more psychometrically robust in discriminating between burnout and nonburnout outpatients suffering from work-related neurasthenia.36

The survey also includes additional work culture domains such as commitment, belonging, safety, teamwork, and work-life balance. The surveys are set to a 5-point Likert response (from 1 = “strongly disagree” to 5 = “strongly agree”). Where appropriate, survey results are reverse scored to account for item valence, such that low domain scores always represent negative outcomes and high domain scores represent positive outcomes. We averaged Likert results from all questions in a subdomain to determine a representative score for that response. Measures, their definitions, and Cronbach’s α values are reported in eTable 2 in the Supplement.

Burnout is transformed to a 100-point scale (0-100) for ease of interpretation, with higher scores representing more burnout. For purposes of graphical visualizations, we categorized burnout into 4 groups—none (0-49), mild (50-74), moderate (75-99), and severe (100) burnout—representing a burnout spectrum.37,38

Statistical Analysis

We used standard descriptive statistics to summarize clinician demographic characteristics, a representative subset of EHR usage metrics, and wellness survey responses. We found all data to be nonparametric and report out summary values as medians with interquartile ranges (IQRs). Work culture survey responses are presented as mean values with standard deviations (SDs) to preserve meaningful variations, which are less evident with IQRs reported as Likert scale results.

We conducted a multivariate analysis to assess the simultaneous association of burnout with clinician demographic characteristics, EHR usage metrics, and well-being domains. For this analysis, burnout was dichotomized using a score of 50 or greater as evidence of burnout.13 We used logistic regression to assess the likelihood of burnout occurring given the covariates in the model.39 The parameter coefficient estimates were converted to odds ratios (OR) for ease of interpretation. Model fit statistics were assessed using McFadden pseudo R² and the likelihood ratio x² test of the fitted vs the intercept model.40 We conducted a hierarchal assessment using different permutations of covariates analyzed separately by clinician demographic characteristics, EHR metrics, and wellness survey domains to determine variables with the strongest contribution to measures of burnout. Race/ethnicity was examined for inclusion in the regression model but was not included because there was no variation of burnout in other racial/ethnic categories other than White. We completed an interaction analysis of sex with other model covariates to help define the relationship sex has on burnout given levels of other metrics. The Akaike information criteria was used as a relative fit statistic for model comparison.41 Finally, we completed likelihood ratio tests to examine the significance of variance explained by the contributions between demographic characteristics, EHR metrics, and wellness domain blocks to the final model.

Statistical analysis was conducted with STATA/SE version 16.1 (StataCorp LLC). Significance was set at α < .05.
Results

Of the 1310 clinicians included for analysis, 542 (41.4%) were men (mean [SD] age, 47.3 [11.6] years; 448 [82.7%] White clinicians, 52 [9.6%] Asian clinicians, and 21 [3.9%] Black clinicians) and 768 (58.6%) were women (mean [SD] age, 42.6 [10.3] years; 573 [74.6%] White clinicians, 105 [13.7%] Asian clinicians, and 50 [6.5%] Black clinicians). Further information on demographic characteristics, specialty, and wellness survey responses are presented in Table 1.

Female clinicians reported more burnout than their male counterparts (score ≥50, median [IQR] percentage: men, 45% [30%-60%] vs women, 50% [35%-70%]; P < .001) (Table 2). Analysis of burnout by sex and clinician type found significant differences for attending physicians (men, 45% [30%-65%] vs women, 50% [35%-70%]; P < .001) and APPs (men, 35% [25%-60%] vs women, 45% [35%-60%]; P = .03) but not house staff (men, 55% [35%-75%] vs women, 50% [35%-75%]; P = .89).

We found nonsignificant differences with EHR usage by sex for related clinical time and volume activities. Female clinicians spent more time in the EHR by total time in minutes (median [IQR] minutes: men, 1551 [748-2750] vs women, 1780 [792-3041]; P = .14) but not more days in the EHR (median [IQR] days: men, 18 [13-22] vs women, 18 [14-21]; P = .41). Metrics for volume of clinical work showed that female clinicians had more days with appointments (median [IQR] days: men, 9 [5-14] vs women, 11 [5-15]; P = .09) and more clinical encounters (median [IQR] total encounters: men, 43 [9-104] vs women, 48 [12-112]; P = .32), although these differences were not statistically significant.

