News in October 2022

1. Risk of Radiation Low for Pregnant Operators When Precautions Taken

Women needn’t avoid the cath lab if they don’t want to, according to a new review that says risks to a fetus are very small.

There isn’t a lot of evidence regarding the risks of radiation exposure to interventional cardiologists, interventional radiologists, and electrophysiologists who are pregnant, but the available data suggest the risk of harm is small, according to a new review.

While women often don’t work in the labs once they become pregnant—the level of allowable radiation during pregnancy varies around the world and can preclude them from even practicing once pregnant—experts believe it is possible to work without harming the developing fetus.

“The instinct today is that whenever somebody is pregnant, whether it’s a technologist, nurse, or physician, they are not allowed to enter the cath lab,” said senior author Ariel Roguin, MD, PhD (Hillel Yaffe Medical Center/Technion—Israel Institute of Technology, Hadera). “When you look at the literature, and you see what the numbers are, we may be exaggerating [the risk]. . . . It’s an area of missing data, so the regulations are cautious because that’s preferred rather than allowing everybody to be exposed.”

For example, there are no studies looking at the risk of spontaneous abortion of women working in the cath lab and none documenting the risk of other adverse events, such as fetal or birth defects. Exposure to high doses of radiation can cause birth defects, malformations, and intellectual impairments, but at doses nearly 10 times higher than safety limits recommended by the American College of Obstetricians and Gynecologists and the National Council on Radiation Protection and Measurements (NCRP), according to the review. Studies of children born to radiologic technologists have not shown any heightened risk of cancer compared with the general population.

To TCTMD, Roguin pointed out that 50% of all medical students are women, and their numbers are increasing every year. While more than 40% of internal medicine trainees are female, women make up just 23% of cardiology fellowships. When looking at fields involving fluoroscopically guided interventions, such as interventional radiology, interventional cardiology, and electrophysiology, their numbers drop off even further.

“It’s really rare to see a woman in the cath lab,” said Roguin, noting they have to plan their training and careers around a pregnancy that can take them away
from the cath lab for at least a year. “We have many women who have to take this into account, about when to plan their family, and they aren’t sure if they should have the child now or wait. It’s a major issue. Women are great doctors, and we’re lacking them in the cath lab.”

**Overlapping Skirts, Aprons on Patients**

In the US, the NCRP recommends limiting occupational exposure of the fetus to 5 mSv or less during the entire pregnancy (or 0.5 mSv per month). In the UK and Norway, though, the levels of allowable radiation during pregnancy are so low that female operators aren’t able to practice during gestation. Elsewhere in Europe, the fetal dose limit is 1 mSv or less for the entire pregnancy.

Despite the limited safety data, there is evidence from dosimeters worn by operators during pregnancy that suggest minimal risks during gestation.

In a Spanish case series of four interventional cardiologists and one electrophysiologist, operators showed that with additional protection, which included overlapping layers of the lead skirt over the abdomen, the risk of exposing the fetus to ionizing radiation was “virtually negligible.” One retrospective study of a fellow who performed neurointerventional procedures before and after pregnancy found there was zero fetal radiation exposure with two lead apron skirts, all without significant changes in the fellow’s case volume or fluoroscopy time.

The reviewers point out that advances in x-ray machines, mapping systems in electrophysiology, and increasing awareness have led to significant declines in radiation doses over time. In one study of electrophysiology procedures, for example, the annual recorded occupational doses declined by approximately 70% for both physicians and nurses.

As part of the review, which was led by Majdi Saada, MD (Hillel Yaffe Medical Center/Technion—Israel Institute of Technology), the authors propose several strategies to protect against radiation during pregnancy in the cath lab. These include a focus on minimizing fluoroscopy times and using technologies, specifically in electrophysiology, that allow operators to perform procedures without radiation. Low frame rates, low magnification, and use of short, intermittent radiation instead of continuous radiation are also recommended. They advise using all possible protection devices, including ancillary shields—ceiling-mounted screens, table curtains, lead skirts over the patient’s waist, and a mobile floor shield—during the procedure.

“Protection from radiation is always good,” said Roguin. “It doesn’t matter your gender, or if you’re pregnant or not. From the report we saw in Spain, where they use double layers of lead skirts, which aren’t as heavy, is something [for pregnant operators] to consider. Also, something that’s very simple is based on a study we
did where we put a lead apron on the patient. This lead apron can reduce radiation to the operator by 50% or more.”

The also recommend using at least two dosimeters during pregnancy, one on the trunk (chest level) inside the lead apron and one at the collar or left shoulder outside the apron. Use of third dosimeter inside the lead apron at the abdomen is also recommended, if possible. During pregnancy, the most valuable information is from the dosimeters worn inside the lead apron, according to the reviewers.

Roguin emphasized that there is a need for future research, including long-term follow-up data on exposed health professionals and their children. Additionally, there is a need for prospective follow-up studies looking at the influence of radiation on fertility and spontaneous abortions, as well as on small birth weight, birth defects, learning disabilities, and cancer in the offspring. Additional studies in men are also warranted, such as the effect of radiation dose on conception, fertility, and child health, particularly in the 3 months prior to conception.

2. Pregnancy in Heart Failure: Concerns For All Clinicians

The rates of maternal mortality in the U.S. have risen steadily over the last 20 years, with cardiovascular disease the leading cause, chiefly from cardiomyopathy among other cardiovascular and cerebrovascular conditions. Maternal mortality is likely to be further impacted by the recent Supreme Court decision regarding Dobbs v. Jackson and subsequent changes at the state level that pose significant challenges to a woman’s access to available health care options. These policies are likely to disproportionately impact racial and ethnic minorities as well as women of lower socioeconomic status.

It is the responsibility of all clinicians who care for women of childbearing age to understand the risks of pregnancy associated with particular cardiovascular conditions or direct them to appropriate cardio-obstetrics teams. This includes understanding the safety of various contraceptive options and obtaining a detailed pregnancy history, including preeclampsia and hypertensive disorders of pregnancy, for those with a previous pregnancy. Here is an overview of the relationship between pregnancy and heart failure (HF).

Women With Pre-Existing Cardiomyopathy

For all women with pre-existing cardiomyopathy, preconception counseling should occur in the context of a shared decision-making model to determine if pregnancy is desired and other related goals and patient preferences. If pregnancy is desired, risk assessment should be undertaken using various risk scores.
Advanced heart failure providers typically see women with pulmonary hypertension and/or severe left ventricular (LV) dysfunction (defined as LV ejection fraction (EF) <30% with NYHA Class III or Class IV disease) or previous peripartum cardiomyopathy (PPCM) with any residual systolic dysfunction. Using the modified WHO classification, these women are Class IV, a group associated with an estimated 50% rate of maternal adverse cardiac events.\(^3\)

These scores help inform discussions with patients regarding the decision to proceed with pregnancy as well as the frequency of cardiac assessment. Management by a multidisciplinary cardio-obstetrics team is advised, including representatives from maternal fetal medicine, cardiology, anesthesia, nutrition and social work, at an experienced center.\(^4\)

It is imperative that members of the treatment team be aware of the potential teratogenic effects of some guideline-directed medical therapy in women with pre-existing cardiomyopathy of childbearing age. Additionally, we should be empowered to ask patients about sexual activity as well as contraception, and ensure patients understand the potential cardiovascular risks of pregnancy, particularly in cases of advanced HF.

The safety of various commonly used medications for HF are shown in the Table. Pregnancy is not recommended for women supported by LV assist devices (LVAD), although cases of successful pregnancy have been reported.\(^3\) After heart transplantation, select women can safely undergo pregnancy. For more detailed information regarding pregnancy after heart transplantation, please refer to dedicated reviews on this topic.\(^3,5\)
Given the potential maternal cardiac risks associated with unplanned pregnancy, clinicians should discuss available contraception options with patients who have concomitant cardiac conditions. According to the Centers for Disease Control and Prevention and the American College of Obstetricians and Gynecologists, intrauterine devices are the recommended reversible option for women with high-risk conditions, such as LVEF <30% or a heart transplant.\textsuperscript{6,7} Combined oral contraceptive pills should be avoided in these patients given the increased risk for thrombotic complications, hypertension and fluid retention. However, progestin-only options may be considered.

