News in November 2023

1. No Racial Disparities Seen in Long-Term MACE for Women With CAD

For women with obstructive coronary artery disease (CAD), there are no racial and ethnic disparities in long-term major adverse cardiovascular events (MACE) or cardiovascular mortality, according to a research letter published online Oct. 25 in the Canadian Journal of Cardiology.

Judy M. Luu, M.D., Ph.D., from McGill University Health Centre in Montreal, and colleagues evaluated long-term adverse outcomes for Black and non-Black women with obstructive CAD from the Women's Ischemia Syndrome Evaluation cohort.

Overall, 38 percent of the 944 women (17 percent non-Hispanic Black) had obstructive CAD. The researchers found that among participants with CAD, Black women had significantly higher body mass index, more hypertension, and higher rates of angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker use when compared with non-Black women. The primary outcome for the composite of MACE included all-cause mortality, nonfatal myocardial infarction, stroke, and hospitalization for angina or heart failure and occurred in 68 and 58.6 percent of Black and non-Black women with CAD, respectively. For women with CAD, the risk for MACE did not differ significantly for Black versus non-Black women; these findings persisted when adjusting for age and cardiovascular risk factors. Being Black was also associated with a similar risk for cardiovascular mortality.

"Despite Black women having a greater burden of cardiovascular risk factors and lower socioeconomic position compared with non-Black women, long-term cardiovascular disease outcomes were similar," the authors write.

2. Key Learning Points: British Society of Haematology Guideline on Anticoagulation Management During Pregnancy for Patients with Mechanical Heart Valves

Pregnancy in individuals with a mechanical heart valve (MHV) is very high risk. According to the modified World Health Organization classification of maternal cardiovascular risks, mechanical valves rank as category III (on a scale of I–IV of ascending risk), and are associated with a significantly increased risk of maternal mortality or morbidity.[1] Key maternal risks associated with MHVs in pregnancy stem from the need for anticoagulation therapy, notably to prevent valve thrombosis and haemorrhagic complications.[2] The fetus is also exposed to significant hazards, including miscarriage, stillbirth, fetal haemorrhage, and warfarin-induced embryopathy.[3]

An Urgent Need for New Guidance

Results from the UK Obstetric Surveillance System (UKOSS) study published in 2017 shone a spotlight on the true extent of the risks faced by pregnant women with MHVs in this country.[4] The UK-specific data noted that only 28% of these pregnancies resulted in good maternal and fetal outcomes—vastly inferior to the 58% of uncomplicated pregnancies found in the European Registry of Pregnancy and Cardiac Disease (RoPAC) study in 2015, although it should be noted that this is based on a relatively small number of cases.[5] Maternal mortality stood at a shocking 9% in the UKOSS study, with a 41% risk of severe morbidity, including a 16% rate of valve thrombosis and 9% risk of cerebrovascular accident.[4] This was a watershed moment, highlighting the urgent need to improve pregnancy care in women with MHVs in the UK.

In response, new guidance from the British Society for Haematology (BSH) for the anticoagulant management of pregnant individuals with mechanical heart valves[3] addresses the key risks encountered, and covers pre-pregnancy counselling, antenatal care, delivery management, and postpartum

complications. The BSH recommendations were developed using observational data and expert opinion, as well as evidence from non-pregnancy situations.[3]

Compared to the top-line advice offered by NICE and the European Society of Cardiology (ESC), the BSH guideline affords a deep dive into the key issues facing cardiologists when managing pregnant individuals with MHVs.[2,3,6] BSH recommendations were designed to be more practical and useful for clinicians, providing a detailed 'how to' guide for navigating the complexities and challenges of pregnancy in this group of patients. Recommendations align closely with other leading guidance in the field—notably the 2021 ESC/European Association for Cardiothoracic Surgery (EACTS) guideline for the management of valvular heart disease.[7]

Perhaps most importantly, BSH guidance was developed by a diverse group of specialists, including obstetricians, neonatologists, cardiologists, anaesthetists, and haematologists, thereby providing the overarching multidisciplinary team (MDT) perspective that is critical to improving maternal and fetal outcomes in this very high-risk setting.[3]

This article focuses on seven key learning points for cardiologists from the BSH guideline for anticoagulant management of pregnant individuals with mechanical heart valves.

1. Plan Ahead by Providing Pre-pregnancy Counselling for All Women of Reproductive Age

The BSH stresses that women with an MHV who are of childbearing age should be offered pre-pregnancy counselling (Box 1) as soon as appropriate.[3] In advance of cardiac surgery, cardiologists should be talking to their female patients about the different valve replacement options available and their potential impact on future pregnancy risk. When there is a viable alternative, mechanical valves should not be used in young women who may wish a future pregnancy.

One of the key pre-pregnancy counselling points for women with MHVs should be a frank discussion about the benefits and risks of different anticoagulation regimens for a mother and her fetus. A clear dichotomy exists in this regard. Although vitamin K antagonists (VKAs) are a superior anticoagulant in preventing mechanical valve thrombosis (MVT), they carry greater risks for a developing fetus.[3] Warfarin crosses the placenta, increasing the risk of fetal, placental, and neonatal haemorrhage, and also causes embryopathy, a fetal warfarin syndrome that occurs in up to 12% of cases.[3] Conversely, low molecular weight heparin (LMWH) anticoagulants do not cross the placenta, and are therefore safer for a fetus, but their use is associated with poorer maternal outcomes.[3]

2. Urgently Refer all Confirmed Pregnancies to the Specialist Team

Echoing guidance from other societies, the BSH urges that all pregnant individuals with MHVs should be managed in a tertiary specialist centre that has the relevant expertise.[3] Referral to the specialist team should be done as a matter of urgency—as soon as pregnancy is confirmed—with review of the patient by the MDT ideally taking place before 6 weeks' gestation.[3] Patients should have been informed how to self-refer as part of their pre-pregnancy counselling, but any healthcare professional who encounters a newly pregnant woman with an MHV can—and should—initiate a referral if this has not already been done.

3. Review Risk–Benefit Ratio and Develop an Anticoagulation Strategy

All anticoagulants carry risks to both a mother and the developing fetus. An anticoagulation plan should therefore be individualised, considering specific maternal risk factors and patient preferences, and ideally developed in the pre-pregnancy setting. This should be a written document that is widely circulated, with a copy also provided to the patient.