Female clinicians received less in-basket messages compared with male clinicians (median [IQR] messages/mo: men, 298.5 [115-534] vs women, 273 [112-498.5]; P = .82) but the difference was not statistically significant. There were no differences in products of clinical encounters, including length of documentation or percentage of encounters closed the same day.

To evaluate whether increased total time in the EHR correlated with increased after-hours time, we examined the percentage of time spent after hours by sex and burnout category. We found no difference in the percentage of time spent after hours (median [IQR] percentage: men, 30.6% [5.8%-49.9%] vs women, 30.5% [8.9%-52.3%]; P = .63). Regardless of level of burnout or sex, all clinicians spent similar time in the EHR after hours (Figure 2). Surprisingly, female clinicians with moderate to severe burnout spent a smaller proportion of time after hours than equivalently burned-out males.

Burnout Logistic Regression Results

We conducted a logistic regression model to assess the association between well-being domains and EHR usage metrics with clinician burnout. The parameter estimates are presented in Table 3. The model fit statistics showed an adequate fit of the data. The likelihood ratio x^2 test was significant (x^2 = 319.82; P < .001; McFadden R^2 = 0.198).

The results of the model indicate sex, total days in the EHR, and 4 survey domains were predictive of burnout. Holding all other variables in the model constant, female clinicians had an increased likelihood of burnout overall (OR = 1.331; 95% CI, 1.010-1.754; P = .04). As total number of days in the EHR increased, the likelihood of burnout modestly decreased (OR = 0.966; 95% CI, 0.937-0.996; P = .03). We found no other EHR metrics to be statistically significant in the full model. However, several of the wellness survey domains were significant. The results show that as the level of commitment increased, the likelihood of burnout decreased (OR = 0.542; 95% CI, 0.427-0.688; P < .001). Similar results were found for work-life balance (OR = 0.643; 95% CI, 0.559-0.739; P < .001), teamwork (OR = 0.525; 95% CI, 0.409-0.672; P < .001), and diversity (OR = 0.837; 95% CI, 0.710-0.985; P = .03).

The significance of variance of explained contributions indicated that EHR metrics accounted for 1.3% of model variance (P = .001) and work culture domains account for 17.6% of variance (P < .001). Interaction effect of sex to variables of interest was only significant for commitment and work-life, indicating that as the levels of these domains increased, the likelihood of burnout decreased more significantly for men compared with women (Figure 2).

Discussion

The etiologies of clinician burnout are multifactorial and likely representative of a combination of the individual, local environment, regulatory requirements, and EHR technology.22 Our study describes the relationship of clinician burnout to EHR usage metrics and work culture across sex for attending physicians, APPs, and house staff.

We found that burnout was associated with commitment and work culture. Our multivariate analysis, taking into consideration clinician demographic characteristics, sex, EHR metrics, and wellness survey, found wellness domains suppressed the significance of EHR metrics for average patient age, total time in system, and in-basket messages. This suggests that wellness domains have greater
The only EHR metric in our multivariate analysis to contribute significantly to burnout was number of days in the system. Interestingly, increasing days in the system were associated with a decreased likelihood of burnout (Table 3), potentially reflecting increased efficiency of usage of the EHR by clinicians for higher volume EHR users. Other EHR metrics derived as products of clinical care, such as length of notes or percentage of appointments closed the same day, did not differ significantly by sex.

