News in May 2023

1. Pregnancy outcomes in women with heart disease: the Madras Medical College Pregnancy And Cardiac (M-PAC) Registry from India

Aims

To evaluate the feto-maternal outcome, identify the adverse outcome predictors and test the applicability of modified WHO (mWHO) classification in pregnant women with heart disease (PWWHD) from Tamil Nadu, India.

Methods and results

One thousand and five pregnant women (mean age: 26.04 ± 4.2) with 1029 consecutive pregnancies were prospectively enrolled from July 2016 to December 2019 in the Madras medical college pregnancy and cardiac (M-PAC) registry. Majority (60.5%; 623/1029) had heart disease (HD) diagnosed for the first time during pregnancy. Rheumatic HD (42%; 433/1029) was most common. One third (34.2%; 352/1029) had pulmonary hypertension (PH). Maternal mortality and composite maternal cardiac events (MCEs) were the primary outcomes. Secondary outcomes were foetal loss and composite adverse foetal events (AFEs). MCEs occurred in 15.2% (156/1029; 95% CI: 13.0–17.5) pregnancies. Heart failure was the most common MCE (66.0%; 103/156; 95% CI: 58.0–73.4). Maternal mortality was 1.9% (20/1029; 95% CI: 1.1–2.8), with highest rates in patients with prosthetic heart valves (PHVs) (8.6%; 6/70). Left ventricular systolic dysfunction (LVSD), PHVs, severe mitral stenosis, PH and current pregnancy diagnosis of HD were independent predictors of MCE. The c-statistic of mWHO classification for predicting MCE and maternal death were 0.794 (95% CI: 0.763–0.826) and 0.796 (95% CI: 0.732–0.860). 91.2% (938/1029; 95% CI: 89.392.8) of pregnancies resulted in live births. 33.7% (347/1029; 95% CI: 30.8–36.7) of pregnancies reported AFEs.

Conclusion

Maternal mortality is high in PWWHD from India. Highest death rates occurred in women with PHVs, PH and LVSD. The mWHO classification for risk stratification may require further adaptation and validation in India.

2. Pregnancy outcomes in women with heart disease: how to improve?

Maternal cardiac disease complicates between 1% and 4% of all pregnancies and is an increasingly important cause of maternal mortality; indeed, it is already the main cause of maternal mortality in developed countries.1 In high-income countries (HICs), the main causes of cardiac death changed from rheumatic heart disease in the 1950s and 1960s to congenital heart disease in the 1970s and 1980s, and—today—to cardiomyopathy, acute coronary events, aortic dissection, valvular heart disease, and arrhythmias. In low-income countries (LICs), that journey is just beginning, with multiple reports identifying rheumatic heart disease as the most important cardiac cause of maternal mortality. However, the true extent of the problem in LICs has been difficult to define not least because maternal mortality rates have been so high. Now, as maternal mortality rates start to decline, the importance of cardiac disease in LICs is becoming clearer.

In this issue of the European Heart Journal, Gnanaraj et al. present the data of the Madras medical college Pregnancy And Cardiac (M-PAC) Registry from India.2 This is the largest single-centre prospective registry of pregnant women with heart disease in a low- and-middle-income country (LMIC). A total of 1029 pregnancies were included of 1005 women with known or newly diagnosed heart disease, aortic disease, or pulmonary vascular disease. This is the first study that also included women with cardiac arrhythmias in an LMIC. Data from registries of pregnant women with heart disease have been very helpful in distinguishing between women with a low or high risk of adverse cardiac events during pregnancy as well as adverse foetal and neonatal outcomes).3–5 The

CARPREG (Cardiac disease in Pregnancy) study also enrolled pregnant women with isolated cardiac arrhythmias, but only from a developed country.5 If we compare the type of underlying cardiac diagnosis from women in the M-PAC cohort with the other registries on pregnancy in women with cardiac disease, there are several differences. Most of the women in the M-PAC cohort had acquired heart disease (66%), whereas congenital heart disease (CHD) was the most common diagnosis in the ROPAC (Registry of Pregnancy And Cardiac disease) and CARPREG II-cohort (57% and 64%, respectively).4,5 The ZAHARA [Zwangerschap bij Aangeboren HARTAfwijking (Pregnancy in Women with Congenital Heart Disease)] study only enrolled women with CHD. Of the women with CHD in the M-PAC cohort (33.6%), fewer had complex CHD than expected. Gnanaraj et al. suggested that this may be because of the reduced survival in this group of patients due to the lack of access to corrective surgery in LMICs. While this is hard to read, it is probably true. The similarities and differences between registry data are highlighted. One striking similarity is in the high rates of complications in women with metallic prosthetic heart valves, particularly valve thrombosis, with the key challenge being optimal anticoagulation both for the mother and for her baby. The failure, in both high- and low-income settings, to safely manage pregnancy in women with a metallic prosthetic heart valves speaks to the need to devise a different approach, be it optimizing anticoagulation regimens or improving the functional life span of bioprosthetic valves, making them a viable alternative to metallic valves and obviating the need for lifelong anticoagulation.

In the current ESC Guidelines for the management of cardiovascular disease during pregnancy, the modified World Health Organization (mWHO) classification advises distinguishing between women with a low, moderate, or high risk for maternal morbidity or mortality.1 In contrast to the mWHO classification distribution of the women enrolled in ROPAC and CARPREG, a relatively high number of women in mWHO class III (18%) and mWHO class IV (19%) were included in the M-PAC cohort. Despite this difference, the maternal

cardiac event rate (15%) is similar to earlier observations.[4,5] In addition, a third of the M-PAC cohort had pulmonary hypertension. The reported rate of heart failure and/or maternal mortality in the literature is 40% in this patient group,[3] so we would have expected a higher maternal cardiac event rate. Although women belonging to mWHO III or IV have a higher predicted maternal cardiac event rate, women in mWHO I, II, or II–III were only followed up through pregnancy and for 1 week post-partum, and therefore the reported rate will in fact be an underestimation. Indeed, many events do occur after delivery. Maternal mortality, on the other hand, occurred in 2%, which is 30-fold higher compared with pregnant women without cardiac disease in the same state during the same period and higher than observed in registries from predominantly HICs.[4,5] This calls for specific programmes to improve pregnancy outcomes, such as implementing pregnancy heart teams and the increased availability of echocardiography, as described by Gnanaraj et al.[2]

One of the most remarkable findings in the M-PAC cohort is the timing of diagnosis, with 60% diagnosed during the current (50%) or an earlier pregnancy (10%). Even women with severe left heart obstruction and cyanotic heart diseases were diagnosed for the first time during pregnancy, which reflects the limited access to cardiac services. Indeed, it is reassuring that, based on preliminary data shared from this study, the Government of Tamil Nadu State established pregnancy and heart disease teams with echocardiography support in all government medical colleges. These changes will improve access to care and hopefully encourage other governments to introduce similar pregnancy heart teams.

As the authors state, data on pregnancy outcomes in women with heart disease living in an LMIC are scarce, which makes this large single-centre study an important addition to the already available registry-based data on pregnancy outcomes in women with heart disease. While the ZAHARA and CARPREG cohorts only included pregnant women in HICs, ROPAC is a large registry

including almost 5800 pregnancies of women with structural heart disease of which 40% were from LMICs.4 Van Hagen et al. investigated the influence of socioeconomic factors on pregnancy outcomes in women with heart disease, based on data from 2924 ROPAC pregnancies from 89 centres.6 They found that the large differences in pregnancy outcomes between individual countries were mainly due to variations in the maternal condition. In a few studies based on ROPAC data, pregnancy outcomes were found to be similar between women living in a HIC and an LMIC.4,7,8 This may be because the care provided in the LMIC centres that participated in the ROPAC was not representative. On the other hand, whether the M-PAC cohort is also representative can be questioned since all women received medical care in a tertiary centre. Unfortunately, it is unlikely that every woman with cardiac disease in an LMIC will receive the same level of care.

In the study of Gnanaraj et al., no data were presented on the presence of chronic hypertension and the occurrence of hypertensive disorders of pregnancy, but this subject is certainly worth considering here. A recently published paper on hypertensive disorders of pregnant women with heart disease showed that adverse outcomes were increased in women with hypertensive disorders, and maternal mortality was strikingly higher in women with pre-eclampsia. The outcomes were also compared between LMICs and HICs, which showed a higher rate of superimposed pre-eclampsia (pre-eclampsia following chronic hypertension) in LMICs as well as a remarkable higher rate of heart failure during pregnancy (31% and 10%, respectively). It is important to consider the occurrence of pre-eclampsia when reporting pregnancy outcomes in women with heart disease.

In our opinion, it is likely that differences in pregnancy outcomes described in registries are due to variations in the nature and severity of the underlying heart disease, the access to medical care, and the underlying socio-cultural environment. The study of Gnanaraj et al. highlights the need for better access

to cardiac care in LMICs for women of childbearing age. Only if underlying heart disease is identified before pregnancy can the clinical state be optimized, and accurate pre-conception counselling given. In the absence of antenatal diagnosis, it is essential that pregnant women with heart disease have access to advanced medical care in the form of pregnancy heart teams as described by Gnanaraj et al. in their timely and important paper.

3. Younger Women With AMI Have More Adverse Outcomes After Discharge

Compared with men, younger women with acute myocardial infarction (AMI) have more adverse outcomes in the year following discharge, according to a study published in the May 9 issue of the Journal of the American College of Cardiology.

Mitsuaki Sawano, M.D., Ph.D., from the Yale School of Medicine in New Haven, Connecticut, and colleagues examined sex differences in causes and timing of one-year outcomes after AMI in individuals aged 18 to 55 years using data from the Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients study. Sex differences in all-cause and cause-specific hospitalizations were compared by calculating incidence rates (IRs) per 1,000 person-years and IR ratios. The sex differences were evaluated by calculating subdistribution hazard ratios accounting for deaths.

The researchers found that at least one hospitalization occurred among 905 of the 2,979 patients (30.4 percent) in the year after discharge. The leading causes of hospitalization were coronary-related (IR, 171.8 versus 117.8 among women versus men) and noncardiac hospitalization (IR, 145.8 versus 69.6). A sex difference was also seen for coronary-related hospitalizations and noncardiac hospitalizations (subdistribution hazard ratios, 1.33 and 1.51, respectively).

"The analysis by Sawano et al adds to decades worth of literature clearly illustrating that young women with AMI experience more adverse outcomes than men," write the authors of an accompanying editorial. "The disparities are

evident. Now it is time to stop adding insult to infarct and to solve these persistent sex gaps in cardiovascular care."

