1). OBESEITY AS A RISK FACTOR FOR COVID-19 DEATH IN WOMEN AND MEN

Abstract

Obesity is associated with severe COVID-19 outcomes, yet, it unclear whether the risk of COVID-19 mortality associated with obesity is similar between the sexes. We used data from the UK Biobank to assess the risk of COVID-19 mortality associated with various anthropometric measures in women and men. To put these results in context, we also compared these estimates with those for mortality from influenza/pneumonia and coronary heart disease (CHD). The analyses included 502,493 individuals (54% women), of whom 410 (36% women) died of COVID-19, 549 (36% women) died of influenza/pneumonia, and 3355 (19% women) died of CHD. A higher BMI, waist circumference, waist-to-hip ratio, and waist-to-height ratio were each associated with a greater risk of death from COVID-19, influenza/pneumonia, and CHD in both sexes, with the exception of the association between higher BMI and the risk of influenza/pneumonia death in men. A higher BMI was associated with a stronger risk of COVID-19 mortality in women than men; the women-to-men ratio of hazard ratios was 1.20 (95% confidence interval: 1.00; 1.43). This study demonstrates the role of obesity in COVID-19 mortality and shows that the relative effects of a higher BMI on COVID-19 mortality may be stronger in women than men.

2). YOUNG WOMEN WITH AMICS: HIGH RISK, INADEQUATE CARE

Women age 55 years or younger who present with acute MI complicated by cardiogenic shock (AMICS) are less likely than young male patients of the same age to receive angiography and mechanical circulatory support and they more likely to die, new data show. The study also found that within this younger population, women who are Black and those with lower socioeconomic status are disproportionately more affected by AMICS.

Lead author Saraschandra Vallabhajosyula, MD, MSc (Emory University School of Medicine, Atlanta, GA), said the findings dispute long-held beliefs that young women of reproductive age are “protected” from more serious CV events because of their hormonal status. Of the 90,648 AMICS admissions in National Inpatient Sample (NIS) from 2000 to 2017 for patients age 55 years or younger, fully 26% were women.

“The rates of cardiogenic shock in these younger women are obviously lower than what is seen in older populations, but regardless, we found it shocking,” Vallabhajosyula said. “These are technically some of the most productive members of our society, and despite that, they frequently receive low rates of angiography and PCI, both of which are proven to be of great mortality benefit and essential in the treatment of cardiogenic shock.”

Indeed, women in the study had higher in-hospital mortality if they did not receive PCI or mechanical circulatory support (MCS), with odds ratios of around 1.2, and female sex itself was an independent predictor of higher in-hospital mortality (OR 1.11; 95% CI 1.07-1.16). Compared with men, however, women with AMICS were less likely to present with STEMI, acute noncardiac organ failure, or cardiac arrest.

In a related editorial, Amanda R. Vest, MBBS, MPH (Tufts Medical Center, Boston, MA), and Leslie Cho, MD (Cleveland Clinic, Cleveland, OH), say that the “sex-specific disconnect” between disease acuity, use of interventions, and survival odds “raises
important questions about both female AMICS pathophysiology and the quality of care delivered."

Vest and Cho further note that some patient-specific factors cannot be accounted for in administrative databases and these might explain why just 50.3% of female patients, compared to 59.5% of male patients, received intra-aortic balloon pump (IABP), percutaneous ventricular assist devices, or extracorporeal membrane oxygenation in this series. Mortality among the female patients here who did not receive these therapies "implies there were women who might have survived if appropriately recognized as mechanical support candidates." Of note, however, randomized controlled trials have not established a clear-cut role for mechanical support in the setting of AMICS; European guidelines currently advise against routine IABP use, while US guidelines are more neutral, giving it a class IIb (B) recommendation.