The BSH guideline states that no single anticoagulation strategy can be recommended above others, based on current evidence.[3] This mirrors ESC/EACTS guidance, which acknowledges that, although therapeutic

anticoagulation during pregnancy is 'of upmost importance', no single anticoagulation regimen is ideal, and the choice must be a balance between maternal and fetal risks.[7]

VKAs are superior to LMWH at preventing valve thrombosis in pregnancy, and constitute the optimal therapy for improving maternal outcomes.[3] According to the BSH, it is therefore reasonable to weight recommendations towards warfarin for women at higher risk of MVT (Box 2). Although the instinct may be to reduce the dose to minimise harm, this is not recommended. There is insufficient evidence that keeping the international normalised ratio (INR) target below range so as to maintain warfarin at less than 5 mg averts adverse fetal outcomes;[3] low-dose warfarin may in fact lead to poorer fetal outcomes.[8]

Box 2: Risk Factors for Mechanical Valve Thrombosis[3,7]

- Prosthesis thrombogenicity
- Mitral, tricuspid, or pulmonary valve replacement
- Previous thromboembolism
- Valve dysfunction or mismatch
- Left ventricular dysfunction
- Atrial fibrillation
- Poor medication adherence.

Given the potential for warfarin embryopathy, in clinical practice most mothers-to-be opt to switch to LMWH. In this case, as soon as a positive pregnancy test is confirmed, the individual should stop taking VKAs and start on twice-daily LMWH; it is not necessary for the INR to already be within the normal range.[3] When switching to LMWH, the BSH advises starting on a dose higher than the standard therapeutic dose, because the risk of MVT

appears to be front-loaded in the first trimester during transition from VKA to LMWH.[3] Despite the perception that MVT risk is highest after birth, in reality, the majority of events occur antenatally rather than postpartum.[3] In the international RoPAC study, half of all MVTs in pregnant women occurred during the transition from VKA to LMWH in the first trimester.[5] Very careful attention is therefore required during this transition in the early stages of pregnancy. The addition of low-dose aspirin to LMWH anticoagulation is also recommended, assuming there are no contraindications.[3]

4. Monitor Anticoagulants Throughout Pregnancy and Take Steps to Maximise Adherence

For patients who opt to remain on warfarin, non-pregnancy INR targets can be used for monitoring. At a minimum, INR should be checked weekly when it is unstable and fortnightly when stable, with women given the option to self-test when appropriate.[3] Warfarin crosses the placenta so avoid a high INR, otherwise a fetus will be more anticoagulated than its mother.[3]

Data suggest that standard therapeutic doses of LMWH in pregnancy are inadequate and that it is prudent to monitor, but controversy persists on whether to use peak or trough testing.[3] Currently, evidence to support the routine use of specific trough levels is lacking.[3] As a 'reasonable compromise', the BSH therefore recommends using an anti-Xa assay—with a peak anti-Xa target between 1.0 and 1.4 IU/ml, taken 3–4 hours after a twice-daily LMWH dose.[3] Monitoring should be carried out at least weekly until the target level is achieved—or when levels are below target at any stage—moving to regular checks every 2–4 weeks thereafter, depending on stability.[3]

The BSH advises a frequency of LMWH injection of not more than twice daily—given that the physical burden and injection site toxicity of such a regimen could prove counterproductive to adherence.[3] Low adherence to the chosen anticoagulation strategy is a leading cause of morbidity and mortality in pregnant women with MHV, underscoring the importance of measures to

boost adherence both during pregnancy and the postpartum period.[3] Women should be made aware, even before embarking on pregnancy, of the need for frequent hospital appointments and the fact that travel to a tertiary specialist centre will be required. This, in turn, may have implications for their work, finances, or ability to care for other children.

5. Maintain a High Index of Suspicion for Valve Thrombosis in Any Pregnant Women with a Mechanical Heart Valve

Given the high risk of MVT in pregnancy, clinicians should remain alert to potential warning signs and symptoms, and act accordingly (Box 3).[3]

Box 3: Red Flags for Mechanical Heart Valve Dysfunction[3]

- Muffled mechanical sounds
    - unable to hear clicks from the valve closure
- New murmur
- Shortness of breath
- Heart failure
- Cardiogenic shock
- Embolic events
    - stroke
    - acute abdominal pain—renal, splenic infarcts
- Pulmonary embolism (when patients have a right-sided MHV).

Box 3: Red Flags for Mechanical Heart Valve Dysfunction[3]

MHV=mechanical heart valve

If an MVT should unfortunately occur, the patient must be managed in a specialist centre under the care of an MDT, with the use of thrombolysis or emergency cardiac surgery when appropriate.[3]

6. Be Ready for Labour and Delivery—and Beyond

Planning is central to a successful outcome of a pregnancy in women with MHV. Birth can prove a hazardous time due to the need to balance the risk of a haemorrhage with that of an MVT from prolonged periods of anticoagulant reduction. Currently, there is an absence of data to support any specific mode of delivery or anticoagulation regimen as optimal, so the decision should be individualised—taking into account benefits and risks.[3] A plan for timing and mode of delivery should be agreed in advance, with input from all members of the MDT and from the patient.[3]

Advertisement

The BSH makes several key recommendations on anticoagulation in the run up to birth and the immediate postpartum period (Box 4).[3]

Box 4: Managing Labour and Delivery[3]

Before

- Switch patients on VKAs to heparin a minimum of 2 weeks before anticipated delivery, and by 36 weeks at the latest

Box 4: Managing Labour and Delivery[3]

- Pause therapeutic LMWH for at least 24 hours before surgical delivery to permit neuraxial analgesia/anaesthesia
- Stop aspirin at least 3 days before delivery given the high risk of PPH.

During

- Consider a caesarean section for women on VKAs presenting in labour ≤2 weeks from their scheduled delivery date to reduce fetal bleeding risks from labour
- Avoid prolonged periods of interruption to anticoagulation—e.g. during induction of labour
- Consider use of intermediate or prophylactic doses of LMWH or intravenous UFH during labour induction.

After

- Use prophylactic or intermediate doses of LMWH for the first 24–48 hours after delivery, before re-introducing therapeutic doses
- Do not restart VKAs until day 5–7 at the earliest
- If using UFH, gradually increase intensity for the first few days.

In contrast to NICE and other guidance which recommends resumption of therapeutic anticoagulation almost immediately after birth, the BSH advises a more cautious approach—reintroducing anticoagulation in a stepwise fashion.[2,3,6] BSH advice is therefore to give prophylactic or intermediate doses of LMWH only for the first 24–48 hours after delivery.[3] The rationale is that, although the risk of MVT exists throughout pregnancy, the risk of major

haemorrhage is concentrated in the period around delivery. If postpartum haemorrhage occurs, further extended pauses in anticoagulation will be required which may be counterproductive. Furthermore, evidence from subjects who are not pregnant argues against immediate anticoagulant escalation, even in patients with MHVs.[7,9]

Postpartum, women should not leave hospital without a firm plan for contraception in place. Insertion of an intrauterine contraceptive device or implant can be undertaken before discharge, or even during delivery, if appropriate. Women should be followed up postnatally to review pregnancy outcomes and discuss plans for any future pregnancies.