**New Diagnosis of HF During Pregnancy**

Pregnancy serves as a "stress test" for the mother as a result of the increased stroke volume, increased cardiac output, increased heart rate and decrease in systemic vascular resistance.\textsuperscript{8}

PPCM, the most common diagnosis for pregnant women with HF, is defined by a nonischemic cardiomyopathy with LVEF <45% that occurs in the third trimester or in the early postpartum period. Risks factors include preeclampsia, maternal age >30 years, African American race and pregnancies with multiple gestations (i.e., twins, triplets).\textsuperscript{9} Notably, there may be a delay in diagnosis because of the overlap in common symptoms in HF and normal pregnancy, including lower extremity swelling or shortness of breath. African-American women are known to have a worse prognosis, further highlighting the importance of improving equitable access to cardiovascular care for these women.

In the U.S., >50\% of women with PPCM will recover cardiac function. However, some women will go on to require an LVAD or transplant or experience cardiac death.\textsuperscript{10}

Women with PPCM should be counseled regarding the risk with future pregnancies and have access to contraception. Subsequent pregnancies can lead to worsening of systolic function as well as progressive symptoms and worsening functional status.\textsuperscript{9} Approximately 20\% of women who fully recover cardiac function will have a decline in ventricular function in a subsequent pregnancy.\textsuperscript{10}

It is worth noting that PPCM is often a diagnosis of exclusion. The differential diagnosis of HF in pregnancy should also include dilated familial cardiomyopathy, stress cardiomyopathy, hypertrophic cardiomyopathy, LV noncompaction and chemotherapy-induced cardiomyopathy, among others, all of which could be unmasked by the hemodynamic changes associated with pregnancy.\textsuperscript{3}
3. Cardiac Biomarkers Reflect Sex Hormones in Transgender People

just as in cisgender individuals, transgender people show variations in cardiac biomarkers that appear related to sex hormones, according to a new cross-sectional study.

Trans men who were taking testosterone saw increased high-sensitivity cardiac troponin (hs-cTn) levels in comparison to trans women who were taking estradiol. For N-terminal pro-brain natriuretic peptide (NT-proBNP), levels were decreased for trans men as compared with trans women. Moreover, the study’s authors say, the extent of these differences matches what’s observed between cis men and cis women.

“Sex hormones, rather than sex assigned at birth, may be a stronger driver of the observed concentration differences between healthy men and women for biomarkers of cardiac disease,” Dina N. Greene, PhD (University of Washington, Seattle), and colleagues note in their paper, published online yesterday in JAMA Cardiology.

Speaking with TCTMD, Greene said she was struck by the clear patterns shown by their results. “Data does not usually look this good,” she noted, adding that it also came as a surprise to see such consistency among the assays they used. “The fact that we saw the exact same trend across the three [troponin] assays was really powerful.”

This work adds a new layer of representation to the literature by focusing on transgender individuals, Greene noted. “For me, that’s the biggest thing: how do we normalize gender expansiveness?”

What their study suggests is that “there is structural remodeling that happens in the heart when people take testosterone or estradiol that we don’t totally understand. Sex hormones influence cardiac physiology,” Greene explained. However, she stressed that their study should be considered basic research and cautioned against applying their findings in practice.

Few data exist on cardiovascular disease in transgender and gender-diverse adults, but there’s growing recognition that the poorer health seen in this population, as compared to cisgender adults, isn’t fully explained by traditional risk factors. As noted by a 2021 American Heart Association scientific statement, psychosocial stressors such as discrimination and lack of access to healthcare are contributing to their excess CV morbidity and mortality.

**There is structural remodeling that happens in the heart when people take testosterone or estradiol that we don’t totally understand.** Dina N. Greene
For their cross-sectional study, Greene and colleagues enrolled 79 trans men who had been prescribed testosterone (mean age 28.8 years) and 93 trans women who had been prescribed estradiol (mean age 35.1 years) for at least 12 months. The mean duration of hormone therapy was 4.8 and 3.5 years, respectively.

Cardiac biomarkers were evaluated by the ARCHITECT STAT (Abbott Diagnostics) and ACCESS (Beckman Coulter) high-sensitivity troponin I assays, the Elecsys Troponin T Gen5 STAT assay (Roche Diagnostic), and the Elecsys proBNP II assay (Roche Diagnostics).

They found that hs-cTnI levels ascertained by the ARCHITECT STAT were higher among trans men as compared with trans women, with similar patterns detected on the other two troponin assays. With NT-proBNP, values were higher for trans women than for trans men.

### Cardiac Biomarkers Among Healthy People: Median (IQR)

<table>
<thead>
<tr>
<th></th>
<th>Trans Men</th>
<th>Trans Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>hs-cTnI, ng/L</td>
<td>0.9 (0.6-1.7)</td>
<td>0.6 (0.3-1.0)</td>
</tr>
<tr>
<td>NT-proBNP, ng/L</td>
<td>17 (13-27)</td>
<td>49 (32-86)</td>
</tr>
</tbody>
</table>

“The observed differences in hs-cTn concentration are likely physiological and not pathological, as concentrations of hs-cTn between healthy cisgender people are also apparent and, as population-based observations, are not thought to portend adverse events,” the study authors note, adding, “Ultimately, the psychosocial benefits of gender-affirming hormones are substantial, and informed consent is likely the ideal method to balance the undetermined risks.”

Greene said her interest in this topic emerged from her earlier work on sex-related differences in cardiac biomarkers among cisgender people and gender-related aspects of cardiovascular medicine.

For instance, female patients tend to have a lower 99th percentile upper reference limit for hs-cTn than do male patients, Greene pointed out. Additionally, prior social-science research performed in cisgender individuals has shown that “different expressions of gender can influence the care you receive,” she noted. “The more masculine you are, the more likely you are to be taken seriously for signs and symptoms of acute myocardial infarction, and the more feminine you are, the less likely you are.”

With more research done in more people, a better understanding of biomarker levels—cardiac and otherwise—in transgender patients could be used to improve
diagnostic tools, Greene noted. Future studies should also include baseline biomarker assessment and cardiac imaging to capture what happens when starting hormone therapy.

“Gender-affirming therapy is essential to the overall well-being and health of transgender persons, and more research is needed to quantify any potential adverse cardiac consequences and develop better strategies to optimize cardiac health in this population,” the paper concludes.

4. **Nifedipine During Labor Controls BP in Severe Preeclampsia**

Women with preeclampsia with severe features benefit from treatment with oral nifedipine during labor and delivery, results of a randomized controlled trial suggest.
The study showed that intrapartum administration of extended-release oral nifedipine was safe and reduced the need for acute intravenous (IV) or immediate-release oral hypertensive therapy. There was a trend toward fewer cesarean deliveries and less need for neonatal intensive care.
The results suggest that providers "consider initiating long-acting nifedipine every 24 hours for individuals with preeclampsia with severe features who are undergoing induction of labor," Erin M. Cleary, MD, with the Ohio State University, Columbus, told theheart.org | Medscape Cardiology.

5. **Sex of Patients With ILD Should Be Considered When Managing Nintedanib-Related Adverse Events**

The researchers sought to evaluate the safety and tolerability of the tyrosine kinase inhibitor nintedanib in patients with autoimmune disease-related ILDs and nonautoimmune disease-related ILDs (ie, other ILDs), according to sex.

Researchers assessed the AEs reported over a 52-week period in the subgroups of individuals, with data on sex collected from case report forms.