4. Impact of Race and Ethnicity on CVD Risk Factors in Women

The American Heart Association has released a scientific statement that addresses the impact of race and ethnicity on cardiovascular disease (CVD) risk factors in women. The report calls for an expanded approach to risk factors and primary prevention strategies for CVD among women of underrepresented races and ethnicities.

The statement highlights the unequal distribution of CVD burden across racial and ethnic groups. Women from minority backgrounds — such as African American, Hispanic, and Native American women — have higher rates of traditional cardiovascular risk factors including hypertension, obesity, diabetes, and smoking than their White counterparts. These disparities are linked to social determinants of health such as structural racism, education, and access to healthcare. Psychosocial factors, such as depression and stress, along with nontraditional sex-specific risk factors, including pregnancy history, premature menopause, and inflammatory conditions, also disproportionately affect women from minority groups.

To reduce these disparities, the report recommends that cardiovascular risk assessment tools for women should consider both traditional and nontraditional sex-specific risk factors as well as social determinants of health. Culturally sensitive cardiovascular health and prevention strategies tailored to the specific needs of women from minority backgrounds are critical. These strategies include improving access to culturally tailored consultation and preventive services, education and awareness campaigns targeted to specific racial/ethnic groups, and addressing social and economic factors that contribute to poor health outcomes.

The report also highlights the need for inclusive research that considers women from diverse racial and ethnic backgrounds to improve our understanding of CVD risk factors and develop targeted interventions that address the unique needs of these populations. Incorporating sex-specific and race-specific data in clinical trials and studies is essential to inform the development of evidence-based interventions that can improve cardiovascular health outcomes for women from all backgrounds.

Overall, the American Heart Association's scientific statement is a critical step towards addressing the inequalities in cardiovascular risk factors and outcomes among women from diverse racial and ethnic backgrounds. It underscores the need for a comprehensive approach that addresses social determinants of health, promotes cultural sensitivity, and incorporates sex-specific and race-specific data in research and clinical practice. By implementing the recommendations outlined in this report, we can work towards reducing the burden of CVD in women from diverse racial and ethnic backgrounds and ultimately improve the health and well-being of all women.

5. Breast Cancer Deaths Lower With Statin Therapy, Taiwanese Data Hint

Statin use is linked to better survival in breast cancer, observational data from Taiwan suggest. Yet researchers only saw a difference for all-cause and cancer-related deaths, not CV death.

The results, from a propensity-score-matched analysis of more than 14,000 patients, were published recently in JAMA Network Open.

It’s well established that statins can “reduce blood cholesterol, mitigate atherosclerosis, and improve cardiovascular outcomes,” Wei-Ting Chang, MD (Chi-Mei Medical Center, Tainan, Taiwan), and colleagues note. The drug class also has drawn attention for its pleiotropic effects, most notably its ability to

reduce inflammation. In the cancer realm, it's been proposed that statins could be antiproliferative as well.

This isn't the first study to tie statin therapy to cancer survival, but "in contrast to Western patients with breast cancer, Asian patients are relatively younger at diagnosis, and a large proportion are premenopausal and have few cardiovascular risk factor," Chang et al explain.

Daniel Lenihan, MD (Saint Francis Healthcare System, Cape Girardeau, MO), immediate past president of the International CardioOncology Society, said that while the concept of statins possibly holding benefit in cancer isn't new, people outside the cardio-oncology space still "might sort of raise an eyebrow" at the idea.

It's "very plausible" that statins could be making this much of a dent in cancer-related death, Lenihan told TCTMD, citing a 2012 paper by Cleveland Clinic researchers that showed, retrospectively, that women with breast cancer treated with anthracycline-based chemotherapy had better heart failure-free survival if they were on statin therapy. Though more proof-of-concept than definitive, he added, "it was a very meaningful initial report."

That work has been followed by other studies with mixed results, but survival signals of better cancer outcomes also have been seen in other cancer types, like multiple myeloma, Lenihan said.

Then there's the added fact that the chemotherapy used to treat cancer can have the side effect of harming the heart. Here, too, it's been suggested statins could help.

In late 2022, the small, randomized PREVENT trial failed to show a cardioprotective effect of statins in breast cancer and lymphoma patients with no existing indication for statin therapy. On its heels in early 2023, however, came another small but randomized trial, STOP-CA, which suggested that

atorvastatin might protect against ventricular dysfunction in lymphoma patients receiving chemotherapy with anthracyclines.

Tomas G. Neilan, MD (Massachusetts General Hospital, Boston), principal investigator for STOP-CA, commenting on the current analysis for TCTMD, stressed that his perspective is that of a cardiologist. This study from Taiwan, by virtue of looking at cancer outcomes, is more tied to oncology, he noted.

With that caveat, “I think most of us would agree that there are no data to suggest that statins have an adverse impact on cancer outcomes, and there’s some nice plausibility that statins may be beneficial from a cancer-outcome perspective. But all the data that may suggest a beneficial role have been retrospective, observational” studies, with the few existing, small trials showing no effects, said Neilan.

W. Gregory Hundley, MD (Virginia Commonwealth University, Richmond), principal investigator of PREVENT, agreed the current report joins a long line of others supporting statins’ link to cancer survival. It appears “statins may amplify the effectiveness of cancer treatments,” Hundley commented to TCTMD. And there is no evidence of negative impact, in breast cancer at least, on survival from the initial disease or risk of recurrence, he added.

Cancer-Related Death but Not CV Death

Using the Taiwanese National Health Insurance Database and National Cancer Registry, Chang and colleagues identified 63,530 female patients with breast cancer between 2012 and 2017. Among them, 12.2% had been taking statins 6 months prior to their diagnosis.

There were no differences in cancer stage, cancer treatments, or socioeconomic status by status use. On the whole, the women on statins tended to be older (mean age 65 vs 54 years); had more coronary artery disease (17% vs 3%), hypertension (66% vs 19%), and diabetes (51% vs 7%); and were more likely to

be taking an ACE inhibitor/ARB (47% vs 10%) or antiplatelet therapy (21% vs 3%).

The researchers used propensity-score matching to account for imbalances in year of diagnosis, age, cancer stage, anticancer therapies, comorbidities, socioeconomic status, and use of cardiovascular drugs before enrollment, so that they were able to compare 7,451 statin users and 7,451 nonusers. In the matched analysis, 15.63% of patients died. The cancer-related death rate was 11.09%, as compared with a cardiovascular death rate of just 0.85%.

Statin use was associated with a lower risk of all-cause death (adjusted HR 0.83; 95% 0.77-0.91), a difference driven by cancer-related death (adjusted HR 0.83; 95% CI 0.75-0.92). There was no relationship between statin use and cardiovascular death.

Contrary to STOP-CA, there was no sign that statins were exerting a protective effect against chemotherapy-induced heart damage, with no significant differences seen between the statin and no-statin groups in the risks of heart failure, arterial events (acute MI and ischemic stroke), or venous events (pulmonary embolism and deep vein thrombosis).

Overall, “our findings provide evidence to support the use of statins in patients with breast cancer; however, randomized studies are necessary,” the researchers conclude.

As for why there was no reduction in CV death risk, Lenihan said this may be simply because these deaths are undercounted. “If you have a cancer and are being treated for cancer, they’re going to follow the cancer really closely. If someone dies for some other reason, they don’t really explore what the reason is,” he pointed out. The mean age of the women studied was also relatively young—mid-60s—when deaths from CVD would have been rare.

Neilan, for his part, observed that the two groups studied—statins and no statins—weren't equally matched from a cardiovascular perspective, which can be hard to fully adjust for, and that the event rates were "relatively low, so I would urge caution in the interpretation of that."

6. Sex Difference in Outcomes of Acute MI in Young Patients

Study Questions:

Do younger women (aged 18-55 years) have higher risk of cardiovascular and noncardiovascular hospitalizations in the year after acute myocardial infarction (AMI)?

Methods:

This analysis used data from the VIRGO (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients) study, which enrolled patients aged 18-55 years across 103 hospitals (2008–2012). Sex differences in all-cause and cause-specific hospitalizations were assessed. Differences in hospitalizations were compared with incidence rates (IRs) (IR per 1,000 person-years) and IR ratios with 95% confidence interval (CI), and sex differences were assessed using sub-distribution hazard ratios (SHRs) accounting for deaths.

Results:

Of 2,979 participants, 2,007 were women, 972 were men, mean age was 47.1 ± 6.2 years, 17.5% self-identified as non-Hispanic Black, and 70% as non-Hispanic White. Median duration of follow-up was 365 days. After AMI, 30.4% had at least one hospitalization in the following year. Most hospitalizations were related to coronary events (IR, 171.8; 95% CI, 153.6-192.2 among women vs. IR, 117.8; 95% CI, 97.3-142.6 among men). Noncardiac hospitalization rates were IR, 145.8; 95% CI, 129.2-164.5 among women vs. IR, 69.6; 95% CI, 54.5-88.9

among men. Women had higher rates of hospitalizations with the calculated SHR of 1.33 (95% CI, 1.04-1.70; p = 0.02) for coronary-related and 1.51 (95% CI, 1.13-2.07; p = 0.01) for noncardiac hospitalizations.

Conclusions:

In the year following AMI, the authors concluded that young women had higher rates of hospitalizations than young men, and the difference in noncardiac hospitalizations was most significant.

7. Sex Difference in Outcomes of Acute Myocardial Infarction in Young Patients

Background

Younger women experience worse health status than men after their index episode of acute myocardial infarction (AMI). However, whether women have a higher risk for cardiovascular and noncardiovascular hospitalizations in the year after discharge is unknown.

Objectives

The aim of this study was to determine sex differences in causes and timing of 1-year outcomes after AMI in people aged 18 to 55 years.

Methods

Data from the VIRGO (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients) study, which enrolled young patients with AMI across 103 U.S. hospitals, were used. Sex differences in all-cause and cause-specific hospitalizations were compared by calculating incidence rates ([IRs] per 1,000 person-years) and IR ratios with 95% CIs. We then performed sequential modeling to evaluate the sex difference by calculating subdistribution HRs (SHRs) accounting for deaths.

