**News in May 2022**

1. **Mediterranean-Style Diet Reduces Risk of Preeclampsia Regardless of Race**

**BACKGROUND**

Preeclampsia is a major cause of maternal and fetal morbidity and mortality. Given its large public health burden, there is a need to identify modifiable factors that can be targeted for preeclampsia prevention. In this study, we examined whether a Mediterranean-style diet is protective for preeclampsia in a large cohort of racially and ethnically diverse, urban, low-income women.

**METHODS AND RESULTS**

We used data from the Boston Birth Cohort. Maternal sociodemographic and dietary data were obtained via interview and food frequency questionnaire within 24 to 72 hours postpartum, respectively. Additional clinical information, including physician diagnoses of preexisting conditions and preeclampsia, were extracted from medical records. We derived a Mediterranean-style diet score from the food frequency questionnaire and performed logistic regression to examine the association of the Mediterranean-style diet score with preeclampsia. Of 8507 women in the sample, 848 developed preeclampsia. 47% were Black, 28% were Hispanic, and the remaining were White/Other. After multivariable adjustment, greatest adherence with MSD was associated with lower preeclampsia odds (adjusted odds ratio comparing tertile 3 to tertile 1, 0.78; 95% CI, 0.64-0.96). A subgroup analysis of Black women demonstrated a similar benefit with an adjusted odds ratio comparing tertile 3 to tertile 1 of 0.74 (95% CI, 0.76-0.96).

**CONCLUSIONS**

Self-report of higher adherence to a Mediterranean-style diet is associated with lower preeclampsia odds, and benefit of this diet is present among Black women as well.
2. Women Underrepresented as Cardiac Electrophysiology Operators

Women cardiac electrophysiology (EP) operators remain significantly underrepresented, according to a study published in the May issue of Heart Rhythm.

Stacey J. Howell, M.D., from University of California in San Francisco, and colleagues assessed temporal and geographical trends in the proportion of women EP operators. The analysis included data extracted from the Medicare Provider Utilization and Payment Database (2013 to 2019).

The researchers found that on average annually, 5 percent of the 3,524 EP operators were women. A similarly low proportion of women EP operators was seen across each procedure type. During the study period, there was a 137 percent increase in the total number of atrial fibrillation ablationists, yet the proportion of women remained unchanged. The numbers remained constant for supraventricular tachycardia/atrial flutter ablationists and device operators, as did the proportion of women operators. Ten states had no women EP operators who performed more than 10 of any given EP procedure annually in 2019 and no women device operators who performed more than 10 of any given type of device implantation annually.

"We hope that by better defining the gender disparity in electrophysiology, our study can highlight the need to recruit and retain more women in this subspeciality," Howell said in a statement.

3. Parental cardiovascular health predicts time to onset of cardiovascular disease in offspring

Background
Cardiovascular disease (CVD) risk factors are transmitted from parents to children. We prospectively examined the association between parental cardiovascular health (CVH) and time to onset of CVD in the offspring.

Methods and results
The study consisted of a total of 5967 offspring–mother–father trios derived from the Framingham Heart Study. Cardiovascular health score was defined using the seven
American Heart Association’s CVH metrics attained at ideal levels: poor (0–2), intermediate (3–4), and ideal CVH (5–7). Multivariable-adjusted Cox proportional hazards regression models, Kaplan–Meier plots, and Irwin’s restricted mean were used to examine the association and sex-specific differences between parental CVH and offspring’s CVD-free survival. In a total of 71,974 person-years of follow-up among the offspring, 718 incident CVD events occurred. The overall CVD incidence rate was 10 per 1000 person-years [95% confidence interval (CI) 9.3–10.7]. Offspring of mothers with ideal CVH lived 9 more years free of CVD than offspring of mothers with poor CVH (P < 0.001). Maternal poor CVH was associated with twice as high hazard of early onset of CVD compared with maternal ideal CVH (adjusted Hazard Ratio 2.09, 95% CI 1.50–2.92). No statistically significant association was observed in the hazards of CVD-free survival by paternal CVH categories.

Conclusions
We found that offspring of parents with ideal CVH had a greater CVD-free survival. Maternal CVH was a more robust predictor of offspring’s CVD-free survival than paternal CVH, underscoring the need for clinical and policy interventions that involve mothers to break the intergenerational cycle of CVD-related morbidity and mortality.

4. Sex-based approach for the clinical impact of polycythaemia on cardiovascular outcomes in the general population

Aims
Although the adverse cardiovascular effect of anaemia has been well described, the effect of polycythaemia on the cardiovascular outcomes of the general population remain unclear. The primary objective is to identify the association between polycythaemia and major adverse cardiovascular events (MACE), and the secondary objective is to identify the specific haemoglobin concentration more associated with an increased risk for MACE.

Methods and results
This was a retrospective cohort study, 451,107 subjects were enrolled who underwent national health examinations from the Korean National Sample Cohort. We estimated the risk of MACE, a composite of cardiovascular mortality, incident myocardial
infarction (MI), and stroke according to haemoglobin-based four categories. During 3.8-year of follow-up, polycythaemia group showed higher MACE [hazard ratio (HR) = 1.27 (1.13–1.44) and HR = 1.76 (1.08–2.88); in men and women, respectively], incident MI [HR = 1.37 (1.05–1.79) and HR = 3.46 (1.06–14.00)], and incident ischaemic stroke [HR = 1.27 (1.10–1.46) and HR = 1.72 (1.02–2.91)] than normal haemoglobin group (P < 0.001 in all cases). In the normal haemoglobin and polycythaemia groups, a 1 g/dL increase in haemoglobin level was associated with increased risks of MACE [HR = 1.04 (1.01–1.07) and HR = 1.05 (1.01–1.10) in men and women, each P < 0.05]. To investigate the specific haemoglobin concentration related to greater MACE incidence, we analysed the sensitivity/specificity of different haemoglobin levels: ≥16.5 g/dL in men and ≥15.0 g/dL in women showed the highest Youden’s index (sensitivity + specificity − 1), with c-indices of 0.82 (0.81–0.83) and 0.83 (0.82–0.84), respectively.

**Conclusion**

Even in the Korean general population, polycythaemia was significantly associated with higher rates of MACE, incident MI, and incident ischaemic stroke. Especially, subjects with haemoglobin levels ≥15.0 g/dL in women and ≥16.5 g/dL among men were associated with increased risks of MACE.

5. As US Abortion Protections Hang in the Balance, Cardiologists Brace for Impact

Leaked Supreme Court documents that may foretell the loss of federal abortion protections in the United States have been making headlines around the globe—they also have profound implications for cardiovascular care.

If the draft opinion from the US Supreme Court, obtained by Politico earlier this month, becomes final, the issue will likely be kicked back to the individual states to legislate as they see fit. The resulting patchwork of abortion laws will drastically affect the options available and influence discussions between patients and doctors about pregnancy termination, which is considered or advised for women with a range of cardiac conditions that place them at extremely high risk for poor outcomes if they proceed. Termination is also considered for a fetus found to have a severe congenital heart defect, for instance, that is incompatible with life.
Mary Norine Walsh, MD (Ascension St. Vincent Heart Center, Indianapolis, IN), a past president of the American College of Cardiology, oversees some patients with high-risk cardiovascular conditions as they navigate decisions around pregnancy. The best example of this type of situation from the world of heart failure is a woman who has had a previous pregnancy affected by peripartum cardiomyopathy. If guideline-directed medical therapy doesn’t lead to recovery of LV systolic function, the risk of severe morbidity or death during a subsequent pregnancy remains very high, and in this situation, contraception is recommended to prevent another pregnancy, Walsh told TCTMD. Then, if LV systolic function eventually recovers, risks are discussed again.

If this type of patient finds herself pregnant unintentionally, Walsh said, “it’s a tough conversation to have about the choice between pregnancy termination and continuing with a very high-risk pregnancy, but it’s one that we have not infrequently.”

Layer in the complex care required for congenital heart disease and severe pulmonary hypertension in which cardiologists are often involved and those heartbreaking discussions become even more sensitive. Loss of protections for abortion access complicate those even further, said Jennifer Haythe, MD, director of the cardio-obstetrics program at NewYork-Presbyterian/Columbia University Irving Medical Center, New York, NY, stressing that “my belief is that women should have the right to choose for any reason.”

**Abortion as Essential Care**

Abortion access has long been a controversial and polarizing issue in the United States. Federal protections have existed since January 1973, under the precedent set by the US Supreme Court’s Roe v. Wade decision. But now, a draft opinion on the Dobbs v. Jackson Women’s Health case indicates those protections are at risk, as elaborated on in an issue brief from the Kaiser Family Foundation.

**I think that the idea that more women will die is a real one, and for reasons that are totally unnecessary.** Jennifer Haythe

If the decision is finalized and Roe v. Wade is overturned, that will likely return the issue to the states. As noted by the Guttmacher Institute, 23 states currently have laws, either
already on the books or ready to be triggered by the overturning of Roe v. Wade, that could be used to severely restrict abortion within their borders, whereas another 16 states and the District of Columbia have laws protecting the right to have an abortion.

The fraught political landscape doesn’t jibe with the medical stance on abortion, with the American College of Obstetricians and Gynecologists (ACOG) calling it “essential healthcare.”

A lot of work has been done in recent years on the link between maternal mortality and CVD, and there are guidelines on the management of pregnant women with CVD, said Afshan Hameed, MD (University of California, Irvine), a member of the task force behind ACOG’s guidance on pregnancy and heart disease. “In literally every single guideline or instruction for care of such women, there are certain conditions where a recommendation is to not continue with the pregnancy because the risk to the mother is so high,” she said.

Indeed, both a 2017 scientific statement on the management of pregnancy in patients with complex congenital heart disease from the American Heart Association (AHA) and ACOG’s guidance refer to a modified World Health Organization (WHO) classification scheme to identify women who carry such a higher risk of mortality or morbidity that pregnancy is not advised (WHO class IV). This category includes women with pulmonary arterial hypertension; severe systemic ventricular dysfunction (LVEF < 30% or NYHA class III or IV heart failure); previous peripartum cardiomyopathy with any residual impairment of LV function; severe mitral stenosis or severe symptomatic aortic stenosis; Marfan syndrome and aortic dilation > 45 mm; aortic dilation > 50 mm in bicuspid aortic valve aortopathy; and native severe coarctation.

“These patients should be counseled to avoid pregnancy. If pregnancy is confirmed in a woman in WHO class IV, then termination is advised,” the AHA document states.

For patients with these types of conditions, Hameed explained, pregnancy can cause changes in the body that push them into dangerous territory, even if they’ve been well controlled with medications and modifications to physical activity. “What happens with pregnancy is that the heart, the cardiovascular system, is significantly stressed,” she said, likening it to putting somebody on a treadmill for the duration of the pregnancy.
In addition, another AHA scientific statement on the diagnosis and treatment of fetal cardiac disease advises discussing termination of pregnancy as an option after a diagnosis of prenatal congenital heart disease is made, with the conversation covering potential restrictions based on timing or legal limits. And it puts decision-making squarely in the hands of the patients, noting: “Counselors should refrain from imposing personal bias into the discussion and should strive for the goal of providing families with all of the tools and support necessary to come to a decision that is best suited for them.”

**Intruding on the Patient-Physician Discussion**

The physicians interviewed by TCTMD said the information provided to women with underlying cardiac conditions about the risks associated with pregnancy won’t necessarily change if federal abortion protections are lost, but there could be an impact on what happens after a woman has made her decision.

“From a cardiovascular practice standpoint, the responsibility that we have is to ensure that pregnant patients know what their risks are [so they can] make their own decisions, and what I would say is this will just complicate that decision for women in many states,” Walsh said, adding that “that secondary decision is truly a woman’s own to make.”

**In literally every single guideline or instruction . . . there are certain conditions where a recommendation is to not continue with the pregnancy because the risk to the mother is so high.** Afshan Hameed

Speaking on behalf of the Society for Maternal-Fetal Medicine, Cara Heuser, MD (University of Utah, Salt Lake City), an expert on high-risk pregnancies, said, “Right now, with there being broad protection for pregnancy termination, we’re able to really counsel people as to when they get pregnant with some of these high-risk conditions what their maternal risks might be, what their fetal risks might be, and then have a nuanced conversation and explore all options with them. And they get to make a decision after they weigh all of those risks and benefits. But once abortion legislation goes back to the state level, it will very much depend on how individual state laws are written.”
And those state laws are not compatible with the complexities of how decisions around pregnancy termination are made, Heuser said. Some of the existing laws restricting abortion in certain states contain exceptions, using phrases like “medical emergency” or “life-threatening situation.” However, those are vague terms, Heuser said. “The laws presume a certainty that is at odds with clinical medicine.”

For example, how great does the risk of death for the mother have to be to justify abortion under that type of law—5%, 10%, 40%, or 100%? Heuser asked. “It takes that nuance out of those discussions that should be between a patient and their physician and whoever their support people are to allow them to explore that nuance and make their own decision.”

If federal protection of abortion access is lost, Hameed said, it’ll be even more important to have discussions about sexuality, pregnancy, and prevention of pregnancy, because if a woman becomes pregnant unexpectedly and would otherwise have been recommended for termination, “your hands are going to be tied.”

Walsh said, “Will we be in situations where physicians are actually providing information about surrounding states and their options to women? That may happen.”

She and others noted that even if a neighboring state is an option for obtaining an abortion, not all women have the means to travel that far for medical care. Some may choose to stay put and explore unsafe, illegal options that can put them at risk for infection, hemorrhage, future infertility, and death, Haythe noted.

There are concerns, also, Haythe said, about how far some state laws will go in trying to prevent female residents from getting an abortion—whether citizens will be able to sue individuals in other states that help facilitate an abortion, whether medications used to induce abortion will be able to be shipped across state lines, and whether women will be charged with murder for terminating a pregnancy. If Roe v. Wade is ultimately overturned, “it’s going to create a lot of confusion,” Haythe said.

An Uptick in Maternal Mortality?
Aside from potential legal complications, the loss of broad protections for abortion is likely to have a real impact on maternal mortality rates, which have been increasing in the United States over the past several decades and are much higher compared with other developed nations. Of note, numbers from the US Centers for Disease Control and Prevention show that the leading cause of pregnancy-related death in the country is cardiovascular disease.

“I think that we are absolutely going to see a rise in the already relatively high maternal morbidity and mortality rates in the United States,” Heuser predicted if Roe v. Wade falls. “We will have patients who have underlying medical conditions that are borderline safe for pregnancy but that we can’t unequivocally say are medical emergencies who may not be able to seek care in another state.”

**Forcing women to carry to term pregnancies that are not viable is just appalling and abhorrent.** Mary Norine Walsh

Heuser noted that there are already worse maternal outcomes among patients from racial/ethnic minority groups, “and it’s possible that that health disparity could worsen.”

Walsh agreed with Heuser’s assessment. If women are more likely to carry to term pregnancies that are considered high risk, “this may well influence our state-by-state maternal cardiovascular mortality rates that we’ve been keeping such a close eye on,” she said. “The concern would be that states with limitations would see an increase in maternal mortality.”

There may be psychological effects as well. When a fetus is nonviable for any reason, women are offered dilation and curettage to terminate the pregnancy, but depending on what a particular state’s restrictions look like, women may be forced to carry these pregnancies to term, Walsh said. “Forcing women to carry to term pregnancies that are not viable is just appalling and abhorrent.”

And the implications of a loss of abortion access stretch beyond pregnancy itself, as parents may be forced into a situation where they’re providing care for a child born with
severe disabilities stemming from a congenital heart defect, for example, but aren’t prepared to do so, Haythe said.

“For people whose contraception fails or who make a mistake or for whatever reason get pregnant and it’s not something they want or it’s not safe, it’s going to be much more challenging, and so it’s going to endanger the lives of those women for sure,” Haythe said. “And it’s going to result in a lot of emotional trauma for women who have to carry fetuses that have congenital heart disease and don’t have the resources to support those children. And it’s not clear to me that the government has any plan to put into action any laws to protect those children and the parents having them to support them through that.”