7. Recognise that Multidisciplinary Collaboration and Individual Ownership are Key to Optimising Outcomes

This new guideline from the BSH fills a clear gap in current care for pregnant women with MHVs, and aims to optimise management for both mother and baby. Communication and collaboration are key to achieving the improvement in outcomes that are clearly needed, given the stark findings from the UKOSS study.[4] The importance of MDT input is reiterated in ESC/EACTS guidelines, which recommend close collaboration with a Pregnancy Heart Team, both when choosing the initial prosthesis and when managing any subsequent pregnancy.[7] Similarly, the WHO advocates the need for expert-led preconception counselling and care during pregnancy to mitigate maternal cardiovascular risk posed by mechanical valves.[1] The MDT team charged with managing pregnant women with MHVs should include representation from obstetrics, cardiology, cardiac surgery, anaesthetics, neonatology, haematology, and specialist midwives.

Clinicians must also recognise that pregnancy is an emotive time for women and, although it is not possible to make the process entirely safe, patients can be empowered to take charge of their own care by being involved in proactive planning, anticoagulation choices, and adherence. Many cardiologists will have direct experience of adverse outcomes with MHVs during pregnancy, so

individual ownership is important, despite the constraints of workload. By reading and referring to these BSH guidelines—and reaching out to MDT colleagues as and when required—cardiologists can put themselves in the best possible position to help their pregnant patients with MHVs.

Conclusion

Pregnancy represents a high-risk time for women with MHVs, but proactive intervention, specialist care, and guidelines-led anticoagulation management are key tools for minimising risk and maximising outcomes. To improve the prospects of pregnant women with MHVs in the UK, rapid optimisation of management according to the latest guidance is crucial.

Caring for women with MHVs in pregnancy is a huge clinical challenge that can only be improved through raised awareness of the risks, education on the current guidance, and advocacy within the NHS on behalf of women of childbearing age with MHVs.

3. Waiting times of women vs. men undergoing transcatheter aortic valve implantation

Aims

Increasing transcatheter aortic valve implantation (TAVI) rates have resulted in prolonged waiting times. These have been associated with heart failure hospitalizations (HFH) and mortality yet sex differences have not yet been reported.

Methods and results

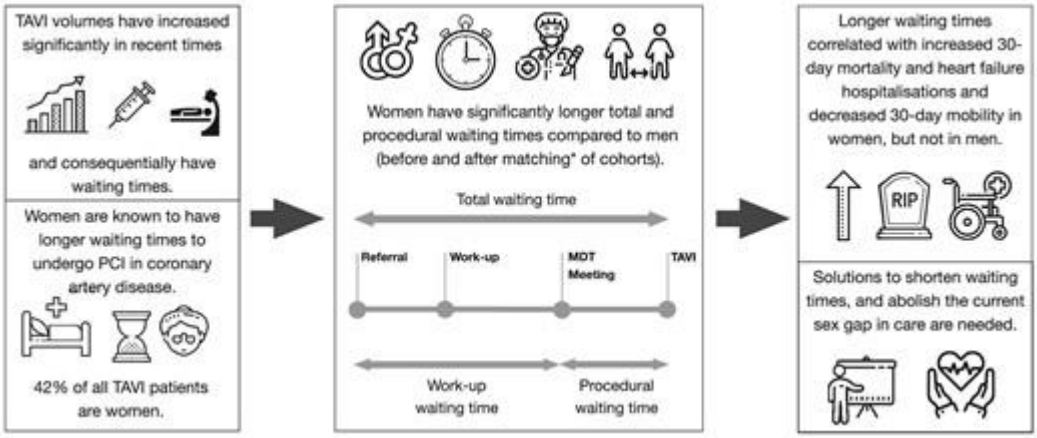
All patients who underwent TAVI for severe aortic stenosis at a tertiary referral hospital in Australia were prospectively included. Total waiting time was divided into 'work-up' waiting time (period from referral date until heart team approval) and, 'procedural' waiting time (period from heart team approval until procedure date). Patients were analysed according to sex. Cohorts were matched to correct for differences in baseline and procedural variables. The

primary endpoints were waiting times. Secondary outcomes included a composite of 30-day mortality and HFH, quality of life, and mobility. A total of 407 patients (42% women) were included. After matching of the two cohorts (345 patients), women had significantly longer total waiting times than men: median 156 [interquartile range (IQR) 114–220] days in women vs. 147 [IQR 92–204] days in men (P = 0.037) including longer work-up (83 [IQR 50–128] vs. 71 [IQR 36–119], P = 0.15) and procedural waiting times (65 [IQR 44–100] vs. 58 [IQR 30–93], P = 0.042). Increasing waiting times were associated with higher 30-day mortality and HFH (P = 0.01 for work-up waiting time, P = 0.02 for procedural waiting time) and decreased 30-day mobility (P = 0.044 for procedural waiting time) in women, but not in men.

Conclusion

TAVI waiting times are significantly longer in women compared to men and are associated with increased mortality and HFH and reduced mobility at 30-days.

Graphical Abstract



4. **Sex differences in the etiology and burden of heart failure across country income level: analysis of 204 countries and territories 1990–2019**

Background

Heart failure (HF) is a global epidemic.

Objective

To assess global sex differences in HF epidemiology across country income levels.

Methods and results

Using Global Burden of Disease (GBD) data from 204 countries and territories 1990–2019, we assessed sex differences in HF prevalence, etiology, morbidity, and temporal trends across country sociodemographic index or gross national income. We derived age-standardized rates. Of 56.2 million (95% uncertainty interval [UI] 46.4–67.8 million) people with HF in 2019, 50.3% were females and 69.2% lived in low- and middle-income countries; age-standardized prevalence was greater in males and in high-income countries. Ischaemic and hypertensive heart disease were top causes of HF in males and females, respectively. There were 5.1 million (95% UI 3.3–7.3 million) years lived with disability, distributed equally between sexes. Between 1990 and 2019, there was an increase in HF cases, but a decrease in age-standardized rates per 100 000 in males (9.1%, from 864.2 to 785.7) and females (5.8%, from 686.0 to 646.1). High-income regions experienced a 16.0% decrease in age-standardized rates (from 877.5 to 736.8), while low-income regions experienced a 3.9% increase (from 612.1 to 636.0), largely consistent across sexes. There was a temporal increase in age-standardized HF from hypertensive, rheumatic, and calcific aortic valvular heart disease, and a decrease from ischaemic heart disease, with regional and sex differences.

Conclusion

Age-standardized HF rates have decreased over time, with larger decreases in males than females; and with large decreases in high-income and small increases in low-income regions. Sex and regional differences offer targets for intervention.

5. PTSD Symptoms Linked to Higher Carotid Atherosclerosis in Women

For midlife women, posttraumatic stress disorder (PTSD) symptoms are associated with higher carotid atherosclerosis and with greater brain small vessel disease and poorer cognitive performance among APOE ε4 carriers, according to a study published online Nov. 2 in JAMA Network Open.

