News in August 2021

1. Women Present With More Advanced Acute Aortic Dissection

Women with acute aortic dissection are older and have more advanced disease at presentation than men, according to a study published online June 1 in The Annals of Thoracic Surgery.

Lauren V. Huckaby, M.D., from the University of Pittsburgh Medical Center, and colleagues queried the Interventional Cohort of the International Registry of Acute Aortic Dissection database to examine sex differences in presentation, operative approach, and outcomes.

The researchers found that women comprised 34.3 percent of the 2,823 patients and were significantly older than men (mean age, 65.4 versus 58.6 years). Women more often had hypotension or coma and were more likely to present with intramural hematoma, periaortic hematoma, or complete or partial false lumen thrombosis. The proportion of Bentall, complete arch, and elephant trunk procedures was greater among men. During the study period, in-hospital mortality was significantly higher in women (16.7 versus 13.8 percent; P = 0.039). Female sex trended toward higher in-hospital mortality overall (odds ratio, 1.40; 95 percent confidence interval, 1.00 to 1.98; P = 0.053) after adjustment, but not in the last decade of enrollment (odds ratio, 0.93; 95 percent confidence interval, 0.54 to 1.62; P = 0.807). There were no significant differences noted between the sexes in five-year mortality and reintervention rates.

2. White Coat Beats Casuals in Patient Perceptions, With Gender Caveats

Physician who wears a traditional white coat appears more professional and experienced compared with one who is dressed in more-casual attire, according to new survey data. That said, biases to the detriment of women physicians remain blatant regardless of what they wear.

“Physician attire is only a small aspect of the practice of medicine and does not embody the wearer’s qualifications, nor does it necessarily affect their performance, practice, and contributions,” write lead author Helen Xun, MD (Johns Hopkins University School of Medicine, Baltimore, MD), and colleagues. “However, as physician attire evolves, the healthcare community should be attuned to the potential associations attire may have with the primary objective of the profession to provide excellent patient care.”

The paper, published online last week in JAMA Network Open, is the latest to address attire and professionalism in healthcare. Last years’ #MedBikini paper spurred debate about physicians posting photos of themselves in “inappropriate attire” on social media.

But in the clinic, patient perceptions matter, as physician attire is linked with “building rapport with patients, reducing risks of nosocomial pathogen transmission, and communicating physicians’ role in patient care,” the authors write. “Physicians in casual physician attire should be conscious of the different impression they may give to patients compared with physicians in a white coat and mitigate this through other methods of building patient rapport.”
Amalia Cochran, MD (Bozeman, MT), who co-wrote an accompanying editorial with Gilbert R. Upchurch Jr, MD (University of Florida Health, Gainesville), told TCTMD that the survey “provides an important contribution in terms of highlighting the fact that there is a diversity of opinions out there in terms of what constitutes professional attire—that there’s not one single right answer to that question—and unfortunately for women physicians, it kind of didn’t matter what we showed up in. There was still the ‘wait for the doctor’ question that came into play.”

Does this mean that women should show up to work in whatever they want? Maybe, Cochran said. “Perhaps the [fact] that there really wasn’t a clear-cut answer for women really does still highlight a lot of unconscious bias that is still present regarding the role of women as physicians, which is unfortunate but that’s just something that takes time. And then I think the other piece of that is that for women, perhaps we really do have a broader bandwidth in terms of what we should wear, because if a white coat isn’t necessarily giving us any additional cachet, maybe we should kind of make our own rules.”

‘A Disruptive Opportunity’

Casual attire, defined in this survey as either fleece or softshell jackets often emblazoned with an institution’s insignia, was associated with lower perceptions of both professionalism and experience compared with white coats, according to 487 respondents to the online image survey sent out between May and June 2020.

Attire Comparison

<table>
<thead>
<tr>
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<th>White Coat</th>
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<td>3.1</td>
<td>&lt;0.001</td>
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<tr>
<td>Professionalism</td>
<td>4.9</td>
<td>3.2</td>
<td>3.3</td>
<td>&lt;0.001</td>
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The preferred outfit changed according to specialty, with respondents reacting most positively to a white coat with scrubs for surgeons and a white coat with business attire for family physicians and dermatologists.

Notably, regardless of what women wore in the survey images, respondents rated them as less professional than men (56.2 vs 65.8; P < 0.001). When dressed similarly in white coats with business wear, female and male models were most frequently identified as physicians, although men were thought to be doctors more often than women (71.7% vs 88.3%; P < 0.001). In contrast to the male model, for example, the female model was mistaken by more respondents as a medical technician (8.0% vs 3.3%; P < 0.005), physician assistant (11.5% vs 2.3%; P < 0.001), or nurse (33.1% vs 27.3%; P = 0.050).

“The introduction of new physician attire presents a disruptive opportunity to address persistent gender biases in medicine,” Xun and colleagues write. “With exposure and education, public perception of physicians can be broadened to reflect increasing diversity as the new status quo. This includes clear identification of professional roles during introductions,
immediate correction of role misidentifications, and increased visibility (such as more diverse representation at all levels of training; spotlight features; representation on boards, as speakers, and in leadership positions; and presence on social media).”

Tradition, Practicality

Cochran said she has noticed more physicians moving away from the white coat, suggesting that certain regions may be less tied to the tradition or that this attire might not be practical for specific specialties. “I have practiced for the bulk of my career in the West, and specifically in the Mountain West, and I felt like white coats were largely out of favor amongst my colleagues. Not just my surgeon colleagues, not just my critical care colleagues, but across the board.”