Data were pooled from the 2 INPULSIS trials (ClinicalTrials.gov Identifiers: NCT01335464 and NCT01335477) in patients with idiopathic pulmonary fibrosis (IPF), the SENSCIS trial (ClinicalTrials.gov Identifier: NCT02597933) in patients with fibrosing ILDs associated with systemic sclerosis (SSc), and the INBUILD trial (ClinicalTrials.gov Identifier: NCT02999178) in patients with progressive fibrosing ILDs other than IPF.

In each of the trials, participants were randomly assigned to receive treatment with oral nintedanib 150 mg twice daily or matched placebo. The post hoc analyses were descriptive and included patients who received at least 1 dose of nintedanib.
In the INPULSIS trials, 79% of the treated patients were men and 21% were women, of whom 21% of men and 25% of women discontinued the trial medication prior to week 52.

In the SENSCIS trial, 25% of the treated patients were men and 75% were women, of whom 12% of men and 16% of women discontinued the study medication before week 52.

In the INBUILD trial, 54% of the treated patients were men and 46% were women, of whom 19% of men and 20% of women discontinued the trial medication prior to week 52.

The pooled data set of patients with autoimmune disease-related ILDs included 746 individuals, of whom 70% were women. A total of 82% in this subgroup had SSc-associated ILD. Women had a lower mean body weight, lower forced vital capacity (FVC), and greater % predicted mean diffusing capacity of the lungs for carbon monoxide (DLCO). Further, a small percentage of women vs men were receiving treatment with corticosteroids.

The pooled dataset of patients with other ILDs included a total of 1554 individuals, of whom 28% were women. Among the patients in this subgroup, 68% had IPF. Women vs men had a lower mean body weight and lower FVC; a higher percentage of men were receiving treatment with corticosteroids.

Overall, patients with autoimmune disease-related ILDs compared with those with other ILDs were younger, had lower body mass index (BMI), lower % predicted FVC, higher % predicted DLCO (women), and were more likely to be receiving treatment with corticosteroids.

Among patients with autoimmune disease-related ILDs, the median exposure to the trial drug (regardless of whether the dose of nintedanib was reduced) was 12.2 months (minimum to maximum, 0.0-12.2 months) in the nintedanib group and 12.2 months (minimum to maximum, 0.4-12.2 months) in the placebo group among men. Corresponding values among women were 12.2 months (minimum to maximum, 0.0-12.2 months) in the nintedanib group and 12.2 months (minimum to maximum, 0.3-12.2 months) in the placebo group.

Among the participants with other ILDs, the median exposure to the trial drug (regardless of whether the dose of nintedanib was reduced) was 11.9 months (minimum to maximum, 0.0-12.5 months) in the nintedanib group and 11.9 months (minimum to maximum, 0.0-13.1 months) in the placebo group among men. Corresponding values among women were 11.9 months (minimum to maximum, 0.0-12.7 months) in the nintedanib group and 12.1 months (minimum to maximum, 0.2-12.8 months) in the placebo group.

Among patients with autoimmune disease-related ILDs, the AE profile of nintedanib was generally similar between men and women, although the occurrence of nausea, vomiting, elevations in liver enzymes, dose reductions,
and treatment interruptions were more common among women vs men. Observations were similar among participants with other ILDs.

Several limitations of the current analysis should be noted. The group of participants with autoimmune disease-related ILDs predominantly included individuals with SSc-associated ILD, whereas most of the patients with other ILDs had IPF. Therefore, these populations should not be considered representative of patients with autoimmune disease-related ILDs and other ILDs. Further, the analyses were based on data from only 1 year of treatment, with the trials differing in the co-medications that were used.

The investigators emphasized the importance of shared decision-making between patient and provider. They concluded, “Sex should be considered in patient education and in the monitoring and management of [AEs] that might be associated with nintedanib.”

6. Use of Hormone Replacement Therapy Assessed Among Postmenopausal Women With Hand OA

Researchers conducted a randomized placebo-controlled double-blind trial (HOPE-e; ClinicalTrials.gov Identifier: NCT04036929) to determine the feasibility and acceptability of a form of HRT (ie, conjugated estrogens plus bazedoxifene) in postmenopausal women with moderate to severe symptoms of hand OA.

It is well recognized that the female sex is an established risk factor for symptomatic OA, particularly hand OA. Hand OA is most common among women in the decade associated with menopause. However, sparse data are available in this regard from large HRT trials.

In the HOPE-e study, the researchers enrolled women aged between 40 and 65 years with definite hand OA in at least 2 painful hand joints and for whom 1 to 10 years had passed after their final menstrual period. Participants were enrolled from 3 primary or secondary care sites, as well as from the community, and were randomly assigned 1:1 for treatment with conjugated estrogens plus bazedoxifene or placebo, administered orally once daily for 24 weeks, then weaned for 4 weeks until the study conclusion.

The primary feasibility outcomes for determining feasibility included enrollment and randomization rates from different enrollment sources; retention rates; study medication compliance (ie, participant-reported adherence, based on daily recording in diaries); and likelihood of unintentional unmasking. Secondary outcomes included patient-reported hand pain during the 14 days prior to each visit, which was measured by 2 methods on a scale of 0 to 10 (0 indicating no pain and 10 indicating the worst pain).
An intention-to-treat analysis was used, with criteria for progression to a full trial predefined as enrollment of at least 30 participants across all sites in 18 months; a dropout rate of 30% or less after randomization; and acceptability. Including rates of adverse events (AEs), to the majority of participants. The enrollment window was reduced to 12 to 15 months because of the COVID-19 pandemic.

Between May 2019 and December 2020, a total of 434 inquiries/referrals were received. Following 96 telephone prescreens and of 35 eligible participants, 7 were excluded from the study. The remaining 28 patients were randomly assigned to the conjugated estrogen/bazedoxifene group (n=14) or the placebo group (n=14). Among the 406 individuals who were not randomly assigned into either group, 250 (62%) were considered ineligible, 101 (25%) did not respond to additional inquiries, and 55 (14%) elected not to proceed with the study (with the most common reason being not wanting to take a hormone-based medication).

All 28 participants completed follow-up evaluations with high compliance and completeness of outcomes measures.

Three AE-related treatment withdrawals were in the placebo group; however, no serious AEs were reported in either group. All participants and investigators were successfully masked (participant Bang’s blinding index placebo group, 0.50; 95% CI, 0.25-0.75). The trial fulfilled the prespecified criteria for progression to a full trial.

Several limitations of the study warrant mention. The number of study participants was at the lower end of the target, thus limiting what could be analyzed from proof-of-concept data; the findings were not generalizable to a larger population; acceptability measures were collected from a small percentage of participants, which most likely led to increased approval rates; and possible biases may have been introduced due to the COVID-19 pandemic.

The investigators concluded that although powered to detect a clinical effect, the outcome of the study “indicates that a full trial of an HRT in this population is feasible and acceptable and identifies potential refinements with regard to the design of such a trial.”

7. **Tadalafil May Ease Voiding Problems in Women**

Single-dose tadalafil, a medication used to treat erectile dysfunction, may have beneficial effects in the treatment of voiding dysfunction in women, according to data presented at the International Continence Society’s 2022 annual meeting (ICS 2022) in Vienna, Austria.

In a randomized, placebo-controlled trial, Thea Christoffersen, MD, of the University of Copenhagen in Denmark, and colleagues evaluated the effects of tadalafil, a phosphodiesterase-type 5 (PDE5) inhibitor, on opening urethral
pressure (OUP) in 24 healthy women. The investigators randomly assigned women to receive either a single 40 mg dose of tadalafil or placebo at the first visit and then crossed over to the opposite treatment at the second visit. To avoid carry-over effects, the visits were separated by a washout period of at least 6 days. Using urethral pressure reflectometry, the investigators measured OUP during resting and squeezing of the pelvic floor 2 hours after administration of study treatment, the reported time of peak plasma drug concentration for tadalafil. They performed uroflowmetry with a prefilled bladder volume of 300 mL of natrium chloride immediately following the urethral pressure measurements.