Rebecca C. Thurston, Ph.D., from the University of Pittsburgh, and colleagues examined whether PTSD symptoms among midlife women are associated with carotid intima media thickness (IMT), brain white matter hyperintensity volume (WMHV), and cognitive performance in a cross-sectional study. Participants included 274 community-based women ages 45 to 67 years (64 were APOE ε4 carriers) who completed questionnaires (PTSD Checklist-Civilian Version), physical measures, phlebotomy, neuropsychological testing, a carotid ultrasonographic examination, and 3-Tesla brain magnetic resonance imaging.

The researchers observed an association for higher PTSD symptoms with greater carotid IMT (multivariable β = 0.07). There was significant variation noted by APOE ε4 status in the association of PTSD symptoms with neurocognitive outcomes. In multivariable models, PTSD symptoms were associated with greater whole-brain WMHV, periventricular WMHV, deep WMHV, and frontal WMHV (β = 0.96, 0.90, 1.21, and 1.25, respectively) among women with APOE ε4, as well as poorer cognition, specifically attention and working memory, semantic fluency, perceptual speed, and processing speed (β = −3.37, −6.01, −12.73, and −11.05, respectively).

"Our findings point to an at-risk population that may warrant early intervention and prevention efforts to reduce cardiovascular and neurocognitive risk at midlife and beyond," the authors write.

6. **Women More Likely to Have Obesity in Low- and Middle-Income Countries**

TOPLINE:

Women are 2-3 times more likely than men to have obesity in low- and middle-income countries, with the disparity as much as 10 times higher among women in the sub-Saharan region of Africa. Key factors believed to contribute to the higher obesity rates include weight gain during pregnancy and menopause, poor dietary habits, sedentary lifestyles, and sociocultural

aspects such as beliefs that larger body types suggest high socioeconomic status and fertility.

METHODOLOGY:

- A systematic review and meta-analysis of 345 studies involved 3.9 million people with data on associations between sex, obesity and cardiometabolic diseases.
- Three hundred of the studies reported data on obesity in women and men in low- and middle-income countries.
- Key metabolic diseases evaluated included type 2 diabetes, impaired glucose tolerance, dyslipidemia, and nonalcoholic fatty liver disease (now known as MASLD [metabolic dysfunction–associated steatotic liver disease].
- Hypertension, coronary heart disease, myocardial infarction, and stroke were included as obesity-related cardiovascular diseases.
- Obesity was defined as a body mass index (BMI) of ≥27.5 kg/m^2 in studies in the South Asian community, and ≥30 kg/m^2 in other populations.
- Studies including children, adolescents, and those in high-income countries, as well as smaller studies and secondary analyses, were excluded.

TAKEAWAY:

- Overall, the odds of obesity were 2.7-fold higher among women than men (odds ratio [OR] 2.72).
- There were significant disparities in the differences between genders and obesity based on regions, with significantly higher odds for women in studies from Sub-Saharan Africa (OR, 3.91), followed by the Middle East and North Africa (OR, 2.69), and Latin America and Caribbean regions (OR, 2.17).
- Studies from Sub-Saharan Africa reported odds that were 3-fold to as much as 10-fold higher in women than men.

- The lowest differences between gender in terms of obesity odds were observed in studies from South Asia (OR, 1.43) and East Asia and Pacific (OR, 1.43).
- Gender disparities were observed regardless of the country's income status, setting and year of study being before or after 2000, as well as age.
- Women had a slight decrease in the risk for hypertension vs men (OR, 0.95), and a slight increase in the risk for type 2 diabetes (OR, 1.07).

IN PRACTICE:

"To our knowledge, ours is the first meta-analysis to quantify the sex-related disparities in low- and middle-income countries for obesity, hypertension, and type 2 diabetes," the authors report.

7. Association of Age and Sex With Use of Transcatheter Aortic Valve Replacement in France

Background

Current guidelines recommend selecting surgical aortic valve replacement (SAVR) or transcatheter aortic valve replacement (TAVR) based on age, comorbidities, and surgical risk. Nevertheless, reports from the United States suggest a rapid expansion of TAVR in young patients.

Objectives

The authors sought to evaluate the trends in TAVR uptake at a nationwide level in France according to age and sex.

Methods

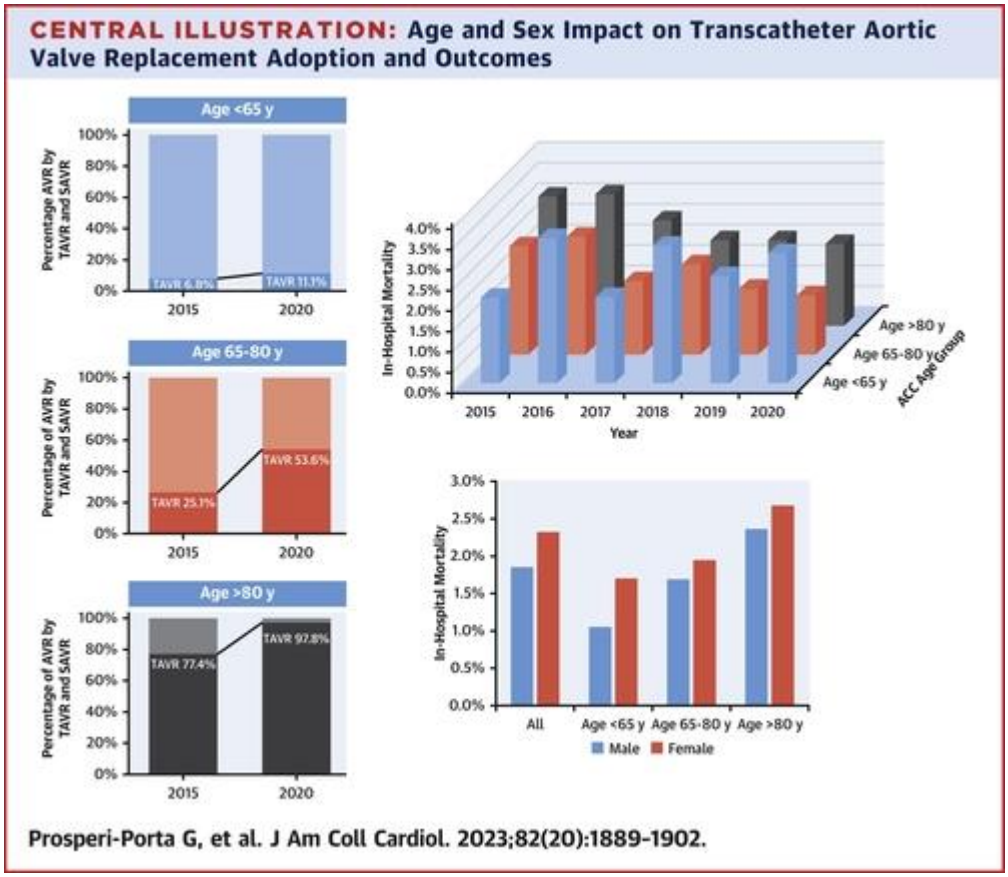
Using a nationwide administrative database, we evaluated age- and sex-related trends in TAVR uptake, patient demographics, and in-hospital outcomes between 2015 and 2020.