There is a diversity of opinions out there in terms of what constitutes professional attire . . . and unfortunately for women physicians, it kind of didn’t matter what we showed up in. Amalia Cochran

Moving away from the white coat is a good thing, she continued. “It does help to smooth the power differential between the physician and patients and families to not have it. . . . There are times, of course, that you as a physician would perhaps want to be recognized for your expertise and your knowledge and your experience. I think that’s understandable. But hopefully that can be done through really thoughtful conversations with patients and family members, and perhaps it doesn’t require that marker that a white coat has traditionally been thought to provide for us.”

There does still remain the question of whether white coats may enable infection to spread more easily in the hospital setting, Cochran acknowledged. “The data around that is equivocal, it’s imperfect. But I think at least acknowledging that there is that possibility is another reason that people in critical care environments have stepped back from wearing white coats,” she said.

Ultimately, the evolution of professionalism in medicine is ongoing and attire is only part of that.

“One of the challenges that I really see us having is that a lot of us want to think about professionalism as something that’s positive, and that’s creating an inclusive culture and a place of civility and kindness,” Cochran said. “But I also know there are times, particularly in education, that professionalism is being weaponized, and if someone acts in a way or dresses in a way that you don’t think is quite right, . . . boy, it’s a fine line sometimes. I think we’re all definitely trying to navigate that professionalism space in a way that it’s supportive of everybody and really acknowledging that times are changing still, and this is one piece of that. I think #MedBikini is one piece of that. I think any time these professionalism questions come up, they get really complicated, really quickly.”

3. **Progestin OCs Triple CV Events in Women With Congenital Long QT**

Women with congenital long QT syndrome (LQTS) need to be cautious when taking an oral contraceptive (OC), observational data suggest those on progestin-only pills are nearly three
times more likely to experience recurrent cardiac events than if they hadn’t been on birth control. The same risks aren’t seen with estrogen-only or combination pills.

Yet the potential harm posed by a progestin-based OC can be sharply reduced by beta-blockers in female patients with LQTS, Ilan Goldenberg, MD (University of Rochester Medical Center, NY), reported today at the Heart Rhythm Society (HRS) 2021 Scientific Sessions. The results were simultaneously published in the journal Heart Rhythm.

LQTS on its own “is commonly associated with cardiac events such as syncope, cardiac arrest, and sudden cardiac death,” Goldenberg and colleagues point out in their paper. Women with the disorder are known to be at increased risk of such events after the onset of adolescence, after pregnancy, and during perimenopause, especially if they have the LQT2 genotype. Men with LQTS, however, see their risk attenuate after they reach adolescence.

“Those opposing trends may possibly be due to the effects of sex hormones on the potassium channels that are associated with this inherited arrhythmic disorder,” Goldenberg said in a press conference. Oral contraceptives, which contain various combinations of sex hormones, thus merit attention in the LQTS setting, he explained.

Goldenberg told TCTMD this study is the first to draw a connection between cardiac events and OC use among women with LQTS. “Before there was very little awareness of the fact that oral contraceptives may be harmful,” he said. “This also has implications for the wider population, because . . . there are many patients [with] drug-induced long QT syndrome: simple antibiotics, antianxiety medications, antipsychotic medications.” If those medications are affecting QTc, they may interact with sex hormones and perhaps OCs, as well, Goldenberg noted. They are now looking into this possibility in an American Heart Association-funded study.

The takeaway for now, he stressed in his presentation, is that “progestin oral contraceptives should not be administered in congenital LQTS women without concomitant beta-blocker treatment. We also believe that careful consideration should be exercised before prescribing any oral contraceptive to women with the LQT2 genotype, especially those who cannot tolerate maximal dosages of beta-blockers.”

**Long QT Syndrome Registry**

Using data from the Rochester, NY-based Long QT Syndrome Registry, the researchers identified 1,659 women with LQTS who completed yearly questionnaires about menstruation, OC use, pregnancy, and menopause. The information was collected from September 2010 through March 2021. To account for changes in OC type over the years, use was modeled as a time-dependent variable.

Around one-quarter of women (22%) took OCs at some point in the study; among them 57% were on combined formulations, while 21% were on estrogen-only OC and 22% on progestin-only OC. Those not taking an OC also did not use other forms of hormone-based contraception.

Age of menarche was similar with versus without OC use (mean 12.3 years), as were the proportion of women who became pregnant (72% overall) and the distribution of genotype (26% LQT1, 23% LQT2, and 7% LQT3). Those on OC had an average QTc duration that was slightly shorter (491 ms vs 495 ms). They also were more likely to receive beta-blockers (79% vs 40%) and to have an implantable cardioverter-defibrillator (35% vs 15%). That said, beta-blocker use
did not vary among the different OC types (79%, 80%, and 77%, respectively, for combined, estrogen, and progestin).

Forty-one percent of the women with LQTS had a first cardiac event after their periods began; slightly more than half of the events were syncope, 19% aborted cardiac arrest, 11% LQTS-related death. Calculated over a cumulative follow-up of 35,797 years, there were 2,027 first and recurrent cardiac events after menarche.

Adjusted for genotype, QTc duration, and time-dependent beta-blocker use, progestin-only OCs were linked to an almost tripled risk of recurrent cardiac events compared with no OC use. Adding a beta-blocker on top of a progestin-only OC was associated with a 78% lower risk (HR 0.22; 95% CI 0.07-0.74) compared with an OC alone. Neither estrogen-only nor combined OC types were associated with cardiac events, though in the latter group there was a “marginally statistically significant risk” difference by beta-blocker use, the researchers note, suggesting that here, too, the drug class might be protective.