In the context of this discussion, Heuser stressed the importance of providing clear information to patients about pregnancy and its associated risks, noting that sometimes when physicians tell women they “can’t get pregnant,” they mean they “shouldn’t get pregnant,” a miscommunication that could result in ill-advised pregnancies.

“How we communicate with patients and how we talk about their reproductive lives is also really important even if you’re not a doctor that always does reproductive care,” Heuser said. “I think that reproductive life planning should be part of all medical care and especially care of underlying serious medical conditions, and that’s probably something that we could ask our cardiology colleagues to help us with and refer people who have serious underlying medical conditions to us sooner, so that we can have these conversations with them ahead of time.”

Ultimately, if Roe v. Wade is overturned, Haythe predicted, “I think it will unfortunately not necessarily change the number of abortions that happen. It will just make them more unsafe. It will isolate poor, socioeconomically disadvantaged, and minority populations specifically. And so I think it’s going to be a terrible thing for the country. I think that the idea that more women will die is a real one, and for reasons that are totally unnecessary.”

Treatment of non-severe chronic hypertension in pregnancy
The standard of care before a 2022 RCT has been to only treat severely elevated blood pressures for chronic hypertension in pregnancy.¹ Some have been concerned that the treatment of non-severely elevated blood pressures could lead to hypoperfusion of the placenta, which puts the fetus at risk for fetal growth restriction (FGR) or stillbirth.

A 2018 Cochrane Review found that the treatment of non-severe chronic hypertension decreased the risk of developing severe hypertension (RR, 0.49; 95% CI, 0.40–0.60; 20 RCTs; 2558 women); however, it did not decrease the risk of preeclampsia (aRR, 0.92; 95% CI, 0.75–1.14; 23 RCTs; 2851 women), fetal or neonatal death (aRR 0.72; 95% CI, 0.50–1.04; 29 RCTs; 2265 women), or preterm birth at <37 weeks of gestation (aRR, 0.96; 95% CI, 0.83–1.12; 15 RCTs; 2141 women).¹ In addition to no significant increase in fetal or neonatal death, there was no increase in the delivery of small for gestational age (SGA) babies (aRR 0.96; 95% CI, 0.78–1.18; 21 RCTs; 2686 babies).²

**2022 RCT supporting treatment of mild chronic hypertension in pregnancy³**

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

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

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

Summary

A 2022 RCT demonstrates improved outcomes with a good safety profile when pharmacologic treatment is used for non-severe chronic hypertension in pregnancy. This counters a 2018 Cochrane Review which included over 20 RCTs and over 2000 women for each of the outcomes evaluated and ACOG’s previous clinical guidance. Due to the quality of the 2022 RCT, The ACOG now recommends treating non-severe hypertension in pregnancy with a blood pressure goal of <140/90 mm Hg.

6. Association of SARS-CoV-2 Infection During Pregnancy With Maternal and Perinatal Outcomes

IMPORTANCE

There are limited high-quality, population-level data about the effect of SARS-CoV-2 infection on pregnancy using contemporaneous comparator cohorts.

OBJECTIVES

To describe maternal and perinatal outcomes associated with SARS-CoV-2 infection in pregnancy and to assess variables associated with severe disease in the pregnant population.

DESIGN, SETTING, AND PARTICIPANTS
CANCOVID-Preg is an observational surveillance program for SARS-CoV-2-affected pregnancies in Canada. This analysis presents exploratory, population-level data from 6 Canadian provinces for the period of March 1, 2020, to October 31, 2021. A total of 6012 pregnant persons with a positive SARS-CoV-2 polymerase chain reaction test result at any time in pregnancy (primarily due to symptomatic presentation) were included and compared with 2 contemporaneous groups including age-matched female individuals with SARS-CoV-2 and unaffected pregnant persons from the pandemic time period.

EXPOSURE

SARS-CoV-2 infection during pregnancy. Incident infections in pregnancy were reported to CANCOVID-Preg by participating provinces/territories.

MAIN OUTCOMES AND MEASURES

Maternal and perinatal outcomes associated with SARS-CoV-2 infection as well as risk factors for severe disease (ie, disease requiring hospitalization, admission to an intensive care unit/critical care unit, and/or oxygen therapy).

RESULTS

Among 6012 pregnant individuals with SARS-CoV-2 in Canada (median age, 31 [IQR, 28-35] years), the greatest proportion of cases were diagnosed at 28 to 37 weeks' gestation (35.7%). Non-White individuals were disproportionately represented. Being pregnant was associated with a significantly increased risk of SARS-CoV-2-related hospitalization compared with SARS-CoV-2 cases among all women aged 20 to 49 years in the general population of Canada (7.75% vs 2.93%; relative risk, 2.65 [95% CI, 2.41-2.88]) as well as an increased risk of intensive care unit/critical care unit admission (2.01% vs 0.37%; relative risk, 5.46 [95% CI, 4.50-6.53]). Increasing age, preexisting hypertension, and greater gestational age at diagnosis were significantly associated with worse maternal outcomes. The risk of preterm birth was significantly elevated among SARS-CoV-2-affected pregnancies (11.05% vs 6.76%; relative risk, 1.63 [95% CI, 1.52-1.76]), even in cases of milder disease not requiring hospitalization, compared with unaffected pregnancies during the same time period.

CONCLUSIONS AND RELEVANCE
In this exploratory surveillance study conducted in Canada from March 2020 to October 2021, SARS-CoV-2 infection during pregnancy was significantly associated with increased risk of adverse maternal outcomes and preterm birth.

7. **Dietary total antioxidant capacity is associated in Polish men and women with the prevalence of cardiovascular diseases and their risk factors**

**Background**
Cardiovascular diseases (CVD) are the main cause of mortality in the Polish population. Improper diet and lifestyle are among the risk factors for CVD. Previous studies have suggested that dietary total antioxidant capacity (DTAC) is a measure of diet quality.

**Purpose**
The aim of the study was to investigate the relationship between diet quality measured by DTAC and the prevalence of CVD and CVD risk factors in the representative sample of men and women in Poland.

**Methods**
The study evaluated participants (2594 men, 3136 women) of the population-based cross-sectional Polish National Multicenter Health Examination Survey (WOBASZ II), which was conducted in 2013-2014. Dietary data were collected using a single 24-hour dietary recall method. The database on dietary antioxidants was compiled from published and own experimental data. DTAC was calculated taking into account the antioxidant capacity of individual foods and the amount of food intake. Men and women were divided into quartiles of CVD prevalence and its risk factors (diabetes; hypertension; BMI≥25; central obesity, CO; low level of leisure-time physical activity, LTPA) according to DTAC. Statistical calculations were performed using the Statistical Analysis System (SAS), version 9.4 (SAS Institute Inc., Cary, NC, USA).

**Results**
DTAC in men ranged from 0.47 to 95.69 mmol/day, while in women it was 0.32-191.82 mmol/day. In men, the prevalence of CVD was 23.7% in the lowest DTAC quartile (Q1) versus 14.9% in the highest quartile (Q4) (p<0.0001), while in women it was 23.4% (Q1) and 17.4% (Q4), respectively (p<0.0002). In women, but not in men, DTAC was inversely
associated with diabetes (p<0.0002), hypertension (p<0.0001), CO (p<0.02) and low LTPA (p<0.0006).

**Conclusions**

DTAC is inversely related to the prevalence of CVD in both genders. In women, but not in men, there is a significant inverse association of DTAC with CVD risk factors such as metabolic diseases, central obesity and lower physical activity. In order to reduce the risk of CVD, Polish men and women should be advised to improve the quality of their diet by increasing the dietary intake of antioxidants.

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**8. Distribution of CAC by Age-Sex-Race Among Patients Aged 30-45 Years**

**Study Questions:**

Use of the coronary artery calcium score (CAC) to assist in risk stratification of asymptomatic men and women is effective but limited to ages 45-84 years. What is the probability of CAC >0, and what are the age-sex-race percentiles for US adults aged 30-45 years?

**Methods:**

The authors harmonized three datasets—CARDIA (Coronary Artery Risk Development in Young Adults), the CAC Consortium (multicenter cohort physician referred for risk stratification), and the WRC (Walter Reed Cohort; armed forces)—to study CAC in 19,725 asymptomatic Black and White individuals aged 30-45 years without known atherosclerotic cardiovascular disease (ASCVD). After weighting each cohort equally, the probability of CAC >0 and age-sex-race percentiles of CAC distributions were estimated using nonparametric techniques.

**Results:**

Mean age was 41 (3.3) years, 27% were women, 17% were Black, and 45% were in the WRC. CV risk factors included hyperlipidemia in 41%, hypertension in 17%, smokers 10%, and diabetes 3%. The prevalence of CAC >0 was 26% among White males, 16% among Black males, 10% among White females, and 7% among Black females. CAC >0 automatically placed all females at the >90th percentile. In White males aged 36 years,
15% had a CAC >0. An observed CAC of 8 is at the 91st percentile for individuals of the same age, sex, and race who are free of clinical ASCVD.

Conclusions:

In a large cohort of US adults aged 30-45 years without symptomatic ASCVD, the probability of CAC >0 varied by age, sex, and race. Estimated percentiles may help interpretation of CAC scores among young adults relative to their age-sex-race matched peers and can henceforth be included in CAC score reporting.

Perspective:

The CAC score has become an important tool for helping both the patient and physician decision regarding treatment and intensity. Among the convincing data has been the utility of CAC = 0 and that CAC score provides better discrimination than age for incident ASCVD over long-term follow-up. The three study cohorts were convenient but very much unrelated, and despite the ‘equal weighting to one third each’ may have introduced bias and thus not be readily generalizable; in particular, the 40% prevalence of hyperlipidemia, which is much higher than the US population of 30-45 years. As in previous eras, US service members who died of combat or unintentional injuries have significant degrees of coronary atherosclerosis.

Comparing coronary atherosclerosis prevalence among those with no CV risk factors (11%), there was a significantly greater prevalence of those with dyslipidemia (50%), hypertension (43.6%), obesity (22%), and smoking (14%). Of the risk factors, each was associated with a significant age-adjusted prevalence ratio, except for smoking (Webber BJ, et al., JAMA 2012;308:2577-83). A recent review concluded that identifying high-risk features that predict early-onset ASCVD among young adults (ages 20-39 years) can assist providers and their patients in modifying ASCVD risk factors earlier (Stone NJ, et al., J Am Coll Cardiol 2022;79:819-36).
9. Worse Survival for Women After Ruptured AAA Repair

nearly 20-year analysis sheds new light on sex disparities following abdominal aortic aneurysm (AAA) rupture and subsequent repair.

The study found that women were older than men, had aneurysms that ruptured at smaller diameters than the traditional threshold, and had worse in-hospital and long-term survival.

“Future studies would be useful to assess the reasons for these disparities and whether opportunities exist to improve AAA care for women, including more-frequent screening, better rupture-risk stratification, and strategies to reduce gender bias and discrimination,” write Ben Li, MD (Toronto General Hospital, Canada), and colleagues in the paper, published online May 10, 2022, in JAMA Network Open.

Overall, AAA is more prevalent in men than women and screening guidelines, while varied, primarily target older men. The US Preventive Services Task Force does not recommend that women undergo AAA screening. However, the Society for Vascular Surgery recommends a one-time screening for anyone aged 65 to 75 with a smoking history.

An expert who was not involved in the study agreed that the data deserve a “deep dive” to understand potential gaps in care that occur for women with AAA, or who are at risk for it, and how they can be addressed.

“We’re still learning about the impact that sex differences have on aneurysm treatment, screening, and survival,” Grayson H. Wheatley, MD (Wheatley Surgical, Nashville, TN), told TCTMD. “This article certainly moves that analysis forward, but it also highlights that there’s a lot more that we still have to learn.”

VQI Findings

For the study, Li and colleagues examined data on 1,160 women and 4,148 men from the Society for Vascular Surgery’s Vascular Quality Initiative (VQI) database who underwent AAA repair between 2003 and 2019. Compared with men, the female patients were older, more than twice as likely to be underweight, and more likely to be Black.
Additionally, more women than men presented with chronic kidney disease (CKD) and chronic obstructive pulmonary disease. While the number of endovascular and surgical procedures was similar between women and men, there were physiologic differences seen in women, including smaller aortic neck diameters and aortic neck angle > 60 degrees.

In-hospital mortality was 34.4% in women and 26.6% in men \( (P = 0.002) \). The disproportionately higher death rate in women versus men remained in a subanalysis of patients aged 70 years or older \( (P = 0.008) \), and regardless of whether repair type was endovascular \( (P = 0.03) \) or open \( (P = 0.01) \). While in-hospital mortality decreased for both women and men over the course of the study, it remained higher for women at every individual time period.

Women’s 8-year survival rates were lower at 36.7% versus 49.5% for men \( (P = 0.02) \). Again, the difference persisted regardless of age or type of AAA repair. An additional analysis of differences in all-cause mortality rates beyond the perioperative period found that women continued to have lower survival at 8 years when only patients who survived beyond 30 days after the repair were included \( (P = 0.03) \).

In multivariable Cox regression analysis, older age, CKD, preoperative dialysis, congestive heart failure, previous carotid revascularization, unconscious at presentation, cardiac arrest, and open repair all were associated with 8-year all-cause mortality. The study authors say the latter finding deserves further research, since it is among the first to suggest a possible long-term mortality benefit of endovascular over open AAA repair.

**Sex Bias and Ongoing Concerns**

According to Li and colleagues, ruptured aneurysms were about 1 cm smaller in women than men. Along with the older age at presentation and prior studies documenting the underdiagnosis and undertreatment of AAA in women, they say these data suggest that “unconscious and conscious sex bias and discrimination prevalent in medicine and society may extend to AAA management.”
To TCTMD, Wheatley said accumulating data, including the finding of smaller size at rupture, point to a possible need to reevaluate screening recommendations for women, recognizing that these recommendations have traditionally been based on data from men.

“I think this presents a double opportunity not only to screen women earlier and more broadly, but to look seriously at the data to understand whether different treatment guidelines for elective aneurysm repair are warranted,” he said. “Women may have a different pathophysiology, . . . and different screening and treatment guidelines therefore may apply.”

Wheatley cautioned that without looking at aorta-related mortality, however, it is hard to draw strong conclusions about the mortality differences or to rule out selection bias as a possible factor.

10. Acute MI Workup in Emergency Departments Varies by Sex and Race

Young women with chest pain who present to the emergency department (ED) are seen less quickly and are less likely to be admitted to hospital than men who present with similar symptoms, according to results of a new study.

Investigators observed racial differences in treatment, too, with people of color, mostly non-Hispanic Black individuals, waiting longer for a physician evaluation than white patients.

Senior investigator Harmony Reynolds, MD (NYU Langone Health, New York, NY), said that previous studies, including the VIRGO study, have also demonstrated differences in care between men and women. For example, chest pain in women is less likely to be recognized as a symptom of acute MI compared with men.

“That’s consistent with my clinical experience,” Reynolds told TCTMD. “I take care of young women with myocardial infarction, and I have heard many stories of the initial
encounter where the healthcare provider did recognize immediately that this might be a heart attack."

It’s known that women are less likely to undergo cardiac testing when presenting with chest pain and less likely to undergo coronary revascularization or be prescribed guideline-recommended medical therapy once acute MI is diagnosed, she said. “It runs the gamut from the initial presentation with chest pain all the way to sex-based differences in the ISCHEMIA trial where everyone was known to have obstructive coronary artery disease and women received less intensive care,” said Reynolds.

The same trends hold true for people of color, with Black adults having poorer outcomes than white adults with acute MI and also being less likely to receive an ECG or troponin testing when presenting with chest pain. Black patients are also less likely to be undergo coronary revascularization compared with white adults.