3). PREECLAMPSIA: PATHOPHYSIOLOGY AND CLINICAL PRESENTATIONS

The following are key points to remember from this JACC state-of-the-art review on preeclampsia—pathophysiology and clinical presentations:

1. Preeclampsia is a hypertensive disorder of pregnancy that occurs in 2-8% of pregnancies and causes substantial morbidity and mortality.
2. Preeclampsia is defined as new-onset hypertension and new-onset end-organ damage after 20 weeks' gestation. Proteinuria is no longer required for the diagnosis.
3. The complex pathophysiology of preeclampsia begins with abnormal placental development, endothelial dysfunction, and immunologic aberrations, possibly related to genetic susceptibility. Clinical features of preeclampsia include hypertension, proteinuria, renal dysfunction, neurological abnormalities, eclampsia, cardiac dysfunction, pulmonary edema, hepatic dysfunction, hematologic dysfunction, and fetal growth restriction.
4. Hypertension is necessary for the diagnosis of preeclampsia, defined as systolic blood pressure (SBP) ≥140 mm Hg or diastolic BP (DBP) ≥90 mm Hg on two occasions ≥4 hours apart after 20 weeks’ gestation in a woman with previously normal BP; or SBP ≥160 mm Hg or DBP ≥110 mm Hg on one occasion.
5. Proteinuria: The imbalance between proangiogenic and antiangiogenic factors likely causes podocyte injury leading to increased risk of hypertension and chronic kidney disease. Proteinuria can take up to 2 years to resolve after preeclampsia.
6. Renal dysfunction in preeclampsia is defined as serum creatinine >1.1 mg/dl or a doubling of baseline creatinine. Inflammatory cytokines lead to endothelial dysfunction and thrombotic microangiopathy of the kidneys and decreased intravascular volumes in preeclampsia increases sodium and free-water retention.
7. Neurologic dysfunction includes headaches, visual disturbances, seizure, posterior reversible encephalopathy syndrome, and hemorrhagic stroke. The classic preeclampsia headache is progressive, bilateral, pulsating/throbbing, associated with visual changes, worse with higher BP, worsened by physical activity, and not relieved by over-the-counter medications.
8. Eclampsia is defined as new-onset tonic-clonic, focal or multifocal seizures in the setting of pregnancy-related hypertension. Magnesium reduces the risk of eclampsia by 59%.
9. Cardiac dysfunction: Impaired placentation in preeclampsia causes increased vascular resistance and higher afterload, resulting in mild-to-moderate left ventricular diastolic dysfunction with concentric left ventricular hypertrophy. Preeclampsia is also a risk factor for peripartum cardiomyopathy (defined as left ventricular systolic function <45%).
10. Pulmonary edema is rare in preeclampsia and is related to: 1) increased vascular permeability, 2) cardiac dysfunction, 3) corticosteroids/tocolytics, and 4) iatrogenic volume overload.
11. Hepatic dysfunction is defined as transaminases ≥2x the upper limit of normal (AST typically < ALT) with right upper quadrant or epigastric tenderness.

12. Hematologic disturbances in preeclampsia include thrombocytopenia (due to increased platelet activation, aggregation, and consumption) and disseminated intravascular coagulopathy (due to consumption coagulopathy, hepatic injury and decreased clotting factors, and/or inflammatory response).

13. Fetal growth restriction (defined as an estimated fetal weight <10th percentile for gestational age) occurs commonly in pregnancies complicated by preeclampsia. Several mechanisms of uterine and placental dysfunction contribute to intrauterine growth restriction.

14. Low-dose aspirin is recommended for prevention of preeclampsia in high-risk women. Possible benefits of exercise, pravastatin, and metformin are being investigated. The definitive treatment for preeclampsia is delivery.

15. Further research to understand the link between preeclampsia and subsequent short- and long-term cardiovascular disease is needed.

4) CONSIDERABLE STATE-LEVEL VARIATION FOUND IN PREVALENCE OF ECLAMPSIA

Abstract

Importance - Hypertensive disorders of pregnancy are important causes of maternal and perinatal morbidity in the US. However, the extent of statewide variation in the prevalence of chronic hypertension, pregnancy-induced hypertension or preeclampsia, and eclampsia in the US remains unknown.

Objective - To examine the extent of statewide variation in the prevalence of chronic hypertension, hypertensive disorders of pregnancy (including pregnancy-induced hypertension or preeclampsia), and eclampsia in the US.

Design, setting, and participants - A cross-sectional study using 2017 US birth certificate data was conducted from September 1, 2019, to February 1, 2020. A population-based sample of 3,659,553 women with a live birth delivery was included.

Main outcomes and measures - State-specific prevalence of chronic hypertension, hypertensive disorders of pregnancy, and eclampsia was assessed using multilevel multivariable logistic regression, with the median odds ratio (MOR) to evaluate statewide variation.