Results

Among 2,979 patients, at least 1 hospitalization occurred among 905 patients (30.4%) in the year after discharge. The leading causes of hospitalization were coronary related (IR: 171.8 [95% CI: 153.6-192.2] among women vs 117.8 [95% CI: 97.3-142.6] among men), followed by noncardiac hospitalization (IR: 145.8 [95% CI: 129.2-164.5] among women vs 69.6 [95% CI: 54.5-88.9] among men). Furthermore, a sex difference was present for coronary-related hospitalizations (SHR: 1.33; 95% CI: 1.04-1.70; P = 0.02) and noncardiac hospitalizations (SHR: 1.51; 95% CI: 1.13-2.07; P = 0.01).

Conclusions

Young women with AMI experience more adverse outcomes than men in the year after discharge. Coronary-related hospitalizations were most common, but noncardiac hospitalizations showed the most significant sex disparity.

8. Prognostic value of combined coronary CT angiography and myocardial perfusion imaging in women and men

Aims

Combined anatomical and functional imaging enables detection of non-obstructive and obstructive coronary artery disease (CAD) as well as myocardial ischaemia. We evaluated sex differences in disease profile and outcomes after combined computed tomography angiography (CTA) and positron emission tomography (PET) perfusion imaging in patients with suspected obstructive CAD.

Methods and results

We retrospectively evaluated 1948 patients (59% women) referred for coronary CTA due to suspected CAD during the years 2008–2016. Patients with a suspected obstructive lesion on coronary CTA (n = 657) underwent ^{15}O-water PET to assess stress myocardial blood flow (MBF). During a mean follow-up of 6.8 years, 182 adverse events (all-cause death, myocardial infarction, or

unstable angina) occurred. Women had more often normal coronary arteries (42% vs. 22%, P < 0.001) and less often abnormal stress MBF (9% vs. 28%, P < 0.001) than men. The annual adverse event rate was lower in women vs. men (1.2% vs. 1.7%, P = 0.02). Both in women and men, coronary calcification, non-obstructive CAD, and abnormal stress MBF were independent predictors of events. Abnormal stress MBF was associated with 5.0- and 5.6-fold adverse event rates in women and men, respectively. There was no interaction between sex and coronary calcification, non-obstructive CAD, or abnormal stress MBF in terms of predicting adverse events.

Conclusion

Among patients evaluated for chronic chest pain, women have a lower prevalence of ischaemic CAD and a lower rate of adverse events. Combined coronary CTA and PET myocardial perfusion imaging predict outcomes equally in women and men.

9. Preterm Birth, Large for Gestational Age Increase A-Fib Risk Up to Middle Age

Preterm birth and being large for gestational age (GA) at birth are associated with increased risks for atrial fibrillation (AF) up to middle age independently of familial factors, according to a study published online April 24 in JAMA Pediatrics.

Fen Yang, M.D., from the Karolinska Institutet in Stockholm, and colleagues investigated whether preterm birth, small for GA, or large for GA are associated with increased risks for AF later in life. The analysis included more than 8 million live, singleton births in Denmark from 1978 through 2016, in Sweden from 1973 through 2014, and in Finland from 1987 through 2014, with follow-up through 2016, 2021, and 2014, respectively, in the three countries.

The researchers found that being preterm and large for GA were each associated with increased AF risk in both the full population cohort (hazard ratios, 1.30 and

1.55, respectively) and the sibling analyses. The association between preterm birth and AF was stronger in childhood than in adulthood. For small for GA, children had an increased risk for AF in the first 18 years of life but not afterwards.

"Preterm births and large for GA births were associated with increased risks of AF up to middle age independently of familial confounding factors," the authors write. "Individuals born small for GA had an increased AF risk only during childhood."

10. Women More Likely to Return to Hospital 12 Months After Heart Attack, Study Concludes

Women with acute myocardial infarction (AMI) experience more adverse outcomes and are more likely to end up back in the hospital compared to men in the year following discharge, suggests a new study.

Led by Mitsuaki Sawano, MD, PhD, from the Yale School of Medicine in New Haven, Connecticut, the research team found that these women have persistently worse outcomes compared with men immediately and 1 year after discharge.

Further study results revealed that coronary-related hospitalizations were the most common cause of hospitalizations, but noncardiac hospitalizations show the greatest sex disparity among young patients after AMI.

“This all begins with public awareness towards preventing heart attacks and screening programs to detect traditional risk factors before a patient has a heart attack. Many people think heart attacks only occur in middle-aged or older men, which is not true,” said Sawano in a news release announcing the study results. ““People need to be aware that heart attacks occur in young women as well and they can present with atypical symptoms. “After experiencing a heart attack, young women will be more likely to need a 360-level approach.”

The study was published Monday online and in the May 9 issue of the Journal of the American College of Cardiology.

Data from the VIRGO observational study

Researchers used data from the Prospective, Multicenter Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients (VIRGO) observational study.

The study included young women and men with AMI aged 18 to 55 years across 103 hospitals in the U.S. from August 2008 to January 2012 using a strict 2:1 enrollment ratio of women to men.

For the present study, 2,985 U.S. patients (n=2,009 women, n=976 men) hospitalized for AMI were included. After excluding in-hospital deaths (n=6), this resulted in a cohort of 2,979 participants.

The primary outcomes of the study were all-cause and cause-specific acute events requiring hospitalization, defined as any hospital or observation stay >24 hours within 1 year of discharge.

Results revealed that among the patients, at least one hospitalization occurred among 905 patients (30.4%) in the year after discharge.

The leading causes of hospitalization were coronary-related (incidence rate [IR]: 171.8; 95% confidence interval [CI]: 153.6-192.2) among women compared to an IR of 117.8 (95% CI: 97.3-142.6) among men.

This was followed by noncardiac hospitalization (IR: 145.8; 95% CI: 129.2-164.5) among women compared to men (IR: 69.6; 95% CI: 54.5-88.9).

Sex disparity for hospitalizations

Further findings revealed a sex difference was present for coronary-related hospitalizations (subdistribution hazard ratio [SHR]: 1.33; 95% CI: 1.04-1.70; P=0.02) and noncardiac hospitalizations (SHR: 1.51; 95% CI: 1.13-2.07; P=0.01).

"We think young women who present with heart attacks tend to have a greater burden of cardiovascular risk factors compared with men. In general, young, premenopausal women are protected by their own estrogen hormone to have lower incidence of heart attacks.," Sawano said in the news release. "Thus, to overcome this physiological protection, we think a higher accumulation of risk factors, such as obesity, high blood pressure, high cholesterol, cigarette smoking, etc., is needed to cause a 'breakthrough' effect."

Sawano suggested that for women, this greater number of risk factors is likely to cause difficulty controlling them after discharge.

Worse control of risk factors is associated with worse outcomes, including recurrence of heart attacks, chest pain due to the heart, as well as other atherosclerotic diseases like stroke, he commented.

MI-CAD and MINOCA populations

On the sex disparity for non-cardiac hospitalizations compared to all other hospitalizations, Sawano said: "We think that the accumulation of risk factors seen in the myocardial infarction with obstructive coronary artery disease (MI-CAD) population is associated with the high incidence of hospitalization one year after heart attack. We must emphasize, however, that does not mean that patients with myocardial infarction with non-obstructive coronary arteries (MINOCA) are 'low risk.' We know from recent studies that MINOCA is not a benign disease compared with similarly aged women and these cases warrant further evaluation to understand the underlying mechanism and treatment of certain conditions."

In an accompanying editorial, Martha Gulati, MD, of the Cedars-Sinai Heart Institute in Los Angeles, and colleagues, wrote that the study highlights the "increased rate of cardiovascular and non-cardiovascular rehospitalization in women as compared to men, with a clear association between psychosocial and demographic factors."

"Yet the root cause of sex differences in psychosocial factors and rates of comorbid conditions remains elusive, the editorialists continued. "Why are more women than men identified as low-income in this cohort? Why does this cohort demonstrate a nearly two-fold greater prevalence of depression in women as compared to men? As a cardiovascular community, by continuing to ask why perhaps we can arrive at 'what next.,'"

Study limitations

The expert commenters identified details of non-cardiac hospitalizations that were not collected as a study limitation.

Other limitations include the results that may not be generalizable to population groups underrepresented in the study cohort.

11. Impact of Race and Ethnicity on CVD Risk Factors in Women

The American Heart Association has released a scientific statement that addresses the impact of race and ethnicity on cardiovascular disease (CVD) risk factors in women. The report calls for an expanded approach to risk factors and primary prevention strategies for CVD among women of underrepresented races and ethnicities.

The statement highlights the unequal distribution of CVD burden across racial and ethnic groups. Women from minority backgrounds — such as African American, Hispanic, and Native American women — have higher rates of traditional cardiovascular risk factors including hypertension, obesity, diabetes,

and smoking than their White counterparts. These disparities are linked to social determinants of health such as structural racism, education, and access to healthcare. Psychosocial factors, such as depression and stress, along with nontraditional sex-specific risk factors, including pregnancy history, premature menopause, and inflammatory conditions, also disproportionately affect women from minority groups.

To reduce these disparities, the report recommends that cardiovascular risk assessment tools for women should consider both traditional and nontraditional sex-specific risk factors as well as social determinants of health. Culturally sensitive cardiovascular health and prevention strategies tailored to the specific needs of women from minority backgrounds are critical. These strategies include improving access to culturally tailored consultation and preventive services, education and awareness campaigns targeted to specific racial/ethnic groups, and addressing social and economic factors that contribute to poor health outcomes.

The report also highlights the need for inclusive research that considers women from diverse racial and ethnic backgrounds to improve our understanding of CVD risk factors and develop targeted interventions that address the unique needs of these populations. Incorporating sex-specific and race-specific data in clinical trials and studies is essential to inform the development of evidence-based interventions that can improve cardiovascular health outcomes for women from all backgrounds.

Overall, the American Heart Association's scientific statement is a critical step towards addressing the inequalities in cardiovascular risk factors and outcomes among women from diverse racial and ethnic backgrounds. It underscores the need for a comprehensive approach that addresses social determinants of health, promotes cultural sensitivity, and incorporates sex-specific and race-specific data in research and clinical practice. By implementing the recommendations outlined in this report, we can work towards reducing the burden of CVD in

women from diverse racial and ethnic backgrounds and ultimately improve the health and well-being of all women.