### Risk of Recurrent Cardiac Events With vs Without OC

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<thead>
<tr>
<th></th>
<th>HR</th>
<th>95% CI</th>
<th>P for Interaction</th>
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<tbody>
<tr>
<td>Progestin</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Beta-blocker</td>
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<td>No Beta-blocker</td>
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<td>Estrogen</td>
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<td></td>
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<tr>
<td>Combined</td>
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<tr>
<td>Beta-blocker</td>
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<tr>
<td>No Beta-blocker</td>
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<td>0.87-1.91</td>
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For women with the LQT2 genotype, a progestin-only OC without beta-blockers was particularly risky, carrying an eightfold increase in risk of recurrent cardiac events in comparison to no OC (HR 8.03; 95% CI 4.22-15.29). Estrogen-only OCs also were linked to harm in this subgroup, carrying a tenfold higher risk (HR 10.05; 95% CI 2.60-38.89), while combination pills were not.

Mark S. Link (UT Southwestern, Dallas, TX), discussing the findings, said they have “incredible practical applications.”

“What I took away from this [is that] progestin alone is a problem and should probably not be used in these patients, that long QT, too, is a problem and has to be of special concern, and...
that nonuse of beta-blockers is a real problem,” said Link. In his own practice, he now believes all women with LQTS “should be on beta-blockers to the maximally tolerated dose.”

The session’s other discussant, Kimberly A. Selzman, MD (George E. Wahlen VA Medical Center, Salt Lake City, UT), agreed the study addresses a “practical and clinically relevant question.”

While the patterns it found are clear, she said it’s worth remembering a few caveats. Only 81 patients within the entire data set were on progestin, for instance. Selzman also questioned whether there may be confounders, such as ICD use and baseline QT interval, influencing risk and asked for more details on the timing of events. “I just want to stress that those are fully adjusted models” that account for those characteristics, as well as time, Goldenberg replied.

Moderator Andrew D. Krahn, MD (University of British Columbia, Vancouver, Canada), forwarded a question from the audience: if progestin is responsible, why didn’t the combo pill also augment risk and fall along a “dose-response curve,” with estrogen at the low end?

Goldenberg said that, in fact, based on basic research and the clinical course of women with LQTS over their lifetimes, the researchers had expected estrogen to be the culprit—their data on progestin-based drugs came as a surprise. It may be that progestin itself isn’t the issue. Rather, it may be that newer-generation progestin OCs, in order to reduce side effects, contain antiandrogenic components; these, he proposed, may be the true root of the risk. “This may be the reason the combined medication [which lack these elements] did not increase the risk. It’s more balanced. This is the hypothesis.”

4. Women Underrepresented in CV Clinical Trials Despite Inclusivity Requirements

Women remain underrepresented in cardiovascular drug and device clinical trials clinical trials despite guidelines and legal requirements developed almost 30 years ago to ensure broader inclusivity, according to a perspective from ACC’s Cardiovascular Disease in Women Committee published Aug. 9 in the Journal of the American College of Cardiology. This lack of representation “limits progress of both the development and adoption of new therapies among women.”

Leslie Cho, MD, FACC, et al., sought to better understand the current barriers to enrollment and retention of women in clinical trials, as well as to offer novel strategies to help increase participation of women and, more specifically, underrepresented minority women, while also looking at women of childbearing age and pregnant women.

1. Differential Care–Low rates of referral to cardiologists and specialty programs for more aggressive care leads to fewer women being treated by specialists recruiting for clinical trials.

2. Lack of Awareness, Trust and Logistical Barriers – Previous surveys and studies have shown that women are more reluctant than men to participate in clinical trials.
3. Lack of Diversity in Clinical Trial Leadership – Women are underrepresented in clinical trial leadership, and research has shown that trials led by women tend to recruit more women participants.

4. Underrepresented Minority Women in Cardiovascular Clinical Trials – Clinical trials that enrolled predominantly racial/ethnic minority groups have proven that it is possible to have representation of underrepresented groups in clinical trial leadership, enrollment and retention; however, rates of minority representation in the majority of major cardiovascular trials remains low.

5. Special Consideration for Pregnant Women and Women of Childbearing Age – Pregnant women and women of “child-bearing potential” are frequently excluded from clinical research as a vulnerable population, resulting in not only reduced numbers of eligible women, but a lack of data on how certain drugs impact pregnant patients.

6. Sex Differences in Disease – Women have a higher risk of developing certain types of cardiovascular disease and/or present with different symptoms than men when experiencing cardiovascular disease, potentially leading to lower numbers of women in clinical trials studying less prevalent types of cardiovascular disease.

7. Study Retention – Little is known about potential sex differences in study drug discontinuation and patient follow up once patients are successfully enrolled since reasons for study drug discontinuation and withdrawal of consent are not routinely captured in clinical trial case reports.

Recommendations for breaking down each barrier are also discussed.

“Historically, drug therapies for women were determined based on male data that was extrapolated to women,” explains Cho, lead author of the paper and a member of the ACC Cardiovascular Disease in Women Committee. “However, research has shown that women respond differently than men and may even be harmed or experience side effects from some drugs when taken at the same dosage as men. Sex-specific data is essential to optimal care.”

The authors conclude that moving forward, to address barriers to recruitment and retention of women in cardiovascular clinical trials, “a comprehensive and targeted approach that involves partnership with all stakeholders – patients, referring clinicians, research teams (investigators and coordinators), health care systems, the FDA, payers, sponsors, professional and community organizations – is essential. We owe it to our patients to increase representation of women and underrepresented minorities in cardiovascular disease trials.”