Results

A total of 107,397 patients (44.0% female) underwent an isolated aortic valve replacement (AVR) (59.1% TAVR, 40.9% SAVR). In patients <65 years of age, the proportion of TAVR increased by 63.2% (P < 0.001) from 2015 to 2020 but remained uncommon at 11.1% of all AVR by 2020 (12.4% in females, 10.6% in males) while TAVR was the dominant modality in patients ≥65 years of age. In patients undergoing TAVR, the Charlson comorbidity index (CCI) (P = 0.119 for trend) and in-hospital mortality (P = 0.740 for trend) remained unchanged in patients <65 years of age but declined in those ≥65 years of age irrespective of sex (all P < 0.001 for trends). Females were older (P < 0.001), had lower CCI (P < 0.001), were more likely to undergo TAVR (P < 0.001), and experienced higher in-hospital mortality (TAVR, P = 0.015; SAVR, P < 0.001) that persisted despite adjustment for age and CCI.

Conclusions

In France, the use of TAVR remained uncommon in young patients, predominantly restricted to those at high risk. Important sex differences were observed in patent demographics, selection of AVR modality, and patient outcomes. Additional research evaluating the long-term impact of TAVR use in young patients and prospective data evaluating sex differences in AVR modality selection and outcomes are needed.



Prosperi-Porta G, et al. J Am Coll Cardiol. 2023;82(20):1889-1902.

8. **Impact of Female Sex on Cardiogenic Shock Outcomes: A Cardiogenic Shock Working Group Report**

Background

Studies reporting cardiogenic shock (CS) outcomes in women are scarce.

Objectives

The authors compared survival at discharge among women vs men with CS complicating acute myocardial infarction (AMI-CS) and heart failure (HF-CS).

Methods

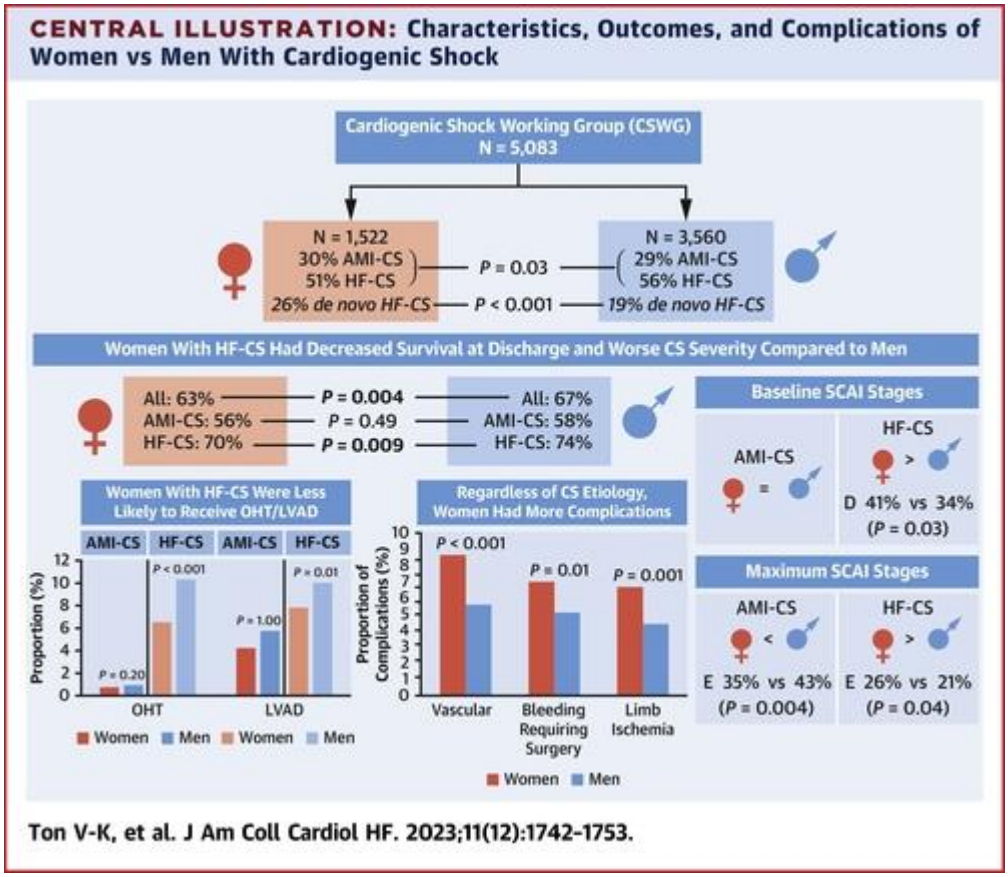
The authors analyzed 5,083 CS patients in the Cardiogenic Shock Working Group. Propensity score matching (PSM) was performed with the use of baseline characteristics. Logistic regression was performed for log odds of survival.

Results

Among 5,083 patients, 1,522 were women (30%), whose mean age was 61.8 ± 15.8 years. There were 30% women and 29.1% men with AMI-CS (P = 0.03). More women presented with de novo HF-CS compared with men (26.2% vs 19.3%; P < 0.001). Before PSM, differences in baseline characteristics and sex-specific outcomes were seen in the HF-CS cohort, with worse survival at discharge (69.9% vs 74.4%; P = 0.009) and a higher rate of maximum Society for Cardiac Angiography and Interventions stage E (26% vs 21%; P = 0.04) in women than in men. Women were less likely to receive pulmonary artery catheterization (52.9% vs 54.6%; P < 0.001), heart transplantation (6.5% vs 10.3%; P < 0.001), or left ventricular assist device implantation (7.8% vs 10%; P = 0.01). Regardless of CS etiology, women had more vascular complications (8.8% vs 5.7%; P < 0.001), bleeding (7.1% vs 5.2%; P = 0.01), and limb ischemia (6.8% vs 4.5%; P = 0.001). More vascular complications persisted in women after PSM (10.4% women vs 7.4% men; P = 0.06).

Conclusions

Women with HF-CS had worse outcomes and more vascular complications than men with HF-CS. More studies are needed to identify barriers to advanced therapies, decrease complications, and improve outcomes of women with CS.



9. **Do Outcomes Vary by Race in Women With Obstructive CAD?**

Treatment in universities and academic centers may be associated with a reduction in racial or ethnic disparities in long-term major adverse cardiovascular events (MACE) or cardiovascular disease (CVD) mortality among women with obstructive coronary artery disease (CAD), new research suggests.

An analysis of 364 women with obstructive CAD found that Black race was associated with the same risk for MACE (hazard ratio [HR], 0.87) after adjustment for age and CV risk factors and a similar risk for CVD mortality (age-adjusted HR, 1.56) as non-Black race.