The difference in the evaluation and treatment of men and women, as well as across race/ethnic lines, is an old refrain, according to C. Noel Bairey Merz, MD (Cedars-Sinai Medical Center, Los Angeles). Roughly 30 years ago, in fact, psychology experiments using case vignettes revealed cardiologists would provide different care depending on the sex and race of the patient.

“It’s kind of old news, unfortunately,” Merz told TCTMD. “It’s not a hypothetical anymore.”

**More Than 4,000 ED Visits**

For the new analysis, which was published May 4, 2022, in the Journal of the American Heart Association, investigators evaluated 4,152 ED visits for adults aged 18 to 55 years presenting with chest pain between 2014 and 2018 who were included in the National Hospital Ambulatory Medical Care Survey. Women accounted for 56.8% of the chest-pain ED visits and people of color—89% who identified as non-Hispanic Black—comprised 34.9% of the study population. The mean age of the female was 37.6 years, and for male patients it was 38.8 years.
I have heard many stories of the initial encounter where the healthcare provider did recognize immediately that this might be a heart attack. Harmony Reynolds

Overall, women presenting to the ED with chest pain were less likely to be triaged as requiring immediate/emergent care compared with men (19.1% vs 23.3%; P = 0.001), waited longer to be seen by a healthcare provider (48.1 vs 37.2 minutes; P < 0.001), and were less likely to be given an ECG (74.2% vs 78.8%; P = 0.024). During the ED visit, women were less likely to be treated with antiplatelet agents than men and were less likely to receive antianginal medications.

After multivariate adjustment, which accounted for a range of clinical features, there was no difference in the use of ECG or emergent triage, but men were significantly more likely to be seen than women at any time point and were more likely to be admitted to hospital or the observation unit.

Women of color waited longer than white women for their initial evaluation (57.8 vs 42.7 minutes; P = 0.006), as did men of color compared with white men (44.0 vs 34.0 minutes; P =0.006). Women of color were less likely to be prescribed antiplatelets, while men of color were less likely to receive antianginal medications, although they were more likely to be given an NSAID.

In multivariable regression analysis, people of color were significantly less likely to be seen by a provider at any time point compared with white patients, but there were no other differences observed, including differences in triage, use of ECG, or cardiac troponin testing between people of color and white adults.

‘Needle in the Haystack’

Overall, acute MI was diagnosed in 1.4% of all adults in the ED and in 6.5% of those admitted to hospital. The database contained too few details to evaluate differences by race and sex in the diagnosis of acute MI, say investigators.

“We recognize that most people who come to the emergency room don’t have a myocardial infarction,” said Reynolds. “That makes it a particular challenge for ED providers—they’re essentially trying to find the needle in the haystack.”
Maybe our awareness campaigns are actually working. Other than that, it’s an example of how things change but they don’t change enough. C. Noel Bairey Merz

Merz, who is the scientific advisor to the Women’s Heart Alliance (WHA) and wasn’t involved in this study, said there are snippets of good news from the new analysis. For example, men and women with chest pain were equally likely to arrive at hospital by ambulance, a contrast with previous data showing that women weren’t calling emergency medical services. Additionally, of the ED visits, women were in the majority (n = 2,319).

“It’s possibly progress,” said Merz. “Maybe our awareness campaigns are actually working. Other than that, it’s an example of how things change but they don’t change enough.”

Merz pointed out that the new analysis doesn’t include data on the outcomes of these ED patients, including those with acute MI. While women did wait longer to be seen by physicians, as did people of color, that increase might be clinically justified. “It’s an ambulatory data set and, as [the researchers] acknowledge up front, they don’t have the outcomes,” said Merz. “Without the outcomes, it might have been appropriate care. It’s what physicians do all the time—they triage and strategize.”

That said, however, the delay in treating Black males compared with white males doesn’t appear appropriate. “Black men are at a higher risk than white men for heart attacks,” said Merz. “That would lead you believe that at least some of this care wasn’t appropriately triaged.”

**Comes Down to Education**

In terms of why care differed for women and people of color, Reynolds stressed that the study can’t get at the underlying reasons, underscoring that ED physicians and staff have a challenging job in identifying patients with acute MI. Reynolds speculated these younger patients, particularly women, might not be the typical demographic for MI, which may lead them to be overlooked. Studies have also shown that women may articulate their symptoms differently than men, which may make it difficult for providers to recognize patterns.
“It might not be a textbook description of chest pain, particularly in women, which might make it difficult to identify rapidly that this might be a concerning chest-pain story,” she said. There might even be a perception that women are at lower risk for MI than men, even though women have worse outcomes after MI diagnosis than men.”

Regarding the racial differences, Reynolds said it might be the result of resource availability, although that is just a hypothesis.

To TCTMD, Merz emphasized the importance of education. The WHA, which is continuing to raise awareness about the risks of cardiovascular disease in young women, has initiated work with the Association of American Medical Colleges as part of their equity, diversity, and inclusion initiatives to develop physician leaders aware of these risks.

An additional limitation of the analysis is its lack of information on the sex of the providers, said Merz. In 2019, researchers published data in PNAS on patient-physician gender concordance and higher risks of mortality among female MI patients. That study showed men and women had similar mortality risks when treated by female ED physicians, but that women had a higher risk of death when treated by male doctors. It also showed that the presence of female physicians on staff influenced the outcomes of patients treated by male ED doctors.

“It really is about education,” said Merz. There are similar trends suggesting there are benefits of patient/physician race/ethnicity concordance, she said.

11. History of Female Infertility Tied to Risk for Heart Failure

HealthDay News — Infertility is significantly associated with later incident heart failure, according to a study published in the April 26 issue of the Journal of the American College of Cardiology.
Emily S. Lau, M.D., from Massachusetts General Hospital in Boston, and colleagues examined the development of heart failure and heart failure subtypes in women with and without a history of infertility. The analysis included 38,528 postmenopausal women.

The researchers found that 14% of participants reported a history of infertility. Incident heart failure was detected in 2,373 women during a median follow-up of 15 years, including 807 with heart failure with reduced ejection fraction and 1,133 with heart failure with preserved ejection fraction. There was an association between infertility and future risk for overall heart failure (hazard ratio, 1.16; 95% confidence interval, 1.04 to 1.30; P = 0.006), independent of traditional cardiovascular risk factors. Infertility was associated with future risk for heart failure with preserved ejection fraction (hazard ratio, 1.27; 95% confidence interval, 1.09 to 1.48; P = 0.002) but not heart failure with reduced ejection fraction (hazard ratio, 0.97; 95% confidence interval, 0.80 to 1.18).

12. **Sex-Specific Added Value of Cardiac Biomarkers for 10-Year Cardiovascular Risk Prediction**

**Background**

Sex-specific risk predictive performance of N-terminal pro B-type natriuretic peptide (NT-proBNP), high sensitivity cardiac troponin T (hs-cTnT) and creatine kinase myocardial band (CK-MB), for individual and composite cardiovascular outcomes remains unclear.

**Objectives**

To evaluate the sex-specific predictive value of NT-proBNP, hs-cTnT and CK-MB for 10-year risk prediction of coronary heart disease (CHD), stroke, heart failure (HF) and composite outcomes.

**Methods**

5430 individuals (mean age 68.6 years, 59.9% women) from the Rotterdam Study, with biomarker measurements between 1997-2001, were included. Participants were followed until 2015. We fitted ‘basic’ models using traditional cardiovascular risk factors. Improvements in c-statistics and net reclassification improvement (NRI) for events and non-events were calculated.
Results
During a median follow-up of 14 years, 747 (13.8%), 563 (10.4%), and 664 (12.2%) participants were diagnosed with CHD, stroke, and HF respectively. NT-proBNP improved the discriminative performance of the ‘basic’ model for all endpoints (c-statistic improvements ranging from 0.007 to 0.050) and provided significant event-net reclassification improvement (NRI) for HF (14.3% in women; 10.7% in men) and for stroke in men (9.3%). The addition of hs-cTnT increased c-statistic for CHD in women by 0.029 (95%CI, 0.011-0.047) and for HF in men by 0.034 (95%CI, 0.014-0.053), and provided significant event-NRI for CHD (10.3%) and HF (7.8%) in women, and for stroke (8.4%) in men. The added predictive value of CK-MB was limited.

Conclusion
NT-proBNP and hs-cTnT provided added predictive value for various cardiovascular outcomes above traditional risk factors. Sex differences were observed in the predictive performance of these biomarkers.

13. Findings May Explain Link Between Obesity and Endometrial Cancer

New research suggests that lifelong excess body weight is associated with an increased risk of developing endometrial cancer, and testosterone, insulin, and sex hormone binding globulin may play a causal role in this relationship. The research was published in BMC Medicine.¹

“Links between obesity and womb cancer are well known, but this is one of the largest studies which has looked into exactly why that is on a molecular level,” lead study author Emma Hazelwood, a PhD student at the University of Bristol in the United Kingdom, said in a statement.²

Hazelwood and colleagues conducted a meta-analysis of 17 genome-wide association studies, which included data from 12,906 patients with endometrial cancer and 108,979 control individuals.

The researchers identified single-nucleotide polymorphisms associated with 14 molecular risk factors for endometrial cancer. The team then used Mendelian
randomization (MR) to evaluate the mediating roles of these risk factors in the relationship between body mass index (BMI) and endometrial cancer.

BMI was strongly associated with the risk of developing endometrial cancer, with an odds ratio (OR) of 1.88 per 4.7 kg/m² increase in BMI (95% CI, 1.69-2.09; \( P = 3.87 \times 10^{-31} \)).

Other factors significantly associated with an increased risk of endometrial cancer were total testosterone, bioavailable testosterone, fasting insulin, sex hormone binding globulin, and total serum cholesterol.

Three of these factors appeared to play a mediating role in the relationship between BMI and endometrial cancer risk. These factors were fasting insulin (19% total effect mediated; 95% CI, 5%-34%; \( P = 9.17 \times 10^{-3} \)), bioavailable testosterone (15% mediated; 95% CI, 10%-20%; \( P = 1.43 \times 10^{-8} \)), and sex hormone binding globulin (7% mediated; 95% CI, 1%-12%; \( P = 1.81 \times 10^{-2} \)).

“Our comprehensive MR analysis provides insight into potential causal mechanisms linking BMI with endometrial cancer risk and suggests targeting of insulinemic and hormonal traits as a potential strategy for the prevention of endometrial cancer,” the researchers concluded.

14. Gender Bias Common in Online Reviews of Physicians

Online consumer reviews in 2022 are playing a bigger role in almost every consumer industry from travel to technology. Medicine is no exception. Physicians’ practices are being increasingly impacted by online comments, both good and bad. In a recent study, investigators at Harrisburg University of Science and Technology in Harrisburg, Pennsylvania, revealed gender bias in online reviews.

While bias may come in various forms, patients’ biases and perceptions have been understudied and may impact adherence to treatment, leading to unequal outcomes, according to the investigators. Online reviews of doctors are considered a naturalistic
way to study gender bias. Their findings, published in Psychology of Language and Communication, suggest that both patients and physicians may need to increase their awareness of how their biases affect how they give and receive vital health information.

“There can be severe implications of gender bias on the overall patient outcome if patients allow stereotypes and biases to color their interaction with their physicians, potentially leading to an incomplete or improper course of treatment,” investigators Sonam Gupta, a doctoral candidate, and Kayla Jordan, PhD, an assistant professor of social analytics, wrote. “On the other hand, if doctors project gender bias towards their patients or allow their stereotypes to impact their interactions with patients, it can impact the overall patient care negatively.”

Advertisement

The investigators analyzed data from 2 different online patient review databases: RateMDs and ZocDoc. They used psychological text analysis to determine how patients reviewed male and female doctors and examined the informality, socio-emotional content, and gendered-ness in the text of the reviews.

In an interview, Gupta said, “Knowing that patients go to their doctors with preconceived notions based on the gender of the doctor and then judge them is mind-boggling. Such notions and biases can be an obstacle for the doctors to do their jobs. “We were surprised that female doctors were reviewed more on their interpersonal skills and not much on their technical competence, as well as how the reviews explicitly mentioned gender of the women surgeons and physicians.”

“Patient reviews should be carefully considered to determine which criticisms are true points for improvement, like spending more time talking with patients or explaining instructions in more understandable ways, and which reviews may be unreasonable or biased, like personal appearance,” Dr Jordan said.

“Online reviews provide physicians an opportunity to improve the social aspects of their craft, which could influence patient decisions when and where to seek care,” said Andrew M. Placona, of Virginia Commonwealth University in Richmond. “Unless something displaces them, I would say online reviews are likely here to stay in some form, such as Facebook, Healthgrades, etc. Whether they can be utilized to improve
processes and outcomes will probably depend on the extent to which platforms get better at asking questions that could help healthcare providers to provide better care,” Placona said.

Patient online reviews can contain valuable information for gaining better insights into quality of care and the patient-doctor relationship, said Sophia C. Kamran, MD, an assistant professor of radiation oncology at Massachusetts General Hospital and Harvard Medical School in Boston, Massachusetts. Physicians can use patient feedback to learn about aspects of care they might not be aware of, she said.

It can be difficult to get honest feedback from patients. Patients might not want to tell doctors face-to-face what matters to them most, but would be willing to do so anonymously, she said.

On the one hand, Dr Kamran pointed out, patients may post online reviews containing biases that are out of physicians’ control, including about gender, appearance, race, and ethnicity. Unless online reviews are curated to remove those that clearly are biased in this way, they are not very helpful, she said.

On the other hand, thoughtful reviews can help a physician understand what works for patients and what does not. In some ways, the reviews can help improve physicians’ bedside manner, and this could translate improved patient adherence to treatment. “Physician reviews that are truly helpful may lead to decreased morbidity or mortality,” Dr Kamran said. “For example, if a review leads to a physician spending more time explaining details with a patient or talking with a patient in a more understandable manner, this may translate to improved patient compliance with treatment or recommendations, improved patient-doctor trust, and potentially decreased morbidity/mortality. This needs to be studied in greater detail.”

If online reviews contain frequent unhelpful or biased criticisms, physicians may not be able to tease out legitimate criticisms on which physicians could reflect in an effort to make improvements, she noted. Although online reviews may provide key information about whether the staff is courteous, they are not a reliable indicator of the overall quality of care in a medical practice, she said.
15. Pregnancy and Progression of Cardiomyopathy in Women With LMNA Genotype Positivity

BACKGROUND

We aimed to assess the association between number of pregnancies and long-term progression of cardiac dysfunction, arrhythmias, and event-free survival in women with pathogenic or likely pathogenic variants of gene encoding for Lamin A/C proteins (LMNA+).

METHODS AND RESULTS

We retrospectively included consecutive women with LMNA+ and recorded pregnancy data. We collected echocardiographic data, occurrence of atrial fibrillation, atrioventricular block, sustained ventricular arrhythmias, and implantation of cardiac electronic devices (implantable cardioverter defibrillator/cardiac resynchronization therapy defibrillator). We analyzed retrospectively complications during pregnancy and the peripartum period. We included 89 women with LMNA+ (28% probands, age 41±16 years), of which 60 had experienced pregnancy. Follow-up time was 5 [interquartile range, 3-9] years. We analyzed 452 repeated echocardiographic examinations. Number of pregnancies was not associated with increased long-term risk of atrial fibrillation, atrioventricular block, sustained ventricular arrhythmias, or implantable cardioverter defibrillator/cardiac resynchronization therapy defibrillator implantation. Women with previous pregnancy and nulliparous women had a similar annual deterioration of left ventricular ejection fraction (-0.5/year versus -0.3/year, P=0.37) and similar increase of left ventricular end-diastolic diameter (0.1/year versus 0.2/year, P=0.09). Number of pregnancies did not decrease survival free from death, left ventricular assist device, or need for cardiac transplantation. Arrhythmias occurred during 9% of pregnancies. No increase in maternal and fetal complications was observed.