Compared with placebo, tadalafil caused significant decreases of 6.8 cmH₂O during resting OUP and 8.8 cmH₂O during squeezing, Dr Christoffersen’s team reported. Tadalafil caused no significant change in voiding parameters compared with placebo, including average and maximum flow rate and voiding volume. The investigators observed a significant period effect for average and maximum flow rates, both of which were increased at the second visit compared with the first.

8. Dedicated Care at Women’s Heart Center May Aid Diagnosis, Outcomes

Mahraz Parvand, from the University of British Columbia in Vancouver, Canada, and colleagues assessed whether visiting a women’s heart center is associated with improved outcomes among patients with ischemia or myocardial infarction. The analysis included questionnaire responses from 154 women with no obstructive coronary artery disease.

The researchers found that the most common referral was for chest pain (94 percent of those with ischemia and 66 percent of those with myocardial infarction). At baseline, a substantial number of patients did not have specific diagnoses (64 percent of those with ischemia and 43 percent of those with myocardial infarction). Following care at the women’s heart center, 71.4 percent of patients with ischemia established a new or a changed diagnosis (most commonly coronary microvascular dysfunction, 68 percent), while 60 percent of patients with myocardial infarction established new or changed diagnoses (most commonly coronary vasospasm, 60 percent). At one year, there were significant decreases in chest pain and improved quality of life and mental health.

“We hope our findings highlight the importance of having a dedicated women-specific heart center, which provides comprehensive care for women resynchronization with heart disease by providing risk factor assessment, referral to psychiatrists, exercise classes, smoking cessation treatment, and consultation with a dietitian in addition to a focus on conditions such as ischemia with no obstructive coronary artery disease that are more common in women,” a coauthor said in a statement.

The Dobbs v Jackson Women’s Health Organization ruling has led to abortion bans and restrictions in some US states and may result in additional restrictions in the future. These changes have not yet affected assisted reproductive technology (ART) and other fertility preservation efforts, but some health care providers and patients are worried about what the future holds.

A recent report by the American Society for Reproductive Medicine (ASRM) analyzed the so-called trigger laws in 13 states that ban or severely restrict abortions. Some of these laws have already taken effect, and others are expected to take effect in the near future.

The ASRM report concluded that most of the laws should not impact in vitro fertilization (IVF) or other ART procedures because they define abortion specifically as terminating a pregnancy and do not apply to embryos and other tissue outside the body.

An exception may be the trigger law in Utah, which has not yet taken effect. The report stated that this law “could be interpreted to have an impact on ART under the provision that defines abortion to include ‘[any] intentional killing or attempted killing of a live unborn child through a medical procedure carried out by a physician or through a substance used under the direction of a physician.’”

10. sex differences in arterial Hypertension

There is strong evidence that sex chromosomes and sex hormones influence blood pressure (BP) regulation, distribution of cardiovascular (CV) risk factors and co-morbidities differentially in females and males with essential arterial hypertension. The risk for CV disease increases at a lower BP level in females than in males, suggesting that sex-specific thresholds for diagnosis of hypertension may be reasonable. However, due to paucity of data, in particularly from specifically designed clinical trials, it is not yet known whether hypertension should be differently managed in females and males, including treatment goals and choice and dosages of antihypertensive drugs. Accordingly, this consensus document was conceived to provide a comprehensive overview of current knowledge on sex differences in essential hypertension including BP development over the life course, development of hypertension, pathophysiologic mechanisms regulating BP, interaction of BP with CV risk factors and co-
morbidity, hypertension-mediated organ damage in the heart and the arteries, impact on incident CV disease, and differences in the effect of antihypertensive treatment. The consensus document also highlights areas where focused research is needed to advance sex-specific prevention and management of hypertension.

11. **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.

**12. Nifedipine to Prevent Severe Hypertension in Pregnant Individuals With Preeclampsia With Severe Features**

**BACKGROUND**

Preeclampsia is associated with maternal and perinatal morbidity. Besides acute therapy for severe hypertension, best practices are lacking for intrapartum hypertension management. Our objective was to test the hypothesis that intrapartum initiation of extended-release nifedipine in individuals with preeclampsia with severe features prevents severe hypertension.

**METHODS**

Randomized, triple-blind, placebo-controlled trial of individuals with preeclampsia with severe features undergoing labor induction between 22⁰/⁷ and 41⁶/⁷ weeks gestation. Participants were randomized to oral extended-release nifedipine 30 mg or identical placebo every 24 hours. Primary outcome is defined as receipt of ≥1 dose of acute hypertension therapy for severe blood pressure (≥160/110 mm Hg) sustained ≥10 minutes. Secondary outcomes included route of delivery, neonatal intensive care unit admission, and a composite of adverse neonatal outcomes.

**RESULTS**

Of 365 individuals screened, 55 were randomized to nifedipine and 55 to placebo. Primary outcome was observed in 34.0% of individuals in nifedipine group versus 55.1% in placebo group (relative risk [RR] 0.62 [95% CI, 0.39-0.97]); number needed to treat to prevent receipt of acute treatment was 4.7 (95% CI, 2.5-44.3). Fewer individuals in nifedipine group required cesarean delivery compared with placebo group (20.8% versus 34.7%, RR, 0.60 [95% CI, 0.31-1.15]). Neonatal intensive care unit admission rate was lower in nifedipine group compared with placebo (29.1% versus 47.1%; RR 0.62 [95% CI, 0.37-1.02]). Neonatal composite was similar between groups (35.8% versus 41.2%, RR, 0.83 [95% CI, 0.51-1.37]).
CONCLUSIONS

Initiation of extended-release nifedipine is effective in reducing intrapartum acute hypertensive therapy among individuals with preeclampsia with severe features.

13. Assessment Of Left and Right Ventricular Functions In Overweight and Obese Females by Different Echo-Doppler Modalities

Aim of work

Assessment of left and right ventricular functions in overweight and obese females using different echo-Doppler modalities.

Methods

This study included 32 obese females (group I), 26 overweight females (group II) -both of them have no chronic illnesses- in addition to 25 healthy females (group III) as a control group. All of them had hsCRP level measured. The following parameters were measured using 2D echocardiography: LA, Ao, LA/Ao ratio, LV measures included LV dimensions, 2D LVEF, 2D LV global longitudinal strain (LVGLS), average LV Sm, Em, Am, LV E/Em ratio, LV E, A and LV E/A ratio. RV measures included LV dimensions, RV FAC, RV Tei index, TAPSE, RV Sm, Em, Am, Em/Am ratio, RV E, A, E/A ratio and PASP.

Results

hsCRP, LA, Ao, LV dimensions, Average LV Am, E/Em, RVD1, RV Tei and PASP were significantly higher in group I compared to group III, but group I had significantly lower LV E/A, LV Sm, Em, LVGLS, RV E/A, Em/Am and RVGLS compared to group III. Group II had significantly higher hsCRP, Ao and RV Tei and significantly lower LV E/A ratio and LV Em compared to group III. On the other hand, group I had significantly lower average Sm, LVGLS and RVGLS than group II but no significant difference detected between two groups as regard LV and RV diastolic function. Pulse, BMI, BSA, waist circumference, waist to hip ratio, hsCRP were negatively correlated with LVGLS and RVGLS. Cut-off values for BMI showed good sensitivity and specificity to predict impaired LVGLS and RVGLS. Cut-off point 31.9 kg/m2 for impaired LVGLS with sensitivity 80%,
specificity 76.81% and p value <0.001, cut-off point >30.73kg/m² for impaired RVGLS with sensitivity 80%, specificity 69.57% and p value 0.001.

Waist circumference was the most sensitive predictor for impaired LVGLS and hsCRP for impaired RVGLS.

**Conclusion**

Isolated obesity and overweight are independent predisposing factors for impaired LV and RV systolic and diastolic dysfunctions. TDI and 2D STE are good echo-Doppler modalities to detect subclinical effects on LV and RV functions.

14. **CVD Risk Factors Similar for Men, Women**

Most cardiovascular disease (CVD) risk factors are similar for women and men, according to a study published in the Sept. 10 issue of *The Lancet*.