"It was surprising to find that despite black women having a relatively higher burden of CV risk factors and overall lower socioeconomic position, compared to non-Black women, long-term CVD outcomes were similar," lead author Judy M. Luu, MD, PhD, junior scientist at McGill University Health Centre in Montreal, Canada, told Medscape Medical News.

"This key point supports emerging areas of intervention that could impact outcomes, including education," she said. "It also supported the hypothesis that other risk factors contribute to CVD, beyond the traditional ones, including perhaps experience of systemic racism."

The study was published online October 25 in the Canadian Journal of Cardiology.

Similar Outcomes

The investigators studied 944 women (mean age, 58 years; 17% non-Hispanic black) enrolled in the Women's Ischemia Syndrome Evaluation (WISE). Of those 944, more than one third (38%) had obstructive CAD.

Among the participants with CAD, black women (mean age, 59 years) had a higher BMI (31.4 vs 28.8), greater prevalence of high blood pressure (89.7% vs 63.5%), and higher rates of use of ACE inhibitors or angiotensin II receptor blockers (ARB, 82.6% vs 63.4%) compared with non-Black women. Statin, beta-blocker, calcium-channel blocker, and hormone replacement therapy use did not differ between black women and non-Black women.

In addition, a larger proportion of Black women had lower levels of education (50% vs 18.5%), lower levels of income, and public health insurance.

The primary outcome, MACE, included all-cause mortality, nonfatal myocardial infarction, stroke, and hospitalization for angina or heart failure. This outcome occurred in 47 Black women (68%) with CAD and 173 non-Black women (58.6%) with CAD.

Among patients with CAD, Black race was associated with the same risk for MACE (age-adjusted HR, 1.15). After accounting for age and CV risk factors, the adjusted HR was 0.87, driven largely by angina hospitalization (50.7% in black vs 33.8% in non-Black women).

Age and Duke Activity Status Inventory were independent predictors of long-term MACE at 10 years for both groups. Race or ethnicity, however, were not predictors.

10. **Hypothetical interventions and risk of atrial fibrillation by sex and education: application of the parametric g-formula in the Tromsø Study**

Aims

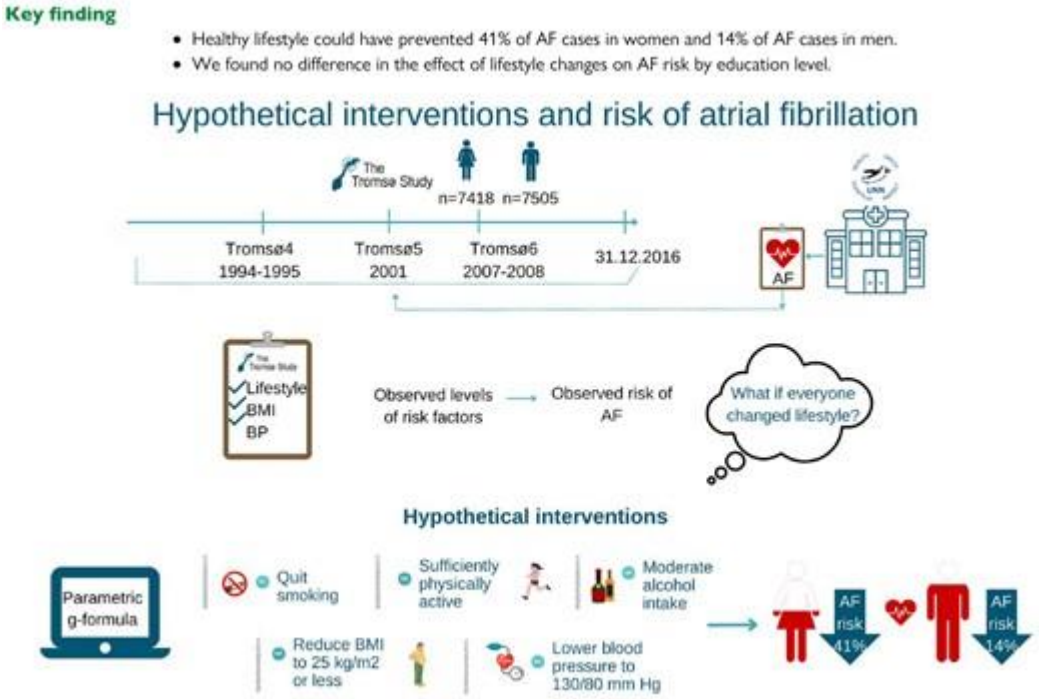
To use the parametric g-formula to estimate the long-term risk of atrial fibrillation (AF) by sex and education under hypothetical interventions on six modifiable risk factors.

Methods and results

We estimated the risk reduction under hypothetical risk reduction strategies for smoking, physical activity, alcohol intake, body mass index, systolic, and diastolic blood pressure in 14 923 women and men (baseline mean age 45.8 years in women and 47.8 years in men) from the population-based Tromsø Study with a maximum of 22 years of follow-up (1994–2016). The estimated risk of AF under no intervention was 6.15% in women and 13.0% in men. This cumulative risk was reduced by 41% (95% confidence interval 17%, 61%) in women and 14% (−7%, 30%) in men under joint interventions on all risk factors. The most effective intervention was lowering body mass index to ≤ 25 kg/m^2, leading to a 16% (4%, 25%) lower risk in women and a 14% (6%, 23%) lower risk in men. We found significant sex-differences in the relative risk reduction by sufficient physical activity, leading to a 7% (-4%, 18%) lower risk in women and an 8% (−2%, −13%) increased risk in men. We found no association between the level of education and differences in risk reduction by any of the interventions.

Conclusion

The population burden of AF could be reduced by modifying lifestyle risk factors. Namely, these modifications could have prevented 41% of AF cases in women and 14% of AF cases in men in the municipality of Tromsø, Norway during a maximum 22-year follow-up period.



11. **Sex-specific presentation, care, and clinical events in individuals admitted with NSTEMI: the ACVC-EAPCI EORP NSTEMI registry of the European Society of Cardiology**

Aims

Women have historically been disadvantaged in terms of care and outcomes for non-ST-segment elevation myocardial infarction (NSTEMI). We describe patterns of presentation, care, and outcomes for NSTEMI by sex in a contemporary and geographically diverse cohort.