CONCLUSIONS

In our cohort of women with LMNA+, pregnancy did not seem associated with long-term adverse disease progression or event-free survival. Likewise, women with LMNA+ generally well-tolerated pregnancy, with a small proportion of patients experiencing arrhythmias.
16. Sex Disparities in Re-Employment Among Stroke Patients With Large-Vessel Occlusion After Mechanical Thrombectomy

BACKGROUND

Strokes in the working-age population represent a relevant share of ischemic strokes and re-employment is a major factor for well-being in these patients. Income differences by sex have been suspected a barrier for women in returning to paid work following ischemic stroke. We aim to identify predictors of (not) returning to paid work in patients with large vessel occlusion treated with mechanical thrombectomy (MT) to identify potential areas of targeted vocational rehabilitation.

METHODS

From 6635 patients enrolled in the German Stroke Registry Endovascular Treatment between 2015 and 2019, data of 606 patients of the working population who survived large vessel occlusion at least 90 days past MT were compared based on employment status at day 90 follow-up. Univariate analysis, multiple logistic regression and analyses of area under the curve were performed to identify predictors of re-employment.

RESULTS

We report 35.6% of patients being re-employed 3 months following MT (median age 54.0 years; 36.1% of men, 34.5% of women [P=0.722]). We identified independent negative predictors against re-employment being female sex (odds ratio [OR], 0.427 [95% CI, 0.229-0.794]; P=0.007), higher National Institutes of Health Stroke Scale (NIHSS) score 24 hours after MT (OR, 0.775 [95% CI, 0.705-0.852]; P<0.001), large vessel occlusion due to large-artery atherosclerosis (OR, 0.558 [95% CI, 0.312-0.997]; P=0.049) and longer hospital stay (OR, 0.930 [95% CI, 0.868-0.998]; P=0.043). Positive predictors favoring re-employment were excellent functional outcome (modified Rankin Scale score of 0-1) at 90 day follow-up (OR, 11.335 [95% CI, 4.864-26.415]; P<0.001) and combined treatment with intravenous thrombolysis (OR, 1.904 [95% CI, 1.046-3.466]; P=0.035). Multiple regression modeling increased predictive power of re-employment status significantly over prediction by best single functional outcome parameter (National
Institutes of Health Stroke Scale 24 hours after MT ≤5; \( R^2: 0.582 \) versus 0.432; area under the receiver operating characteristic curve: 0.887 versus 0.835, \( P<0.001 \).

CONCLUSIONS

There is more to re-employment after MT than functional outcome alone. In particular, attention should be paid to possible systemic barriers deterring women from resuming paid work.

17. **Sex-related differences in treatment and outcome of chronic limb-threatening ischaemia: a real-world cohort**

**Aims**

The prevalence of chronic limb-threatening ischaemia (CLTI) is increasing and available data often derive from cohorts with various selection criteria. In the present study, we included CLTI patients and studied sex-related differences in their risk profile, vascular procedures, and long-term outcome.

**Methods and results**

We analysed 199,953 unselected patients of the largest public health insurance in Germany (AOK: Local healthcare funds), hospitalized between 2010 and 2017 for a main diagnosis of CLTI. A baseline period of 2 years before index hospitalization to assess comorbidities and previous procedures, and a follow-up period until 2018 were included. Female CLTI patients were older (median 81.4 vs. 73.8 years in males; \( P<0.001 \)) and more often diagnosed with hypertension, atrial fibrillation, chronic heart failure, and chronic kidney disease. Male patients suffered more frequently from diabetes mellitus, dyslipidaemia, smoking, cerebrovascular disease, and chronic coronary syndrome (all \( P<0.001 \)). Within hospitalized CLTI patients, females represent the minority (43% vs. 57%; \( P<0.001 \)) and during index hospitalization, women underwent less frequently diagnostic angiographies (67 vs. 70%) and revascularization procedures (61 vs. 65%; both \( P<0.001 \)). Moreover, women received less frequently guideline-recommended drugs like statins (35 vs. 43%) and antithrombotic therapy (48 vs. 53%; both \( P<0.001 \)) at baseline. Interestingly, after including age and comorbidities in a Cox regression analysis, female sex was associated with increased overall-survival.
(OS) [hazard ratio (HR) 0.95; 95% confidence interval (CI) 0.94–0.96] and amputation-free survival (AFS) (HR 0.84; 95% CI 0.83–0.85; both P < 0.001).

**Conclusion**

Female patients with CLTI were older, underwent less often vascular procedures, and received less frequently guideline-recommended medication. Nevertheless, female sex was independently associated with better OS and AFS during follow-up.

18. **Sex equality or sex equity: what are we looking for in treating limb-threatening ischaemia?**

![Sex Equality or Sex Equity: what are we looking for?]

19. **Women, People of Color Wait Longer to See ED Doctor for Chest Pain**

Among young adults with chest pain (CP) presenting to the emergency department, women and people of color wait longer to be seen by physicians, according to a study published online May 4 in the Journal of the American Heart Association.
Darcy Banco, M.D., M.P.H., from New York University Langone Hospital in New York City, and colleagues examined sex and racial differences in evaluation of CP among young adults (age 18 to 55 years) presenting to the emergency department. Data were included for 4,152 records, representing 29,730,145 visits.

The researchers found that compared with men, women were less likely to be triaged as emergent, to undergo electrocardiography, or to be admitted to the hospital or observation unit, but they had similar ordering of cardiac biomarkers. Men were seen more quickly (hazard ratio, 1.15) and were more likely to be admitted (adjusted odds ratio, 1.40) after multivariable adjustment. In adjusted analyses, people of color waited longer than White adults for physician evaluation (hazard ratio, 0.82), but there were no differences observed in hospital admission, triage level, electrocardiography, or cardiac biomarker testing according to race. Overall, 1.4 percent of adults in the emergency department and 6.5 percent of admitted adults were diagnosed with acute myocardial infarction.

"Whether or not the differences in chest pain evaluation directly translate into differences in outcomes, they represent a difference in the care individuals receive based on their race or sex, and that is important for us to know," Banco said in a statement.

20. **Can pregnancy hypercholesterolaemia cause myocardial infarction in young adults?**

Human pregnancy is characterized by upraised lipid metabolism to meet the lipid demands for foetal growth and development, besides other modifications that are also necessary and are commonly assumed to be a natural phenomenon. Cholesterol the best-known lipid is vital for normal foetal cell membranes development (formation and maintaining integrity (fluidity and passive permeability)) and membrane-associated signalling cascades and is a precursor to many foetal hormones. Foetal cholesterol demands are covered from foetal de novo synthesis and from maternal circulation (supplies >20% to the foetal cholesterol pool).\(^1\) Therefore, serum total cholesterol (TC) levels raise as pregnancy progresses,\(^2\) causing maternal hypercholesterolaemia in pregnancy (MCP). Of note, that in MCP the maximum serum TC levels are unlikely to exceed 250 mg/dL at any time during normal pregnancy. Although earlier studies have
found women with TC levels of 280–290 mg/dL at the end of pregnancy and named it maternal supraphysiological hypercholesterolaemia. Desoye et al. reported for TC levels to raise from 167 mg/dL (4.3 mmol/L) pre-/early pregnancy to 286 mg/dL (7.3 mmol/L) near term. This can be particularly seen in pregnant women with heterozygous familial hypercholesterolaemia (heFH). Although the relative increases of TC do not differ between the heFH and referral women, the absolute increases are much higher in heFH women, since their TC levels are usually >355 mg/dL (9.1 mmol/L) at pre-/early-pregnancy and raised up to 452 mg/dL (11.6 mmol/L) near term. Studies concerning heFH and cardiovascular disease (CVD) in offspring reported increased risk for CVD. Thus, the presence of MCP (besides maternal and foetal development issues) raises the question of potential risk of atherosclerosis to the offspring. In this issue of Eur J Prev Cardiol, in the study linking to a cohort of patients from seven hospitals in the Regione Campania, the association of offspring’s acute myocardial infarction (AMI) and MCP has been evaluated. In the MCP cohort, the TC above 240 mg/dL was reported in 72.3%. In the AMI cohort, even though the sample size was small, MCP was correlated with AMI’s severity (number of vessels, left ventricular ejection fraction, creatine kinase/creatine kinase-myocardial band, and survival time). Furthermore, in the multivariate analysis of patients stratified by AMI severity, MCP predicted AMI severity independently of age, gender, body mass index (BMI), and coronary heart disease risk factors. Although this is a retrospective study, the data likely reflect that MCP is associated with adult BMI, atherosclerosis-related risk, and severity of AMI. MCP is thought to be clinically not significant and, therefore, TC levels are not routinely tested during pregnancy; consequently, there are not many clinical studies. The first suggestion that MCP may lead to adult CVD came from the Fate of Early Lesions in Children study. It was found that maternal hypercholesterolaemia increased considerably the number of early fatty streaks, suggesting that the onset of early fatty streaks detected in children and young adults may be formed much earlier than was believed. Direct experimental data for the causal role of MCP and atherosclerosis in offspring came from transgenic [low density lipoprotein (LDL) receptor deficient (LDLR−/−)] pregnant mice and indicated that utero foetus exposure to hypercholesterolaemia may, for long time, modify the gene expression in the aorta, implicated in early life origins of CVD. The epigenome phenomenon is very active throughout the pregnancy and early postnatal periods. The Framingham Heart Study
found that mother’s dyslipidaemia before pregnancy is associated with dyslipidaemia in offspring during adulthood in addition to CVD and genetic risk factors (Table 1).9 The maternal epigenetic (DNA methylation, histone acetylation) can lead to constant modifications in the function and structure of genes involved in LDL metabolism and cholesterol transport between mother and foetus across the placenta and interfere, not always beneficially, with utero foetal programming.10 In contrast, lowering MCP with cholestyramine (recommended by guidelines as safe treatment of hypercholesterolaemia in pregnancy) or with antioxidant or vitamin E reduced the offspring atherosclerosis.11 Also, a treatment of pregnant mice with MCP with statin (cornerstone drug in management dyslipidemias) during pregnancy (not recommended in humans) reduced atherogenic programming in mice.12 There are still few questions arise such as: (1) Do we deal with new risk factor for adults aged 40–50 years, who were exposed to MCP? (2) Do we have enough evidence? (3) Should they be advice for routine lipid analysis and lifestyle modifications?

**Table 1**

Maternal hypercholesterolaemia in pregnancy and its potential effect on foetus and on young adults’ health

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<th>Mother</th>
<th>Modifications</th>
<th>Foetus</th>
<th>Offspring</th>
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<td>Obesity, dyslipidemia, metabolic syndrome, pre-eclampsia, gestational DM, polycystic ovary syndrome, assisted</td>
<td>• Endothelial dysfunction, Differential expression of LDL receptors • Upregulation of lipid metabolism • Changes in gene expression</td>
<td>• High cholesterol • Atherogenic programming • Lesion formation</td>
<td>• Obesity • Dyslipidaemia • MetS • AMI/CHD • Unknown disease</td>
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<tr>
<td>Mother</td>
<td>Modifications</td>
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The pre-pregnancy mother’s metabolic conditions can further increase levels of total cholesterol observed in MCP. These lipid changes can increase levels of foetal cholesterol and interfere with foetal programming and because of that foetus unfavourable cardiometabolic conditions that are likely to provoke cardiovascular diseases in adult life. AMI, acute myocardial infarction; CHD, coronary heart disease; DM, diabetes mellitus; LDL, low density lipoprotein; MCP, maternal hypercholesterolaemia in pregnancy; MetS, metabolic syndrome.

Therefore, the evaluation of lipid profile routinely in pregnant women may be of great help for managing their offspring lately in their life. Although there are no specific recommendations for such group, until more clinical studies and data will be presented, they can be advised to undergo lifestyle modifications and routine lipid profiling at specific intervals to initiate statin therapies, if required. On the end of the day, the answers to question if the MCP is responsible for myocardial infarction in young adults are still open. It is more likely that foetus exposed to MCP and environmental CVD risk factors lately in their life are more prone to develop CVD in younger age compared with foetus not exposed to MCP.
21. Maternal hypercholesterolaemia during pregnancy affects severity of myocardial infarction in young adults

Aims
Elevated maternal cholesterol during pregnancy (MCP) enhances atherogenesis in childhood, but its possible impact on acute myocardial infarction (AMI) in adults is unknown.

Methods and results
We retrospectively evaluated 310 patients who were admitted to hospital and whose MCP data were retrievable. Eighty-nine AMI patients with typical chest pain, transmural infarction Q-waves, elevated creatinine kinase, and 221 controls hospitalized for other reasons were identified. The AMI cohort was classified by MI severity (severe = involving three arteries, left ventricle ejection fraction ≤35, CK-peak >1200 mg/dL, or CK-MB >200 mg/dL). The association of MCP with AMI severity was tested by linear and multiple regression analysis that included conventional cardiovascular risk factors, gender, age, and treatment. Associations of MCP with body mass index (BMI) in patients were assessed by linear correlation. In the AMI cohort, MCP correlated with four measures of AMI severity: number of vessels (β = 0.382, P = 0.001), ejection fraction (β = −0.315, P = 0.003), CK (β = 0.260, P = 0.014), and CK-MB (β = 0.334, P = 0.001), as well as survival time (β = −0.252, P = 0.031). In multivariate analysis of patients stratified by AMI severity, MCP predicted AMI severity independently of age, gender, BMI, and CHD risk factors (odds ratio = 1.382, 95% confidence interval 1.046–1.825; P = 0.023). Survival was affected mainly by AMI severity.

Conclusions
Maternal cholesterol during pregnancy is associated with adult BMI, atherosclerosis-related risk, and severity of AMI.

22. Striking Sex Differences in Acute MI Risk Factors in Younger Adults
Young adults who have an acute MI before age 55 have many risk factors in common no matter their sex, but a new analysis of data from the VIRGO study shows that psychosocial risk factors carry special weight among women.

Yuan Lu, ScD (Yale New Haven Hospital, CT), the study’s lead author, pointed out to TCTMD that while young women account for a just a sliver of the overall population with cardiovascular disease, this translates to 40,000 MI-related hospitalizations in the United States each year. Yet awareness about the risk is lacking among both patients and clinicians, she noted.

For women, acute MIs carry a high mortality burden after they occur, making the case for better primary prevention, Lu stressed. “Understanding the risk factors would be very important to inform the target of the intervention.”

The sex differences they found were striking, she said, and they point to the need for targeted prevention strategies. Mental health and income level, for instance, mattered more for women than they did for men. High cholesterol, on the other hand, was more instrumental for men, possibly because many of the female patients in the below-55 age bracket are premenopausal, she suggested.

Their study, published online in JAMA Network Open, is one of the most comprehensive on this topic to date, said Lu.

**Income, Mental Health, and More**

VIRGO, a multicenter registry, was designed to study the effects of sex on outcome in young MI patients. Lu and colleagues performed a matched case-control study comparing 2,264 patients in VIRGO who had an acute MI before age 55 with 2,264 population-based controls from the National Health and Nutrition Examination Survey. Among them, 68.9% were women and the median age was 48 years.

The researchers identified seven risk factors that, taken together, accounted for around 85% of the total MI risk in men and women. However, there were differences in the strengths of the associations. Notably, low household income was significantly linked to acute MI in women but not in men.
## Risk Factors for Acute MI in Young Adults

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diabetes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>3.59</td>
<td>2.72-4.74</td>
</tr>
<tr>
<td>Men</td>
<td>1.76</td>
<td>1.19-2.60</td>
</tr>
<tr>
<td><strong>Depression</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>3.09</td>
<td>2.37-4.04</td>
</tr>
<tr>
<td>Men</td>
<td>1.77</td>
<td>1.15-2.73</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>2.87</td>
<td>2.31-3.57</td>
</tr>
<tr>
<td>Men</td>
<td>2.19</td>
<td>1.65-2.90</td>
</tr>
<tr>
<td><strong>Current Smoking</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>3.28</td>
<td>2.65-4.07</td>
</tr>
<tr>
<td>Men</td>
<td>3.05</td>
<td>2.28-4.10</td>
</tr>
<tr>
<td><strong>Family History of Premature MI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>1.48</td>
<td>1.17-1.88</td>
</tr>
<tr>
<td>Men</td>
<td>2.42</td>
<td>1.71-3.41</td>
</tr>
<tr>
<td><strong>Low Household Income</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>1.79</td>
<td>1.28-2.50</td>
</tr>
<tr>
<td>Men</td>
<td>1.35</td>
<td>0.82-2.23</td>
</tr>
<tr>
<td><strong>Hypercholesterolemia</strong></td>
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</tbody>
</table>
Diabetes, depression, hypertension, and current smoking contributed more toward the total risk of acute MI in women than in men, whereas hypercholesterolemia and family history of premature MI were larger contributors for men.