Female clinicians reported more burnout than their male colleagues did across all 3 clinician types. These results support previous findings related to sex differences in burnout and EHR use metrics. While female clinicians spent more total time in the EHR and had more days with appointments, these measures did not lead to more clinician encounters or more total in-basket messages than male clinicians. The incongruence of the EHR time metric to volume metrics may be derivative of other workflow processes outside of the EHR to support clinicians that are not captured directly in the data. For example, some clinical workflows may allow other personnel to attach and complete in-basket metrics that would not be captured in the time spent completing messages. Differences by sex in how clinicians deliver clinical care may also be driving these differences in EHR usage metrics. For example, female clinicians spend more time in direct patient care, even to the disadvantage of their overall volume of encounters. They may also be responding to different gendered expectations for care encounters reflected in the time spent in front of the patient. Regardless, Chen et al found trends of improved clinical quality of care also taking more time, thus validating the time spent.

All clinicians, regardless of sex or burnout category, spent approximately one-third of their total EHR usage after hours. After-hours time in the EHR has been of significant concern as a driver of burnout. The consistency of EHR use after hours and across all burnout categories appears to be more reflective of the flexibility to utilize the EHR at times that are more effective for them to complete their work. The relative decrease in after-hours time for female clinicians with moderate-to-severe burnout may be indicative of other competing priorities outside of work for these clinicians that necessitate improved efficiency with the EHR. Our results suggest that the time of day when a clinician works is not as important as the volume of time that they work.

Among the clinician groups, house staff shared the most similar work volume metrics for number of days in the system and days with appointments. These similarities can likely be attributed to larger Graduate Medical Education time constraints and training requirements. However, we still found differences in female house staff EHR time metrics, with increased total time and after-hours time. These findings were more consistent with female clinicians' peers overall.

Our results found sex differences across clinician types for increased time spent and differences in clinical volume in the EHR for female clinicians. Our data set did not include a full-time-equivalency (FTE) metric, so normalization of work volume to overall encounter volumes cannot be determined. The differences for EHR usage metrics were most significant for attending physicians, less so for APPs, and generally not present for house staff, which is suggestive of potential variations in FTE.

**Limitations**

There are a number of limitations to our study. Our sample included clinicians from only 1 academic institution. While the data are limited in originating from a single institution, this is counterbalanced by the size of our cohort and inclusion of multiple specialties in our multivariate analysis. Attending physicians and APPs represented significant portions of active clinicians. A minority of the GME house staff (approximately 10%) participated in the organization survey and thus the house staff results are less generalizable. Overall, our results may not be as generalizable to other health systems owing to the contextual effect related to our EHR implementation and local work culture.

There are inherent limitations to using vendor EHR usage metadata. The Signal report consists of preprocessed summative data of the voluminous UAL Lite. As such, it represents a secondary data source of metadata of various activities in the EHR in varied formats for time (both by day and by activity), volume, and clinician panel demographic. Additionally, the data does not include delineation of metrics for clinicians who work concurrently in both outpatient and inpatient settings. We saw evidence of clinical crossover, with in-basket messages for some clinicians including hospital medical chart completion notifications.

For this study, we focused on metrics based upon total time and volume for consistency of comparisons across clinicians. Without a relative clinical FTE, understanding of volume EHR metrics
is limited. We note that attending physicians especially can have significant variation in the timing of clinical duties with other responsibilities. Consequently, we only analyzed 1 month of EHR usage metrics vs averaged month-to-month data.

We developed secondary derivations of EHR metrics when the available measures were not specific for work volume or too granular for comparison across clinicians. For example, the SecondsPerCompletedMsg Denominator metric represents all completed messages for a month. Since these can be completed by other support staff, we calculated the total number of in-basket messages as more comparable of volume across clinicians. To limit introduction of errors and ensure the data used were representative of the metrics we calculated, definitions and data interpretation were cross-referenced with vendor representatives.

Finally, our study does not include patient outcomes. Without measures of potential value of EHR activities to the care of the patient, discrimination of the time and volume of work in the EHR cannot be fully assessed. Future research should include the combination of patient outcomes, measures of severity of illness in tandem with EHR usage metrics, sex, and measures of burnout.

Conclusions

This study provides insight into variations of EHR usage by sex and across 3 types of clinicians. We found that clinician burnout was associated with commitment and local work culture factors. Burnout was greater for female clinicians irrespective of differences with male counterparts in EHR usage.

