1. Sex differences in left ventricular remodelling in patients with severe aortic valve stenosis

AIMS

WOMEN WITH SEVERE AORTIC STENOSIS (AS) HAVE BETTER LONG-TERM OUTCOME AFTER TRANSCATHETER AORTIC VALVE IMPLANTATION (TAVI) BUT WORSE SURVIVAL AFTER SURGICAL AORTIC VALVE REPLACEMENT COMPARED WITH MEN. WHETHER THIS IS RELATED TO SEX DIFFERENCES IN LEFT VENTRICULAR (LV) REMODELLING IS UNKNOWN. THE AIM OF THIS STUDY WAS TO EXAMINE THE SEX DIFFERENCES IN LV REMODELLING WITH MULTIDETECTOR ROW COMPUTED TOMOGRAPHY (MDCT) AND OUTCOME IN PATIENTS WITH SEVERE AS UNDERGOING TAVI BETWEEN 2007 AND 2018.

METHODS AND RESULTS

A TOTAL OF 289 PATIENTS (AGE 80 ± 6 YEARS, 54% MALE) WERE INCLUDED. LV VOLUMES, MASS, AND FUNCTION WERE ANALYSED ON PRE-PROCEDURAL MDCT SCANS. WOMEN SHOWED SMALLER LV VOLUMES AND MASS COMPARED WITH MEN. PATIENTS WERE CLASSIFIED INTO FOUR LV REMODELLING PATTERNS: CONCENTRIC HYPERTROPHY (50%) WAS THE MOST FREQUENT PATTERN OF LV REMODELLING FOLLOWED BY ECCENTRIC HYPERTROPHY (33%), NORMAL GEOMETRY (13%), AND CONCENTRIC REMODELLING (4%). MEN SHOWED MORE CONCENTRIC REMODELLING COMPARED WITH WOMEN (91% VS. 9%, RESPECTIVELY, \( P = 0.011 \)). HOWEVER, NO DIFFERENCES WERE OBSERVED IN THE REMAINING LV REMODELLING PATTERNS. DURING A MEDIAN FOLLOW-UP OF 3.8 (IQR 2.2–5.1) YEARS AFTER TAVI, 87 (30%) PATIENTS DIED. WOMEN DEMONSTRATED BETTER OUTCOME AFTER TAVI COMPARED WITH MEN.
LOG-RANK $X^2 = 4.29, P = 0.038)$. NO ASSOCIATION WAS OBSERVED BETWEEN THE INTERACTION OF THE LV REMODELLING PATTERNS AND SEX WITH OUTCOME.

CONCLUSION

LV CONCENTRIC HYPERTROPHY AND ECCENTRIC HYPERTROPHY ARE SIMILARLY OBSERVED IN MEN AND WOMEN WITH SEVERE AS BUT CONCENTRIC REMODELLING WAS MORE COMMON IN MEN. WOMEN DEMONSTRATED BETTER OUTCOME AFTER TAVI WHEN COMPARED WITH MEN. THE INTERACTION BETWEEN THE LV REMODELLING PATTERNS AND SEX WAS NOT ASSOCIATED WITH SURVIVAL.

2. Syncope in a pregnant woman with repaired Tetralogy of Fallot: a case report

Background

Tetralogy of Fallot (TOF) is one of the most widespread cyanotic congenital heart disease (CHD), which can be successfully repaired in the neonatal period. However, residual problems and the surgical technique itself can create a favourable basis for arrhythmias and conduction abnormalities in these patients. Sometimes, these arrhythmias may worsen during pregnancy and require urgent intervention.

Case summary

This is a case of a 25-year-old woman, who underwent a surgical repair of TOF at the age of 2 years. She suffered an ischaemic stroke postoperatively, which was complicated with secondary seizures and syncope. These episodes were evaluated as epilepsy. The patient was admitted to our hospital with the above-mentioned complaints in the 10th week of pregnancy. A comprehensive cardiac
examination was performed. Her presyncopal event was captured during Holter monitoring, which documented a severe dysfunction of the sinus node. She was diagnosed with postoperative sick sinus syndrome and implanted with a permanent dual-chamber pacemaker (PM). After the operation, the patient did not have any episodes of syncope or seizures and the PM check-up showed almost 30% of atrial pacing.

**Conclusion**

No matter how obvious the neurological or other nature of syncope may seem, it is advised to exclude the cardiac origin of syncope, especially in patients with repaired CHD. One of the most common complications after surgery of CHD is rhythm and conduction disturbances. In some of these cases, permanent PM implantation can be unavoidable, even during pregnancy. The implantation of the PM device during pregnancy can be performed safely.

3. **Sex disparity in secondary prevention pharmacotherapy and clinical outcomes following acute coronary syndrome**

**Aims**

We sought to investigate if sex disparity exists for secondary prevention pharmacotherapy following acute coronary syndrome (ACS) and impact on long-term clinical outcomes.