Results - Of the 3,659,553 women, 185,932 women (5.1%) were younger than 20 years, 727,573 women (19.9%) were aged between 20 and 24 years, 1,069,647 women (29.2%) were aged between 25 and 29 years, 1,037,307 women (28.3%) were aged between 30 and 34 years, 523,607 women (14.3%) were aged between 35 and 39 years, and 115,487 women (3.2%) were 40 years or older. Most women had Medicaid (42.8%) or private insurance (49.4%). Hawaii had the lowest adjusted prevalence of chronic hypertension (1.0%; 95% CI, 0.9%-1.2%), and Alaska had the highest (3.4%; 95% CI, 3.0%-3.9%). Massachusetts had the lowest adjusted prevalence of hypertensive disorders of pregnancy (4.3%; 95% CI, 4.1%-4.6%), and Louisiana had the highest (9.3%; 95% CI, 8.9%-9.8%). Delaware had the lowest adjusted prevalence of eclampsia (0.03%; 95% CI, 0.01%-0.09%), and Hawaii had the highest (2.8%; 95% CI, 2.2%-3.4%). The degree of statewide variation was high for eclampsia (MOR, 2.36; 95% CI, 1.88-2.82), indicating that the median odds of eclampsia were 2.4-fold higher if the same woman delivered in a US state with a higher vs lower prevalence of eclampsia. Modest variation between states was observed for chronic hypertension (MOR, 1.27; 95% CI, 1.20-1.33) and hypertensive disorders of pregnancy (MOR, 1.17; 95% CI, 1.13-1.21).
Conclusions and relevance - The findings of this study suggest that after accounting for patient-level and state-level variables, substantial state-level variation exists in the prevalence of eclampsia. These data can inform future public-health inquiries to identify reasons for the eclampsia variability.

5). GENDER DISPARITIES IN HIGH-RISK ANGIOPLASTY: STILL ROOM FOR IMPROVEMENT

The use of ventricular support is indicated in several high-risk percutaneous coronary intervention (PCI) scenarios. However, the uses of complex or advanced interventions are being underutilized in females when compared with males. There is limited information related to the use and outcomes of ventricular support devices in high-risk PCI by gender.

Dr. Alraies and collaborators assessed utilization, in-hospital, and short-term outcomes differences between females and males who underwent high-risk PCI with left ventricular support. They included 1,053 high-risk patients who underwent PCI with mechanical support using Impella 2.5 or Impella CP, in which a total 261 (24.79%) were females. These were more likely to be at higher risk of clinical events and more comorbid, which is better expressed or summarized as a higher mean STS score (8.21 ± 8.21 vs. 5.04 ± 5.97, *p* < .001). Despite that, there was no difference in in-hospital mortality, stroke, myocardial infarction or need for recurrent revascularization when compared with males. Females had higher risk of bleeding requiring transfusion compared than males (9.58 vs. 5.30%, *p* = .019). Authors conclude that female patients undergoing high-risk PCI were older and had more comorbidities, but had comparable similar outcomes compared with males.

The article emphasizes that only 25% of patients undergoing high-risk PCI with ventricular support are female is actually low. Is important to note that the prevalence of female patients in incident acute coronary syndromes is around 30%, not very different than 25%. However, this small difference may actually concentrate the highest risk people, so let us dig in a little deeper on this issue.

If there is a difference in the use of ventricular support in high-risk PCI, there are few explanations. The first one, is that female patients are more likely to be treated by cardiac surgery, but the article indirectly shows that female patients are more likely to be declined from cardiac surgery than males (females more likely to be evaluated by surgeons, but a higher proportion found not to be suitable for surgery). Second, those female patients are less likely to receive a ventricular support device for their high-risk PCI. This may make sense given potential issues with peripheral arterial size in the presence of the same degree of atherosclerotic disease burden, but is rarely present in clinical practice for a 14 French system. Finally, female patients are less likely to receive high-risk PCI, with or without ventricular support. Then, the truth likely falls in one or a combination between the last two hypotheses.