11) AHA OFFERS GUIDANCE FOR CVD RISK IN BREAST, PROSTATE CANCER

In a scientific statement issued by the American Heart Association and published online April 26 in Circulation: Genomic and Precision Medicine, recommendations are presented for cardiovascular disease (CVD) management in patients with breast and prostate cancer receiving hormone therapy.

Tochi M. Okwuosa, D.O., from the Rush University Medical Center in Chicago, and colleagues describe the CVD risks associated with hormone treatment for breast and prostate cancer and provide an evidence-based approach to detect and prevent adverse cardiovascular outcomes.

The authors note that tamoxifen may have protective to neutral effects on CVD risk burden and CVD events, although it increases the risk for venous thromboembolic events. In contrast, aromatase inhibitors increase CVD risk factors and event risks, including myocardial infarctions. For prostate cancer, androgen deprivation therapy seems to increase the risk for cardiovascular events; there is a lower risk for cardiovascular events with gonadotropin-releasing hormone (GnRH) agonists than GnRH antagonists. An increased risk for CVD was also seen with oral antiandrogens, especially when used for complete androgen blockade as combination GnRH/antiandrogen therapy. The authors did not find the effects of baseline cardiovascular risk factors and CVD on hormone therapy-associated cardiovascular events to be consistent. Evidence suggests that patients with breast and prostate cancer who are receiving hormonal therapy are more likely to be at risk for CVD, especially if they already have CVD risk factors, and consequently should receive close monitoring.

"For patients who have two or more cardiovascular risk factors, it is likely that referral to a cardiologist would be appropriate prior to beginning hormone treatment," Okwuosa said in a statement.

Two authors and one reviewer disclosed financial ties to the pharmaceutical and technology industries.

11) Sleep arousal burden is associated with long-term all-cause and cardiovascular mortality in 8001 community-dwelling older men and women

Abstract

Aims

To quantify the arousal burden (AB) across large cohort studies and determine its association with long-term cardiovascular (CV) and overall mortality in men and women.

Methods and results

We measured the AB on overnight polysomnograms of 2782 men in the Osteoporotic Fractures in Men Study (MrOS) Sleep study, 424 women in the Study of Osteoporotic Fractures (SOF) and 2221 men and 2574 women in the Sleep Heart Health Study (SHHS). During 11.2 ± 2.1 years of follow-up in MrOS, 665 men died, including 236 CV deaths. During 6.4 ± 1.6 years of follow-up in SOF, 105 women died, including 47 CV deaths. During 10.7 ± 3.1 years of follow-up in SHHS, 987 participants died, including 344 CV deaths. In women, multivariable Cox proportional hazard analysis adjusted for
common confounders demonstrated that AB is associated with all-cause mortality [SOF: hazard ratio (HR) 1.58 (1.01–2.42), \( P=0.038 \); SHHS-women: HR 1.21 (1.06–1.42), \( P=0.012 \)] and CV mortality [SOF: HR 2.17 (1.04–4.50), \( P=0.037 \); SHHS-women: HR 1.60 (1.12–2.28), \( P=0.009 \)]. In men, the association between AB and all-cause mortality [MrOS: HR 1.11 (0.94–1.32), \( P=0.261 \); SHHS-men: HR 1.31 (1.06–1.62), \( P=0.011 \)] and CV mortality [MrOS: HR 1.35 (1.02–1.79), \( P=0.034 \); SHHS-men: HR 1.24 (0.86–1.79), \( P=0.271 \)] was less clear.

Conclusions

Nocturnal AB is associated with long-term CV and all-cause mortality in women and to a lesser extent in men.