**Methods and results**

We analysed data on medical management 30-day post-percutaneous coronary intervention (PCI) for ACS in 20,976 patients within the multicentre Melbourne Interventional Group registry (2005–2017). Optimal medical therapy (OMT) was defined as five guideline-recommended medications, near-optimal medical therapy (NMT) as four medications, sub-optimal medical therapy (SMT) as ≤3 medications. Overall, 65% of patients received OMT, 27% NMT and 8% SMT. Mean age was 64 ± 12 years; 24% (4931) were female. Women were older (68 ± 12
vs. 62 ± 12 years) and had more comorbidities. Women were less likely to receive OMT (61% vs. 66%) and more likely to receive SMT (10% vs. 8%) compared to men, \( P < 0.001 \). On long-term follow-up (median 5 years, interquartile range 2–8 years), women had higher unadjusted mortality (20% vs. 13%, \( P < 0.001 \)). However, after adjusting for medical therapy and baseline risk, women had lower long-term mortality [hazard ratio (HR) 0.88, 95% confidence interval (CI) 0.79–0.98; \( P = 0.02 \)]. NMT (HR 1.17, 95% CI 1.05–1.31; \( P = 0.004 \)) and SMT (HR 1.79, 95% CI 1.55–2.07; \( P < 0.001 \)) were found to be independent predictors of long-term mortality.

Conclusion

Women are less likely to be prescribed optimal secondary prevention medications following PCI for ACS. Lower adjusted long-term mortality amongst women suggests that as well as baseline differences between gender, optimization of secondary prevention medical therapy amongst women can lead to improved outcomes. This highlights the need to focus on minimizing the gap in secondary prevention pharmacotherapy between sexes following ACS.

4. **Thirteen-year trends in cardiovascular risk in men and women with chronic coronary syndrome**

**Aims**

To examine combined and sex-specific temporal changes in risks of adverse cardiovascular events and coronary revascularization in patients with chronic coronary syndrome undergoing coronary angiography.

**Methods and results**

We included all patients with stable angina pectoris and coronary artery disease examined by coronary angiography in Western Denmark from 2004 to 2016. Patients were stratified by examination year interval: 2004–2006, 2007–2009, 2010–2012, and 2013–2016. Outcomes were 2-year risk of myocardial infarction, ischaemic stroke, cardiac death, and all-cause death estimated by
adjusted incidence rate ratios using patients examined in 2004–2006 as reference. A total of 29,471 patients were included, of whom 70% were men. The 2-year risk of myocardial infarction [2.8% vs. 1.9%, adjusted incidence rate ratio 0.65, 95% confidence interval (CI) 0.53–0.81], ischaemic stroke (1.8% vs. 1.1%, adjusted incidence rate ratio 0.48, 95% CI 0.37–0.64), cardiac death (2.1% vs. 0.9%, adjusted incidence rate ratio 0.38, 95% CI 0.29–0.51), and all-cause death (5.0% vs. 3.6%, adjusted incidence rate ratio 0.65, 95% CI 0.55–0.76) decreased from the first examination interval (2004–2006) to the last examination interval (2013–2016). Coronary revascularizations also decreased (percutaneous coronary intervention: 51.6% vs. 42.5%; coronary artery bypass grafting: 24.6% vs. 17.5%). Risk reductions were observed in both men and women, however, women had a lower absolute risk.

**Conclusion**
The risk for adverse cardiovascular events decreased substantially in both men and women with chronic coronary syndrome from 2004 to 2016. These results most likely reflect the cumulative effect of improvements in the management of chronic coronary artery disease.

5. **COVID-19 Vaccination During Pregnancy and Incidence of SARS-CoV-2 Infection in Infants**

**IMPORTANCE**

Pregnant women are recommended to receive COVID-19 vaccination to reduce risk of severe COVID-19. Whether vaccination during pregnancy also provides passive protection to infants after birth remains unclear.

**OBJECTIVE**

To determine whether COVID-19 vaccination in pregnancy was associated with reduced risk of COVID-19 in infants up to age 4 months during COVID-19 pandemic periods dominated by Delta and Omicron variants.

**DESIGN, SETTING, AND PARTICIPANTS**
This nationwide, register-based cohort study included all live-born infants born in Norway between September 1, 2021, and February 28, 2022.

EXPOSURES

Maternal messenger RNA COVID-19 vaccination during second or third trimester compared with no vaccination before or during pregnancy.

MAIN OUTCOMES AND MEASURES

The risk of a positive polymerase chain reaction test result for SARS-CoV-2 during an infant’s first 4 months of life by maternal vaccination status during pregnancy with either dose 2 or 3 was estimated, as stratified by periods dominated by the Delta variant (between September 1 and December 31, 2021) or Omicron variant (after January 1, 2022, to the end of follow-up on April 4, 2022). A Cox proportional hazard regression was used, adjusting for maternal age, parity, education, maternal country of birth, and county of residence.