Marjan Walli-Attaei, Ph.D., from McMaster University in Hamilton, Ontario, Canada, and colleagues enrolled 155,724 participants aged 35 to 70 years at baseline. Participants came from 21 high-income, middle-income, and low-income countries and were followed for about 10 years to examine the prevalence of metabolic, behavioral, and psychosocial risk factors for CVD.

The researchers found that 4,280 and 4,911 major CVD events had occurred in women and in men, respectively, as of the data cutoff (Sept. 13, 2021). Women presented with a more favorable cardiovascular risk profile than men, especially at younger ages. The hazard ratios (HRs) for metabolic risk factors were similar for men and women, except for high non-high density lipoprotein (HDL) cholesterol (HRs, 1.11 in women and 1.28 in men, for major CVD). For other lipid markers, the pattern was consistent. For symptoms of depression, the HRs were 1.09 and 1.42 in women and men, respectively. Consumption of a diet with a PURE (Prospective Urban Rural Epidemiological) score of 4 or lower was associated with major CVD more strongly in women than men (1.17 versus 1.07). The total population-attributable fractions associated with behavioral and psychosocial risk factors were greater in men than women (15.7 versus 8.4 percent).

"Women and men have similar CVD risk factors, which emphasizes the importance of a similar strategy for the prevention of CVD in men and women," Walli-Attaei said in a statement.

One author disclosed financial ties to the pharmaceutical industry.
15. **Sex differences in cardiac operations: Are we being fair to our female patients?**

**Introduction**

Research suggests that whilst men have a higher cardiovascular disease (CVD) rate, women are more likely to suffer a poor prognosis following CVD, possibly due to incorrect diagnosis and treatments. A question infrequently asked is whether this inequality is due to sex bias when selecting patients for operation.

**Methods**

Patients who had been admitted to hospital with a cardiovascular diagnosis within the Scottish Heart Health Extended Cohort (SHHEC) were studied. Participants were recruited between 1984–1995 and followed up until 2017 via data linkage to NHS hospital records. Using propensity score nearest neighbour matching, admissions for women were matched with men within the cohort on a 1:1 basis. Admissions were matched for common CVD risk factors and generalised logistic mixed models were used to estimate Odds Ratios (OR) and 95% Confidence Intervals (95% CI).

**Results and conclusions**

A total of 25,318 admissions to hospital for cardiac reasons were recorded over the study period (20,520 following matching). Women were less likely to have a cardiac procedure (4.57% males, 2.77% females; OR 0.59; 95% CI 0.50–0.70). Women were significantly less likely to have a cardiac operation (2.65% males, 1.47% females; OR 0.55; 95% CI 0.45–0.67), but not endovascular procedures (1.89% males, 1.30% females; OR 0.66; 95% CI 0.37–1.16) following hospital admission. Within the SHHEC cohort, a matched cohort of 20,520 admissions to hospital over a 30-year period, demonstrated that women were less likely to undergo surgical procedures, even when matched with men on common CVD risk factors.
A Case of Post Thrombotic Syndrome and AV Fistula arising from Recurrent DVT Secondary to May–Thurner Syndrome (MTS) in an Elderly Woman

Abstract

May-Thurner Syndrome (MTS) remains to be an overlooked condition wherein the right common iliac artery compresses the left common iliac vein. Rarely reported, MTS has other different variants with the iliac vein being compressed by an ipsilateral artery. Iliofemoral DVT poses a significant impact because of venous claudication and DVT recurrence. MTS usually occurs in women, ages 20–40 y/o, and is thus rarely included in differential diagnosis of DVT in elderly patients presenting with persistent unilateral leg swelling. Treatment of DVT alone with anticoagulation is insufficient to address thrombotic MTS. Failure to address the mechanical compression leads to poor quality of life due to high predisposition to recurrent DVT, and at times to other complications such as post-thrombotic syndrome and formation of AV fistulas.

We present a case of an 89 year old woman, hypertensive, non-smoker, no history of cancer, presenting with progressive left lower extremity swelling with erythema, violaceous discoloration, varicosities, telangiectatic skin lesions, hyperpigmentation and calf tenderness. Ultrasound revealed DVT at common iliac vein extending to the popliteal veins. CT studies showed a left common iliac artery compressing the left common iliac vein with early enhancement of the common femoral vein, indicating presence of fistula. Peripheral angiography and venography findings were consistent with CT scan findings, with incidental findings of multiple small AV fistulas.

Anti-coagulation was given and IVC filter was inserted. An attempt to do catheter-directed thrombolysis was unsuccessful. Subsequently, she underwent Palma's surgery which provided significant improvement and was sent home ambulatory.
17. Age at menopause and risk of heart failure and atrial fibrillation: a nationwide cohort study

**Aims**
This study aimed to examine the association of premature menopause and age at menopause with the risk of heart failure (HF) and atrial fibrillation (AF).

**Methods and results**
A total of 1,401,175 postmenopausal women, who had undergone health examination provided by the Korean National Health Insurance Service, were included, and their reproductive histories were collected. Multivariable Cox proportional hazard models were performed to determine the hazard ratios (HRs) and 95% confidence intervals (CIs) of incident HF and AF, according to the history of premature menopause and age at menopause. At a mean follow-up of 9.1 years, there were 42,699 (3.0%) and 44,834 (3.2%) new cases of HF and AF, respectively. Women with history of premature menopause had an increased risk of HF (HR: 1.33, 95% CI: 1.26–1.40) and AF (HR: 1.09, 95% CI: 1.02–1.16), compared to women without the history. Compared with women aged ≥50 years at menopause, those aged 45–49, 40–44, and <40 years at menopause showed a significantly increased trend in HRs for the incident risk of both HF and AF (P for trend <0.001). The robustness of the results of a series of sensitivity analyses further strengthens the main findings.

**Conclusion**
Our findings suggest that postmenopausal women with a history of premature menopause or early menopausal age may have an increased risk of HF and AF. These reproductive factors need to be considered for preventing the future risk of HF and AF.
18. **Premature menopause and cardiovascular disease: can we blame estrogen?**

19. **Maternal Exposure to PFAS Tied to Reproductive Function of Male Offspring**

Katia Keglberg Hærvig, Ph.D., from Copenhagen University Hospital-Bispebjerg and Frederiksberg in Denmark, and colleagues examined associations between maternal plasma PFAS levels during early pregnancy and male offspring reproductive function in adulthood. The analysis included 864 young men and first-trimester samples from their mothers.

The researchers found that for a 1-unit increase in the weighted quantile sum index, combined maternal PFAS exposure was associated with lower sperm concentration, lower total sperm count, and a higher proportion of nonprogressive and immotile sperm in the young men. There was variance noted in the strength of associations for different PFAS; however, perfluoroheptanoic acid was identified as the main contributor in the analyses of all three outcomes despite the low concentration. There was no association between exposure to maternal PFAS and testicular volume or reproductive hormones.

“A man’s reproductive capacity is largely defined in the first trimester of pregnancy when the testicles are developed,” a coauthor said in a statement. “It makes sense that exposure to substances that mimic and interfere with the...
hormones involved in this delicate process can disrupt normal development and have consequences for semen quality later in life.”

20. Serial 7-Day ECG Screening for AF in High-Risk Older Women

Study Questions:

Can serial electrocardiogram (ECG) patch monitoring increase the detection of atrial fibrillation (AF) among women at increased risk for AF?

Methods:

Postmenopausal female participants (50-79 years of age) from the WHISH (Women's Health Initiative Strong and Healthy), a trial to assess the impact of hormone therapy and lifestyle, were potentially eligible for this ancillary study (WHISH STAR [Health Initiative Silent Atrial Fibrillation Recording Study]). Women with an increased risk for AF, defined as a 5-year predicted risk of new-onset AF >5%, but without prior evidence or diagnosis of AF at baseline, were included in the present study. Risk for AF was defined using the CHARGE (Cohorts for Heart and Aging Research in Genomic Epidemiology)-AF clinical prediction score (variables included age, race/ethnicity, height, weight, blood pressure, smoking, diabetes, heart failure, myocardial infarction, and use of antihypertensive medications). Screening for AF was completed using 7-day ECG patch monitors worn at baseline, 6 months, and 12 months from study enrollment. AF was defined as at least 30 seconds of AF or atrial flutter on an ECG patch monitor recording.