Methods and results

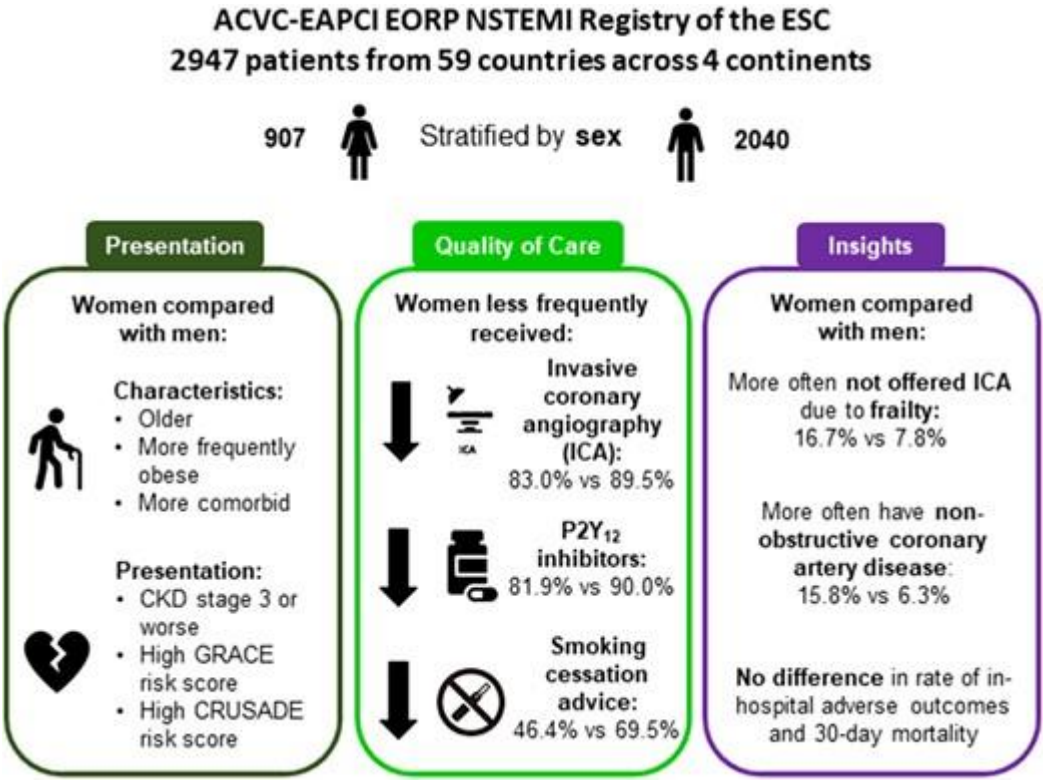
Prospective cohort study including 2947 patients (907 women, 2040 men) with Type I NSTEMI from 287 centres in 59 countries, stratified by sex. Quality of care was evaluated based on 12 guideline-recommended care interventions. The all-or-none scoring composite performance measure was used to define receipt of optimal care. Outcomes included acute heart failure, cardiogenic shock, repeat myocardial infarction, stroke/transient ischaemic attack, BARC Type ≥3 bleeding, or death in-hospital, as well as 30-day mortality. Women admitted with NSTEMI were older, more comorbid, and more frequently categorized as at higher ischaemic (GRACE >140, 54.0% vs.

41.7%, P < 0.001) and bleeding (CRUSADE >40, 51.7% vs. 17.6%, P < 0.001) risk than men. Women less frequently received invasive coronary angiography (ICA; 83.0% vs. 89.5%, P < 0.001), smoking cessation advice (46.4% vs. 69.5%, P < 0.001), and $P2Y_{12}$ inhibitor prescription at discharge (81.9% vs. 90.0%, P < 0.001). Non-receipt of ICA was more often due to frailty for women than men (16.7% vs. 7.8%, P = 0.010). At ICA, more women than men had non-obstructive coronary artery disease or angiographically normal arteries (15.8% vs. 6.3%, P < 0.001). Rates of in-hospital adverse outcomes and 30-day mortality were low and did not differ by sex.

Conclusion

In contemporary practice, women presenting with NSTEMI, compared with men, less frequently receive antiplatelet prescription, smoking cessation advice, or are considered eligible for ICA.

Graphical Abstract



12. **Left atrial stiffness and sex differences in atrial fibrillation recurrence after catheter ablation.**

Background

Atrial fibrillation (AF) occurs more frequently in men, but women suffer more AF recurrence; mechanisms are not completely understood.

Purpose

To explore whether sex related differences in LA stiffness (LAstiffn) in patients with AF ablation could potentially explain differences in AF recurrence.

Methods

We screened patients with catheter ablation for AF, in sinus rhythm at 3 months post-ablation, with no significant mitral valve disease (< moderate), and with prospectively measured LA volumes [maximum (LAVI) and minimum volume index] by echocardiography. LAStiffn index was estimated as (E/e')/LA emptying fraction. Outcome endpoint was AF recurrence up to 14 years post ablation.

Results

A total of 591 patients with AF ablation were studied (mean age 60±10 years; 25% women; Table1). At 3 months post-ablation, LAVI was 36±10 mL/m2 and LAstiffn was 0.31±0.21 1/%. Compared to males, female patients were slightly older, had more frequently hypertension, congestive heart failure, prior stroke/TIA, higher CHA2DS2-VASc score; they less often had persistent AF, coronary artery disease, or dilated cardiomyopathy. Women also had higher LAstiffn (0.37±0.24 vs. 0.29±0.19, P <.0001, Figure 1), despite similar indexed LA volumes (Table1). Rates of AF recurrence at follow-up (median 7.5 years; 347 patients with events) were higher in women vs. men (Figure 2, left; log-rank P<.001) and persisted after adjustment for age, type and duration of AF, body mass index, cardiovascular risk factors and comorbidities, CHA2DS2-VASc score ≥2, LV ejection fraction, and LAVI (adjusted HR 1.58 [1.20-2.08], P=.001). Overall, LA volumes and LAstiffn were higher in patients with older age and more comorbidities (hypertension, congestive heart failure, coronary artery disease, persistent AF, CHA2DS2-VASc score ≥2, etc; P<.01 for all). At multivariable regression analysis, LAVI and LAstiffn correlated with E/e', LV

size and mass, degree of mitral/tricuspid regurgitation, and LV stroke volume index (only LAVI). In addition, LAstiffn was higher in patients with elevated right ventricular systolic pressure (RVSP) >35 mmHg and increase in RVSP more than 10 mmHg from pre-ablation (P<.0001) (correlation R=0.44, P<.0001). At follow-up, after adjusting for age and LAVI, higher LAstiffn remained associated with AF recurrence in women (P=.02, HR 2.82 per unit change, 95% CI, 1.08-6.72; Figure 2, right), but not in men (P=.30).

Conclusions

LAStiffn is higher in women vs. men and correlates with burden of comorbidities, aging, diastolic dysfunction and pulmonary hypertension, possibly reflecting more extensive LA myopathy, and potentially contributing to sex differences in AF recurrence.