Additionally, traditional CV risk factors were both more prevalent and more strongly associated with type 1 MI as compared with type 2 MI.

How to apply this information in practice remains a difficult question, said Lu. “I think the first step [is] to raise awareness in clinicians and patients about heart attack in young women.” It’s important, she continued, to ask younger women about things like depression, stress, and income. “Once we identify those young women that could potentially be at high risk of developing heart disease, then we can connect them, say, to social workers or community health workers.” Patients with lower incomes might benefit from coupons to use at the pharmacy or discounts on parking and transportation, for instance.

Unlike lab values, “social factors are not commonly documented in electronic health records,” she observed, adding, “Because they are not documented, the next time you come to see the doctor, the doctor cannot view your social history, and they cannot weigh in and make clinical decisions to address that.” It can be hard to standardize these details in a way that fits on a typical “dashboard,” she acknowledged, and to fit the screening process into a 15-minute appointment.

In terms of research, Yu said that the next step is an analysis focused on female VIRGO study participants, exploring how things like their menopausal and reproductive history relate to MI risk in comparison to population-based controls. Another area ripe for further study is a risk prediction tool tailored to young patients.
23. Catheter-Based Interventions for the Management of Valvular Heart Disease During Pregnancy

Pregnancy is associated with a significant increase in hemodynamic burden. These changes can lead to maternal morbidity and mortality as well as unfavorable fetal outcomes in patients with valvular heart disease and limited cardiac reserve. Mechanical interventions may be needed for the management of severe hemodynamic deterioration not responding to medical therapy. Catheter-based percutaneous interventions can provide an alternative therapy to surgery during pregnancy. The purpose of this article is to review indications, potential advantages, and limitations of catheter-based interventions for the management of women with valvular heart disease in pregnancy.

**Highlights**

- Invasive interventions may be needed for the management of severe hemodynamic deterioration in pregnant women with valvular disease.

- Cardiac surgery during pregnancy is associated with high fetal loss and prosthetic valves with risk of complications and early deterioration.

- Catheter-based percutaneous interventions can provide an alternative therapy to surgery during pregnancy.

- Discussions regarding decision-making and performance of catheter-based interventions should be undertaken by an experienced multidisciplinary cardio-obstetrics valve team.

24. Time-Restricted Eating May Lower CVD Risk For Older Breast Cancer Survivors

Older breast cancer survivors with cardiometabolic risk factors who restrict food intake to eight hours during the weekday, followed by 16 hours of fasting, may lower their risk
of cardiovascular disease after a few weeks, according to a research letter published May 17 in JACC: CardioOncology.

Amy A. Kirkham, PhD, et al., looked at 22 individuals with a body mass index who were classified as overweight or obese (>25kg/m²), had completed cardiotoxic treatment (anthracyclines, a commonly used chemotherapy drug) within the past one to six years, and were an average age of 66 years. For eight weeks, participants were allowed to eat freely between 12-8 p.m. on weekdays and at any time on the weekends. Outside of those hours, participants were asked to consume only water, black coffee or black tea.

Using the Canadian Cardiovascular Society scoring system to calculate the 10-year Framingham Risk Score, results showed that cardiovascular risk decreased from 10.9% (IQR: 8.6% to 13.7%) to 8.6% (IQR: 7.6% to 10.0%), a −15% relative change (P=0.037) at the end of the trial period.

In addition, the modifiable Framingham components (i.e., total cholesterol, high-density lipoprotein, and systolic blood pressure) did not significantly change overall, indicating interindividual differences in each of these measures and the risk reduction etiology.

“Randomized controlled trials are needed to confirm these findings and to evaluate the health benefits, including potential health care cost savings and safety of longer-term [time-restricted eating],” the authors conclude.

“This rigorously designed, well-executed single-arm feasibility study generates important hypotheses and questions about the role of time restricted eating relevant to cancer survivors,” commented Bonnie Ky, MD, MSCE, FACC, editor-in-chief of JACC: CardioOncology. “For example, what is the basis of the inter-individual variation of the response to time restricted eating in the Framingham Risk Score, and will this help identify patients who are most likely to benefit from this strategy? How does diet quality affect these findings? We look forward to seeing research using practical lifestyle interventions continue to evolve and advance to improve the lives of our patients and survivors.”
25. In-Hospital STEMI Death Rates Soar for COVID-19 Infected Patients Regardless of Sex: NACMI Registry Analysis

Around 30% of ST-segment elevation myocardial infarction (STEMI) patients with COVID-19 in the North American COVID-19 STEMI (NACMI) registry died in the hospital, a rate which – while elevated from pre-pandemic times – remained similar between men and women.

This was despite differing clinical characteristics and management strategies between the sexes.

The findings from the new NACMI analysis were reported Thursday in a late breaking session at the Society for Cardiovascular Angiography & Interventions (SCAI) 2022 Scientific Sessions in Atlanta, by lead author Odayme Quesada, MD, MHS, from the Christ Hospital Women’s Heart Center, Cincinnati. A manuscript reporting the results was simultaneously published online in the Journal of the Society for Cardiovascular & Interventions.

NACMI was established as a collaboration of SCAI, the American College of Cardiology and the Canadian Association of Interventional Cardiology in 2020 to define baseline characteristics, management strategies and outcomes data for COVID-19 patients presenting with STEMI.

Prior to the pandemic, it was well-established that women with STEMI suffered worse outcomes than men, said Quesada.

Although worse COVID-19 prognoses in the general population have been associated with men, sex differences in STEMI patients infected with COVID-19 had not been reported, she noted.

The current study, therefore, set out to describe the differences between men and women in the prospective multicenter (64 sites in the U.S. and Canada) NACMI registry of hospitalized patients with STEMI and concomitant COVID-19 infection in terms of clinical characteristics, management strategies and outcomes.
Among the 585 enrolled from March 1, 2020, to Dec. 31 2021, 154 (26.3%) were women.

Compared to men, the women were significantly older (65% vs. 37% aged ≥66 years), Quesada noted. According to the study abstract, women also had higher rates of diabetes and stroke/transient ischemic attack, and were more often on a statin medication at presentation.

Men were more likely to present with chest pain (59% vs. 47%), whereas women presented more often with dyspnea.

Meanwhile, women were more likely to have STEMI without an identified culprit lesion compared to men (33% vs. 18%; P < 0.01).

Treatment differed between men and women, with use of primary and rescue percutaneous coronary intervention (PCI) used significantly more in men (76% vs. 61%), whereas medical therapy use was higher in women.

In-hospital mortality was 33% for women and 27% for men (P = 0.217), and there were no significant sex differences for in-hospital stroke, re-infarction or “composite primary endpoint.”

Regardless of differences between the sexes, the mortality figures in the study represent a significant increased risk of in-hospital mortality for STEMI patients who are also infected with COVID-19, Quesada pointed out. Pre-COVID-19 STEMI mortality was below 5%, the press released notes, citing figures published in the Journal of the American College of Cardiology.

“The significant increase in mortality among both men and women in this study highlights the need for continued research to better understand the long-term effects of COVID-19 on cardiovascular health,” Quesada said.

“Our study also points to the lack of research and clear guidance on how to treat STEMI patients without an identified culprit lesion, many of which are women.”
The researchers added in the abstract that evaluation of specific underlying etiologies are underway to better define the full impact of COVID-19 on STEMI outcomes, and better understand the observed sex differences.

“We hope additional analysis of these patient characteristics will help further inform clinicians on best the treatment approach and ultimately improve patient outcomes,” Quesada concluded.

26. Call to Action for Cardiovascular Disease in Women: Epidemiology, Awareness, Access, and Delivery of Equitable Healthcare

Addressing the pervasive gaps in knowledge and care delivery to reduce sex-based disparities and achieve equity is fundamental to the American Heart Association's commitment to advancing cardiovascular health for all by 2024. This presidential advisory serves as a call to action for the American Heart Association and other stakeholders around the globe to identify and remove barriers to health care access and quality for women. A concise and current summary of existing data across the areas of risk and prevention, access and delivery of equitable care, and awareness and education provides a framework to consider knowledge gaps and research needs critical toward achieving significant progress for the health and well-being of all women.

27. Sex-specific anthropometric and blood pressure trajectories and risk of incident atrial fibrillation: the Rotterdam Study

Aims
To investigate sex-specific longitudinal trajectories of various obesity-related measures and blood pressure at the population level and further assess the impact of these trajectories on new-onset atrial fibrillation (AF).

Methods and results
Participants with ≥2 repeated assessments for various risk factors from the population-based Rotterdam Study were included. Latent class linear mixed models were fitted to
identify the potential classes. Cox proportional-hazard models were used to assess the association between risk factors’ trajectories and the risk of new-onset AF, with the most favourable trajectory as reference. Among 7367 participants (mean baseline age: 73 years, 58.8% women), after a median follow-up time of 8.9 years (interquartile range: 5.3–10.4), 769 (11.4%) participants developed new-onset AF. After adjustments for cardiovascular risk factors, persistent-increasing body mass index (BMI) trajectory carried a higher risk for AF [hazard ratio, 95% confidence interval: (1.39; 1.05–1.85) in men and (1.60; 1.19–2.15) in women], compared with the lower-and-stable BMI trajectory. Trajectories of elevated-and-stable waist circumference (WC) in women (1.53; 1.09–2.15) and elevated-and-stable hip circumference (HC) in men (1.83; 1.11–3.03) were associated with incident AF. For systolic blood pressure (SBP), the initially hypertensive trajectory carried the largest risk for AF among women (1.79; 1.21–2.65) and men (1.82; 1.13–2.95). Diastolic blood pressure trajectories were significantly associated with AF risk among women but not among men.

**Conclusion**
Longitudinal trajectories of weight, BMI, WC, HC, and SBP were associated with new-onset AF in both men and women. Diastolic blood pressure trajectories were additionally associated with AF in women. Our results highlight the importance of assessing long-term exposure to risk factors for AF prevention among men and women.


During 2017 to 2019, there was an increase in the prevalence of hypertensive disorders of pregnancy (HDP) among delivery hospitalizations, according to research published in the April 29 issue of the U.S. Centers for Disease Control and Prevention Morbidity and Mortality Weekly Report.

Nicole D. Ford, Ph.D., from the CDC in Atlanta, and colleagues calculated the annual prevalence of HDP among delivery hospitalizations and by maternal characteristics using data from the National Inpatient Sample.
The researchers found that the prevalence of HDP among delivery hospitalizations increased from 13.3 to 15.9% during 2017 to 2019. During the same period, the prevalence of pregnancy-associated hypertension increased from 10.8 to 13.0% and the prevalence of chronic hypertension increased from 2.0 to 2.3%. Among delivery hospitalizations, HDP prevalence was highest for non-Hispanic Black or African American women, non-Hispanic American Indian and Alaska Native women, and women aged 35 years or older residing in zip codes in the lowest median household income quartile or delivering in hospitals in the South or the Midwest Census regions. Overall, 31.6% of deaths that occurred during delivery hospitalization had any HDP documented.

“Severe HDP-associated maternal complications and mortality are preventable with equitable implementation of public health and clinical strategies,” the authors write. “These include efforts across the life course for preventing HDP, identifying, monitoring, and appropriately treating those with HDP with continuous and coordinated care, increasing awareness of urgent maternal warning signs, and implementing quality improvement initiatives to address severe hypertension.”

29. Menopause Tied to Proatherogenic Changes in Circulating Metabolites

Menopause is associated with proatherogenic circulating metabolome alterations, according to a study published online May 12 in the European Journal of Preventive Cardiology.

Jari E. Karppinen, from the University of Jyväskylä in Finland, and colleagues analyzed longitudinal data from 218 Finnish women, of whom 35 started menopausal hormone therapy during the study. Participants were followed for a median of 14 months. Menstrual diaries and serum hormone measurements were used to measure the menopausal transition. Targeted nuclear magnetic resonance metabolomics were used to quantify serum metabolites.

The researchers found that menopause was associated with 85 metabolite measures. Increases were seen in the concentration of apolipoprotein B, very-low-density lipoprotein triglycerides and particles, low-density lipoprotein (LDL) cholesterol and particles, high-density lipoprotein (HDL) triglycerides, glycerol, and leucine. Decreases were seen in concentrations of citrate and 3-hydroxybutyrate. Most metabolite changes
were associated with the hormonal shift of menopause; this explained 11 and 9 percent of the increase in LDL cholesterol and particle concentration, respectively. Increased medium-to-large HDL particle count and decreased small-to-medium LDL particle and glycine concentration were seen in association with menopausal hormone therapy.

"Menopause-induced hormonal shift is associated with a proatherogenic metabolomic fingerprint," the authors write. "These findings broadly agree with earlier metabolomics studies on menopause, and now connect the previous and present observations to the female sex hormone levels."

30. **Sex-based approach for the clinical impact of polycythaemia on cardiovascular outcomes in the general population**

**Aims**
Although the adverse cardiovascular effect of anaemia has been well described, the effect of polycythaemia on the cardiovascular outcomes of the general population remain unclear. The primary objective is to identify the association between polycythaemia and major adverse cardiovascular events (MACE), and the secondary objective is to identify the specific haemoglobin concentration more associated with an increased risk for MACE.

**Methods and results**
This was a retrospective cohort study, 451,107 subjects were enrolled who underwent national health examinations from the Korean National Sample Cohort. We estimated the risk of MACE, a composite of cardiovascular mortality, incident myocardial infarction (MI), and stroke according to haemoglobin-based four categories. During 3.8-year of follow-up, polycythaemia group showed higher MACE [hazard ratio (HR) = 1.27 (1.13–1.44) and HR = 1.76 (1.08–2.88); in men and women, respectively], incident MI [HR = 1.37 (1.05–1.79) and HR = 3.46 (1.06–14.00)], and incident ischaemic stroke [HR = 1.27 (1.10–1.46) and HR = 1.72 (1.02–2.91)] than normal haemoglobin group (P < 0.001 in all cases). In the normal haemoglobin and polycythaemia groups, a 1 g/dL increase in haemoglobin level was associated with increased risks of MACE [HR = 1.04 (1.01–1.07) and HR = 1.05 (1.01–1.10) in men and women, each P < 0.05]. To investigate the specific haemoglobin concentration related to greater MACE incidence, we analysed
the sensitivity/specificity of different haemoglobin levels: ≥16.5 g/dL in men and ≥15.0 g/dL in women showed the highest Youden’s index (sensitivity + specificity − 1), with c-indices of 0.82 (0.81–0.83) and 0.83 (0.82–0.84), respectively.

**Conclusion**

Even in the Korean general population, polycythaemia was significantly associated with higher rates of MACE, incident MI, and incident ischaemic stroke. Especially, subjects with haemoglobin levels ≥15.0 g/dL in women and ≥16.5 g/dL among men were associated with increased risks of MACE.

### 31. Sex and Race Differences in the Evaluation and Treatment of Young Adults Presenting to the Emergency Department With Chest Pain

**BACKGROUND**

Acute myocardial infarctions are increasingly common among young adults. We investigated sex and racial differences in the evaluation of chest pain (CP) among young adults presenting to the emergency department.