5. Men Dominate Discussions at Academic Medical Conferences

When Dr. Victoria Salem mentioned that she rarely heard women comment or ask questions at an otherwise gender-balanced endocrinology conference, her dinner companions at the meeting responded with incredulity.

"People at the table were laughing at me, saying: 'What are you talking about? At least half of the delegates are women,' " said Salem, an endocrinologist at Imperial College London. She recalled people around the table asking, "So really, are you sure there’s a problem?"
Yes, she is sure. Six years later, Salem is the lead author of a new study in The Lancet Diabetes & Endocrinology that proves her point. Women spoke less - significantly less - than men at the UK Society for Endocrinology's annual national conference in 2017.

Although nearly half of the conference attendees were women, they asked less than one quarter of the questions, the study showed.

In an intervention to improve female participation at the following year's conference, the researchers emailed organizers urging them to invite more women to chair sessions. In a separate email, they encouraged session chairs to offer the opening question to a female audience member, whenever possible.

Researchers credit the intervention with increasing the number of female session chairs from 34% in 2017 to 47% in 2018 and with increasing the proportion of females asking questions from 24% in 2017 to 35% in 2018.

"Small interventions had a big difference," Salem told Reuters Health in an email. "The removal of all male-chaired sessions will clearly help."

"I loved how simple their intervention was," said Dr. Erin Brown, a pediatric surgeon at UC Davis Medical Center in Sacramento. Every medical association could easily have more women chair conference sessions and try to offer the first question to a woman, said Brown, who was not involved with the study.

6. Mammographic Features Are Associated With Cardiometabolic Disease Risk and Mortality

AIMS

In recent years, microcalcifications identified in routine mammograms were found to be associated with cardiometabolic disease in women. Here, we aimed to systematically evaluate the association of microcalcifications and other mammographic features with cardiometabolic disease risk and mortality in a large screening cohort and to understand a potential genetic contribution.

METHODS AND RESULTS

This study included 57 867 women from a prospective mammographic screening cohort in Sweden (KARMA) and 49 583 sisters. Cardiometabolic disease diagnoses and mortality and medication were extracted by linkage to Swedish population registries with virtually no missing data. In the cardiometabolic phenome-wide association study, we found that a higher number of microcalcifications were associated with increased risk for multiple cardiometabolic diseases, particularly in women with pre-existing cardiometabolic diseases. In contrast, dense breasts were associated with a lower incidence of cardiometabolic diseases. Importantly, we observed similar associations in sisters of KARMA women, indicating a potential genetic overlap between mammographic features and cardiometabolic traits. Finally, we observed that the presence of microcalcifications was associated with increased cardiometabolic mortality in women with pre-existing cardiometabolic diseases (hazard ratio and 95% confidence interval: 1.79 [1.24-2.58], P = 0.002) while we did not find such effects in women without cardiometabolic diseases.
CONCLUSIONS

We found that mammographic features are associated with cardiometabolic risk and mortality. Our results strengthen the notion that a combination of mammographic features and other breast cancer risk factors could be a novel and affordable tool to assess cardiometabolic health in women attending mammographic screening.


OBJECTIVE

The aim of this study was to determine the association between SARS-CoV-2 infection at the time of birth and maternal and perinatal outcomes.

METHODS

This is a population-based cohort study in England. The inclusion criteria were women with a recorded singleton birth between 29th May 2020 and 31st January 2021 in a national database of hospital admissions. Maternal and perinatal outcomes were compared between pregnant women with a laboratory-confirmed SARS-CoV-2 infection recorded in the birth episode and those without. Study outcomes were fetal death at or beyond 24 weeks' gestation (stillbirth), preterm birth (<37 weeks gestation), small for gestational age infant (SGA; birthweight <10th centile), pre eclampsia/eclampsia, induction of labor, mode of birth, specialist neonatal care, composite neonatal adverse outcome indicator, maternal and neonatal length of hospital stay following birth (3 days or more), 28-day neonatal and 42-day maternal hospital readmission. Adjusted odds ratios (aOR) and their 95% confidence interval (CI) for the association between SARS-CoV-2 infection status and outcomes were calculated using logistic regression, adjusting for maternal age, ethnicity, parity, pre-existing diabetes, pre-existing hypertension and socioeconomic deprivation measured using Index of Multiple Deprivation 2019. Models were fitted with robust standard errors to account for hospital-level clustering. The analysis of the neonatal outcomes was repeated for those born at term (≥ 37 weeks' gestation) since preterm birth has been reported to be more common in pregnant women with SARS-CoV-2 infection.

RESULTS

The analysis included 342,080 women, of whom 3,527 had laboratory-confirmed SARS-CoV-2 infection. Laboratory-confirmed SARS-CoV-2 infection was more common in women who were younger, of non-white ethnicity, primiparous, residing in the most deprived areas, or had comorbidities. Fetal death (aOR, 2.21, 95% CI 1.58-3.11; P<0.001) and preterm birth (aOR 2.17, 95% CI 1.96-2.42; P<0.001) occurred more frequently in women with SARS-CoV-2 infection than those without. Risk of pre eclampsia/eclampsia (aOR 1.55, 95% CI 1.29-1.85; P<0.001), birth by emergency Cesarean delivery (aOR 1.63, 95% CI 1.51-1.76; P<0.001) and prolonged admission following birth (aOR 1.57, 95%CI 1.44-1.72; P<0.001) were significantly higher for women with SARS-CoV-2 infection than those without. There were no significant differences in the rate of other maternal outcomes. Risk of neonatal adverse outcome (aOR 1.45, 95% CI 1.27-1.66; P<0.001), need for specialist neonatal care (aOR 1.24, 95% CI 1.02-
1.51; P=0.03), and prolonged neonatal admission following birth (aOR 1.61, 95% CI 1.49-1.75; P<0.001) were all significantly higher for infants with mothers with laboratory-confirmed SARS-CoV-2 infection. When the analysis was restricted to pregnancies delivered at term (≥37 weeks), there were no significant differences in neonatal adverse outcome (P=0.78), need for specialist neonatal care after birth (P=0.22) or neonatal readmission within four weeks of birth (P=0.05). Neonates born at term to mothers with laboratory-confirmed SARS-CoV-2 infection were more likely to have prolonged admission following birth (21.1% compared to 14.6%, aOR 1.61, 95% CI 1.49-1.75; P<0.001).