12. Maternal Third Dose of the BNT162b2 mRNA Vaccine and the Risk of Infant COVID-19 Hospitalization

Infants are at a higher risk of Coronavirus Disease 2019 (COVID-19)-related hospitalizations compared to older children. In this study, we investigated the effect of the recommended third maternal dose of BNT162b2 COVID-19 vaccine during pregnancy on rates of infant COVID-19-related hospitalizations. We conducted a nationwide cohort study of all live-born infants delivered in Israel between 24 August 2021 and 15 March 2022 to estimate the effectiveness of the third booster dose versus the second dose against infant COVID-19-related hospitalizations. Data were analyzed for the overall study period, and the Delta and Omicron periods were analyzed separately. Cox proportional hazard regression models estimated hazard ratios and 95% confidence intervals (CIs) for infant hospitalizations according to maternal vaccination status at delivery. Among 48,868 live-born infants included in the analysis, rates of COVID-19 hospitalization were 0.4%, 0.6% and 0.7% in the third-dose, second-dose and unvaccinated groups, respectively. Compared to the second dose, the third dose was associated with reduced infant hospitalization with estimated effectiveness of 53% (95% CI: 36-65%). Greater protection was associated with a shorter interval between vaccination and delivery. A third maternal dose during pregnancy reduced the risk of infant hospitalization for COVID-19 during the first 4 months of life, supporting clinical and public health guidance for maternal booster vaccination to prevent infant COVID-19 hospitalization.

13. Seven 'Simple' Cardiovascular Health Measures Linked to Reduced Dementia Risk in Women

Women with better indicators of cardiovascular health at midlife saw reduced risk of later dementia, according to results of a study that was released early, ahead of its scheduled presentation at the annual meeting of the American Academy of Neurology.

Epidemiologist Pamela M. Rist, ScD, assistant professor of medicine at Harvard Medical School and associate epidemiologist at Brigham and Women's Hospital, both in Boston, and colleagues, used data from 13,720 women whose mean age was 54 when they enrolled in the Harvard-based Women's Health Study between 1992 and 1995. Subjects in that study were followed up in 2004.

Dr. Rist and colleagues used the Harvard data to discern how well closely women conformed, during the initial study period and at 10-year follow up, to what the American Heart Association describes as "Life's Simple 7," a list of behavioral and biometric measures that indicate and predict cardiovascular health. The measures include four modifiable behaviors – not smoking, healthy weight, a healthy diet, and being physically active – along with three biometric measures of blood pressure, cholesterol, and blood sugar (AHA has since added a sleep component).

Researchers assigned women one point for each desirable habit or measure on the list, with subjects' average Simple 7 score at baseline 4.3, and 4.2 at 10 years' follow-up.

The investigators then looked at Medicare data for the study subjects from 2011 to 2018 – approximately 20 years after their enrollment in the Women's Health Study – seeking dementia diagnoses. Some 13% of the study cohort (n = 1,771) had gone on to develop dementia.

Each point on the Simple 7 score at baseline corresponded with a 6% reduction in later dementia risk, Dr. Rist and her colleagues found after adjusting for variables including age and education (odds ratio per one unit change in score,

0.94; 95% CI, 0.90-0.98). This effect was similar for Simple 7 scores measured at 10 years of follow-up (OR, 0.95; 95% CI, 0.91-1.00).

"It can be empowering for people to know that by taking steps such as exercising for a half an hour a day or keeping their blood pressure under control, they can reduce their risk of dementia," Dr. Rist said in a statement on the findings.

'A simple take-home message'

Reached for comment, Andrew E. Budson, MD, chief of cognitive-behavioral neurology at the VA Boston Healthcare System, praised Dr. Rist and colleagues' study as one that "builds on existing knowledge to provide a simple take-home message that empowers women to take control of their dementia risk."

Each of the seven known risk factors – being active, eating better, maintaining a healthy weight, not smoking, maintaining a healthy blood pressure, controlling cholesterol, and having low blood sugar – "was associated with a 6% reduced risk of dementia," Dr. Budson continued. "So, women who work to address all seven risk factors can reduce their risk of developing dementia by 42%: a huge amount. Moreover, although this study only looked at women, I am confident that if men follow this same advice they will also be able to reduce their risk of dementia, although we don't know if the size of the effect will be the same."

14. Association of Prenatal Depression With New CVD Within 24 Months After Childbirth

BACKGROUND

Although depression is well established as an independent risk factor for cardiovascular disease (CVD) in the nonpregnant population, this association has largely not been investigated in pregnant populations. We aimed to estimate the cumulative risk of new CVD in the first 24 months postpartum among pregnant individuals diagnosed with prenatal depression compared with patients without depression diagnosed during pregnancy.

METHODS AND RESULTS

Our longitudinal population-based study included pregnant individuals with deliveries during 2007 to 2019 in the Maine Health Data Organization's All Payer Claims Data. We excluded those with prepregnancy CVD, multifetal gestations, or no continuous health insurance during pregnancy. Prenatal depression and CVD (heart failure, ischemic heart disease, arrhythmia/cardiac arrest, cardiomyopathy, cerebrovascular disease, and chronic hypertension) were identified by International Classification of Diseases, Ninth Revision (ICD-9)/International Classification of Diseases, Tenth Revision (ICD-10) codes. Cox models were used to estimate hazard ratios (HRs), adjusting for potential confounding factors. Analyses were stratified by hypertensive disorder of pregnancy. A total of 119 422 pregnancies were examined. Pregnant individuals with prenatal depression had an increased risk of ischemic heart disease, arrhythmia/cardiac arrest, cardiomyopathy, and new hypertension (adjusted HR [aHR], 1.83 [95% CI, 1.20-2.80], aHR, 1.60 [95% CI, 1.10-2.31], aHR, 1.61 [95% CI, 1.15-2.24], and aHR, 1.32 [95% CI, 1.17-1.50], respectively). When the analyses were stratified by co-occurring hypertensive disorders of pregnancy, several of these associations persisted.

CONCLUSIONS

The cumulative risk of a new CVD diagnosis postpartum was elevated among individuals with prenatal depression and persists even in the absence of co-occurring hypertensive disorders of pregnancy. Further research to determine the causal pathway can inform postpartum CVD preventive measures.

15. Sex Differences in hs-cTnI Concentration Trajectories Over the Life Course

BACKGROUND

Cardiac troponin concentrations are lower in women than men. We examined whether age- and risk factor-related changes in cardiac troponin over the life course differ by sex and if the trajectory of cardiac troponin was informative in respect of cardiovascular outcomes in women and men in the general population.

METHODS

In the Whitehall II cohort, high-sensitivity cardiac troponin I concentrations were measured on 3 occasions over a 15-year period. Using linear mixed-effects models, the sex-specific trajectories of cardiac troponin were evaluated, and the relationship with conventional cardiovascular risk factors determined. Using multistate joint models, the association between sex-specific trajectories of cardiac troponin and a composite outcome of nonfatal myocardial infarction, nonfatal stroke, or cardiovascular death was evaluated.

RESULTS

In 2142 women and 5151 men (mean, 58±7 and 57±7 years of age, respectively), there were 177 (8.3%) and 520 (10.1%) outcome events, respectively, during a median follow-up of 20.9 (25th to 75th percentile, 15.8-21.3) years. Cardiac troponin concentrations were persistently lower in women than in men (median baseline concentration: 2.4 [25th to 75th percentile, 1.7-3.6] ng/L versus 3.7 [25th to 75th percentile, 2.6-5.8] ng/L, respectively, $P<0.001$), with women exhibiting a relatively larger increase with advancing age as compared with men ($P_{interaction}<0.001$). Apart from age, a significant and divergent interaction with sex was found for the association between cardiac troponin and body mass index (BMI) ($P_{interaction}=0.008$) and diabetes ($P_{interaction}=0.003$). During follow-up, cardiac troponin concentrations were associated to the outcome in both women and men (adjusted hazard ratio per 2-fold difference [95% CI, 1.34 (1.17-1.52) and 1.30

(1.21-1.40), respectively], $P_{interaction}$=0.752). The slope of cardiac troponin was significantly associated with the outcome in women, but not in men (adjusted hazard ratio [95% CI, 2.70 (1.01-7.33) and 1.31 (0.62-2.75), respectively], $P_{interaction}$=0.250).

CONCLUSIONS

Trajectories of cardiac troponin differ between women and men in the general population, with differing associations to conventional risk factors and cardiovascular outcomes. Our findings highlight the importance of a sex-specific approach when serial cardiac troponin testing is applied for cardiovascular risk prediction.

16. Female Reproductive Factors and the Risk of New-Onset Heart Failure

BACKGROUND

A comprehensive evaluation of woman-specific risk factors in relation to incident heart failure (HF) is limited.

OBJECTIVES

The study sought to investigate the association of multiple female reproductive factors with the risk of HF.

METHODS

Between 2007 and 2010, 229,026 women (mean age: 56.5 years) without prevalent HF from the UK Biobank cohort were included and followed until December 2020. The relation between (self-reported) reproductive factors and HF was analyzed using Cox proportional hazards models with adjustment for potential confounding.

RESULTS

Menarche at age <12 years, compared to age 12-13 years, carried a 9% larger risk of HF (HR: 1.09 [95% CI: 1.01-1.18]). Younger age at menopause was associated with a higher risk of HF ($HR_{age < 45\ y\ vs\ 50\text{-}51\ y}$: 1.15 [95% CI: 1.03-1.28]; $HR_{age\ 45\text{-}49\ y\ vs\ 50\text{-}51\ y}$: 1.11 [95% CI: 1.01-1.23]). Younger maternal age at first live birth ($HR_{age < 21\ y\ vs\ 24\text{-}26\ y}$: 1.42 [95% CI: 1.28-1.59]; $HR_{age\ 21\text{-}23\ y\ vs\ 24\text{-}26\ y}$: 1.14 [95% CI: 1.03-1.26]) and at last live birth ($HR_{age < 26\ y\ vs\ 29\text{-}31\ y}$: 1.19 [95% CI: 1.07-1.33]) were associated with higher risk of HF. Compared to women with 1 or 2 children, having 3 or 4 children (HR: 1.09 [95% CI: 1.02-1.17]) or >4 children (HR: 1.24 [95% CI: 1.05-1.47]) was associated with higher HF risk. Experiencing miscarriages or abortions was not significantly associated with incident HF, whereas experiencing 1 stillbirth and recurrent stillbirths conferred a 20% and 43% larger risk of HF, respectively, compared to no stillbirth.

CONCLUSIONS

The findings emphasize the importance of female reproductive history in the assessment of HF risk.