**METHODS AND RESULTS**

Emergency department visits for adults aged 18 to 55 years presenting with CP were identified in the National Hospital Ambulatory Medical Care Survey 2014 to 2018, which uses stratified sampling to produce national estimates. We evaluated associations between sex, race, and CP management before and after multivariable adjustment. We identified 4152 records representing 29 730 145 visits for CP among young adults. Women were less likely than men to be triaged as emergent (19.1% versus 23.3%, respectively, P<0.001), to undergo electrocardiography (74.2% versus 78.8%, respectively, P=0.024), or to be admitted to the hospital or observation unit (12.4% versus 17.9%, respectively, P<0.001), but ordering of cardiac biomarkers was similar. After multivariable adjustment, men were seen more quickly (hazard ratio [HR], 1.15 [95% CI, 1.05–1.26]) and were more likely to be admitted (adjusted odds ratio, 1.40 [95% CI, 1.08–1.81]; P=0.011). People of color waited longer for physician evaluation (HR, 0.82 [95% CI, 0.73–0.93]; P<0.001) than White adults after multivariable adjustment, but there were no racial differences in hospital admission, triage level, electrocardiography,
or cardiac biomarker testing. Acute myocardial infarction was diagnosed in 1.4% of adults in the emergency department and 6.5% of admitted adults.

CONCLUSIONS

Women and people of color with CP waited longer to be seen by physicians, independent of clinical features. Women were independently less likely to be admitted when presenting with CP. These differences could impact downstream treatment and outcomes.

32. Pregnant women living under negative social conditions may face higher heart disease risk

Pregnant women in the U.S. who face adverse social conditions where they live, work, learn and play are at higher risk for poor heart health, a new study suggests.

That can lead to early cardiovascular disease and death – and it can affect their children’s health, said senior study author Dr. Khurram Nasir, division chief of Cardiovascular Prevention and Wellness at Houston Methodist DeBakey Heart & Vascular Center in Texas. "We need to identify and work on the social risks that are truly impacting their cardiovascular risks."

Cardiovascular disease is driving a rise in the maternal death rate, which has been steadily rising over the past few decades. It now accounts for one-third of all pregnancy-related deaths. Recent years also have seen a rise in cardiovascular risk factors among pregnant women, including Type 2 diabetes, high blood pressure and obesity. At the same time, other poor pregnancy outcomes have been growing, such as preeclampsia, gestational diabetes, premature births and low birthweight babies.

The new study, published Tuesday in the Journal of the American Heart Association, measured risk factors for cardiovascular disease among pregnant women living under multiple adverse social conditions, including economic instability, low education levels, high psychological distress, unstable housing, food insecurity, insufficient access to
quality health care, and a lack of social support. These factors are collectively referred to as the social determinants of health.

While other studies have looked at individual factors affecting the social conditions under which pregnant women live, Nasir said this is the first to look at the cumulative impact of those conditions upon pregnant women's heart health.

"We took a more robust look at the issue than just looking at income and access to health care," said Nasir, a professor of cardiology at Houston Methodist Academic Institute. "There are many other factors that used to get ignored. But it's very hard to disentangle the individual risks, which are interconnected. We needed a more comprehensive approach in capturing them."

Nasir and his team looked at six categories of social determinants affecting the lives of 1,433 pregnant women, scoring 38 individual sociodemographic variables. Using data from the National Health Interview Survey, their cardiovascular health was rated based on the presence of risk factors such as high blood pressure, obesity, Type 2 diabetes, high cholesterol, current smoking and insufficient physical activity.

Overall, they found about one-third of the women had less than optimal heart health, no matter their sociodemographic scores. But women facing the greatest cumulative burden of negative social conditions were twice as likely to have two or more risk factors for heart disease, such as smoking, obesity and insufficient physical activity, compared to those living under much better social conditions.

"Many women in the United States enter pregnancy with suboptimal cardiovascular health," said Dr. Sadiya Khan, an assistant professor of medicine and preventive medicine at Northwestern University Feinberg School of Medicine in Chicago. "But the upstream drivers of poor cardiovascular health at the time of pregnancy are social determinants of health. Pregnancy represents a time during which we can intervene to address both clinical and social risk factors to reduce risks associated with pregnancy and beyond."

Khan, who was not involved in the new study, was part of the writing committee for last year's American Heart Association statistical update on heart disease and stroke. It was
updated to include data on heart-related pregnancy complications, recognizing the increasing threat heart disease poses to pregnant women and their children.

The risks are higher for some women.

Black women are more than twice as likely to die during or soon after pregnancy than their white counterparts and three times as likely as Hispanic women. They also are 50% more likely to give birth to a baby prematurely and nearly twice as likely to have low birthweight babies.

"If you want to prevent these outcomes, optimizing cardiovascular health in pregnant women gives us a huge window of opportunity to do so," said lead study author Dr. Garima Sharma, director of cardio-obstetrics at Johns Hopkins University School of Medicine in Baltimore.

She said women who are pregnant or thinking of becoming pregnant may be more motivated to make lifestyle changes to reduce their heart health risks if they are made aware of ways to do so. "We really need to start reaching out to them as early as possible to help break down some of these barriers. We need to focus on primordial and primary prevention in young women and focus on intervening before they have adverse pregnancy outcomes," said Sharma, an assistant professor of medicine at Johns Hopkins University.

She said the next step is to study interventions that can improve access to preventive care and to take a closer look at how social determinants may be affecting pregnant women in rural areas compared to urban places.

"Then we can have a conversation about where best to allocate public health resources."
33. B.C. journalist honoured for exposing inequity in care for women's heart disease

A medical journalist based in Kelowna, B.C., has received a media award from a major U.S. health advocacy group for exposing how the medical profession fails to take heart disease in women as seriously as it does in men.

Shelley Wood, editorial director of New York-based nonprofit Cardiovascular Research Foundation and managing editor of its medical news portal TCTMD.com, was awarded the Wenger Award for Excellence in Media from the U.S.’s National Coalition for Women with Heart Disease in Washington on Monday.

Presenting the award, University of Arizona cardiologist Martha Gulati said the profession needs Wood’s challenging questions and sharp insight into gaps in health care to promote better awareness of the condition in women.

Inadequate support for women’s heart disease has been documented on both sides of the border.

Over the past decade, medical researchers across Canada have found women often don’t receive care for heart attacks as quickly as men do, while medical professionals tend to downplay women’s risk of heart attack — which may explain the higher rate of death by heart disease among women.

- **Women need to be aware of risks of heart attack, cardiologist says**
- **Women are unnecessarily suffering and dying from heart disease, new report says**

Wood graduated from the master’s program in journalism from the University of British Columbia, where she specialized in medical journalism. She has been a medical journalist covering cardiology since 2000.
She spoke to CBC's Radio West host Sarah Penton about why she's passionate about improving care for women with heart disease.

- **Why heart attack care may be less timely for women**

The following transcript has been edited for clarity and length.

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**Where does that passion come from?**

The number of women working in cardiology hovers somewhere between 15 and 20 per cent, and yet obviously women going into medical school these days make up either 50 per cent of a class or even slightly more.

So when I first noticed there weren't that many female cardiologists, it immediately took me to the fact that female cardiologists are also the ones that are going to be perhaps advocating for their female patients better. They're going to be doing research that affects women.

That's how I became interested in this — I thought this must be an area that's being overlooked, only because the people that would champion work in women are actually not going into the field.
Wood, pictured holding her award at the ceremony in Washington, says there aren't many female cardiologists and not many female patients enrolled in cardiological research. (Submitted by Shelley Wood)

**How long ago did this begin for you?**

I noticed it right away — you go to these conferences and there are just not a lot of women presenting research. If you look at the studies themselves, there are not that many women enrolled in the clinical trials.

**How are you feeling about the advancement? Where are we now?**

At the awards ceremony, there were these women getting up to talk about their experience of not receiving medication that a man would receive, or complaining to their doctor or to a paramedic about symptoms and being told: "Oh, you're young; that's not what it is; do you really want to go to the hospital? Are you sure you want to do that?"

Women are just really not being taken seriously.

I can't help but think that if more was being done to remind physicians that women need to be included in studies and they need to be paid attention to, the National Coalition for Women with Heart Disease wouldn't need to exist.
Wood, right, pictured with Nanette Wenger, the American cardiologist who the award is named after, at the award ceremony. (Submitted by Shelley Wood)

Why are things the way they are when it comes to not including women in research?

I think a big problem is that women actually tend to develop heart disease later. When you're studying a new drug or a new device, it's often that enrolling people in clinical trials only happens up to a certain age. You don't, for example, enrol women over 65 in an experimental study. But if women don't develop cardiovascular disease in many cases until they're later, they don't get enrolled.

What are you most proud of in the work that you've done?
I'm glad that my work is touching physicians' lives in that they may be thinking a little bit differently about how they treat their patients that they see every day.

34. Gender Differences in Takotsubo Syndrome

Study Questions:

What are gender-based differences among patients presenting with takotsubo syndrome (TTS)?

Methods:

TTS patients enrolled in the international multicenter GEIST (GERman Italian Spanish Takotsubo) registry were analyzed. Comparisons between sexes were performed within the overall cohort and using an adjusted analysis with 1:1 propensity-score matching for age, comorbidities, and kind of trigger.

Results:

In total, 286 (11%) of 2,492 TTS patients were men. Male patients were younger (ages 69 ± 13 years vs. 71 ± 11 years; p = 0.005), with higher prevalence of comorbid conditions (diabetes mellitus 25% vs. 19%; p = 0.01; pulmonary diseases 21% vs. 15%; p = 0.006; malignancies 25% vs. 13%; p < 0.001, and physical trigger (55 vs. 32%; p < 0.01). Propensity-score matching yielded 207 patients from each group. After 1:1 propensity matching, male patients had higher rates of cardiogenic shock and in-hospital mortality (16% vs. 6% and 8% vs. 3%, respectively; both p < 0.05). Long-term mortality rate was 4.3% per patient-year (men 10%, women 3.8%). Survival analysis showed a higher mortality rate in men during the acute phase in both cohorts (overall: p < 0.001; matched: p = 0.001); mortality rate after 60 days was higher in men in the overall (p = 0.002) but not in the matched cohort (p = 0.541). Within the overall population, male sex remained independently associated with both in-hospital (odds ratio, 2.26; 95% confidence interval [CI], 1.16-4.40) and long-term (hazard ratio, 1.83; 95% CI, 1.32-2.52) mortality.

Conclusions:
Male TTS is featured by a distinct high-risk phenotype requiring close in-hospital monitoring and long-term follow-up.

Perspective:

This analysis from a multicenter international registry reported on sex-based differences among patients with TTS. Men represented 10% of the total cohort and had more comorbidities. Among propensity-matched patients, men had significantly higher in-hospital mortality; however, long-term mortality was similar in men and women. Although these findings are limited by retrospective design, they do bring to light the possibility that minority men with TTS might have worst outcomes compared to women. Mechanisms to explain the sex-based differences remain poorly understood and deserve further study.

35. Timing of Cardiac Surgery During Pregnancy

Study Questions:

How does the timing of cardiac surgery during pregnancy impact maternal and fetal outcomes?

Methods:

This was a meta-analysis of studies that included individual patient data related to cardiac surgery during pregnancy. Patients who underwent cesarean delivery prior to cardiac surgery were compared with patients who had cardiac surgery while still pregnant. The trimester of pregnancy, maternal and fetal mortality, and predictors of adverse outcomes were analyzed using multivariable logistic regression.

Results:

Of 179 included studies, 386 patients were identified (120 had cesarean delivery prior to cardiac surgery). The overall maternal mortality was 7.3%, without significant differences based on trimester of pregnancy nor whether cardiac surgery was performed while still pregnant versus postpartum. The overall fetal mortality was 26.5%. Fetal
mortality (6.7%) was lowest when cesarean delivery of the fetus occurred prior to the mother undergoing cardiac surgery.

Conclusions:

Cardiac surgery during pregnancy was associated with an overall maternal mortality rate of 7%, and this did not differ significantly by the trimester of pregnancy nor whether delayed until after cesarean. Due to high rates of fetal mortality (26% overall), the authors suggest considering delivery by cesarean prior to cardiac surgery if feasible.

Perspective:

Cardiac surgery is avoided during pregnancy due to maternal and fetal risks. When necessary, expert guidelines have recommended surgery be performed during the second trimester (between 13 and 28 weeks of gestation). This study showed no significant difference for fetal or maternal mortality by the trimester of pregnancy. Fetal survival was highest when cesarean delivery could occur prior to cardiac surgery; however, waiting for fetal viability may not be feasible in many situations and caution is needed. Importantly, 95% of the patients in this study had an urgent or emergent indication for surgery. Fetal mortality during pregnancy may be related to the maternal condition (e.g., severe valve disease, endocarditis, aortic dissection) rather than the effects of cardiac surgery. Delaying urgent cardiac surgery can also lead to maternal and fetal deaths that would not have been measured in this study. Multidisciplinary maternal care teams are necessary, and ideally, patients with known cardiovascular disease will undergo preconception counseling and risk assessment.

36. Long-Acting Reversible Contraception With Contraceptive Implants and Intrauterine Devices

Long-acting reversible contraception (LARC), including contraceptive implants and intrauterine devices (IUDs), is highly effective, with typical-use failure rates of less than
1 pregnancy per 100 person-years of use. Fertility returns rapidly after discontinuation of LARC.2

Contraceptive Implants
The contraceptive implant available in the US is a single radiolucent rod inserted subdermally. The implant contains 68 mg of the progestin etonogestrel and is effective for up to 5 years of use (Figure). The primary mechanism of action is ovulation suppression. Progestins also thicken cervical mucus, inhibiting sperm penetration.2

Contraceptive implants are safe for almost all users; the only absolute contraindication is recent breast cancer.3 Implant-related complications are rare and include pain, insertion site hematoma, and excessively deep insertion, which increases risks of neurovascular injury and difficult removal.2 Both amenorrhea and frequent unscheduled light bleeding are common with implant use.1

Contraceptive implant insertion may be performed any time in the menstrual cycle. Pregnancy testing is recommended if pregnancy cannot be excluded based on history. Pregnancy risk is low after implant insertion with a negative pregnancy test result, regardless of menstrual cycle day.4 Patients with recent unprotected intercourse may take oral progestin emergency contraception the day of implant insertion.4

Intrauterine Devices
One copper-containing and 4 levonorgestrel-releasing IUDs (LNG-IUDs) are available in the US. Copper IUDs and LNG-IUDs are not abortifacients.2 The copper IUD is a polyethylene T wrapped with copper wire and is effective for up to 12 years of use. It primarily prevents fertilization by inhibiting sperm migration.2 Heavier, longer, or more painful menses are associated with copper IUD use.2 LNG-IUDs are T-shaped devices that contain the progestin levonorgestrel at doses ranging from 13.5 mg to 52 mg and with varying durations of effectiveness, from 3 to 8 years of use. LNG-IUDs prevent fertilization through progestin effects on cervical mucus; they do not consistently suppress ovulation.2 Most users have light menses; some have amenorrhea, particularly users of 52-mg LNG-IUDs (Figure).
Most patients can safely use IUDs. Current pregnancy, pelvic infection, endometrial or cervical cancer, and a distorted uterine cavity are absolute contraindications. Additionally, LNG-IUDs are contraindicated in patients with recent breast cancer. IUD complications include bleeding, infection, pain, expulsion, and uterine perforation. Serious complications, including perforation, are rare (<1%).

Prophylactic antibiotics are not necessary before IUD insertion. Screening for Chlamydia trachomatis and Neisseria gonorrhoeae should be performed according to sexually transmitted infection (STI) screening guidelines. When indicated, STI testing may occur at the time of IUD insertion. The absolute risk of pelvic infection after IUD insertion is low with or without an STI. Patients with positive STI test results should receive treatment as soon as possible; IUD removal is not necessary.