CONCLUSIONS

SARS-CoV-2 infection at the time of birth is associated with higher rates of fetal death, preterm birth, preeclampsia and emergency Cesarean delivery. There were no additional adverse neonatal outcomes, other than those related to preterm delivery. Pregnant women should be counseled regarding risks of SARS-COV-2 infection and should be considered a priority for vaccination.

8. In-Hospital Mortality in a Cohort of Hospitalized Pregnant and Non-Pregnant Patients With COVID-19

Background: Studies examining pregnant patients with COVID-19 have shown an increased risk for death in pregnant versus nonpregnant patients of reproductive age (1). However, these data are based on registries that are limited by a significant proportion of missing data, including pregnancy status, and likely have biased case ascertainment.

Objective: To evaluate the risk for in-hospital death among pregnant and nonpregnant patients of reproductive age hospitalized with COVID-19, because studies with more thorough ascertainment of COVID-19 in pregnancy are needed to provide the foundation for clinical management and health care policy.

Methods and Findings: We did a retrospective cohort study of patients in the Premier Healthcare Database, an all-payer data repository that captures 20% of U.S. hospitalizations. We included all female inpatients aged 15 to 45 years hospitalized from April to November 2020 with COVID-19. A patient was defined as pregnant if the encounter included any pregnancy-related diagnosis. This study did not include personally identifiable information and was exempted from review by the institutional review board of the University of Maryland, Baltimore.

To exclude asymptomatic patients with COVID-19 diagnoses due to positive results on screening tests, we used only patients with a viral pneumonia diagnosis. We then did sensitivity analyses using subgroups of patients with an intensive care unit admission or mechanical ventilation.

Analyses were done using SAS, version 9.4 (SAS Institute). The cohort consisted of 1062 pregnant and 9815 nonpregnant patients hospitalized with COVID-19 and viral pneumonia. Pregnant patients were younger and more likely to have public insurance than nonpregnant patients (2) Pregnant patients were also less likely to have most comorbid conditions, including hypertension, chronic pulmonary disease, diabetes, and obesity.
In-hospital death occurred in 0.8% \( (n = 9) \) of pregnant patients and 3.5% \( (n = 340) \) of nonpregnant patients hospitalized with COVID-19 and viral pneumonia. Median time from admission to death was 18 days (interquartile range, 6 to 28 days) for pregnant patients and 12 days (interquartile range, 5 to 23 days) for nonpregnant patients. Among the subgroup of patients admitted to an intensive care unit, in-hospital mortality was 3.5% \( (9 \text{ of } 255) \) in pregnant patients and 14.9% \( (283 \text{ of } 1898) \) in nonpregnant patients. Among those who received mechanical ventilation, in-hospital death occurred in 8.6% \( (9 \text{ of } 105) \) of pregnant patients and 31.4% \( (294 \text{ of } 937) \) of nonpregnant patients.

Their ages ranged from 23 to 44 years. Eight were non-Hispanic Black or Hispanic. All died between April and July. Six were obese, and 7 had at least 1 comorbid condition. Gestational ages ranged from 23 to 39 weeks, and 7 of 9 deliveries were live births.

Discussion: Overall and within multiple subgroups, we found a substantially lower rate of in-hospital mortality in pregnant patients than nonpregnant patients hospitalized with COVID-19 and viral pneumonia. The rates found in this study are consistent with results of multiple other studies \( (3, 4) \). A cohort study including all symptomatic patients with COVID-19 aged 20 to 39 years hospitalized throughout the United Kingdom reported mortality of 0.8% in pregnant and 3.1% in nonpregnant persons \( (3) \).

Our study suggests lower mortality among pregnant patients than was initially reported. Using data collected from a voluntary reporting registry, the U.S. Centers for Disease Control and Prevention observed a mortality rate of 0.15% among pregnant and 0.12% among nonpregnant patients, including both hospitalized and nonhospitalized patients \( (1) \). That study was limited in that pregnancy status was available for only 36% of patients, creating potential for case ascertainment bias \( (1) \).

A strength of our study is the use of a large database including patient discharge data from 853 hospitals. It is hospital-based, providing a clearly defined population without the biases of registry-based studies. However, some amount of collider bias is expected because both severity of disease and pregnancy affect the likelihood of hospitalization.

Other limitations include the small number of deaths, with resultant lack of adjustment for confounding. Results cannot be extrapolated to patients who are not hospitalized. Laboratory test results were unavailable, but prior research showed a strong correlation between COVID-19 diagnosis and laboratory-confirmed SARS-CoV-2 infection \( (5) \).

In this large, geographically diverse cohort of reproductive-aged patients hospitalized with COVID-19, we found that in-hospital mortality was low in pregnant patients.