Results:

From a total of 14,290 active participants enrolled in the WHISH trial, 4,791 women were randomly selected to participate in the present study, 1,257 (51.8%) to be enrolled in the study, 1,067 returned a baseline monitor, 866 returned the 6-month monitor, and 777 returned the 12-month monitor and had readable data. The mean age of all participants who returned a readable baseline monitor was 79 years, and 92% were white, 4.6% were African American, and 1.5% were Hispanic. With baseline monitoring, 2.5% of the women had AF detected. At 6 months and 12 months, 3.7% and 4.9% of the cohort were diagnosed with AF, respectively. A higher CHARGE-AF score was associated with higher rates of AF detection. A CHARGE-AF score, which predicted AF ≥10%, was associated with 4.2% of women with AF detected at baseline, 5.9% at 6 months, and 7.2% at 12 months. Most participants with patch-identified AF never had a clinical diagnosis of AF (36 of 46 [78%]).
Conclusions:

The investigators concluded that older women with an elevated CHARGE-AF score had a high prevalence of AF on 7-day ECG patch screening. Serial screening over 12 months substantially increased the detection of AF. These data can be useful in helping identify high-risk participants for enrollment in future studies of the management of asymptomatic AF.

21. Race and Sex Dictate Publication Rate for Med Students

Publication rates among US medical students vastly differ based on sex, race, and ethnicity, according to new data released online yesterday in JAMA Network Open. Researchers say there may be career consequences for women and racial/ethnic groups underrepresented in medicine (URIM).

Previous studies in the cardiology field have shown similar alarming trends, with men being more likely than women to author invited commentaries and women in general publishing less than men, although there are hints that this could be improving.

“We expected to find some gender disparity and some race/ethnic disparity, based on prior studies at the faculty level,” lead author Mytien Nguyen, MS (Yale School of Medicine, New Haven, CT), told TCTMD. “What was surprising when we looked at intersectionality between the two identities was that we found data that actually mirrors [previous research] among [US National Institutes of Health] faculty where URIM and women face the most inequity, essentially.”

With every one of these individuals, we're impacting not only the professional societies but also all patient populations as clinician scientists. Mytien Nguyen

The study speaks to a broader “pipeline problem,” commented Sunil Rao, MD (NYU Langone Health, New York), editor-in-chief of Circulation: Cardiovascular Interventions. “That's where I think we need to focus, as well as continue to try and make sure that there's adequate representation in the field,” he told TCTMD. “You can't just have one single approach to this issue.”

Similarly, Bruce Ovbiagele, MD (University of California, San Francisco), who will take over as editor-in-chief of the Journal of the American Heart Association next year, told TCTMD: “Clearly, there are lots of factors that contribute to what we see, which is not surprising. But having it quantified in
such a rigorous way is I think very helpful to support what many of us see in reality.”

Also, Armin Zadeh, MD, PhD, MPH (Johns Hopkins University, Baltimore, MD), editor-in-chief of the Journal of Cardiovascular Computed Tomography, told TCTMD in an email that these findings “raise important awareness of persistent bias in our training programs. Clearly, we have more work to do. Our training programs should monitor the research opportunities as well as productivity in relation to sex, race, and ethnicity.”

**Significant Gaps**

For the study, Nguyen and colleagues included data from the Association of American Medical Colleges on 31,474 medical school graduates (48.2% women; 13.8% URIM) who matriculated between 2014 and 2016.

Students attending top 40 research-ranked schools by the NIH reported more research experiences as well as publications (median 1.60 vs 1.25; P < 0.001) compared with students from non-top 40 schools.

While women reported a higher number of research experiences than men, they published significantly less regardless of whether they attended a top 40 (mean 7.32 vs 8.22) or non-top 40 school (mean 4.81 vs 5.15; P ≤ 0.001 for both). This resulted in a significantly lower adjusted publication rate among women than men, as well, at both top 40 schools (adjusted RR 0.85; 95% CI 0.83-0.86) and non-top 40 schools (adjusted RR 0.91; 95% CI 0.90-0.92).

Compared with white students, those of Asian descent reported higher publication rates at both NIH top 40 schools (adjusted RR 1.10; 95% CI 1.08-1.12) and non-top 40 schools (adjusted RR 1.07; 95% CI 1.05-1.08). However, Black students reported lower publication rates than white regardless of school ranking (top 40: adjusted RR 0.83; 95% CI 0.80-0.86; non-top 40: adjusted RR 0.88; 95% CI 0.85-0.95), and Hispanic students attending non-top 40 schools also reported fewer publications (adjusted RR 0.93; 95% CI 0.90-0.95).

*Clearly, there are lots of factors that contribute to what we see, which is not surprising. But having it quantified in such a rigorous way is I think very helpful to support what many of us see in reality.* Bruce Ovbiagele

The findings regarding NIH funding specifically indicate that the organization can greatly help to “mitigate and reduce gender and race inequity” by spreading out the wealth more than has been done in the past, Nguyen said. “Right now, what I’ve seen is that money begets money, so schools that are already well funded pretty well get more NIH funding, and schools that are minority serving—like your historically Black colleges and universities—are not among the top 40.”
By “intentionally match[ing] funding with diversity outcomes,” schools can better generate more diversity in the pool of physician scientists, Nguyen added.

As for some of the gender disparities observed, she said, “we can infer that women are seeking out on research opportunities and are more proactive in finding research opportunities and mentors, but for each of these research opportunities, women students are getting out of it less than men do.” The mechanism for this is unclear, Nguyen added, but she guessed that it could be tied to mentorship trends.

She called for change to start “at the elementary school level” to really have a lasting effect. “We've seen that there is increased diversity in medical school in general, but there’s still students who are leaving medicine,” Nguyen said. “It's key to support the continuum for students across their training. . . . With every one of these individuals, we’re impacting not only the professional societies but also all patient populations as clinician scientists.”

**Mentorship Is ‘Fundamental’**

Commenting on the study for TCTMD, Ann Marie Navar MD, PhD (UT Southwestern Medical School, Dallas, TX), who serves as the deputy editor for equity, diversity, and inclusion at JAMA Cardiology, urged caution in overinterpreting the data since they show average publication rates across a large population. “It’s not clear what proportion of each group really wanted to have research experiences that led to publications versus those who had other goals or priorities in medical school including community outreach, service, quality improvement, or education,” she said in an email.

“And while number of publications is important, publication count doesn’t necessarily correlate with the quality of the experience(s) for the trainee. This highlights the importance for residency programs and ultimately academic leadership to look beyond publication count when evaluating potential trainees and faculty,” Navar added.

**You can't just have one single approach to this issue.** Sunil Rao

Rao agreed that publication counts on their own don’t matter all that much, but funding does if the goal is to have a career in research. Still, the discrepancies highlighted in this paper are “challenging,” he said. And, if the study was done among cardiology trainees, Rao said he expects the gaps would be “worse.”

This may be “rooted in a lot of different things,” Rao observed. “It may be systematic bias. It may be rooted in opportunity. It may be rooted in lack of mentorship.”
Mentorship is “fundamental” to the solution of these issues, he said. “What a good mentor does is they provide opportunities for their mentees that they themselves could benefit from. . . . If you are mentoring someone who is underrepresented, my sense is that they’re probably not getting as many opportunities as other mentees. I don’t have any data to back that up except to say that there’s a reason why we don’t have representation in science, and maybe that’s one of them.”