RESULTS

Of 21,643 live-born infants, 9,739 (45.0%) were born to women who received a second or third dose of a COVID-19 vaccine during pregnancy. The first 4 months of life incidence rate of a positive test for SARS-CoV-2 was 5.8 per 10,000 follow-up days. Infants of mothers vaccinated during pregnancy had a lower risk of a positive test compared with infants of unvaccinated mothers and lower risk during the Delta variant-dominated period (incidence rate, 1.2 vs 3.0 per 10,000 follow-up days; adjusted hazard ratio, 0.29; 95% CI, 0.19-0.46) compared with the Omicron period (incidence rate, 7.0 vs 10.9 per 10,000 follow-up days; adjusted hazard ratio, 0.67; 95% CI, 0.57-0.79).

CONCLUSIONS AND RELEVANCE

The results of this Norwegian population-based cohort study suggested a lower risk of a positive test for SARS-CoV-2 during the first 4 months of life among infants born to mothers who were vaccinated during pregnancy. Maternal
COVID-19 vaccination may provide passive protection to young infants, for whom COVID-19 vaccines are currently not available.

6. Hypertensive Disorders of Pregnancy Carry 2.4-Fold Greater Risk of Hypertension in 10 Years Post-Pregnancy, Study

Hypertensive disorders during pregnancy are associated with a 2.4 times higher risk of hypertension even in the 10 years after pregnancy, according to a new study involving predominantly Black women.

Longer-term cardiovascular (CV) risk – i.e., over 20 to 30 years – is already well-established following hypertensive disorders of pregnancy (HDP), including gestational hypertension and pre-eclampsia.

The new findings – published Monday online ahead of the June 21 issue of the Journal of the American College of Cardiology – are some of the first to demonstrate ongoing risk in the intervening decade post-HDP, particularly within a predominantly Black (85% self-identifying as Black) cohort.

“The importance of studying a more diverse population, including a larger percentage of Black patients, is of critical importance given that both HDP and [cardiovascular disease – CVD] disproportionally affect Black women,” lead author Lisa Levine, MD, MSCE, from the University of Pennsylvania, said in an accompanying press statement.

HDP impacts close to 20% of all pregnancies and is the leading cause of maternal death around the world, and carries higher long-term risk of heart disease and stroke.

Study population

A total 135 patients were enrolled into the prospective cross-sectional study from April 2016 to December 2019 from a previous observational study, conducted
from 2005 to 2007, which had enrolled 439 patients with obstetrician-confirmed HDP.

Subjects were included both with (84 subjects) and without (51 subjects) a history of HDP in a pregnancy ≥10 years earlier, and who underwent in-person visits with echocardiography, arterial tonometry and flow-mediated dilation of the brachial artery. Only patients without a history of cardiac disease, chronic hypertension or pregestational diabetes at the time of enrollment into the original parent study, 10 years earlier, were included.

In the group without a history of HDP, 78.4% were Black and 21.6% white, while 91.7% of those in the group who had a history of HDP were Black vs. 8.3% white (P = 0.037).

At study visit, those with no HDP history had a median age of 39.1 years compared to 35.7 years in HDP, while those with HDP history were heavier (median body mass index [BMI] of 31.4 kg/m² vs. 29.9 kg/m²), more likely to smoke (25% vs. 21.6% current tobacco users), and more likely to have a history of preterm birth (50% vs. 19.6%; P = 0.001).

HDP severity was most commonly marked as “severe preeclampsia (including [hemolysis, elevated liver enzymes, low platelets])” (61.9%), while 38.1% had mild gestational hypertension or preeclampsia. For 39.3%, HDP was recurrent.

Stage 2 chronic hypertension more than twice as likely following HDP

The researchers found that patients with a history of HDP had a 2.4-fold increased risk of new stage 2 chronic hypertension vs. those without HDP (56% vs. 23.5%, respectively) a relative risk of 2.38 (95% confidence interval [CI]: 1.40 – 4.40), “even when adjusting for race, maternal age, BMI, and history of preterm birth” (adjusted relative risk: 2.4; 95% CI: 1.39-4.14).

Criteria for stage 1 or 2 chronic hypertension were met in 82.1% of those with HDP history and 60.7% of those without (P < 0.001).
There was no association with other identifiable clinical CV risk factors such as diabetes, obesity or metabolic syndrome, the researchers found.

The researchers also found that there were no differences in non-invasive subclinical measures of CV risk, including left ventricular structure, global longitudinal strain, diastolic function, arterial stiffness or endothelial function.