**9. Risk Associated With Valvular Regurgitation During Pregnancy**

**BACKGROUND**

Pregnancies in women with regurgitant valve lesions are generally considered low risk, but this has not been well studied.

**OBJECTIVES**
This study determined the frequency of adverse cardiac events (CEs) in pregnant women with moderate or severe regurgitant valve lesions.

METHODS

Maternal and fetal outcomes in women with moderate or severe chronic valve regurgitation enrolled in a prospective multicenter study on pregnancy outcomes were examined. Adverse CEs included heart failure, sustained arrhythmias, cardiac arrest, or death. A multivariate logistic regression model was used to identify determinants of CEs in women at the highest risk.

RESULTS

Outcomes of 430 pregnancies in women with moderate or severe regurgitant lesions were examined: 145 with mitral regurgitation (MR), 101 with pulmonary regurgitation (PR), 71 with multivalve disease, 73 with tricuspid regurgitation (TR), and 40 with aortic regurgitation (AR). Most women had associated congenital or acquired heart disease. Adverse CEs occurred in 13% of pregnancies: 27% of pregnancies with multivalve disease; 15% with MR; 15% with TR; 5% with AR; and 3% with PR. Maternal mortality was rare. In women with MR, TR, or multivalve disease \( n = 289 \), left ventricular systolic dysfunction \( p = 0.001 \), pulmonary hypertension \( p = 0.005 \), and cardiac events before pregnancy \( p < 0.001 \) were important determinants of CEs during pregnancy.

CONCLUSIONS

Women with AR and PR are at low risk for cardiac complications during pregnancy. While many women with MR, TR, and multivalve regurgitation do well during pregnancy, additional clinical variables help stratify those at highest risk. This new information will enhance the quality and precision of preconception counseling and pregnancy planning

10. Increasing Participation of Women in Cardiovascular Trials: JACC Council Perspectives

Abstract

Although some progress has been made in the last 3 decades to increase the number of women in clinical cardiology trials, review of recent cardiovascular literature demonstrates that women and underrepresented minority women are still underrepresented in most clinical cardiology trials. This is especially notable in trials of patients with coronary artery disease, heart failure with reduced ejection fraction, and arrhythmia studies, especially those involving devices and procedures. Despite the call from National Institutes of Health, Food and Drug Administration, Institute of Medicine, and various professional societies, the gap remains. This paper seeks to identify the barriers for low enrollment and retention from patient, clinician, research team, study design, and system perspectives, and offers recommendations to improve recruitment and retention in the current era.
Highlights

• Women, especially members of ethnic and racial minorities, are underrepresented in the leadership and enrolled cohorts of CVD clinical trials.

• Differential care, ageism, logistical barriers, lack of diversity in leadership, and systemic societal factors contribute to the underrepresentation of women in clinical trials.

• Increasing sex and racial diversity among trial leadership and site investigators, innovative approaches to participant recruitment, broader distribution of site locations, remote monitoring, and other measures could be used to narrow the sex gap in clinical CVD trials.

11. Sex Differences in Outcomes After CABG
Study Questions:

What are the sex differences in outcomes after coronary artery bypass grafting (CABG)?

Methods:

The investigators undertook a systematic review and pooled analysis of high-quality individual patient data from large CABG trials to compare the adjusted outcomes of women and men. The primary outcome was a composite of all-cause mortality, myocardial infarction (MI), stroke, and repeat revascularization (major adverse cardiac and cerebrovascular events [MACCE]). The secondary outcome was all-cause mortality. The effect of sex on the primary endpoint was calculated using a two-stage approach pooling β coefficients and relative standard error obtained from individual study multivariable Cox regression models.

Results:

Four trials involving 13,193 patients (10,479 males; 2,714 females) were included. Over 5 years of follow-up, women had a significantly higher risk of MACCE (adjusted hazard ratio [aHR], 1.12; 95% confidence interval [CI], 1.04-1.21; p = 0.004) but similar mortality (aHR, 1.03; 95% CI, 0.94-1.14; p = 0.51) compared to men. Women had higher incidence of MI (aHR, 1.30; 95% CI, 1.11-1.52) and repeat revascularization (aHR, 1.22; 95% CI, 1.04-1.43) but not stroke (aHR, 1.17; 95% CI, 0.90-1.52). The difference in MACCE between sexes was not significant in patients aged 75 years and older. The use of off-pump surgery and multiple arterial grafting did not modify the difference between sexes.

Conclusions:

The authors concluded that women have worse outcomes than men in the first 5 years after CABG.

Perspective:

This study reports that after CABG, women have higher adjusted incidence of adverse cardiac and cerebrovascular events, but similar mortality compared to men. The higher incidence of MACCE is mostly driven by a higher rate of MI and repeat revascularization. Of note, the difference in outcomes between the sexes is not evident after 75 years of age and is significantly affected by preoperative left ventricular ejection fraction (LVEF), but not by variations in the surgical technique used. Women have a higher risk of perioperative MI possibly related to technical factors and may be one of the reasons for the difference in mid-term outcomes. Additional studies focused on improving the outcome of women (especially younger women) undergoing CABG are indicated.

12. Mammographic Features and Cardiometabolic Disease

Study Questions:

What is the association of microcalcifications and other mammographic features with cardiometabolic disease risk and mortality?

Methods:
The investigators included 57,867 women from a prospective mammographic screening cohort in Sweden (KARMA) and 49,583 sisters. Cardiometabolic disease diagnoses and mortality and medication were extracted by linkage to Swedish population registries with virtually no missing data. The authors used logistic regression for the phenome-wide association study (PheWAS).