Further, Rao said it’s “everybody’s” responsibility to create change, echoing Nguyen’s comment about starting at the elementary school level. “We need to start . . . getting people interested in science who traditionally have been excluded from science,” Rao said. “All of us benefit when there’s diversity. That’s what I think people misunderstand. People think of diversity efforts as inclusion of one group at the exclusion of the other group. But that’s not what it’s about. It’s about making sure that we have all the voices of the room heard because that makes all of us better.”

**How Should Journals Adjust?**

Journals will play a large role in increasing diversity going forward, according to several people interviewed for this article.

Ovbiagele said his experience fostering an editor-in-training program for Stroke has successfully upped diversity for that journal’s editorial board, and he intends to continue a similar program in his new role.

Still, he acknowledged, “at some point, you can only do so much based on who's out there.” In trying to recruit board members for JAHA, Ovbiagele said he has encountered challenges. “Because there are so few underrepresented minorities, everybody wants them,” he said. “When I approach them, they all go: ‘I’m already taken on this board and that board.’”

Similarly, Rao said it’s important to not “overburden specific people who may be asked repeatedly to be on editorial boards or review or write.” Because of this, he also plans to continue his assistant editor program at Circulation: Cardiovascular Interventions.

“I think things are going to change, but let’s not be naive about how hard it's going to be,” Rao said. “I think things are changing, but I do think that we have a long way to go.”
22. Differences in Demographics and Outcomes Between Men and Women With Spontaneous Coronary Artery Dissection

Background

Spontaneous coronary artery dissection (SCAD) is an increasingly recognized cause of myocardial infarction (MI) that most frequently affects women. The characteristics of men with SCAD are less well described.

Objectives

The aim of this study was to describe the characteristics of men with SCAD.

Methods

We compared baseline demographics, clinical presentation, angiographic findings and cardiovascular outcomes of men and women in the Canadian SCAD Study. Major adverse cardiovascular events (MACE) were composite of death, MI, stroke or transient ischemic attack, heart failure hospitalization, and revascularization.

Results

Of 1,173 patients with SCAD, 123 (10.5%) were men. Men with SCAD were younger than women (mean age 49.4 ± 9.6 years vs 52.0 ± 10.6 years; P = 0.01). Men had lower rate of prior MI than women (0.8% vs 7.0%; P = 0.005). Men were less likely to have fibromuscular dysplasia (FMD) (27.8% vs 52.7%; P = 0.001), depression (9.8% vs 20.2%; P = 0.005), emotional stress (35.0% vs 59.3%; P < 0.001), or high score on the Perceived Stress Scale (3.5% vs 11.0%; P = 0.025) but were more likely to report isometric physical stress (40.2% vs 24.0%; P = 0.007). There was no difference in angiographic types of SCAD, but men had more circumflex artery (44.4% vs 30.9%; P = 0.001) and fewer right coronary artery (11.8% vs 21.7%; P = 0.0054) dissections. At median follow-up of 3.0 (IQR: 2.0-3.8) years, men had fewer hospital presentations with chest pain (10.6% vs 24.8%; P < 0.001). There were no differences in in-hospital events or follow-up MACE (7.3% vs 12.7%; P = 0.106).

Conclusions

Ten percent of SCAD patients were men. Men were younger and more likely to have a physical trigger but were less likely to have FMD, depression, or an emotional trigger. Men had less recurrent chest pain but no significant difference in MACE.
23. Worse Effects of Thrombus Burden or Undertreatment in Women With ST-Segment Elevation Myocardial Infarction?

Sex differences in long- and short-term outcomes following ST-segment elevation myocardial infarction (STEMI) have long been recognized worldwide. Women have higher in-hospital rates of mortality, recurrent myocardial infarction (MI), stroke, and major bleeding. Reasons may include older age, more comorbidities, smaller vessels, undertreatment, and higher bleeding risk. Delayed presentation and delayed recognition of symptoms in women by health care providers, and lower likelihood of receiving guideline-based MI therapies, contribute to poorer outcomes in women.

Successful primary percutaneous coronary intervention (PCI) may be hampered by distal embolization of thrombus, leading to slow flow or no-reflow. Therefore, it seems logical that a large thrombus burden (TB) would lead to worse results. Demonstrating sex differences in TB may contribute to understanding differential long-term outcomes.

This topic is evaluated in this issue of JACC: Cardiovascular Interventions. Manzi et al³ combine data from the TAPAS (Thrombus Aspiration during Percutaneous coronary intervention in Acute myocardial infarction Study), the TASTE (Thrombus Aspiration in ST-Elevation myocardial infarction in Scandinavia), and the TOTAL (Thrombectomy with PCI vs. PCI Alone in Patients with STEMI) trials, focusing on sex-specific differences in outcomes according to TB. These large randomized clinical trials of thrombus aspiration (TA) during PCI for STEMI within 12 to 24 hours of symptom onset reported thrombus grade and at least 1-year clinical outcome. In TAPAS, routine TA was associated with improved procedural success with lower cardiac death and nonfatal reinfarction at 1 year (secondary endpoints). This was subsequently refuted by TASTE, designed to specifically evaluate hard endpoints, even taking TB into consideration, and confirmed by TOTAL, which also demonstrated increased stroke following TA. High TB (HTB) was identified as an independent risk factor for cardiovascular (CV) mortality and increased stroke risk in patients post-TA.

In the current analysis by Manzi et al³, the combined study population was dichotomized according to sex and TB, categorized as HTB in patients with TIMI (Thrombolysis In Myocardial Infarction) thrombus grade ≥3, or low (LTB) for TIMI thrombus grade <3. Primary outcome was CV death at 1 year. Secondary outcomes included all-cause mortality, recurrent MI, heart failure stroke/transient ischemic attack, and stent thrombosis or target vessel revascularization up to 1 year. The final study population comprised 18,256 patients, of whom 24.9% were women. Most patients at presentation had a HTB (74.5%). Women had a lower incidence of HTB compared with men (71.4% vs 75.5%; P < 0.0001).
As expected, clinical outcomes were worse in women. Patients with HTB had worse 1-year outcomes, with a HR for both CV and vascular death of 1.52. Women had an increased risk of the primary outcome regardless of TB, especially in the first 30 days following PCI. Women with HTB had higher CV death and all-cause mortality, and higher risk for stent thrombosis and MI at 1 year and from heart failure through 30 and 180 days. After adjusting for confounders, the risk of the primary outcome was higher only in women with HTB. There was no difference in outcome with respect to treatment arm (thrombus aspiration vs none).

The importance of this study lies in the demonstration of the excess risk for poor outcomes in women with HTB, which may represent a further therapeutic target. As amply demonstrated, routine thrombus aspiration is not helpful. How then could this excess mortality associated with HTB be mitigated?

It is known that the size of the thrombus and especially its composition (not analyzed in this retrospective study) depend on the time since the onset of symptoms. Literature lacks relevant data about the potential influence of differences between sexes and ages in patients with STEMI. Therefore, profiling TB in women and men may be a strategy to identify potential distinguishing features between sexes to clarify differential pathophysiological mechanisms of coronary thrombosis. Moreover, the influence of sex on the thrombogenic response in STEMI has not been systematically researched in vivo. A recent study reported that men and women with STEMI had a similar thrombus composition, except in a group of patients aged ≤55 years, where younger women had significantly lower thrombogenic content in their thrombi than young men, even though the association between the thrombus content with prognosis was not analyzed. Several studies have pointed out that estrogens may modulate the risks and outcomes of atherosclerotic disease, and we can speculate that a potential protective effect of estrogens on the formation of TB is present in premenopausal women.