12) ADVERSE PREGNANCY OUTCOMES AND CVD RISK

Abstract

This statement summarizes evidence that adverse pregnancy outcomes (APOs) such as hypertensive disorders of pregnancy, preterm delivery, gestational diabetes, small-for-gestational-age delivery, placental abruption, and pregnancy loss increase a woman’s risk of developing cardiovascular disease (CVD) risk factors and of developing subsequent CVD (including fatal and nonfatal coronary heart disease, stroke, peripheral vascular disease, and heart failure). This statement highlights the importance of recognizing APOs when CVD risk is evaluated in women, although their value in reclassifying risk may not be established. A history of APOs is a prompt for more vigorous primordial prevention of CVD risk factors and primary prevention of CVD. Adopting a heart-healthy diet and increasing physical activity among women with APOs, starting in the postpartum setting and continuing across the life span, are important lifestyle interventions to decrease CVD risk. Lactation and breastfeeding may lower a woman’s later cardio metabolic risk. Black and Asian women experience a higher proportion APOs, with more severe clinical presentation and worse outcomes, than White women. More studies on APOs and CVD in non-White women are needed to better understand and address these health disparities. Future studies of aspirin, statins, and metformin may better inform our recommendations for pharmacotherapy in primary CVD prevention among women who have had an APO. Several opportunities exist for health care systems to improve transitions of care for women with APOs and to implement strategies to reduce their long-term CVD risk. One proposed strategy includes incorporation of the concept of a fourth trimester into clinical recommendations and health care policy.

13) GENETIC AND PHENOTYPIC LANDSCAPE OF PERIPARTUM CARDIOMYOPATHY

Abstract

Background: Peripartum cardiomyopathy (PPCM) occurs in approximately 1:2000 deliveries in the US and worldwide. The genetic underpinnings of PPCM remain poorly defined. Approximately 10% of women with PPCM harbor truncating variants in \( TTN \) (TTNtv). Whether mutations in other genes can predispose to PPCM is not known. It is also not known if the presence of TTNtv predicts clinical presentation or outcomes. Nor is it known if the prevalence of TTNtv differs in women with PPCM and preeclampsia, the strongest risk factor for PPCM.

Methods: Women with PPCM were retrospectively identified from several US and international academic centers, and clinical information and DNA samples were acquired. Next-generation sequencing was performed on 67 genes, including \( TTN \), and evaluated for burden of truncating and missense variants. The impact of TTNtv on severity of clinical presentation, and on clinical outcomes, was evaluated.

Results: 469 women met inclusion criteria. 10.4% of women with PPCM bore TTNtv (Odds ratio [OR]=9.4 compared with 1.2% in reference population; Bonferroni-corrected P \( [P*]=1.2x10^{-46} \)). We additionally identified overrepresentation of truncating variants in FLNC (OR=24.8, \( P=7.0x10^{-46} \)), DSP (OR=14.9, \( P=1.0x10^{-48} \)), and BAG3 (OR=53.1, \( P=0.02 \)), genes not previously associated with PPCM. This profile is highly similar to that found in non-ischemic dilated cardiomyopathy (DCM). Women with TTNtv had lower left ventricular ejection fraction (LVEF) on presentation than did women without TTNtv (23.5% vs 29%, \( P=2.5x10^{-4} \)), but did not differ significantly in timing of presentation after delivery, in prevalence of preeclampsia, or in rates of clinical recovery.

Conclusions: This study provides the first extensive genetic and phenotypic landscape of PPCM, and demonstrates that predisposition to heart failure is an important risk factor for PPCM. The work reveals a degree of genetic similarity between PPCM and DCM, suggesting that gene-specific therapeutic approaches being developed for DCM may also apply to PPCM, and that approaches to
genetic testing in PPCM should mirror those taken in DCM. Finally, the clarification of genotype/phenotype associations has important implications for genetic counseling.

**14) GENS X AND Y SHOW WORRISOME TREND OF DECLINING HEALTH**

Gen X and Gen Y are showing poorer physical health and higher levels of unhealthy behaviors compared with older generations, according to a study published online March 18 in the *American Journal of Epidemiology*.

Hui Zheng, Ph.D., and Paola Echave, both from The Ohio State University in Columbus, examined trends in mental and physical health among 62,833 adults participating in the National Health and Nutrition Examination Surveys (1988 to 2016) and 625,221 adults participating in the National Health Interview Surveys (1997 to 2018).