Results:

In the cardiometabolic PheWAS, the investigators found that a higher number of microcalcifications were associated with increased risk for multiple cardiometabolic diseases, particularly in women with pre-existing cardiometabolic diseases. In contrast, dense breasts were associated with a lower incidence of cardiometabolic diseases. Importantly, they observed similar associations in sisters of KARMA women, indicating a potential genetic overlap between mammographic features and cardiometabolic traits. Finally, they observed that the presence of microcalcifications was associated with increased cardiometabolic mortality in women with pre-existing cardiometabolic diseases (hazard ratio, 1.79; 95% confidence interval, 1.24-2.58; p = 0.002), while they did not find such effects in women without cardiometabolic diseases.

Conclusions:

The authors concluded that mammographic features are associated with cardiometabolic risk and mortality.

Perspective:

This study reports that a higher number of microcalcifications resulted in an increased occurrence of cardiometabolic diseases in participants and their sisters as well as in a higher cardiometabolic mortality in women with pre-existing cardiometabolic diseases. In contrast, women with high dense breasts as well as their sisters were less likely to be diagnosed with cardiometabolic diseases. Of note, a family history of breast cancer and a breast cancer-specific genetic risk score were generally associated with lower risk for cardiometabolic diseases. These data suggest that automated quantification of microcalcifications and breast density could be useful at no additional cost or radiation to improve cardiometabolic risk projection in women undergoing mammography.

13. LAAO Registry Study Shows Women at Higher Risk of Adverse Events After LAAO Procedure

Women may have a significantly higher risk of in-hospital adverse events following left atrial appendage occlusion (LAAO), according to a study published Aug. 11 in JAMA Cardiology.

Douglas Darden, MD, et al., used data from ACC’s LAAO Registry to look at sex differences in baseline characteristics among patients undergoing LAAO with the WATCHMAN device and in-hospital outcomes. The study’s primary outcomes were aborted or canceled procedure, major adverse event, any adverse event, a hospital stay longer than one day and death.

The study cohort consisted of 49,357 patients with an average age of 76.1 years, 20,388 (41.3%) of whom were women and 28,969 (58.7%) of whom were men. Men were more likely to be older and had a higher prevalence of paroxysmal atrial fibrillation, prior stroke and uncontrolled hypertension, but had a lower prevalence of congestive heart failure, diabetes and coronary artery disease.
The results show no differences in aborted or canceled procedures between women and men (3% vs. 2.9%). Women were more likely than men to experience a major adverse event (4.1% vs. 2%) or any adverse event (6.3% for women vs. 3.9% for men). Women also were more likely than men to require a hospital stay longer than one day (16% for women vs. 11.6% for men). In addition, although death was rare, it was more common among women than men (0.3% vs. 0.1%).

According to the researchers, women undergoing LAAO had a twofold higher risk of a major adverse event and a greater likelihood of experiencing any in-hospital event. They note that women comprise a larger proportion of patients receiving LAAO implants in real-world practice than in clinical trials, noting that the study’s findings underscore the need to “continue to advocate for increased participation of women in clinical trials to better inform clinical decision-making and adequately delineate sex-based safety and efficacy outcomes.” They conclude that additional research is needed to “identify the reasons for sex-based differences in outcomes and the strategies to reduce the risk of adverse events among women [undergoing LAAO].”

14. **Maternal Cardiovascular Health in Pregnancy Tied to Offspring Cardiovascular Health**

Better maternal cardiovascular health (CVH) at 28 weeks of gestation is significantly associated with better offspring CVH at ages 10 to 14 years, according to a study published in the Feb. 16 issue of the *Journal of the American Medical Association*.

Amanda M. Perak, M.D., from the Northwestern University Feinberg School of Medicine in Chicago, and colleagues used data from the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study (July 2000 to April 2006) and HAPO Follow-Up Study (February 2013 to December 2016) to examine associations between maternal gestational CVH (at 28 weeks of gestation) and offspring CVH (measured at ages 10 to 14 years). The analysis included 2,302 dyads.

The researchers found that 32.8 percent of pregnant mothers had all ideal metrics, while 6 percent had two or more poor metrics. The distribution of CVH categories among offspring varied by maternal CVH category. In an adjusted analysis, poorer maternal CVH categories were associated with higher relative risks for offspring to have one poor and two or more poor metrics versus all ideal maternal and offspring metrics. When further adjusting for an extended set of birth factors (e.g., preeclampsia), the significant associations remained (relative risk for association between two or more poor maternal metrics and two or more poor offspring metrics, 6.23).

"Knowledge of maternal gestational CVH level may have clinical utility to identify newborns at higher risk for poor CVH by early adolescence, even beyond other measures available at birth," the authors write.

15. **Pregnancy, Postpartum Care, and COVID-19 Vaccination in 2021**
Pregnancy is often thought to be a joyous and celebratory time; however, for women experiencing pregnancy during the COVID-19 pandemic there is often a sense of fear and stress about the unknowns surrounding the virus. Fears are plentiful and questions are often asked; how does the virus affect my pregnancy, does pregnancy increase my risks of getting sick, is the vaccine safe? As highlighted in both of these reports,1,2 pregnant women have experienced a disproportionate burden of morbidity and mortality from COVID-19 compared with their reproductive-aged peers. Despite the maternal concern of COVID-19, there are reassuring data that neonatal risk is quite low, with transplacental viral transmission even more seldom seen. Vaccinations in pregnancy are quite common; Tdap, influenza, and RhoGAM are components of routine prenatal care; however, the exclusion of pregnant women in COVID-19 vaccination trials has opened the door for safety and efficacy questions during pregnancy. To address this, the American College of Obstetricians and Gynecologists (ACOG), the Society for Maternal-Fetal Medicine (SMFM), and the Centers for Disease Control and Prevention (CDC) have each supported that the currently available vaccines (Pfizer-BioNTech and Moderna) be made accessible to pregnant women, acknowledging a conversation with their clinicians may be beneficial. ACOG and SMFM go even further in their recommendations for vaccination during lactation, as the theoretical risks do not outweigh the potential benefits.