In the Manzi et al study, the clinical trials that were carried out had heterogenous methods for patients with STEMI: the TAPAS and TOTAL studies included patients with a 12-hour interval from the onset of symptoms, whereas in the TASTE trial, patients were included up to an interval of 24 hours. Furthermore, TB was analyzed at different times until thrombi were obtained from the patients (from the onset of symptoms, from admission to emergency room, and from the time they arrived at the interventional lab). Another aspect to consider is that thrombus grade was assessed before wire crossing in both TAPAS and TOTAL, and after wire crossing in TASTE. The definition of HTB and LTB was roughly reduced to stratification by thrombus in LTB and HTB, respectively, without more details. These factors may influence the different levels of TB assessed and cause a bias in the interpretation of the data.
Moreover, the data sets of the individual trials should be interpreted cautiously, given that this is a post hoc analysis. Outcomes in the TASTE trial were from administrative databases, clinical registries, and death certificates. As expected, HTB was associated with an increased risk of cardiovascular events in both men and women, but HTB was associated with worse outcomes in women compared with men. However, we cannot safely rule out that such higher mortality in female patients was due to the absence of the same adequate antithrombotic treatment as the one received by men. As a matter of fact, antithrombotic treatment prescribed before, during, and after discharge was less often used in women than in men, and the Cox models were not adjusted for these variables. In this regard, some studies report lower rates of P2Y$_{12}$ inhibitor use in women, as well as in other antithrombotic treatments used in during PCI, even though a higher bleeding risk of women did not imply the absence of these treatments in this scenario.

In summary, the Manzi et al study provides new insights into thrombosis burden in women and leads to the speculation that the worse outcomes often reported in women could be due to a higher effect of TB. Some gaps remain unexplained, and future prospective research is necessary. In the meanwhile, emphasis should be placed on ensuring that women with STEMI receive equal guideline-based MI therapies as men.

24. Peripartum Outcomes Associated With COVID-19 Vaccination During Pregnancy

IMPORTANCE

The risk and benefits of COVID-19 vaccination during pregnancy are under investigation. Pooled evidence regarding neonatal and maternal outcomes in association with COVID-19 vaccination during pregnancy is scarce.

OBJECTIVE

To evaluate the association between COVID-19 vaccination during pregnancy and peripartum outcomes.

DATA SOURCES

PubMed and EMBASE databases were searched on April 5, 2022. Language restrictions were not applied.

STUDY SELECTION

Prospective trials and observational studies comparing the individuals who received at least 1 COVID-19 vaccination during pregnancy with those who did not and reporting the neonatal outcomes, including preterm birth, small for gestational age, low Apgar score, neonatal intensive care units (NICU) admission, and intrauterine fetal death (IFD).
DATA EXTRACTION AND SYNTHESIS

Two independent investigators extracted relevant data from each study. Odds ratios (ORs) were calculated using a random-effects model. This study followed the Preferred Reporting Items for Systematic Reviews and Meta-analysis guidelines.

MAIN OUTCOMES AND MEASURES

The primary outcomes were the neonatal outcomes, including preterm birth, small for gestational age, low Apgar score, NICU admission, and IFD. The secondary outcomes were maternal outcomes, including maternal SARS-CoV-2 infection, cesarean delivery, postpartum hemorrhage, and chorioamnionitis.

RESULTS

Nine observational studies involving 81,349 vaccinated (mean age, 32-35 years) and 255,346 unvaccinated individuals during pregnancy (mean age, 29.5-33 years) were included. COVID-19 vaccination during pregnancy was associated with lower risk of NICU admission (OR, 0.88; 95% CI, 0.80-0.97) and IFD (OR, 0.73; 95% CI, 0.57-0.94), whereas there was no statistically significant association with preterm birth (OR, 0.89; 95% CI, 0.76-1.04), small for gestational age (OR, 0.99; 95% CI, 0.94-1.04), and low Apgar score (OR, 0.94; 95% CI, 0.87-1.02). COVID-19 vaccination during pregnancy was associated with a lower risk of maternal SARS-CoV-2 infection (OR, 0.46; 95% CI, 0.22-0.93), whereas it was not associated with increased risk of cesarean delivery (OR, 1.05; 95% CI, 0.93-1.20), postpartum hemorrhage (OR, 0.95; 95% CI, 0.83-1.07), and chorioamnionitis (OR, 0.95; 95% CI, 0.83-1.07).

CONCLUSIONS AND RELEVANCE

COVID-19 vaccination during pregnancy was not associated with an increase in the risk of peripartum outcomes, was associated with a decreased risk of NICU admission, IFD, and maternal SARS-CoV-2 infection. Thus, COVID-19 vaccination should be encouraged for pregnant individuals.

25. Irregular, Long Menstrual Cycles Up Risk for Cardiovascular Disease

Irregular and long menstrual cycles are associated with increased rates of cardiovascular disease (CVD), according to a study published online Oct. 25 in JAMA Network Open.

Yi-Xin Wang, M.D., Ph.D., from the Harvard T.H. Chan School of Public Health in Boston, and colleagues explored associations between menstrual cycle characteristics across the reproductive life span and the risk for CVD. The analysis included 80,630 participants in the Nurses' Health Study II with 24 years of follow-up.
The researchers found that compared with women reporting very regular cycles at the same ages, women who had irregular cycles or no periods at ages 14 to 17, 18 to 22, or 29 to 46 years had a higher risk for CVD (hazard ratios [95 percent confidence intervals], 1.15 [0.99 to 1.34], 1.36 [1.06 to 1.75], and 1.40 [1.14 to 1.71], respectively). Women reporting a cycle length ≥40 days or a cycle too irregular to estimate from ages 18 to 22 or 29 to 46 years also had higher CVD risk (hazard ratios [95 percent confidence intervals], 1.44 [1.13 to 1.84] and 1.30 [1.09 to 1.57], respectively) compared with women reporting a cycle length of 26 to 31 days. Subsequent development of hypercholesterolemia, chronic hypertension, and type 2 diabetes only explained 5.4 to 13.5 percent of the observed associations.

"These results suggest that menstrual cycle characteristics throughout the reproductive lifespan may be used as additional markers of CVD risk in women," the authors write.

26. Effects of Empagliflozin in Women and Men With HFpEF

BACKGROUND

Women and men with heart failure (HF) and preserved ejection fraction may differ in their clinical characteristics and their response to therapy. The aim of this study was to evaluate the influence of sex on the effects of empagliflozin in patients with HF and preserved ejection fraction enrolled in the EMPEROR-Preserved trial (Empagliflozin Outcome Trial in Patients With Chronic Heart Failure With Preserved Ejection Fraction).

METHODS

The effects of empagliflozin on the primary outcome of cardiovascular death or hospitalization for HF and on secondary outcomes (including total HF hospitalization, cardiovascular and all-cause mortality, and Kansas City Cardiomyopathy Questionnaire scores) were compared in women and men in the overall cohort and in subgroups defined by left ventricular ejection fraction (41%-49%, 50%-59%, and ≥60%). The effects of empagliflozin on physiological measures, including changes in systolic blood pressure, uric acid, hemoglobin, body weight, and natriuretic peptide levels, were also assessed.

RESULTS

Of the 5988 patients randomized, 2676 (44.7%) were women. In the placebo arm, women tended to have lower risk for adverse outcomes, including a lower risk of all-cause mortality (hazard ratio, 0.69 [95% CI, 0.56, 0.84]). Compared with placebo, empagliflozin reduced the risk of cardiovascular death or hospitalization for HF to a similar degree in both sexes (hazard ratio, 0.81 [95% CI, 0.69, 0.96] for men; and hazard ratio, 0.75 [95% CI, 0.61, 0.92] for women; \( P_{\text{interaction}}=0.54 \).
Sex did not modify the relationship between empagliflozin and outcomes across ejection fraction groups. Similar results were seen for secondary outcomes and physiological measures. Compared with placebo, empagliflozin improved the Kansas City Cardiomyopathy Questionnaire Clinical Summary Score to a similar extent in both sexes (1.38 for men versus 1.63 for women at 52 weeks; $P_{\text{interaction}}=0.77$); the results were similar for Kansas City Cardiomyopathy Questionnaire overall summary score and total summary score.

CONCLUSIONS

Empagliflozin produced similar benefits on outcomes and health status in women and men with HF and preserved ejection fraction.