17. Women Have About 12-Year Delay in Onset of Atherosclerosis

Women have an approximately 12-year delay in the onset of coronary atherosclerosis, but those in the highest atherosclerotic burden group have a higher risk for major adverse cardiovascular events (MACE), according to a study published online May 11 in the European Heart Journal: Cardiovascular Imaging. The research was published to coincide with EACVI 2023, the congress of the European Association of Cardiovascular Imaging, held from May 10 to 12 in Barcelona, Spain.

Sophie E. van Rosendael, M.D., from the Leiden University Medical Center in the Netherlands, and colleagues examined the differences in age onset and prognostic significance of atherosclerotic plaque burden between sexes in 11,678 women and 13,272 men who were followed for 3.7 years. The Leiden coronary

computed tomography angiography (CCTA) score was calculated for all participants.

The researchers found that in women, the age where the median risk score was greater than 0 was 12 years higher than in men (64 to 68 versus 52 to 56 years). There was an independent association for the Leiden CCTA risk score with MACE (hazard ratios for scores 6 to 20 and >20, respectively: 2.29 and 6.71 in women and 1.64 and 2.38 in men). Within the highest-score group, the risk was significantly higher for women. The risk score was equally predictive and comparable for premenopausal women and men. In postmenopausal women, the prognostic value was higher than for men (hazard ratios for scores 6 to 20 and >20, respectively, 2.21 and 6.11 in women and 1.57 and 2.25 in men), with a significant interaction seen for the highest-risk group.

18. Sex differences and disparities in cardiovascular outcomes of COVID-19

Aims

Previous analyses on sex differences in case fatality rates at population-level data had limited adjustment for key patient clinical characteristics thought to be associated with coronavirus disease 2019 (COVID-19) outcomes. We aimed to estimate the risk of specific organ dysfunctions and mortality in women and men.

Methods and results

This retrospective cross-sectional study included 17 hospitals within 5 European countries participating in the International Survey of Acute Coronavirus Syndromes COVID-19 (NCT05188612). Participants were individuals hospitalized with positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from March 2020 to February 2022. Risk-adjusted ratios (RRs) of in-hospital mortality, acute respiratory failure (ARF), acute heart failure (AHF), and acute kidney injury (AKI) were calculated for women vs. men. Estimates were evaluated by inverse probability weighting and logistic regression models. The overall care cohort included 4499 patients with COVID-19-associated

hospitalizations. Of these, 1524 (33.9%) were admitted to intensive care unit (ICU), and 1117 (24.8%) died during hospitalization. Compared with men, women were less likely to be admitted to ICU [RR: 0.80; 95% confidence interval (CI): 0.71–0.91]. In general wards (GWs) and ICU cohorts, the adjusted women-to-men RRs for in-hospital mortality were of 1.13 (95% CI: 0.90–1.42) and 0.86 (95% CI: 0.70–1.05; $p_{interaction}$ = 0.04). Development of AHF, AKI, and ARF was associated with increased mortality risk (odds ratios: 2.27, 95% CI: 1.73–2.98; 3.85, 95% CI: 3.21–4.63; and 3.95, 95% CI: 3.04–5.14, respectively). The adjusted RRs for AKI and ARF were comparable among women and men regardless of intensity of care. In contrast, female sex was associated with higher odds for AHF in GW, but not in ICU (RRs: 1.25; 95% CI: 0.94–1.67 vs. 0.83; 95% CI: 0.59–1.16, $p_{interaction}$ = 0.04).

Conclusions

Women in GW were at increased risk of AHF and in-hospital mortality for COVID-19 compared with men. For patients receiving ICU care, fatal complications including AHF and mortality appeared to be independent of sex. Equitable access to COVID-19 ICU care is needed to minimize the unfavourable outcome of women presenting with COVID-19-related complications.

19. Association of Adverse Pregnancy Outcomes and Chronic Hypertension With the Risk of 12 CVDs Among Parous Women

BACKGROUND

Evidence on the association between chronic hypertension and the risk of cardiovascular disease (CVD) in mothers with adverse pregnancy outcomes (APOs) is limited. We investigated the association between chronic hypertension and risk of CVD, considering the role of APOs.

METHODS

We used linked electronic health records in the CALIBER platform to define a UK cohort of women with recorded births between 1997 and 2016. We conducted multivariable Cox regression to estimate the association between chronic hypertension, with and without APOs, and 12 subsequent CVD events.

RESULTS

The study cohort comprised 1 784 247 births (1.2 million women); of these 12 698 (0.71%) records had chronic hypertension, and 16 499 women had incident CVD during follow-up, of which 66% occurred in women under 40 years. Chronic hypertension (versus no chronic hypertension) was associated with a 2-fold higher risk of first subsequent CVD (adjusted hazard ratios, 2.22 [95% CI, 2.03-2.42]). Compared to normotensive women without APOs, the associations were the strongest in women with chronic hypertension and APOs across the 12 CVD outcomes, varying from 9.65 (5.96-15.6) for heart failure to 2.66 (2.17-3.26) for stable angina. In women with chronic hypertension without APOs, adjusted hazard ratios varied from 5.25 (3.47-7.94) for subarachnoid hemorrhage to 1.26 (0.59-2.67) for peripheral arterial disease. In women with APOs, but without chronic hypertension, adjusted hazard ratios varied from 3.27 (2.48-4.31) for intracerebral hemorrhage to 1.33 (1.26-1.41) for stable angina.

CONCLUSIONS

We found strong associations between chronic hypertension and the risk of premature CVD, with greater risk in women who additionally had APOs. Intervention programs focused on these groups might lower their risk of subsequent CVD.

20. Cardiac Complications of Pregnancy in Desmoplakin Cardiomyopathy

Pathogenic variants in the DSP gene, which encodes the desmosomal protein desmoplakin (DSP), are present in approximately 4% of adults who undergo genetic testing for dilated cardiomyopathy.[1] The phenotype of DSP cardiomyopathy is of predominant left ventricular (LV) involvement with episodic myocardial injury or inflammation, heart failure, and a heavy burden of ventricular arrhythmias.[2] Although the overlapping genetic etiology of peripartum and dilated cardiomyopathy was recently described, there are no descriptions of pregnancy outcomes in patients with pre-existing DSP cardiomyopathy. Studies in arrhythmogenic right ventricular cardiomyopathy have described a modest burden of ventricular tachycardia or heart failure (3 and 2 episodes, respectively, in 196 pregnancies).[3] In this study, we identified 3 patients who had a prenatal diagnosis of DSP cardiomyopathy by using the STORCC (Standardized Outcomes in Reproductive Cardiovascular Care) registry from 2011 to 2022,[4] and we report their prospectively observed 4 pregnancies

Patient 1: Pregnancy 1

A 27-year-old gravida 1, para 0 woman underwent in vitro fertilization (IVF) during which preimplantation genetic testing was used to prevent transmission of the DSP variant. She had symptomatic premature ventricular contractions (PVCs) beginning 4 years before pregnancy that were treated with nadolol and radiofrequency ablation on 3 occasions. Prepregnancy evaluations included cardiac magnetic resonance imaging revealing an LV ejection fraction (LVEF) of 50% and nearly circumferential, epicardial late gadolinium enhancement involving the basal and middle left ventricle. Genetic testing revealed a heterozygous, likely pathogenic variant in DSP c.7563_7566del (p. Asp2521Glufs∗39). A primary prevention subcutaneous (SC) implantable cardioverter-defibrillator (ICD) was implanted 2 years before pregnancy. A preconception echocardiogram revealed normal biventricular size, an LVEF of

50%, and mildly depressed right ventricular systolic function. Nadolol was continued during pregnancy for treatment of PVCs.

Throughout pregnancy, she experienced worsening palpitations, orthopnea, and intermittent effort intolerance. However, LVEF by echocardiography remained stable, she did not develop signs of congestion, and N-terminal pro–B-type natriuretic peptide (NT-proBNP) levels remained within the normal range. She underwent induction of labor at 37.9 weeks for nonreassuring fetal testing results and was monitored on telemetry intrapartum without events. Delivery was complicated by a postpartum hemorrhage (estimated blood loss >1,000 mL) and neonatal hypoglycemia. She breastfed without complications.

Some improvement in dyspnea was noted during the postpartum period; however, palpitations increased, and Holter monitoring revealed nonsustained ventricular tachycardia (NSVT) and 2.4% PVCs.

Patient 1: Pregnancy 2

The following year, the same woman presented with a spontaneous pregnancy. Her first trimester echocardiogram imaging was stable. She continued on nadolol, and metoprolol tartrate was taken as needed for increasing palpitations in the first trimester.

At 35 weeks' gestation, she developed orthopnea, paroxysmal nocturnal dyspnea, and increasing palpitations. She was hospitalized at 38 weeks after an echocardiogram revealed worsening systolic function (LVEF, 35%), and venous congestion was noted on examination. NT-proBNP levels were stable from first trimester levels at 251 pg/mL. She was treated with furosemide, and labor was induced at 38 weeks, with telemetry monitoring. She had an uncomplicated vaginal delivery of a healthy infant.

The patient required furosemide in the postpartum period for recurring dyspnea but had no further congestion on examination. However, NT-proBNP levels rose,

and systolic function remained impaired 2 and 4 months after delivery (**Figure 1**). The patient continued taking metoprolol and diuretic agents, including spironolactone and furosemide. She again chose to breastfeed, and angiotensin type II receptor blockers were held.

Patient 2

A 32-year-old gravida 2, para 1 woman presented in her first trimester after a spontaneous conception. Arrhythmia history included a previous cardiac arrest after which an SC ICD was placed, frequent PVCs, and atrioventricular nodal re-entrant tachycardia treated by ablation. Genetic testing before pregnancy revealed a heterozygous, likely pathogenic variant in DSP c.1751delA (p. Glu584fs∗52). Continuing palpitations following ablation prompted implantation of a loop recorder, present during pregnancy. At baseline, the patient reported New York Heart Association functional class II capacity. Metoprolol succinate and aspirin were continued throughout pregnancy.

An echocardiogram obtained 2.5 years before pregnancy revealed an LVEF of 40% and low-normal right ventricular (RV) systolic function. Repeat echocardiogram imaging obtained at 14 weeks' gestation revealed worsening systolic dysfunction (LVEF, 35%). Cardiopulmonary exercise testing performed at 16 weeks revealed a decline in functional capacity, with a peak oxygen consumption of 15 mg/kg/min (56% predicted), blunted systolic blood pressure response (90 and 96 mmHg at rest and peak exercise, respectively), and frequent multifocal PVCs. Given her poor functional capacity and high risk of progressive heart failure, she was advised to consider pregnancy termination; however, she elected to continue the pregnancy. She remained stable from a cardiovascular standpoint throughout the remainder of the pregnancy. Echocardiograms at 22 and 35 weeks' gestation revealed unchanged LVEFs. No additional cardiac medications were required during pregnancy. She was observed antenatally for a short cervix.