IUD insertion may be performed any time during the menstrual cycle if pregnancy is reasonably excluded considering factors such as menstrual cycle day and frequency of unprotected intercourse. Pregnancy testing is recommended if pregnancy cannot be excluded based on history. Data support the use of both copper IUDs and 52-mg LNG-IUDs as highly effective emergency contraception when placed within 5 days of unprotected intercourse.

Special Considerations

**Postpartum and Breastfeeding Patients.** Offering postpartum LARC before hospital discharge can help facilitate obtaining desired contraception. Most studies of progestin-containing LARC placed immediately after delivery demonstrate no effect on lactogenesis, breast milk quantity, exclusive breastfeeding, or infant growth. Immediate postpartum IUD placement is safe and convenient; expulsion risk is higher with IUDs placed less than 10 minutes after delivery (10%-27%) than with interval placement weeks later (2%-10%). Although uterine perforation risk is higher with interval IUD placement among breastfeeding or recently postpartum patients, the absolute risk remains low (<1%). Breastfeeding is associated with lower IUD expulsion risk.

**Nulliparous and Adolescent Patients.** LARC can be safely used in nulliparous and adolescent patients. Studies show no increase in serious IUD complications among these patients, including no increased risk of pelvic inflammatory disease. Although the
success rate for IUD insertions among adolescents is more than 95%, the IUD expulsion rate may be higher in adolescents. Routine pretreatment with misoprostol is unnecessary before IUD insertion. A paracervical block with 20 mL of 1% lidocaine can be offered and reduces insertion pain in nulliparous patients.

“Missing” IUD Strings. Routine follow-up visits are not required after IUD insertion. Patients who suspect IUD expulsion should use backup contraception until IUD location is confirmed. If IUD strings are not visible during speculum examination, pelvic ultrasonography can confirm IUD location; appropriately positioned IUDs require no further follow-up. If an IUD is not visible on ultrasonography, abdominopelvic radiograph should be obtained. Lack of IUD visualization on both ultrasonography and radiographic imaging confirms that the IUD is not present. Surgical removal is necessary when an IUD is intra-abdominal (seen on radiographic imaging but not in the uterine cavity on pelvic ultrasonography).

Nonfundal IUDs. Pelvic imaging may occasionally reveal a nonfundal (low-laying or malpositioned) IUD. Clinicians should remove nonfundal IUDs if any part of the device is below the internal cervical os or if the patient has pain or abnormal bleeding. If desired, another IUD may be placed immediately. It is unknown whether IUD failure rates are higher with nonfundal IUDs or differ between nonfundal copper vs LNG-IUDs. Asymptomatic patients with nonfundal IUDs located entirely above the internal cervical os may choose to continue the IUD in the context of shared decision-making.

Pregnancy With LARC. Because LARC users rarely become pregnant, the absolute risk of ectopic pregnancy is significantly reduced vs those not using contraception, although the relative risk is increased. If a pregnancy occurs with an IUD in place, clinicians should promptly evaluate the location of the pregnancy with pelvic ultrasonography, because the pregnancy is more likely to be ectopic. In a 5-year study of 495 women who received an LNG-IUD, 9 pregnancies occurred, 6 (67%) of which were ectopic (estimated ectopic pregnancy rate through 5 y, 0.13 per 100 person-years). Patients with intrauterine pregnancies in the setting of LARC use should receive pregnancy options counseling. Clinicians should remove IUDs when strings are visible to reduce obstetrical risk or facilitate abortion care; if IUD strings are not visible, removal should not be attempted until the time of delivery or abortion. Clinicians should remove the implant
if a patient becomes pregnant with an implant in place and chooses to continue the pregnancy.

**Noncontraceptive LARC Use.** Evidence supports off-label use of the 52-mg LNG-IUD in endometrial protection for menopausal estrogen therapy and as nonsurgical treatment for endometrial hyperplasia. LARC devices may be left in place through their effective duration when menopausal status is unknown. The contraceptive implant and LNG-IUDs reduce dysmenorrhea; LNG-IUDs also manage heavy menstrual bleeding and endometriosis pain.

**Patient-Centered Counseling.** When approaching contraceptive counseling, clinicians should engage patients in shared decision-making, centering on patient goals and preferences, including any concerns about adverse effects, cost, or ability to obtain care for device removal. Patient priorities should guide contraceptive choice.

Conclusions

LARC methods represent a highly effective reversible contraception that is safe for most patients to use.

**37. Time to Re-Examine Maternity Leave in Cardiology Training: Proactive Rather Than Reactive**

With the lack of a U.S. national paid parental leave policy, directors of cardiology fellowship programs must individually address the concerns over pregnancy and parental leave for their fellows. Directors must also consider the effects of such a policy on all the trainees in relation to coverage policy and compensation for those who cover the additional time. Enough has been said about our need for a greater percentage of women cardiologists. There is no need to further debate that fact. However, it is puzzling that despite >50% of medical students being women, the cardiology specialty is fraught with recent survey reports of hostility in the workplace, concerns of long hours, exposure to radiation, and poor work-life balance that can compel trainees to choose delaying pregnancy or taking unpaid leave, which will, in turn, delay training. Therefore, it is
not surprising that only 14.9% of cardiologist specialists and 21.9% of cardiology fellows are women. To add to the complexity, these issues are occurring in the midst of a national movement to increase diversity, inclusion, and belonging, thus adding to the frustration of both candidates for fellowship and their director leaders. Such challenges are not unique to the United States; however, more international programs have legally mandated and paid maternity leave policies than the United States.

Although speculation exists about the practices of institutions toward pregnancy and parental leave, there is a need for more accurate data to inform the challenges met by programs and trainees which could guide more consistent acceptable approaches.\(^6\) That is exactly what Oliveros et al\(^7\) sought to find through an international survey published in this issue of the Journal of the American College of Cardiology. The anonymous survey was distributed using various forms of social media, thus facilitating the willingness to complete. One unique feature was that the initial question was designed to include training directors whereas subsequent questions were then tailored to the respondents. The creators of the survey were also international, which may also have encouraged participation so that an impressive 573 respondents accessed the link and 73% completed it. The majority of responders were women aged 35-44 years and Caucasian, followed by Asian/Pacific Islanders with smaller percentages of Black and Hispanic respondents. More than one-half were current or past trainees who were not pregnant during training; however, 67.1% were parents at the time of response, lending credence to the importance of the questionnaire. It is of no surprise that 29% of trainees became pregnant during the third year, perhaps because they were willing to become pregnant closer to the end of training and avoid adverse consequences. Pregnancy was less common in those who sought advanced subspecialty training, which also is not unexpected, given the time extension and professional challenges to succeed in such a highly competitive field.

Those training in the United States had the least number of months for parental leave when compared to Europe, Australia, and Latin America, although there is no clarity about whether leave was paid or not. On the director’s responses, less than one-third had received any training or guidance for their individual program on issues of pregnancy or parental leave. Of importance, when policies were present, the majority of trainees were unaware of such policies; hence, the lack of transparency and effective
communication become apparent. Other details concerning this point are shown in the Central Illustration. An area that is not as well covered relates to child care, which is lacking in most large institutions. Trainees may travel away from family and home in the pursuit of cardiology program excellence, which leaves them vulnerable to concerns about child care. Confidence in the availability of child care could enhance recruitment of excellent candidates.

Oliveros et al\textsuperscript{7} understand that it is difficult to change national policies. However, they issue a call to action for organizations including program directors to be called on to demonstrate their leadership by developing approaches for clarity, organization, and dissemination of fair and balanced decisions. Those decisions are so impactful that they can change career trajectories for the better or the worse. Nonetheless, the current status is unacceptable and must change for the benefit of all—trainees, their families, and the program directors. The problem is too important and pervasive. Programs could discuss areas of agreement and offer alternatives in areas where other factors influence policies to allow adaptability. All should strive for clarity of communication with the entire trainee group to minimize ambiguity. Additionally, the survey did not reach a significant population of Hispanic and Black trainees; therefore, they must be included in these discussions.

Oliveros et al\textsuperscript{7} offer suggestions for improvement, including the use of remote technology to maintain inclusiveness—a novel application that the providers have adapted from treatment developments during the COVID-19 pandemic. Perhaps if the women who are the subjects of, and often the unwitting party to, administrative decisions about their lives, choices, and welfare were invited to contribute to the changes, we would finally see an increase in the number of women in cardiology careers. After all, aren’t we about diversity and belonging?

38. **Worsening Obesity Linked to Risk for Heart Failure in Women With Late Menopause**

The presence of obesity modifies the association of menopausal age and incidence of heart failure (HF), with the risk for development of HF becoming significantly higher with worsening obesity. These findings were published in the Journal of the American Heart Association.
Investigators evaluated heterogeneity by obesity on the relationship between age at onset of menopause and HF incidence. A total of 5539 postmenopausal women who experienced natural or surgical menopause at the prospective Atherosclerosis Risk in Communities Study (ARIC) Visit 4 (1996 to 1998) were enrolled in the study. Following exclusion for a variety of reasons, the final sample size comprised 4441 postmenopausal women, including 3636 who had experienced natural menopause and 808 who had undergone surgical menopause. Hazard ratios (HRs) of incident HF associated with menopausal age were estimated with the use of Cox proportional hazards models.

The study participants were categorized according to age at onset of menopause:

- younger than 45 years
- 45 to 49 years
- 50 to 54 years
- 55 years or older

Among the 4441 postmenopausal women (mean age, 63.5±5.5 years), a total of 903 incident HF events were reported over a mean follow-up of 16.5±5.6 years. The incidence rates of HF were 15.6/1000 person-years, 12.1/1000 person-years, 10.3/1000 person-years, and 10.7/1000 person years in those aged younger than 45 years, 45 to 49 years, 50 to 54 years, and 55 years or older, respectively.

Results of the study show that incidence rates of HF were greatest among those women with generalized or central obesity who had also experienced menopause at younger than 45 years of age (21.3/1000 person-years and 16.3/1000 person-years, respectively). The attributable risk for generalized obesity, overweight, and central obesity, however, was greatest among those women who experienced menopause at 55 years of age or older (11.09/1000 person-years, 4.56/1000 person-years, and 7.38/1000 person-years, respectively).

The probability of HF-free survival during the follow-up period was lowest among women who experienced early menopause. A significant interaction was observed between menopausal age and body mass index (BMI) for HF incidence (P\text{interaction} = .02), thus substantiating the presentation of the current findings based on menopausal age categories. A significant interaction was also reported between menopausal age and waist circumference (WC; P\text{interaction} = .001).

The adjusted HRs for incident HF associated with an increase in BMI were 1.39 (95% CI, 1.05-1.84), 1.33 (95% CI, 1.06-1.67), 0.98 (95% CI, 0.73-1.31), and 2.02 (95% CI,
1.41-2.89) for women aged younger than 45 years, 45 to 49 years, 50 to 54 years, and 55 years or older, respectively.

The adjusted HR of incident HF for a decrease in WC was elevated only in those women with a menopausal age of 55 years or older (2.93; 95% CI, 1.85-4.65). As BMI and WC increased, the adjusted HRs of incident HF became greater in those women who had experienced onset of menopause at 55 years of age or older compared with those in the other menopausal age categories.

“Maintenance of a healthy body weight and [WC] may be protective against developing HF, particularly among women who have experienced late menopause,” the study authors noted. “These findings support a public health campaign advocating weight management in postmenopausal women, particularly among those with late menopause.”

39. Blood Pressure Management in Pregnancy: CHAP Through the Lens of SPRINT

Introduction

Rates of chronic hypertension, which is a significant cause of maternal and neonatal morbidity and mortality, have doubled among pregnant individuals aged 15 to 44 years in the US between 2007 and 2018 with persistent disparities (eg, racial and ethnic, socioeconomic, and geographic). In addition to superimposed preeclampsia, chronic hypertension is also associated with an increased risk of a small-for-gestational-age birth, medically indicated preterm birth, and perinatal death. Data recently published from the CHAP (Chronic Hypertension and Pregnancy) trial now support the safety and benefits of lower blood pressure (BP) targets in pregnancy.

The narrative of optimal BP control in pregnancy resembles the narrative about BP control from 5 years ago in nonpregnant individuals. In the latter population, concerns about adverse effects of intensive BP lowering (eg, orthostatic hypotension, syncope), particularly in older adults, as well as variable BP goals for those with different comorbidities contributed to barriers in achieving population-wide optimal BP control. The SPRINT (Systolic Blood Pressure Intervention Trial), which demonstrated a 25% reduction in cardiovascular events in middle- to older-aged adults, led to changes in US
guidelines for those individuals in 2017. However, key implementation gaps exist with continued suboptimal BP control and worsening trends in recent years with persistent disparities in nonpregnant populations. In this viewpoint, we synthesize the evidence base for BP treatment in pregnancy, the key findings of the CHAP trial in redefining US guidelines, and opportunities for translation of these findings to equitably improve outcomes in pregnant individuals and their offspring.

**Blood pressure treatment targets during pregnancy**

A wealth of epidemiologic evidence supports higher risk for adverse maternal and perinatal outcomes in the setting of chronic hypertension. However, a key challenge in managing pregnant individuals with chronic hypertension has been the uncertainty in BP treatment targets, which vary across society guidelines. This is particularly true given that there has not been good evidence to this point that treatment of mild chronic hypertension improves health outcomes and some evidence that it reduces birth weight. Thus, the American College of Obstetricians and Gynecologists guidelines had recommended treatment when systolic blood pressure (SBP) ≥160 mmHg or diastolic blood pressure (DBP) ≥110 mmHg. In contrast, the European Society of Cardiology guidelines had stricter thresholds and recommended treatment when SBP ≥140 mmHg or DBP ≥90 mmHg. In nonpregnant individuals, the American College of Cardiology and American Heart Association guidelines cutoffs for the management of hypertension have an entirely different strategy, recommending not only reclassification but also management of stage 1 hypertension from 140/90 mmHg to less than 130/80 mmHg with antihypertensives. While treatment of BP does provide therapeutic control, the lack of data on preventing adverse pregnancy outcomes and the potential for harm related to reduced uteroplacental blood flow and fetal growth restriction has led to hesitation to lower BP treatment targets in pregnancy. Thus, the treatment thresholds of chronic hypertension in pregnancy vary from what the cardiovascular community uses in the rest of the adult population.

**The CHAP trial**

In order to inform treatment of mild chronic hypertension during pregnancy, the CHAP trial (funded by the National Heart Lung and Blood Institute) was designed as an open-
labeled, randomized controlled, pragmatic clinical trial to evaluate 2 different BP treatment strategies during pregnancy for those in early pregnancy with mild chronic hypertension, regardless of whether they were already being treated with antihypertensive medications: (1) antihypertensive treatment with a target <140/90 mmHg vs (2) no treatment unless BP became severe (ie, SBP ≥ 160 mmHg or DBP ≥ 110 mmHg). The CHAP trial demonstrated that those randomized to early initiation (or continuation) of antihypertensive medications with a target BP <140/90 had a significantly lower incidence of the primary endpoint (a composite of preeclampsia with severe features, preterm birth <35 weeks, placental abruption, or fetal death), with an adjusted risk ratio of 0.82 (95% confidence interval: 0.74–0.92). There was no significant difference in the frequency of small-for-gestational-age between the 2 groups. Both the American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine rapidly responded to the study results with statements endorsing <140/90 mmHg as a treatment target for BP in pregnant individuals.