This analysis showed that female patients were less likely to receive ventricular support, have higher risk profile, but similar clinical outcomes. This combination of findings may preclude the following: female patients at the highest risk of events were more likely excluded from the use ventricular assist devices. If women undergoing protected high-risk PCI have significantly higher outcome event risk profile than males at a population level, this should be translated to clinical outcomes, but clinical outcomes remain similar between genders. If this is the case, there is still significant room for improvement in being more inclusive in terms of ventricular assist devices in female patients. Other methodological reasons explaining these findings could be lack of sufficient statistical power for clinical events, or that risk scores do not discriminate outcome incidence with the same performance in both genders.
Authors also detected a higher risk of bleeding in female patients. Bleeding is a relevant clinical event, strongly associated with mortality. In this article by Alraies and collaborators mentioned that female patients had lower body surface area. Lower body-mass index has been associated with higher risk of major bleeding in acute coronary syndromes. Then, this finding may represent a relative overdosing (per per-kilogram of body-weight) of anticoagulants or antiplatelets in female participants, which usually have a lower body-surface area and lower weight when compared with males.

Overall, this analysis by Alraies and collaborators provide new insights related to gender disparities of ventricular support use in high-risk PCI. Although clinical outcomes look similar between females and males, this is likely due to selection bias rather a real clinical effect. There is a need to better understand the reasons why female patients are less likely to receive best medical therapy when compared with male counterparts.

6). WOMEN WITH AMI-CARDIOGENIC SHOCK TREATED LESS AGGRESSIVELY

Health Day News — among young adults with acute myocardial infarction-cardiogenic shock (AMI-CS), women are treated less aggressively and have higher in-hospital mortality than men, according to a study published online Sept. 29 in Circulation: Heart Failure.

Saraschandra Vallabhajosyula, M.D., from the Emory University School of Medicine in Atlanta, and colleagues identified a retrospective cohort from the National Inpatient Sample of individuals aged 18 to 55 years who were admitted for AMI-CS during 2000 to 2017. Data were included for 90,648 AMI-CS admissions; 26 percent of these admissions were among women.

The researchers found that the rates of CS were higher in men (2.2 percent in 2000 and 4.8 percent in 2017) compared with women (2.6 percent in 2000 and 4 percent in 2017). Women with AMI-CS were more often Black, had lower socioeconomic status and higher comorbidity, and were more often admitted to rural and small hospitals compared with men. Women experienced lower rates of ST-segment elevation presentation, acute noncardiac organ failure, and cardiac arrest; they also received less-frequent coronary angiography, early coronary angiography, percutaneous coronary intervention, and mechanical circulatory support. In-hospital mortality was independently predicted by female sex. Lower hospitalization costs were seen for women, but their length of stay was comparable to that of men.

“Further quantitative and qualitative research is needed in these vulnerable populations to better understand the underlying reasons for these differences in resource utilization in this high-risk population and what can be done to improve the outcome,” the authors write.

7). PROCEDURAL, PREGNANCY, AND SHORT-TERM OUTCOMES AFTER FETAL AORTIC VALVULOPLASTY

Abstract

Objectives

We aimed to evaluate the effect of technical aspects of fetal aortic valvuloplasty (FAV) on procedural risks and pregnancy outcomes.
Background

FAV is performed in cases of severe mid-gestation aortic stenosis with the goal of preventing hypoplastic left heart syndrome (HLHS).

Methods

The International Fetal Cardiac Intervention Registry was queried for fetuses who underwent FAV from 2002 to 2018, excluding one high-volume center.

Results

The 108 fetuses had an attempted cardiac puncture (mean gestational age [GA] 26.1 ± 3.3 weeks). 83.3% of attempted interventions were technically successful (increased forward flow/new aortic insufficiency). The interventional cannula was larger than 19 g in 70.4%. More than one cardiac puncture was performed in 25.0%. Intraprocedural complications occurred in 48.1%, including bradycardia (34.1%), pericardial (22.2%) or pleural effusion (2.7%) requiring drainage, and balloon rupture (5.6%). Death within 48 hr occurred in 16.7% of fetuses. Of the 81 patients born alive, 34 of whom had biventricular circulation. More than one cardiac puncture was associated with higher complication rates ($p<.001$). Larger cannula size was associated with higher pericardial effusion rates ($p = .044$). On multivariate analysis, technical success (odds ratio [OR] = 10.9, 95% confidence interval [CI] = 2.2–53.5, $p = .003$) and later GA at intervention (OR = 1.5, 95% CI = 1.2–1.9, $p = .002$) were associated with increased odds of live birth.