The patient had an uncomplicated spontaneous vaginal delivery at 37.6 weeks. She was monitored with telemetry throughout labor and for 12 hours post partum without events. The infant developed tachypnea resulting in neonatal intensive care unit (NICU) admission. Genetic testing revealed that the infant was positive for the DSP variant. There were no maternal postpartum complications following pregnancy, and the patient breastfed without concerns. At 18 months post partum, she was without congestion or worsening symptoms, and an echocardiogram revealed an LVEF of 25%.

Patient 3

A 32-year-old gravida 2, para 1 woman underwent IVF with preimplantation genetic testing, resulting in a monochorionic, diamniotic twin pregnancy. The patient experienced a cardiac arrest 10 years earlier, for which an SC ICD was placed. Preconception cardiac evaluations included stress testing and echocardiography. Genetic testing performed 1 year before pregnancy revealed a heterozygous pathogenic variant in DSP c.2236del (p. Val746Tyrfs∗19). Cardiac medications included nadolol, continued throughout pregnancy for symptomatic PVCs. An echocardiogram in the first trimester revealed an LVEF of 50% and normal RV size and function. NT-proBNP levels were within the normal range (137 pg/mL). ICD interrogation in the second trimester revealed rare NSVT. The patient remained clinically stable without sustained arrhythmias. In the third trimester, there was a modest decline in LVEF to 45%, although LVEF remained low normal and stable thereafter.

The pregnancy was complicated by intrauterine growth restriction (IUGR) of both twins and oligohydramnios during the third trimester. The patient was consequently admitted at 33.9 weeks' gestation for induction of labor. Vaginal delivery was planned with telemetry monitoring during active labor. However, nonreassuring fetal heart tracings after induction prompted urgent cesarean delivery. The patient tolerated the procedure well, and telemetry was continued

for 6 hours after delivery. Both neonates were admitted to the NICU for prematurity.

The patient remained stable in the postpartum period. Her echocardiogram was unchanged. Nadolol dosage had been decreased (from 80 mg to 40 mg) during the third trimester in response to the finding of IUGR but was increased back to 80 mg post partum for recurrence of palpitations. There were no new arrhythmias or other cardiac complications. The patient successfully breastfed through the postpartum period.

Discussion

Among 4 pregnancies in 3 patients with DSP cardiomyopathy, a decline in systolic function was observed in 2 pregnancies, symptoms of congestive heart failure accompanied by systolic functional decline occurred in 1 patient, and there were no cases of malignant arrhythmias. All patients received preconception counseling with a cardiologist and a maternal-fetal specialist, and the plan for cardiac monitoring and contingencies for worsening cardiac function were discussed. All 4 deliveries were well tolerated from a cardiac perspective, including the postpartum hemorrhage in 1 patient. Of note, vaginal deliveries were completed in 3 of the 4 pregnancies, and the 1 cesarean delivery was performed for noncardiac complications of induction, thus suggesting the safety of vaginal delivery in patients with cardiomyopathies. Findings from these 4 pregnancies suggest that there may be an increased risk of decline in systolic function during pregnancy among patients with DSP cardiomyopathy. These observations suggest that patients will need careful echocardiographic follow-up throughout pregnancy and in the postpartum period. It is important that patients with DSP cardiomyopathy who wish to become pregnant undergo prepregnancy counseling and are followed closely by a multidisciplinary cardio-obstetric team. Furthermore, the unique phenotype of and potentially increased risk for systolic decline during pregnancy in patients with DSP cardiomyopathy support the recommendation for genetic testing in patients with undiagnosed

cardiomyopathies to tailor cardiac and obstetric care to these patients appropriately. Future studies of patients with DSP cardiomyopathy will be necessary to guide clinical recommendations for this group of patients.

21. Anomalous Right Coronary Artery From the Pulmonary Artery Diagnosed in Pregnancy

A 39-year-old gravida 2, para 1 woman presented with palpitations in pregnancy. The palpitation episodes last for 5 minutes with spontaneous resolution. She had been physically active and never had any exertional limitations or anginal symptoms. A tracing from her watch demonstrated supraventricular tachycardia (SVT) at 213 beats/min. An echocardiogram demonstrated dilated epicardial vessels in the interventricular septum and a Doppler signal indicating flow into the proximal pulmonary artery. The flow pattern was diastolic dominant, suggestive of either anomalous coronary artery origin from the pulmonary artery or a coronary-to-pulmonary artery fistula. Her left ventricular (LV) systolic function was normal. LV dilation was appreciated with an end-diastolic volume of 114 mL/m^2. There was trace mitral regurgitation.

Noncontrast cardiac magnetic resonance with steady-state free procession imaging demonstrated a normal origin of the left coronary artery, dilated epicardial coronary collateral vessels, and probable anomalous right coronary artery origin from the pulmonary artery (ARCAPA) with flow going into the proximal pulmonary artery; however, given the limitations of the imaging study, it was inadequate to confirm the diagnosis.

Her SVT, likely atrioventricular nodal re-entrant tachycardia, thought to be unrelated to ARCAPA, was managed medically. On metoprolol, she had a low burden of arrhythmia during pregnancy and none during labor and delivery.

A vaginal delivery was uneventful, with peripartum telemetry, monitoring of volume status, and the use of bubble or particle filters on all intravenous lines

to prevent paradoxical embolus. After delivery, an electrocardiogram-gated computed tomography scan confirmed the diagnosis of ARCAPA (**Figure 1**).

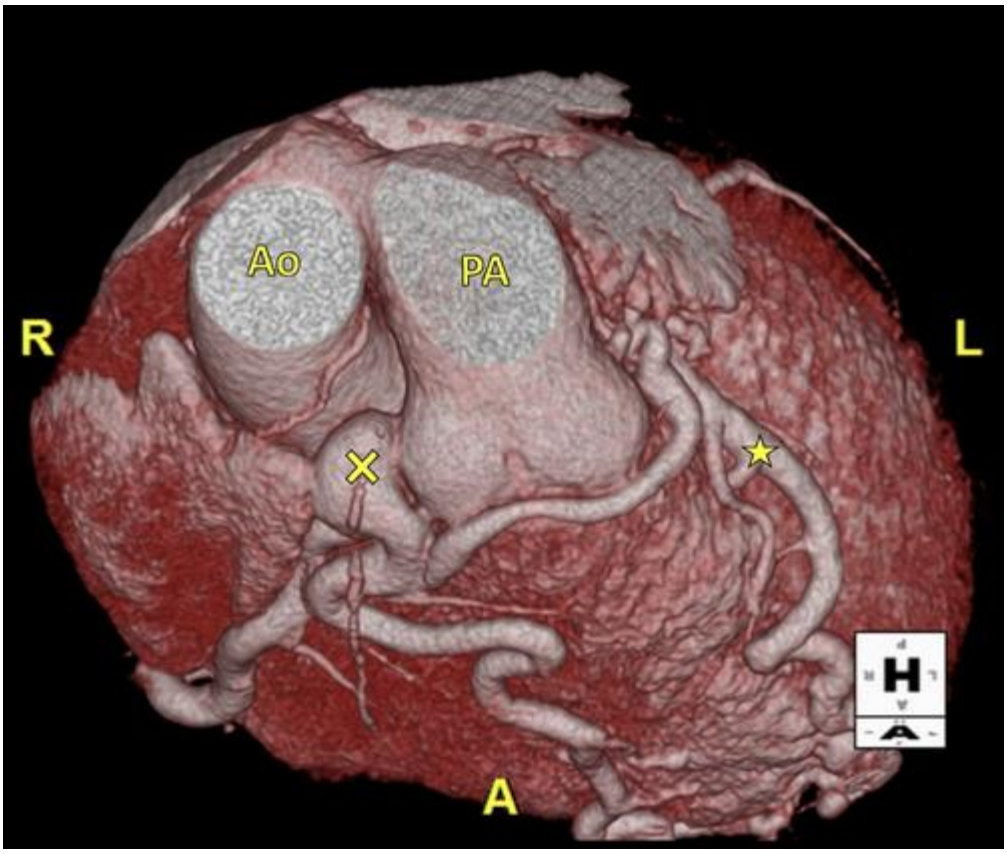

Figure 1

Anomalous Right Coronary Artery From the Pulmonary Artery

A 3-dimensional reconstruction of an electrocardiogram-gated coronary computed tomography angiogram demonstrates anomalous right coronary artery **(x)** from the pulmonary artery. The **star** indicates the left anterior descending coronary artery. A = anterior; Ao = aorta; H = head; L = left; PA = pulmonary artery; R = right.

For women with heart disease who desire pregnancy, the modified World Health Organization (mWHO) risk classification and the CARPREG II (Cardiac Disease

in Pregnancy II) score are used to estimate the risk of maternal cardiac events through pregnancy and the puerperium.[1,2]

The mWHO classification, which focuses on anatomy and complexity of cardiac disease, stratifies patients from class I, with no known increase in maternal morbidity or mortality, to class IV, where pregnancy is contraindicated.[1] The CARPREG II score assigns points on the basis of general, lesion specific, and delivery-of-care predictors.[2] Our patient's SVT would have been classified as mWHO class II, which denotes a 6% to 10% maternal cardiac event rate. Her coronary artery disease and arrhythmia, without previous intervention, corresponds to a CARPREG II score of 6, predicting a 40% to 45% maternal cardiac event rate. However, she was asymptomatic, with good exertional capacity and normal LV systolic function. Therefore, the CARPREG II score may have overestimated the maternal cardiac event rate.

Anomalous origin of a coronary artery from the pulmonary trunk is a rare congenital cardiac lesion.[3] Anomalous left coronary artery from the pulmonary artery (ALCAPA) and ARCAPA can create a left-to-right shunt from the left coronary artery to the pulmonary artery, which may result in a "steal" phenomenon. In this situation, blood flows away from the myocardium, and this can lead to ischemia and infarction.[3] In ALCAPA, coronary flow compromise can beget LV dilation, LV dysfunction, or mitral regurgitation.