Collectively, these two JAMA publications provide the rationale for encouraging pregnant women to consider vaccination during pregnancy and highlight the biology for explaining its safety both during pregnancy and lactation.

16. Furosemide for Accelerated Recovery of BP Postpartum in Women With a Hypertensive Disorder of Pregnancy

Persistent postpartum hypertension is a significant cause of maternal morbidity. Our objective was to study the effect of furosemide on postpartum blood pressure recovery in women with hypertensive disorders of pregnancy. We performed a randomized, double-blind, placebo-controlled trial of a 5-day course of 20 mg oral furosemide versus placebo in women with gestational hypertension and preeclampsia with/without severe features from June 2018 to October 2019. Primary outcomes were persistent hypertension at 7 days postpartum (using generalized linear models to calculate adjusted relative risk) and days to resolution of hypertension (Kaplan-Meier curves), stratified by severe/nonsevere hypertensive disease. Secondary outcomes included readmissions and need for additional hypertensive medication. We randomized 384 women (192 per group). Baseline characteristics were similar except cesarean delivery rate was higher in the furosemide group (29% versus 20%; P=0.04). In women randomized to furosemide, there was a 60% reduction in the prevalence of persistently elevated blood pressure at 7 days when controlling for cesarean (adjusted relative risk, 0.40 [95% CI, 0.20-0.81]). The magnitude of reduction was greater in women with nonsevere disease (adjusted relative risk, 0.26 [95% CI, 0.10-0.67]). Number of days to blood pressure resolution was significantly shorter among women with nonsevere disease randomized to furosemide (8.5 versus 10.5; P=0.001). There were no significant differences in readmissions or need for additional antihypertensive medication postpartum between groups. In this double-blinded randomized trial, a short course of postpartum furosemide significantly improved blood pressure control in women with hypertensive disorders of pregnancy, mostly among women without severe disease.
17. Dance Class May Offer Health Benefits in Postmenopausal Women

A 16-week dance intervention is associated with improvements in lipid profiles, functional fitness, self-image, and self-esteem among postmenopausal women, according to a study published online July 19 in *Menopause*.

Giovana Rampazzo Teixeira, Ph.D., from São Paulo State University in Brazil, and colleagues assessed the impact of dance practice on body composition (body fat and lean mass), blood lipids, functional fitness, self-image, and self-esteem in postmenopausal women. The analysis included 36 postmenopausal women (mean age, 57 years) who danced three times per week for 90 minutes each day, with evaluation before and 16 weeks after initiation.

The researchers found that from baseline to 16 weeks, there were improvements noted in triglyceride, high-density lipoprotein cholesterol, and total cholesterol levels. Furthermore, the dance intervention was associated with improved coordination, agility, and aerobic capability. The classification of general function fitness index, which was considered regular at baseline, improved after 16 weeks of dance participation. The women also reported significantly improved self-esteem and self-image after the dance intervention.

"This study highlights the feasibility of a simple intervention, such as a dance class three times weekly, for improving not only fitness and metabolic profile but also self-image and self-esteem in postmenopausal women," Stephanie Faubion, M.D., medical director of the North American Menopause Society, said in a statement. "In addition to these benefits, women also probably enjoyed a sense of comradery from the shared experience of learning something new."

18. Association of Preterm Birth With Myocardial Fibrosis and Diastolic Dysfunction in Young Adulthood

BACKGROUND

Preterm birth affects about 10% of live births worldwide and is associated with cardiac alterations. Animal models of preterm birth suggest that left ventricular functional impairment may be due to an up-regulation of myocardial fibrosis.

OBJECTIVES

The aim of this study was to determine whether diffuse left ventricular fibrosis is evident in young adults born preterm.

METHODS

One hundred one normotensive young adults born preterm (n = 47, mean gestational age 32.8 ± 3.2 weeks) and term (n = 54) were included from YACHT (Young Adult Cardiovascular Health sTudy). Left ventricular structure and function were quantified by cardiovascular magnetic resonance and echocardiography. Intravenous administration of a gadolinium-based contrast agent during cardiovascular magnetic resonance was used to quantify focal myocardial fibrosis on the basis of late gadolinium enhancement and, in combination with T1 mapping, to quantify diffuse myocardial fibrosis on the basis of assessment of myocardial extracellular volume fraction.
RESULTS

Adults born preterm had smaller left ventricular end-diastolic and stroke volumes, with greater left ventricular mass and wall thickness (P < 0.001). In addition, longitudinal peak systolic strain and diastolic strain rate by both cardiovascular magnetic resonance and echocardiography, and E/A ratio measured by echocardiography, were lower in preterm-born compared to term-born adults (P < 0.05). Extracellular volume fraction was greater in preterm-born compared with term-born adults (27.81% ± 1.69% vs 25.48% ± 1.41%; P < 0.001) and was a significant mediator in the relationship between gestational age and both longitudinal peak diastolic strain rate and E/A ratio.

CONCLUSIONS

Preterm-born young adults have greater extracellular volume fraction in the left ventricle that is inversely related with gestational age and may underlie their diastolic functional impairments.