The researchers found that for all gender and racial groups, physiological dysregulation increased continuously from Baby Boomers through late Gen X and Gen Y. The increase was greater for White men than other groups. Black men had the steepest increase in low urinary albumin (a marker of chronic inflammation). White individuals saw distinctive increases in anxiety, depression, and heavy drinking and additionally had a higher level of smoking and drug use than Black and Hispanic individuals. The increase in physiological dysregulation was not associated with smoking, but the obesity epidemic contributed to the increase in metabolic syndrome.

“The worsening physiological and mental health profiles among younger generations imply a challenging morbidity and mortality prospect for the United States, one that may be particularly inauspicious for Whites,” the authors write.

**15) METABOLICALLY HEALTHY/UNHEALTHY OVERWEIGHT/OBESITY ASSOCIATIONS WITH INCIDENT HEART FAILURE IN POSTMENOPAUSAL WOMEN**

Abstract

Background:

Obesity is associated with an increased risk of heart failure (HF); however, how metabolic weight groups relate to HF risk, especially in postmenopausal women, has not been demonstrated.

Methods:

We included 19,412 postmenopausal women ages 50 to 79 without cardiovascular disease from the Women’s Health Initiative. Normal weight was defined as a body mass index ≥ 18.5 and < 25 kg/m² and waist circumference < 88 cm and overweight/obesity as a body mass index ≥ 25 kg/m² or waist circumference ≥ 88 cm. Metabolically healthy was based on < 2 and unhealthy ≥ 2 cardiometabolic traits: triglycerides ≥ 150 mg/dL, systolic blood pressure ≥ 130 mm Hg or diastolic blood pressure ≥ 85 mm Hg or blood pressure medication, fasting glucose ≥ 100 mg/dL or diabetes medication, and HDL-C (high-density lipoprotein cholesterol) < 50 mg/dL. Risk factor-adjusted Cox regression examined the hazard ratios (HRs) for incident hospitalized HF among metabolically healthy normal weight (reference), metabolically unhealthy normal weight, metabolically healthy overweight/obese, and metabolically unhealthy overweight/obese.

Results:

Among our sample, 455 (2.34%) participants experienced HF hospitalizations over a mean follow-up time of 11.3±1.1 years. Compared with metabolically healthy normal weight individuals, HF risk was greater in metabolically unhealthy normal weight (HR, 1.66 [95% CI, 1.01–2.72], *P*=0.045) and metabolically unhealthy overweight/obese individuals (HR, 1.95 [95% CI, 1.35–2.80], *P*=0.0004), but not metabolically healthy overweight/obese individuals (HR, 1.15 [95% CI, 0.78–1.71], *P*=0.48). Subdividing the overweight/obese into separate groups showed HRs for metabolically unhealthy obese of 2.62 (95% CI, 1.80–3.83; *P*<0.0001) and metabolically healthy obese of 1.52 (95% CI, 0.98–2.35; *P*=0.06).

Conclusions:

Metabolically unhealthy overweight/obese and metabolically unhealthy normal weight are associated with an increased risk of HF in postmenopausal women.

Migraine Linked to Hypertension Among Menopausal Women aura, or unknown migraine type.
Results During 826,419 person years, 12,501 cases of incident hypertension were identified, including 3100 among women with migraine, and 9401 among women without migraine. Migraine was associated with an increased risk of hypertension in menopausal women ($HR_{migraine} = 1.29 [1.24: 1.35]$), and were consistent in post-hoc sensitivity analyses, such as when controlling for common migraine medications. Associations between migraine and hypertension were similar whether or not women reported aura ($HR_{migraine aura} = 1.54 [1.04: 2.30]$, $HR_{migraine no aura} = 1.32 [0.87: 2.02]$, $p$-heterogeneity = 0.60). Associations were slightly stronger among ever users of menopausal hormone therapy ($HR_{migraine} = 1.34 [1.27: 1.41]$), than among never users ($HR_{migraine} = 1.19 [1.11: 1.28]$).

Conclusion Migraine was associated with an increased risk of hypertension amongst menopausal women. In secondary analysis, we didn’t observe a significant difference between migraine with aura and migraine without aura.