Because ALCAPA is considered higher risk, repair is recommended at diagnosis. Indications for repair in ARCAPA include symptoms, ventricular dysfunction, or evidence of coronary ischemia attributed to the anomaly.[3]

22. Sudden Cardiac Arrest in the Postpartum Period Due to Long QT Syndrome and Dilated Cardiomyopathy

A 19-year-old woman presented with sudden cardiac arrest (SCA) 5 weeks after premature delivery. She collapsed in her kitchen and had bystander cardiopulmonary resuscitation for 20 minutes before the arrival of emergency medical services (EMS). She was in ventricular fibrillation and received 2 defibrillations by EMS before the return of spontaneous circulation. On hospital admission, the initial physical examination showed an intubated and sedated patient with a benign cardiopulmonary examination.

Past Medical History

The patient was 5 weeks post partum from delivery at 24 weeks of gestation resulting from placental abruption. This was her second gestation, with a previous uncomplicated term pregnancy. A few weeks after her delivery she had a motor vehicle accident while driving in which she suddenly lost consciousness. She did not seek evaluation by medical personnel after the accident. Pertinent family history included the sudden cardiac death of her mother in her late 20s. The cause of her mother's death was reportedly an unnamed "cardiomyopathy," and no autopsy information was available. Otherwise, the patient was healthy and took no medications.

Differential Diagnosis

The initial differential diagnosis for her SCA included hereditary cardiomyopathy, type 2 long QT syndrome (LQTS), peripartum cardiomyopathy, stress cardiomyopathy, SCA, spontaneous coronary artery dissection, and anomalous coronary artery, with highest concern for hereditary cardiomyopathy given her family history of sudden cardiac death.

Investigations

Initial laboratory investigation revealed an elevated troponin I level, which peaked at 3.07 ng/mL (<0.02 ng/mL) and signs of end-organ dysfunction with elevated creatinine at 1.1 mg/dL (0.6-1.1 mg/dL) from baseline 0.5 mg/dL and lactic acid of 3.3 mmol/L (0.5-2.2 mmol/L). Magnetic resonance imaging of her brain revealed diffuse hypoxic ischemic insults throughout the parieto-occipital cortex and basal ganglia. An initial electrocardiogram before therapeutic cooling revealed a prolonged corrected QT interval at 534 milliseconds by using the Bazett formula (**Figure 1**). The transthoracic echocardiogram showed severely reduced systolic function, with a left ventricular ejection fraction (LVEF) of <15% with otherwise normal wall thickness and valve structure. A cardiac magnetic resonance (CMR) scan obtained 1 week after admission showed an improvement in LVEF to 47% with mildly dilated left ventricular cavity size and a basal to midwall septal stripe late gadolinium enhancement (LGE) consistent with nonischemic dilated cardiomyopathy (DCM) (**Figures 2A** and **2B**). Genetic testing revealed a pathogenic heterozygous sequence variant in both KCNQ1, indicating congenital type 1 LQTS, and BAG3, which is associated with DCM.

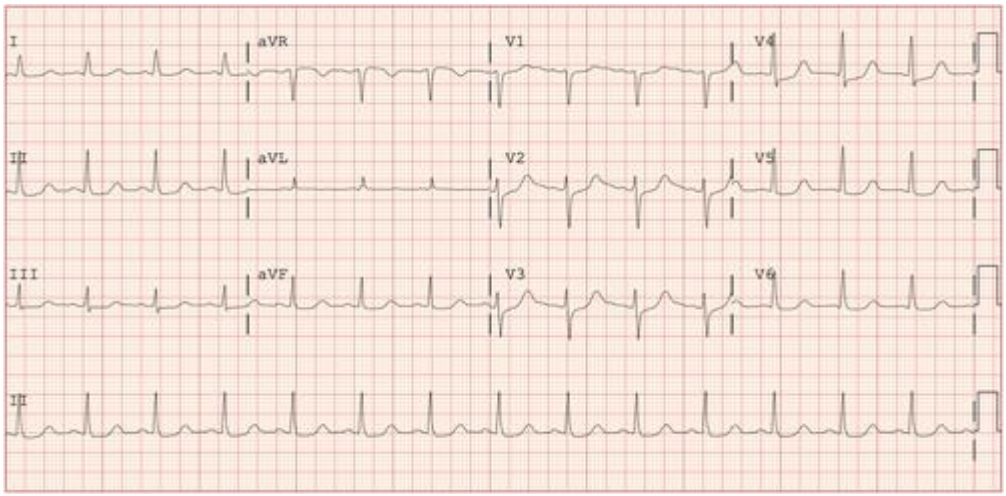

Figure 1

Electrocardiogram on Presentation

Corrected QT interval prolonged at 534 milliseconds.

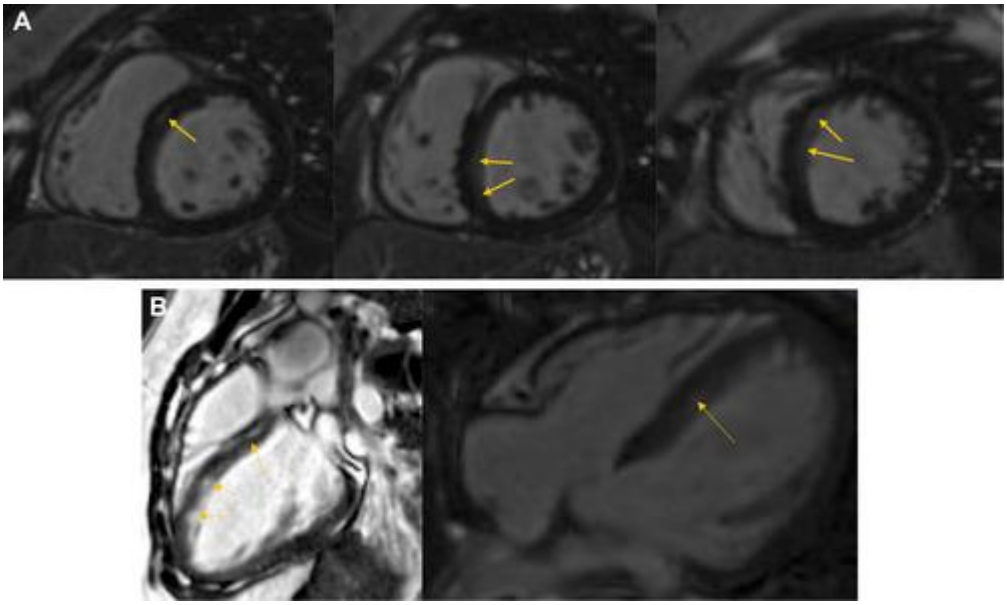

Figure 2

Cardiac Magnetic Resonance

(A) Short-axis views demonstrating late gadolinium enhancement **(arrows)** in the basal to midseptum. **(B)** The 3- **(left)** and 4-chamber views **(right)** demonstrating basal to midseptal late gadolinium enhancement **(arrows).**

Management

Therapeutic hypothermia was initiated following cardiac arrest according to institutional protocol. She was initially given an indefinite prognosis of neurologic recovery by neurology. She had a tracheostomy and percutaneous endoscopic gastrostomy tube placement while awaiting neurologic recovery. Given the diagnosis of congenital type 1 LQTS, she was started on prophylactic nadolol. Her initial low LVEF was presumed to be the result of her postshock state given the rapid improvement in LVEF. She had an implantable cardioverter-defibrillator placed for secondary prevention.

Discussion

LQTS can be either congenital or acquired.[1] Among congenital LQTS cases, 13 genes have been implicated, with the KCNQ1 gene, indicative of type 1 LQTS, the most common variant.[1] Patients with type 1 LQTS have been shown to have a higher risk of cardiac events with sympathetic activation, especially exercise and stress.[2] There has been particular attention paid to the effects of pregnancy on the risk of arrhythmias. Initial studies showed an increased risk of cardiac events for patients with LQTS.[3] Later investigations revealed that the preponderance of cardiac events occurring post partum was in patients with type 2 LQTS rather than type 1 LQTS (16% vs <1%, respectively).[4,5] A follow-up study specifically examining the risk of cardiac events in patients with type 1 LQTS in the peripartum period showed a 1% rate of cardiac events during pregnancy and 2% rate of cardiac events post partum.[6]

In addition to type 1 LQTS, our patient also had a mutation in BAG3, which is a known cause of DCM.[7] BAG3 is present in up to 6.7% of patients with DCM.[8] Among subtypes of LQTS, type 3 LQTS has shown the closest association with DCM.[9,10] In patients with mutations in KCNQ1, there have been case reports of concomitant hypertrophic cardiomyopathy and noncompaction cardiomyopathy.[11] Our patient is the only known case of concomitant KCNQ1 and BAG3 mutations. In a recent study, 15.6% of Kazakh patients with DCM who presented with ventricular tachycardia had a mutation of KCNQ1.[12] This finding suggests an association between channelopathies, such as type 1 LQTS, and the presence of ventricular tachycardia in patients with DCM.

The diagnosis of DCM in our patient was made because of the BAG3 mutation coupled with CMR findings of a dilated left ventricle and nonischemic LGE. CMR is recommended in the work-up of SCA and has important diagnostic and prognostic implications.[13] In patients with SCA, CMR findings such as decreased

LVEF and extent of LGE have been associated with an increased frequency of major adverse cardiac events.[14]

The mainstay of therapy in LQTS is β-blockers, which decrease mortality from 21% in 1 year to 1% in 15 years.[1,6] Preferred agents are propranolol and nadolol over other β-blockers.[1] This therapy is effective in both pregnancy and the postpartum period.[3-6] There is debate about whether implantable cardioverter-defibrillator placement is appropriate for primary prevention in patients with LQTS; however, the consensus is that device placement is indicated for secondary prevention, as performed in our patient.[1]

Follow-Up

She was weaned from sedation and experienced progressive neurologic recovery. Her LVEF normalized to 65% to 70% on repeat transthoracic echocardiogram. Her QTc interval remained prolonged at greater than 500 milliseconds on repeat electrocardiograms throughout hospitalization. She was counseled on the risk of cardiac events in future pregnancies and was started on contraception. Genetic counseling was scheduled for her children and siblings. She was discharged to an acute rehabilitation facility 36 days after the initial event.

Conclusions

This case is a rare example of a previously asymptomatic patient with SCA in the postpartum period resulting from concomitant congenital type 1 LQTS and BAG3 DCM. It highlights the increased risk of peripartum events in patients with LQTS. Additionally, it emphasizes the role of CMR in the work-up of SCA.