Conclusions

FAV is an often successful but high-risk procedure. Multiple cardiac punctures are associated with increased complication and fetal mortality rates. Later GA at intervention and technical success were independently associated with increased odds of live birth. However, performing the procedure later in gestation may miss the window to prevent progression to HLHS.

8) OBESITY AS A RISK FACTOR FOR COVID-19 DEATH IN WOMEN AND MEN

Abstract

Obesity is associated with severe COVID-19 outcomes, yet, it is unclear whether the risk of COVID-19 mortality associated with obesity is similar between the sexes. We used data from the UK Biobank to assess the risk of COVID-19 mortality associated with various anthropometric measures in women and men. To put these results in context, we also compared these estimates with those for mortality from influenza/pneumonia and coronary heart disease (CHD). The analyses included 502,493 individuals (54% women), of whom 410 (36% women) died from COVID-19, 549 (36% women) died from influenza/pneumonia and 3,355 (19% women) died from CHD. A higher body mass index (BMI), waist circumference, waist-to-hip ratio and waist-to-height ratio were each associated with a greater risk of death from COVID-19, influenza/pneumonia and CHD in both sexes, with the exception of the association between higher BMI and the risk of influenza/pneumonia death in men. A higher BMI was associated with a stronger risk of COVID-19 mortality in women than men; the women-to-men ratio of hazard ratios was 1.20 (95% confidence interval 1.00; 1.43). This study demonstrates the role of obesity in COVID-19 mortality and shows that the relative effects of a higher BMI on COVID-19 mortality may be stronger in women than men.

Introduction

Although women and men are approximately as likely to be infected by coronavirus disease 2019 (COVID-19), men have higher death rates from COVID-19 in almost all countries where data are available. Obesity has been identified as one of the key factors associated
with severe COVID-19 outcomes, some of which may be explained by the adverse effects of obesity on diabetes. However, it is unclear whether the risk of COVID-19 mortality associated with obesity is similar between the sexes. We thus assessed the risk of COVID-19 mortality associated with various anthropometric measures in women and men in the UK Biobank. For comparability, we also evaluated the association of these measures with mortality from influenza or pneumonia, the leading causes of death from respiratory disease in usual circumstances, and coronary heart disease (CHD), a condition which has a well-established association with obesity.

Methods

The UK Biobank is a prospective, population-based cohort study of women and men aged 40 to 69 years at baseline between 2006 and 2010. Follow-up for cause-specific mortality was conducted to June 30, 2020 through linkage with the National Death Register. Cox regression was used to estimate the sex-specific hazard ratios (HRs) and 95% confidence intervals (CIs) for mortality from COVID-19, influenza/pneumonia and CHD for overweight and obesity (defined as a body mass index [BMI] ≥25 to <30 kg/m² and ≥30 kg/m², respectively) and an overall 1-standard deviation (SD) increase in BMI (SD 4.8), waist circumference (SD 13.5), waist-to-hip ratio (SD 0.09) and waist-to-height ratio (SD 0.08). Influenza and pneumonia were taken together to avoid unreliable estimation due to small numbers. CIs were estimated using floating absolute risks. Adjustments were made for age, smoking status (never/ex/current), socio-economic status (determined using the Townsend index of area deprivation) and ethnicity (white or not). Interactions between each variable and sex were added to the model, so as to obtain the women-to-men ratio of HRs (RHRs) for each risk factor. Penalized smoothing splines were used to examine the shape of associations between BMI and the study endpoints. In secondary analyses, we additionally adjusted for diabetes. We also stratified our analyses on COVID-19 mortality for ethnicity because a previous UK Biobank analysis suggested that the association between BMI and the risk of testing positive for COVID-19 may vary by ethnicity. Analyses used R version 3.3.0.

2.1 ethics

This research was conducted using the UK Biobank Resource (application No 2495). Permission to use the UK Biobank Resource was approved by the access subcommittee of the UK Biobank Board. UK Biobank has obtained Research Tissue Bank approval from its governing research ethics committee, as recommended by the National Research Ethics Service. No separate ethical approval was required. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Results

Of the 502,493 individuals (54% women) included in the analyses, 410 (36% women) died from COVID-19, 549 (36% women) died from influenza/pneumonia, and 3355 (19% women) died from CHD during a median follow-up of 11.2 years.