The patients who did develop hypertension – regardless of HDP history – had greater left ventricular remodeling, including greater relative wall thickness; worse diastolic function, including lower septal and lateral e’ and E/A ratio; more abnormal longitudinal strain; and higher effective arterial elastance than those without hypertension, the researchers added.

“Differences in noninvasive measures of CV risk were driven mostly by the hypertension diagnosis, regardless of HDP history, suggesting that the known long-term risk of CVD after HDP may primarily be a consequence of hypertension development,” the researchers said.

Underdiagnosis and importance of routine screening

“Importantly, 18% of patients with a history of HDP met criteria for a new diagnosis of hypertension identified through the study visit,” the researchers added.

More than 60% of all patients who met criteria for either stage 1 or 2 hypertension did not have a formal diagnosis before the study, while among those with HDP history, just 39% of patients with either stage 1 or 2 hypertension had a formal diagnosis, “potentially missing the other half of patients in this category if screening had not otherwise been performed outside of our current study,” the researchers noted.

This, together with the effect hypertension has on future CV risk, “highlights the importance of early screening for hypertension in women post-pregnancy
complicated by HDP and the importance of initiating antihypertensive treatments to decrease the long-term risk of CVD,” said the researchers.

“Future studies should evaluate the optimal time period to screen for postpartum hypertension and a monitoring plan for these at-risk women.”

Missed opportunities

In an accompanying editorial, Josephine C. Chou, MD, MS, of the Yale University School of Medicine, went on to highlight studies showing that chronic hypertension increases the risk of symptomatic heart failure in the 3 years after a preeclampsia/eclampsia-related pregnancy, adding “even at 1 year postpartum, patients with HDP have not only a 4-fold increased risk of [chronic hypertension] but also higher 30-year CVD risk scores.”

“The initial postpartum years offer a window of opportunity to impact lifelong CV health, with ample evidence supporting [chronic hypertension] as the most important condition to target for reducing CVD in patients with HDP,” she added.

Yet, the high incidence of undiagnosed hypertension observed in the study highlights that the opportunity is “frequently missed,” said Chou.

“Only [around] 60% of patients with HDP have a continuity care visit by 6 months postpartum,” she said, potentially because of caregiving challenges faced by parents, fatigue, pain and exacerbation of mental health disorders.

“In contrast to the intensity of prenatal visits, postpartum care is relatively episodic and limited,” she lamented, but highlighted “promising strategies” incoming, such as postpartum transitional clinics providing CVD risk assessments with counseling.

Chou went on to call for further studies to evaluate new interventions, adding: “Black patients are known to be disproportionately affected by HDP and their complications. However, it is important to recognize race as a social construct, and not an inherent risk factor for disease.
“Therefore, addressing these disparities requires an understanding of the distinct CV profiles and sociodemographic factors that contribute to HDP and CVD in Black patients.”

The current study paves the way for such efforts, she said.

“[Our trial] along with studies with similar findings, further highlights the importance of routine screening for hypertension in this population,” Levine added. “Future studies should evaluate the optimal time period to screen for postpartum hypertension and a monitoring plan for these at-risk women.”

Sources:


7. Cardiac Microstructural Alterations on Echocardiography Identifies Sex-Specific Risk for Heart Failure

OBJECTIVE

Established preclinical imaging assessments of heart failure (HF) risk are based on macrostructural cardiac remodelling. Given that microstructural alterations may also influence HF risk, particularly in women, we examined associations between microstructural alterations and incident HF.
METHODS

We studied N=2511 adult participants (mean age 65.7±8.8 years, 56% women) of the Framingham Offspring Study who were free of cardiovascular disease at baseline. We employed texture analysis of echocardiography to quantify microstructural alteration, based on the high spectrum signal intensity coefficient (HS-SIC). We examined its relations to incident HF in sex-pooled and sex-specific Cox models accounting for traditional HF risk factors and macrostructural alterations.

RESULTS

We observed 94 new HF events over 7.4±1.7 years. Individuals with higher HS-SIC had increased risk for incident HF (HR 1.67 per 1-SD in HS-SIC, 95% CI 1.31 to 2.13; p<0.0001). Adjusting for age and antihypertensive medication use, this association was significant in women (p=0.02) but not men (p=0.78). Adjusting for traditional risk factors (including body mass index, total/high-density lipoprotein cholesterol, blood pressure traits, diabetes and smoking) attenuated the association in women (HR 1.30, p=0.07), with mediation of HF risk by the HS-SIC seen for a majority of these risk factors. However, the HS-SIC association with HF in women remained significant after adjusting for relative wall thickness (representing macrostructure alteration) in addition to these risk factors (HR 1.47, p=0.02).

CONCLUSIONS

Cardiac microstructural alterations are associated with elevated risk for HF, particularly in women. Microstructural alteration may identify sex-specific pathways by which individuals progress from risk factors to clinical HF.