23. HRS Expert Consensus Statement Focuses on Management of Arrhythmias During Pregnancy

A new expert consensus statement released by the Heart Rhythm Society (HRS) is focused on the management of cardiac arrhythmias during pregnancy. Endorsed by the ACC, the statement offers practical guidance for electrophysiologists, cardiologists and other health care professionals on the optimal management of arrhythmias in pregnant patients and in fetuses worldwide.

Specifically, the statement includes dedicated sections on:

- General concepts related to arrhythmias in both the patient and the fetus during pregnancy
- Optimal approaches to diagnosis and evaluation of arrhythmias during pregnancy
- Approaches for invasive and noninvasive treatments of arrhythmias in pregnant patients
- Disease- and patient-specific considerations when risk stratifying, diagnosing and treating arrhythmias in pregnant patients
- Management of fetal arrhythmias

Shared decision-making with patients and among a multidisciplinary care team is also highlighted throughout the statement. “Managing arrhythmias in pregnant patients requires a multidisciplinary care team approach because both the mother and the fetus can be affected,” said Statement Chair **Jose A. Joglar, MD, FACC**. “Throughout the pregnancy, delivery, and postnatal period it is vital that the patient and care team engage in shared decision-making discussions that consider the risks and benefits of treatment vs. no treatment and eflect each patient’s individual personal preferences.”

According to the Writing Committee, the statement was developed taking into consideration the health benefits, side effects and risks to both the pregnant patient and fetus, as well as current evidence and standards of care. However, Joglar and colleagues note that the availability of resources, technology and health care delivery logistics vary widely in different parts of the world. “Some procedures are better performed, and some disease states are better managed, in settings where there is specific expertise,” said Joglar.

24. Your ACC Joins ABC Statement on Maternal Health Crisis

Urgent action is needed to combat the maternal morbidity and mortality crisis in America and cardiologists have a vital role to play,” reads a joint statement released by the Association of Black Cardiologists (ABC) along with the ACC and the American Heart Association.

The statement highlights multiple factors influencing the maternal health crisis, including increased maternal age, health conditions such as hypertension, diabetes and obesity, and discrimination including bias and racism.

The groups stress the need for “all cardiovascular specialists to double down on their efforts to reduce maternal mortality and to eliminate racial and ethnic gaps in maternal health outcomes,” and to develop a “multi-faceted approach that includes prevention and treatment of underlying cardiovascular risk factors along with education of stakeholders,” all while “addressing social and structural determinants of maternal and cardiovascular risk.”

25. Sex Differences in Heart Failure Following Acute Coronary Syndromes

Study Questions:

Are there sex differences in presentation and outcomes in patients with acute heart failure (HF) with acute coronary syndrome (ACS)?

Methods:

This study used the ISACS (International Survey of Acute Coronary Syndromes) registry, which enrolled ACS patients from 11 European registries. The primary outcome was 30-day all-cause mortality from hospital admission. The secondary outcome was risk of acute HF on admission. Propensity-matched analyses were conducted to examine sex differences in presentations and outcomes.

Results:

Among 87,812 ACS patients, 25,187 (29%) had acute HF on admission, of which 35.2% were women. This included 56,038 ST-segment elevation myocardial infarction (STEMI) with 34% women and 31,774 NSTEMI patients with 38% women. Women were older, more likely to have diabetes and hypertension, and less likely to be current smokers with no difference in time from symptom onset to presentation.

Women with ACS had a higher risk for 30-day mortality than men (absolute difference, 3.5%; risk ratio [RR], 1.43; 95% confidence interval [CI], 1.37-1.50). This elevated 30-day mortality risk was higher for STEMI than NSTEMI. Women also had a higher risk for presenting with acute HF (absolute difference, 2.6%; RR, 1.13; 95% CI, 1.10-1.17). Acute HF risk was higher with STEMI than NSTEMI. Women with acute HF on presentation had a higher 30-day mortality risk (RR, 1.24; 95% CI, 1.17-1.31). In patients with STEMI and acute HF, women were more likely to have HF with reduced ejection fraction (HFrEF) compared with men. In patients with acute HF and NSTEMI, women were less likely to have

HFrEF than men. In multivariable models, female sex was independently associated with acute HF and 30-day mortality.

Conclusions:

In a large study enrolling ACS patients from 11 European countries, female sex was independently associated with a higher risk for 30-day mortality and acute HF. These risks were higher among STEMI patients. In ACS patients with HF, women with STEMI were more likely to have HFrEF but women with NSTEMI were less likely to have HFrEF than men.

Perspective:

Although sex differences and outcomes in ACS have been extensively studied, studies have yielded mixed results. This study provides results of sex disparities and outcomes after ACS from one of the largest ACS cohorts enrolling over 80,000 ACS patients. Results highlight several differences between men and women presenting with ACS. Women remained at a higher risk for 30-day mortality post-ACS and risk for acute HF presentation that persisted despite propensity-score matching. Differences in revascularization strategy and time to presentation did not explain these differences. In addition, these higher risks for mortality and acute HF presentation were higher for women with STEMI than NSTEMI. There were biological differences in type of HF as well with women with STEMI presenting more frequently with HFrEF than men. However, women with NSTEMI presented more frequently with HFpEF than men. While mechanisms behind these differences cannot be assessed in this study, these findings certainly support the need to evaluate sex differences in response to treatment for ACS and HF.

26. Sex Differences in Outcomes After Transcatheter Aortic Valve Replacement: A POPular TAVI Subanalysis

Background

Stroke and bleeding are complications after transcatheter aortic valve replacement (TAVR). A higher incidence of bleeding and stroke has been reported in women, but the role of antithrombotic management pre- and post-TAVR has not been studied.

Objectives

The study sought to compare bleeding and ischemic complications after TAVR between women and men stratified by antiplatelet and oral anticoagulant (OAC) regimen.

Methods

The POPular TAVI (Antiplatelet Therapy for Patients Undergoing Transcatheter Aortic Valve Implantation) trial was a randomized clinical trial to test the hypothesis that monotherapy with aspirin or OAC after TAVR is safer than the addition of clopidogrel. The primary endpoints of interest of this post hoc subanalysis were: 1) all bleeding; and 2) a composite of ischemic events consisting of stroke and myocardial infarction. Secondary endpoints were: 1) nonprocedural bleeding; 2) major or life-threatening bleeding; 3) minor bleeding; 4) stroke; 5) myocardial infarction; and 6) all-cause death.

Results

A total of 978 patients (466 [47.6%] women) were included in this study. All bleeding and the composite of myocardial infarction and stroke rates were similar between sexes (all bleeding: 106 [22.8%] women vs 121 [23.6%] men; P = 0.815; ischemic events: 26 [5.6%] vs 36 [7.0%]; P = 0.429). However, major or life-threatening bleeding occurred more often in women (58 [12.5%]) vs men (38

[7.4%]) (P = 0.011), most of which were access site bleedings. The use of aspirin pre- and post-TAVR increased major or life-threatening bleeding in women but not in men.

Conclusions

After TAVR, overall bleeding and ischemic outcomes were similar between women and men. However, women had more major or life-threatening bleedings, especially those receiving aspirin pre- and post-TAVR.

27. Young Women More Likely to Return to the Hospital in Year Following MI

Young women who experience a myocardial infarction (MI) have more adverse outcomes and are more likely to end up back in the hospital compared to men of a similar age in the year following discharge, according to a study published May 1 in JACC.

Mitsuaki Sawano, MD, PhD, et al., used data from the VIRGO study, an observational study of the presentation, treatment and outcomes of young women and men who experienced a MI between ages 18 and 55 years old. In the current study, after excluding in-hospital deaths, the final cohort included 2,979 patients hospitalized for MI (2,007 women vs. 972 men). The study examined all-cause and cause-specific acute events that required hospitalization, which was defined as any hospital or observation stay longer than 24 hours within one year of discharge following MI. The average age was 47 years and 70% self-identified as non-Hispanic White. A high proportion of women self-identified as non-Hispanic Black compared to men. Women also had a higher prevalence of comorbidities, including obesity, congestive heart failure, prior stroke and renal disease. In the patient cohort, the young women were more likely to be low-income, have a history of depression and significantly worse health status compared to men in the study.

Results showed that women were less likely to present to the hospital with chest pain and more likely to arrive more than six hours after symptom onset. They were also more likely to have a NSTEMI or a MI with nonobstructive coronary arteries (MINOCA). The women experiencing MINOCA were younger, more likely to be a non-Hispanic Black patient, smoker, with a lower education status and the lowest proportion of previous coronary artery disease. These patients also reported lower treatment satisfaction compared with men or women presenting with myocardial infarction with obstructive coronary artery disease (MI-CAD). On average, women stayed in the hospital longer and received lower rates of guideline-recommended medical therapies including aspirin, statins, beta-blockers and ACE inhibitors.

All-cause hospitalization rates within one year of discharge were 34.8% for women and 23% for men. The leading cause of hospitalizations for women were coronary-related, followed by noncardiac then other cardiac and stroke-related hospitalizations. Women with MINOCA had lower rates of one-year outcomes compared with women who experienced MI-CAD. There was a more significant sex disparity between women and men for noncardiac hospitalizations compared to all other hospitalizations (145.8 vs. 69.6 per 1,000 person-years).

"We think that the accumulation of risk factors seen in the MI-CAD population is associated with the high incidence of hospitalization one year after heart attack," Sawano said. "We must emphasize, however, that does not mean that MINOCA patients are 'low risk.' We know from recent studies that MINOCA is not a benign disease compared with similarly aged women and these cases warrant further evaluation to understand the underlying mechanism and treatment of certain conditions."

The researchers conclude that their findings demonstrate the need for continued efforts to optimize secondary preventive strategies to reduce coronary-related hospitalizations, but also highlight the need for further research into the causes

and mechanisms of noncardiac hospitalization especially given the significant sex disparity.

In an accompanying editorial, **Martha Gulati, MD, MS, FACC**, et al., said, "This study importantly identifies an increased rate of cardiovascular and non-cardiovascular rehospitalization in women as compared to men, with a clear association between psychosocial and demographic factors. Yet the root cause of sex differences in psychosocial factors and rates of comorbid conditions remains elusive. Why are more women than men identified as low income in this cohort? Why does this cohort demonstrate a nearly two-fold greater prevalence of depression in women as compared to men? As a cardiovascular community, by continuing to ask why perhaps we can arrive at 'what next.'"