A higher BMI, waist circumference, waist-to-hip ratio and waist-to-height ratio were each associated with a greater risk of death from COVID-19, influenza/pneumonia and CHD in both sexes (Table 1). The only exception was the association between higher BMI and the risk of influenza/pneumonia death in men, which may be attributable to the apparent underlying U-shaped relationship (Figure 1). The shape and magnitude of the relationship between BMI and COVID-19 mortality was similar to the relationship with CHD mortality. Obesity was associated with an increased risk of each cause of death in both sexes, except for influenza/pneumonia in men.
SEX DIFFERENCES AND THE LEFT VENTRICLE: MORPHOLOGY MATTERS

It is well known that alterations in structure and function of the left ventricle are key predictors of cardiovascular disease (CVD) outcomes. Ironically, but not surprisingly, sex differences in left ventricular (LV) morphology have been better recognized and understood in health rather than in disease. For instance, both electrocardiographic and echocardiographic parameters for identifying normal vs. abnormal LV size have been defined using sex-specific criteria since the early 1980s. Acknowledging that cardiac size is not only proportionate to overall body size but also independently differs by sex, cardiac magnetic resonance imaging (cMRI) criteria have been similarly developed to provide guidance for identifying presence of LV hypertrophy (LVH) specifically for women vs. men. In the Multi-Ethnic Study of Atherosclerosis, for example, the formulas for defining LVH differ substantially for women and men: predicted LV mass = 6.82 × (height in metres)0.561 × (weight in kilograms)0.608 for women, compared to 8.17 × (height in metres)0.561 × (weight in kilograms)0.608 for men. Moreover, women demonstrate more concentric remodelling and less dilated (eccentric) hypertrophy than men, and aortic stenosis leads to sex-specific myocardial remodelling with a more concentric form of hypertrophy, less fibrosis, and better reversibility after unloading the ventricle following aortic valve replacement in women than in men.

A new report by Miller et al. adds to this literature, showing sex-specific differences in LV morphology in a large dataset of 3745 women and men who underwent both cMRI and invasive coronary angiography. The participants were stratified into four groups: (i) normal; (ii) concentric remodelling; (iii) eccentric (dilated) hypertrophy; and (iv) concentric (non-dilated) hypertrophy, then related to all-cause mortality and revascularization at 3- to 4-year follow-up. Baseline findings were consistent with prior work showing that women had more concentric remodelling, less eccentric hypertrophy, and a similar prevalence of concentric hypertrophy to men. Notably, while the all-cause mortality and revascularization prognosis was equally elevated for women and men with concentric hypertrophy, women uniquely demonstrated elevated risk with eccentric hypertrophy. Analyses exclusive to all-cause mortality were similar, suggesting that the primary contributor to the findings was cardiac mortality. While these are important novel findings, not accounting for other CVD events, such as heart attack, stroke, and heart failure, is a limitation that likely underestimates differences in major adverse cardiac events, including in those with concentric remodelling. Specifically, sex differences in LV remodelling appear to contribute to the higher prevalence of heart failure with preserved ejection fraction (HFpEF), which is more prevalent and lacks definitive therapies.

Why would sex differences in LV remodelling contribute to greater adverse mortality in women and not in men? We have described in a cohort exclusively of women undergoing cMRI and invasive coronary functional testing that despite a similar LV mass and LV ejection fraction (LVEF), women with impaired myocardial perfusion reserve had greater relative wall thickness compared to women with normal myocardial perfusion reserve, a measure of coronary micro vascular function. We have further demonstrated that women suffer disproportionately from coronary micro vascular dysfunction, now a recognized major contributor to the rising epidemics of ischaemia with no obstructive coronary disease, and myocardial infarction with no obstructive coronary disease, and linked with elevated cardiovascular morbidity and mortality.