Translating CHAP Trial into equitable control of BP during pregnancy

How can we operationalize the findings from the CHAP trial to realize the intended clinical benefits and improve outcomes (Figure 1)? First, we must anticipate the inevitable gaps in implementation of revised BP guidelines and proactively design innovative care delivery models to optimize BP management in pregnant populations with chronic hypertension. An important step in achieving control is BP monitoring, which could incorporate remote monitoring and may lead to greater patient empowerment. However, the pitfalls of remote BP monitoring need to be addressed, including limited validation of measurement devices, lack of methodological standardization, and increased administrative and clinical burden without coverage by health insurers. Another potential solution can be the enhanced integration of care delivery with clinicians who care for individuals when they are not pregnant (eg, physicians [internal medicine, family practitioners or preventive cardiologists], nurses, pharmacists), which may also improve handoffs and transitions between pregnancy and after-pregnancy care. Testing new and innovative care delivery models, such as the incorporations of patient navigators and community health workers who are trained to support patients, could help reduce patient apprehension and anxiety. These care delivery models would need buy-in from all relevant stakeholders including clinicians,
other providers of care, delivery systems, and health plans in both managed care and fee-for-service contract settings and require testing for scalability and sustainability, especially in the rural and resource-limited settings.

Figure 1

**Equitable Management of Blood Pressure in Pregnancy Post the CHAP Trial**

CHAP = Chronic Hypertension and Pregnancy.

Second, prior therapeutic patterns might persist despite guideline updates. The failure to intensify and treat to target BP has been seen in hypertension control in the nonpregnant population despite the results of the SPRINT trial. In fact, using a goal <130/80, only 19.0% (95% confidence interval: 17.0-20.9%) of a representative sample of nonpregnant US adults with hypertension achieved control in 2017 to 2018; persistently lower rates were present among non-Hispanic Black adults. Contemporary studies also point to health system factors, such as differences in treatment intensification and scheduled follow-up as key drivers of racial and ethnic disparities in BP control. The example offered by post-SPRINT practice should provide the impetus to proactively focus on consensus building across a multidisciplinary group of clinicians caring for pregnant people, partnering with community organizations, improving payer
practices, and benchmarking patient quality outcomes to facilitate translation into clinical practice.

Third, fewer than 50% of the population in the CHAP trial were using low-dose aspirin, which is recommended by the United States Preventive Services Task Force for pregnant people with chronic hypertension for prevention of superimposed preeclampsia, at trial entry. Hence, the focus on BP control early in pregnancy might provide a unique opportunity also to focus on uptake of low-dose aspirin therapy. Similarly, the need for more frequent BP monitoring might serve as an impetus to expedite telemedicine and broadband services in resource-limited settings with the promotion of early maternal engagement and health education to optimize cardiovascular health throughout pregnancy.

**Pregnancy as a “window” to intergenerational health**

Pregnancy provides a unique window of opportunity, given increased contact with the healthcare system happening at a time when there is increased patient activation, to improve intergenerational cardiovascular health. Despite improved outcomes, nearly one-third of individuals with well-controlled BP in the CHAP study still experienced an adverse pregnancy outcome. In addition to identifying novel factors associated with this residual risk, actualizing the benefits of lower BP targets needs investment in rigorous dissemination and implementation research and requires recognition of the broader impact of the social determinants of health on BP control at the individual, health system, and community level. There are many lessons to be learned from the post-SPRINT experience for the post-CHAP era in pregnancy care, as we try not just to achieve better BP management but also to design high-value, integrated care aimed at patient empowerment and mitigation of maternal-child health disparities.
40. Risk Factors and Outcomes Associated With Hypertensive Disorders of Pregnancy in Maternal Congenital Heart Disease

Background

Among women with congenital heart disease (CHD), risk factors for hypertensive disorders of pregnancy (HDP) and the association of HDP with adverse outcomes are unknown.

Objectives

To identify risk factors for HDP among women with and without CHD and to assess the association of HDP with adverse events.

Methods

This retrospective cohort study included the first live birth for each woman who was pregnant in Alberta, Canada, between January 1, 2005, and December 31, 2018. The prevalence of HDP among women with and without CHD was compared. Multivariable models were used to determine the independent associations between maternal characteristics and HDP and to assess the strength of associations between HDP and CHD with adverse events.

Results

Of the total birth events, 0.6% (N = 2,575) occurred in women with CHD. HDP were more common among women with CHD (11.2% vs 8.1%, P < 0.0001). Chronic hypertension and diabetes mellitus were strongly associated with HDP among women with CHD (adjusted odds ratio [aOR]: 4.56; 95% confidence interval [CI]: 2.95-7.03; and aOR: 3.33; 95% CI: 1.48-7.49, respectively). Coarctation of the aorta was the only CHD lesion independently associated with increased risk for HDP (aOR: 1.76; 95% CI: 1.02-3.02).
HDP, as opposed to CHD, was more strongly associated with having a complicated delivery admission, preterm delivery, and small for gestational age infant.

**Conclusions**

HDP were more common among women with CHD. The strongest risk factors for HDP among women with CHD were acquired. The presence of HDP, rather than CHD, was more strongly associated with certain adverse outcomes.

41. **Intersection of Acquired and Congenital Cardiovascular Disorders in Pregnancy**

Maternal mortality has been steadily rising in the United States over the last several decades, with cardiovascular disease as the leading cause of maternal deaths. Though the majority of these deaths are related to acquired cardiovascular conditions, the number of pregnant women with congenital heart disease (CHD) continues to increase in the setting of improved pediatric surgical techniques. Unfortunately, it is known that up to 60% of patients with CHD have a significant lapse in CHD care during their transition from pediatric to adult CHD clinics, with pregnancy being one of the leading reasons for return to care. This has important implications for preconception counseling and cardiovascular prevention, which may impact pregnancy outcomes.

In the current issue of JACC: Advances, Goldstein et al evaluate risk factors and outcomes associated with hypertensive disorders of pregnancy (HDPs) in maternal congenital heart disease, through a retrospective cohort analysis of the longitudinal Alberta Pregnancy-Birth cohort. HDPs are an increasingly prevalent complication of pregnancy with serious maternal and fetal consequences. Not only are women at risk of immediate cardiovascular complications of pregnancy including heart failure (HF), stroke, and myocardial infarction when experiencing HDPs, HDP are clearly and consistently associated with an increased risk of long-term cardiovascular complications including HF, stroke, ischemic heart disease, and chronic hypertension (HTN). Thus, identifying risk factors and potentially actionable targets for improving HDP outcomes among high-risk women is essential.
In their analysis, Goldstein et al compared maternal and fetal outcomes, stratified into 4 groups based on the presence or absence of CHD and HDP: +CHD/-HDP, +CHD/+HDP, -CHD/-HDP, -CHD/+HDP. Notably, HDPs were significantly more common among women with CHD (11.2% vs 8.1%, \( P < 0.0001 \)), with both gestational HTN and preeclampsia/eclampsia occurring more commonly in the CHD group. Further, the HDP among women in the CHD group was more severe, as evidenced by early-onset preeclampsia/eclampsia (diagnosed <34 weeks gestation).

Importantly, the key drivers for the increased incidence of HDP among women with CHD were primarily acquired risk factors, namely chronic HTN and diabetes mellitus, with adjusted odds ratios of 4.56 and 3.33, respectively, among women with CHD. Both chronic HTN and diabetes mellitus were significantly more prevalent among the CHD cohort, despite being overall slightly younger than the control group. This truly highlights the importance of preconception and interpregnancy preventive care for the CHD population—with weight management, cardiometabolic screening, and dietary and exercise modifications—essential both for pregnancy health as well as prevention of long-term acquired cardiovascular disease.7-10

The only CHD-specific condition that was associated with HDPs in this study was coarctation of the aorta. CHD disease complexity and other specific CHD lesions were not associated with HDPs, though a true effect may not have been identified due to coding errors which were biased toward simple lesions, and small numbers of complex defects. The findings of increased risk of HDPs in women with coarctation of the aorta is consistent with previous smaller cohort studies and are plausible due to the high prevalence of underlying chronic HTN, as well as persistent endothelial dysfunction and potential for placental hypoperfusion among women with repaired or unrepaired coarctation of the aorta.11,12 Given the known benefit of prophylactic low-dose aspirin in reducing the risk of preeclampsia among women with moderate or strong risk factors, these findings merit further study for confirmation and raise the question of whether this population may also potentially benefit from prenatal aspirin treatment.13

Short-term adverse maternal and fetal outcomes were increased for both women with CHD and those with HDP; however, HDPs conferred a greater risk of delivery hospitalization complications than did CHD. It is known that HDPs are a major driver
of cardiovascular complications of pregnancy and in the early postpartum period, accounting for 7% of all maternal deaths in the United States, including 44% of deaths in the first week postpartum and 21% of deaths between weeks 1 and 6 after delivery.\textsuperscript{14,15} Further, HDPs are the leading cause of postpartum hospital readmissions—reducing both maternal and infant quality of life and driving health care costs.\textsuperscript{16}

Women with both CHD and HDPs carried the highest risk for complicated delivery hospitalization outcomes and 1-year death or readmission, highlighting the need for closely monitoring women with CHD for the development of HDPs, as well as potential complications of HDPs such as HF. The postpartum period is the highest risk period for cardiovascular complications among women with pre-existing cardiovascular disease, and blood pressure is known to increase during this period among women with HDPs.\textsuperscript{7,17,18} Women with underlying CHD are known to be at an increased risk of postpartum HF symptoms,\textsuperscript{19} and HDPs are a known risk factor for peripartum HF.\textsuperscript{7,18,20} Thus, women with CHD who have pregnancies complicated by HDPs warrant close monitoring, especially in the early postpartum period to assess for symptoms of uncontrolled HTN and HF. This study further highlights the importance of adequate blood pressure control and achievement of euvolemia in women with underlying CHD prior to discharge to home, as well as early fourth trimester follow-up.\textsuperscript{7}

The authors of this study should be congratulated on their work investigating a common but serious cardiovascular complication of pregnancy among a high-risk group of patients. The results of this study have implications across the reproductive life span of women with CHD—including early pregnancy and contraception counseling for adolescents, effective transition of care from pediatric to adult CHD clinics, preventive preconception and interpregnancy cardiovascular care, the potential role for prenatal preeclampsia prevention strategies, intensified third and fourth trimester monitoring and management, and longitudinal risk factor modification.
42. Catheter-Based Interventions for the Management of Valvular Heart Disease During Pregnancy

Pregnancy is associated with a significant increase in hemodynamic burden. These changes can lead to maternal morbidity and mortality as well as unfavorable fetal outcomes in patients with valvular heart disease and limited cardiac reserve. Mechanical interventions may be needed for the management of severe hemodynamic deterioration not responding to medical therapy. Catheter-based percutaneous interventions can provide an alternative therapy to surgery during pregnancy. The purpose of this article is to review indications, potential advantages, and limitations of catheter-based interventions for the management of women with valvular heart disease in pregnancy.

Highlights

- Invasive interventions may be needed for the management of severe hemodynamic deterioration in pregnant women with valvular disease.

- Cardiac surgery during pregnancy is associated with high fetal loss and prosthetic valves with risk of complications and early deterioration.

- Catheter-based percutaneous interventions can provide an alternative therapy to surgery during pregnancy.

- Discussions regarding decision-making and performance of catheter-based interventions should be undertaken by an experienced multidisciplinary cardio-obstetrics valve team.

43. Social Factors Contribute to Race Differences in Premature CVD: CARDIA

The significantly higher risk of premature cardiovascular disease seen among Black participants in the CARDIA study compared to their white counterparts can be explained primarily by clinical factors, but neighborhood, socioeconomic, and lifestyle factors also come into play, researchers report.
It is well known that a variety of interrelated psychosocial factors affect cardiovascular outcomes—and that there are major race- and sex-based differences—but the study, published online last week in Circulation, was designed to take a deeper look.

“This approach that we took, it wasn’t just about identifying which factors explain the differences between Black adults and their white adult counterparts, but also what was the relative contribution,” lead author Nilay Shah, MD (Northwestern University Feinberg School of Medicine, Chicago, IL), told TCTMD. “Because the idea was that if we could learn what some of the largest contributors to these differences were, it will start to provide a groundwork for what are likely to be some of the more-effective interventions to narrow the disparities that are prevalent in cardiovascular disease in the US.”

Looking at the web of risk factors that affect CVD, Harriette Van Spall, MD, MPH (McMaster University, Hamilton, Canada), who was not involved in the study, told TCTMD “it’s a complex issue because those clinical factors in themselves are known to be related to socioeconomic factors, and in particular, to structural racism. So, it’s hard to uncouple those factors because we know that even the clinical factors themselves are more common in patients who are Black, who are historically marginalized, who are subjected to systemic racism, and these socioeconomic drivers also give rise to some of the lifestyle factors that are being analyzed, such as smoking.”

**What Affects Race-Based Differences?**

For the study, Shah and colleagues looked at data on 2,785 Black and 2,327 white participants of the CARDIA study who were followed for a median 33.9 years.

After adjustment for age and hospital, Black women (HR 2.44; 95% CI 1.71-3.49) and Black men (HR 1.59; 95% CI 1.20-2.10) were at significantly higher risk for premature CVD than their white counterparts. However, these differences were ameliorated after full adjustment for clinical, lifestyle, psychosocial, socioeconomic, and neighborhood factors.

For women, race-based differences were explained mostly by clinical factors (87% reduction in the β estimate after adjustment), followed by neighborhood (32%) and
socioeconomic (23%) factors. For men, clinical factors also contributed most strongly (64%), but socioeconomic (50%) and lifestyle (34%) factors also contributed.

Shah explained that while the factors affecting race-based differences did change over time, this was accounted for in their analysis. “The CARDIA study followed participants for over 30 years, but in those 30 years, the participants had somewhere on the order of 10 follow-up exams in the interim,” he said. “The way we designed our analysis is that every time a participant had an updated value for one of these factors, we accounted for the change in those factors. So when we were looking at the contribution of these factors to racial differences in premature cardiovascular disease, it wasn’t just the factor at one level, but it was the factor and how it changed over the course of the 30 years.”

Vast Implications

This is powerful data not only for clinicians, but especially for policy makers. “With the growing recognition that these differences in heart disease between racial groups are not because of biological differences, the emphasis at multiple levels is to really understand and address the factors that we identified as contributing to the differences,” Shah continued. For one, he said, clinicians should be inquiring about the social determinants that may affect the health of their patients and how those factors—things like obesity and hypertension—can contribute to race-based disparities.

“At the policy level, when we think about the contribution of things like neighborhood-level environments and lifestyle factors—which account for factors like neighborhood-level poverty and the ability to participate in physical activity in built environments and the quality of diets that individuals are consuming—there are policy interventions that may target these factors that play the largest role in explaining these differences to actually be most effective at reducing disparity,” he added.

Van Spall agreed. “We really need to do a better job at the public health level and the population level in our policy—not just health policy, but social justice, education, and urban design—in order to really tackle the problem of cardiovascular disease and race-based differences in outcomes,” she said.
For physicians, it might be easier prescribe a therapy for hypertension, say, than to address challenging socioeconomic factors that patients live with, but “we see some of those factors manifest themselves in our patients' ability to make it to their appointments, to fill their prescriptions, and engage in self-care activity,” she said. “We need to account for these with compassion.”

Moreover, many of these patient groups have long been “marginalized in our healthcare system such that they don’t receive the care for those risk factors,” Van Spall continued. “It’s different in a registry when patients are routinely being contacted to see how they're doing to measure those risk factors for the incidence of cardiovascular disease, [but] in reality those patients receive less care in real-world situations, so we need to be mindful of that.”

As for next steps, Shah said he would like to better “understand the contribution of social determinants not to cardiovascular disease events, but actually to cardiovascular health and cardiovascular risk factors, because we suspect that a big component of the differences in cardiovascular risk factors or these clinical factors that we identified is actually also due to social determinants.”

Also, he said, clinical assessment of patients can improve by better incorporating consideration of social determinants of health.

Van Spall said “it would be interesting to measure in a robust manner how health policy changes impact population-level risk factors and outcomes. Higher-level interventions are harder to test robustly in clinical trials, and those types of studies need to get done because policy needs to be informed on evidence and it often isn’t. . . . There are different ways to assess relative contributions and each really gives you a different set of results. There’s no doubt that clinical risk factors drive cardiovascular disease, but the clinical risk factors are driven by other factors that we must recognize.”