Given that Miller et al. have confirmed that sex differences in LV remodelling have serious adverse implications, it is best to further understand the genesis in order to respond to the scientific charge of using our understanding of sex differences to improve patient outcomes. Prior sex difference studies have evaluated adult participants of convenience undergoing cardiac testing for CVD, and therefore do not inform us about biological sex differences, i.e. the mechanisms underlying sexual dimorphism in LV responses to stressors that accumulate over a life course. Of value, Goble et al. studied 243 11-year-old girls and boys and found that LV mass differs by sex, adjusted for weight, in healthy pre-pubertal children. Notably, they found LV mass sex difference was strongly related to body fat mass, where the girls’ lower LV mass was related to their higher fat mass. Moreover, although to a
lesser extent, LV mass differences were also related to hemodynamic sex difference, where girls’ higher heart rate contributed to lower LV mass, while boys’ higher systolic blood pressure contributed to higher LV mass. Other work demonstrates that women also have higher LV elastance (systolic stiffness) than men at a given age, and steeper increases in LV elastance are seen in ageing women than men.11 Although cardiomyocyte number is the same in girls and boys at birth, ageing women have a relatively attenuated decline in cardiomyocyte number and mass, with less tendency towards cardiomyocyte hypertrophy and eccentric LV remodelling compared with men.12 It is likely that these sex differences are genetically determined by sex biases in gene expression, a consistent finding reported across organ systems and species.13

10). CAC HELPS ID CVD RISK IN WOMEN RECEIVING RT FOR BREAST CANCER

THURSDAY, Oct. 15, 2020 (Health Day News) -- For women with breast cancer, coronary artery calcium (CAC) detected on radiotherapy (RT)-planning computed tomography (CT) scan is associated with cardiovascular disease (CVD) risk, according to a study presented at the annual European Breast Cancer Conference, held virtually from Oct. 2 to 3.

Roxanne Gal, from the University of Utrecht in the Netherlands, and colleagues examined the association between automated CAC measurement on RT-planning CT scans and the risk for CVD in a cohort of breast cancer patients receiving RT between 2005 and 2016. Data were included from 14,002 patients (mean age, 58 years).

The researchers found that 29 percent of the patients had a CAC score >0. Overall, 8 percent of patients were admitted for CVD and 1 percent died from CVD at a median follow-up of 52 months. The risk for CVD increased with higher CAC after adjustment for age and calendar year at planning CT, from 5 percent for patients without CAC to 28 percent for patients with a CAC score >400. Patients treated with anthracyclines had the strongest association between a high CAC score and CVD (hazard ratio CAC >400 = 5.4).

"In my opinion, treating breast cancer means finding the right balance between maximizing chances of tackling the tumour, while minimizing the risks of side effects, including the risk of cardiovascular disease," a co-author said in a statement.

11). WOMEN WHO EXPERIENCE A MYOCARDIAL INFARCTION AT A YOUNG AGE HAVE WORSE OUTCOMES COMPARED WITH MEN

Abstract

Aims

There are sex differences in presentation, treatment, and outcomes of myocardial infarction (MI) but less is known about these differences in a younger patient population. The objective of this study was to investigate sex differences among individuals who experience their first MI at a young age.

Methods and results

Consecutive patients presenting to two large academic medical centres with a Type 1 MI at ≤50 years of age between 2000 and 2016 were included. Cause of death was adjudicated using electronic health records and death certificates. In total, 2097 individuals (404 female, 19%) had an MI (mean age 44 ± 5.1 years, 73% white). Risk factor profiles were similar between men and women, although women were more likely to have diabetes (23.7% vs. 18.9%, $P=0.028$). Women were less likely to undergo invasive coronary angiography (93.5% vs. 96.7%, $P=0.003$) and coronary revascularization (82.1% vs. 92.6%, $P<0.001$).
Women were significantly more likely to have MI with non-obstructive coronary disease on angiography (10.2% vs. 4.2%, \( P < 0.001 \)). They were less likely to be discharged with aspirin (92.2% vs. 95.0%, \( P = 0.027 \), beta-blockers (86.6% vs. 90.3%, \( P = 0.033 \)), angiotensin-converting enzyme inhibitors/angiotensin-receptor blockers (53.4% vs. 63.7%, \( P < 0.001 \)), and statins (82.4% vs. 88.4%, \( P < 0.001 \)). There was no significant difference in in-hospital mortality; however, women who survived to hospital discharge experienced a higher all-cause mortality rate (adjusted HR = 1.63, \( P = 0.01 \); median follow-up 11.2 years) with no significant difference in cardiovascular mortality (adjusted HR = 1.14, \( P = 0.61 \)).

Conclusions

Women who experienced their first MI under the age of 50 were less likely to undergo coronary revascularization or be treated with guideline-directed medical therapies. Women who survived hospitalization experienced similar cardiovascular mortality with significantly higher all-cause mortality than men. A better understanding of the mechanisms underlying these differences is warranted.

12). RISK FOR CVD IN WOMEN VS MEN WITH DIABETES

Health Day News — Most patients with congenital heart disease (CHD) are not at risk for severe COVID-19 infection, according to a study published online Oct. 14 in the Journal of the American Heart Association.

Matthew J. Lewis, M.D., from the Columbia University Irving Medical Center in New York City, and colleagues assessed the impact and predictors of COVID-19 infection and severity among 53 patients with CHD diagnosed with COVID-19 between March 1 and July 1, 2020.

The researchers found that 10 CHD patients were younger than 18 years old (median age, 34 years). More than half (58 percent) had complex congenital anatomy, including 10 with a Fontan repair. Additionally, eight patients had a genetic syndrome, six had pulmonary hypertension, and nine were obese. Eighteen adults were physiologic class C or D. Among all 53 patients, nine had a moderate or severe infection, including three who died. The presence of a genetic syndrome (odds ratio, 35.82) and physiological Stage C or D in adults (odds ratio, 19.38) were significantly associated with moderate or severe infection.

“While our sample size is small, these results imply that specific congenital heart lesions may not be sufficient cause alone for severe COVID-19 infection,” the authors write.

13). AORTIC DISSECTION, A RARE COMPLICATION OF PREGNANCY

Abstract

Importance - Women with aortopathy conditions are at risk for pregnancy-related aortic dissection, and these conditions may not be recognized until after the aortic dissection occurs.

Objective - To examine the clinical characteristics, imaging features, and outcomes in women with pregnancy-related acute aortic dissection.

Design, Setting, and Participants - A cohort study, comprising data from the International Registry of Acute Aortic Dissection (IRAD) (February 1, 1998, to February 28, 2018). The
Multicenter referral center study included 29 women with aortic dissection during pregnancy or less than 12 weeks post partum in IRAD from 1998 to 2018.

**Main Outcomes and Measures** - Clinical features of pregnancy-related aortic dissection to be studied included underlying aortopathy, aortic size, type of aortic dissection, timing of dissection, hypertension, and previous aortic surgery.

**Results** - A total of 29 women (mean [SD] age, 32 [6] years) had pregnancy-related aortic dissection, representing 0.3% of all aortic dissections and 1% of aortic dissection in women in the IRAD. Among women younger than 35 years, aortic dissection was related to pregnancy in 20 of 105 women (19%). Thirteen women (45%) had type A aortic dissection, and 16 women (55%) had type B. Aortic dissection onset was known in 27 women (93%): 15 during pregnancy, 4 in the first trimester, and 11 in the third trimester; 12 were post partum, occurring a mean (SD) of 12.5 (14) days post partum. At type A aortic dissection diagnosis, the mean (SD) aortic diameters were sinus of Valsalva, 54.5 (5) mm and ascending aorta, 54.7 (6) mm. At type B aortic dissection diagnosis, the mean (SD) descending aortic diameter was 32.5 (5) mm. Twenty women (69%) had an aortopathy condition or a positive family history: 13 women (65%) with Marfan syndrome, 2 women (10%) with Loeys-Dietz syndrome, 2 women (10%) with bicuspid aortic valves, 2 women (10%) with a family history of aortic disease, and 1 woman (5%) with familial thoracic aortic aneurysm. Aortopathy was not recognized until after aortic dissection in 47% of the women. Twenty-eight women (97%) survived aortic dissection hospitalization.

**Conclusions and Relevance** - Aortic dissection complicating pregnancy is rare. Most pregnancy-related aortic dissection is due to an aortopathy often not diagnosed until after aortic dissection. In this study, type A aortic dissections were associated with a dilated aorta, and type B aortic dissections often were not. Recognition of underlying conditions and risks for aortic dissection may improve management of pregnancy in women with aortopathy.