Figure 1

Figure 1. LA stiffness and LA volume index (at 3 months post-ablation)

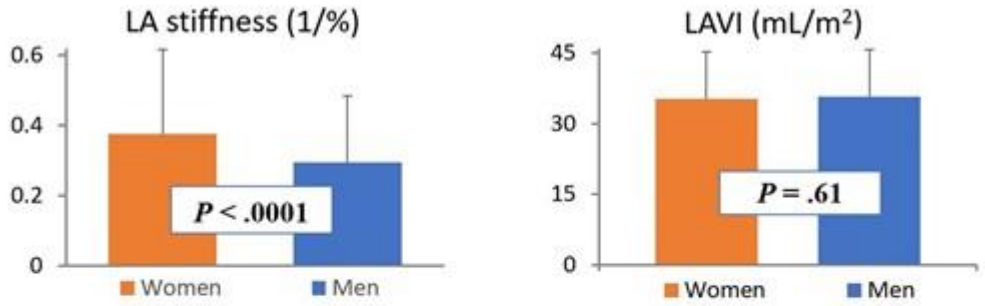
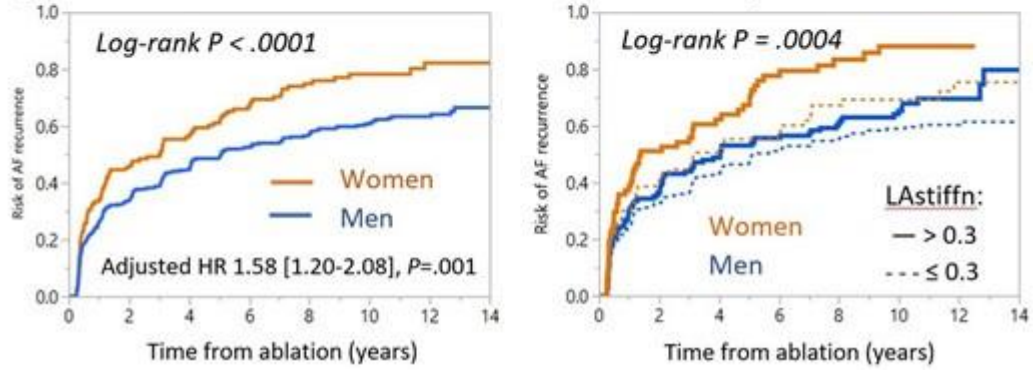


Figure 2. Cumulative rates of AF recurrence at followup



13. **Optimal Mode of Delivery Among Pregnant Patients With Cardiomyopathies**

Study Questions:

What is the optimal mode of delivery among patients with cardiomyopathies?

Methods:

This was a retrospective cohort study of patients with cardiomyopathy using the Premier inpatient administrative database. The primary analysis compared outcomes among patients with intended vaginal delivery versus intended cesarean delivery (intention to treat). The secondary analysis compared outcomes among patients with vaginal versus cesarean deliveries (as treated).

Results:

Of 2,291 deliveries, there was no difference in outcomes in patients with intended vaginal versus cesarean delivery: nontransfusion morbidity (adjusted odds ratio [aOR], 1.17; 95% confidence interval [CI], 0.91–1.51), blood transfusion (aOR, 1.27; 95% CI, 0.81–1.98), or readmission (aOR, 1.03; 95% CI, 0.73–1.44). Among patients who actually had cesarean delivery (as treated), there was a twofold higher risk of nontransfusion morbidity (aOR, 2.44; 95% CI, 1.85–3.22) and blood transfusion (aOR, 2.26; 95% CI, 1.34–3.81) versus vaginal delivery.

Conclusions:

The authors conclude that among patients with cardiomyopathies, a trial of labor does not confer higher risk of adverse outcomes compared with planned cesarean delivery.

Perspective:

Planned cesarean deliveries should be reserved for obstetric indications because cesarean deliveries are associated with increased risk of hemorrhage, thrombotic complications, and infection. Very rarely is there a cardiac indication for planned cesarean delivery; these include: 1) patients with premature labor while actively anticoagulated with warfarin, 2) severe symptomatic aortic stenosis, and 3) acute decompensated heart failure unable to be medically stabilized. There has been a lack of data about outcomes among pregnant patients with cardiomyopathies. This observational study showed that a trial of labor does not confer a higher risk of maternal morbidity, blood transfusion, or readmission compared with planned caesarean delivery. These findings support the current guideline recommendations to avoid cesarean delivery in the absence of an obstetric or fetal indication.

14. **Mortality in Norwegian men and women with an incident myocardial infarction**

Extract

In general, mortality is higher in men than in women. However, it is unsettled whether this is the case after myocardial infarction. Some studies have shown higher mortality in men,[1,2] whereas other have shown higher mortality in women, especially at younger ages.[3–5] We studied mortality according to age in men and women with an incident myocardial infarction (MI).

The Norwegian Cardiovascular Disease Registry (NCDR) is a national health registry that was established in 2012. We used episodes registered with MI in 2016–2018 and with no MI registered in the three previous years. MI was defined as ICD-10 codes I21 or I22 as main We calculated person-years from date of MI episode to date of death or 28. February 2020, whichever came first.

We estimated mortality in age-groups 0–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84, 85–89, ≥90. We used these age-groups as a factor variable in Cox proportional hazard analyses. Percutaneous coronary intervention (PCI, 1 = yes, 0 = no) and number of contributory diagnoses (0, 1, 2,…,5, 6, 7+) registered in NCDR were additional independent factor variables in these analyses. The percentage with PCI was 44 and 33 in men and women below 75 years, and 25 and 17 in men and women 75 or older. The average of contributory diagnoses was 1.6, and 1.5 below 75 and 2.4 and 2.3 in men and women 75 years or older.

15. What Contributes to Worse Outcomes For Women vs. Men With AMI-CS or HF-CS?

Women with heart failure-related cardiogenic shock (HF-CS) had more vascular complications and worse outcomes than men with HF-CS and more studies are needed to advance therapies, decrease complications and improve outcomes for women with CS, according to a working group report being presented at AHA 2023 and simultaneously published Nov. 6 in JACC: Heart Failure.

Van-Khue Ton, MD, PhD, et al., examined data from CS patients in the Cardiogenic Shock Working Group (CSWG), performing propensity score matching with the use of baseline characteristics and logistic regression to analyze odds of survival. The authors compared survival at discharge between women and men with CS complicating acute myocardial infarction (AMI-CS) and HF-CS to assess the impact of female sex in CS outcomes. Of the 5,083 patients, 1,522 were women (30%) with a mean age of 61.8 years. More women than men presented with de novo HF-CS (26.2% vs. 19.3%; $p<0.001$), whereas a similar proportion presented with AMI-CS (30% vs. 29.1%; $p=0.03$). Notably, there were no significant differences between women and men regarding age, race, hypertension or diabetes.

Results showed that women, compared with men, had a worse survival at discharge rate (69.9% vs. 74.4%; $p=0.009$) as well as a higher rate of

maximum Society for Cardiac Angiography and Interventions Stage E (26% vs. 21%; p=0.04). Women were also less likely to receive pulmonary artery catheterization (52.9% vs. 54.6%; p<0.001), heart transplantation (6.5% vs. 10.3; p<0.001) or left ventricular assist device implantation (7.8% vs. 10%; p=0.01).

Furthermore, the researchers found that, regardless of CS etiology, women had more vascular complications (8.8% vs. 5.7%; p<0.001), bleeding (7.1% vs. 5.2%; p=0.01) and limb ischemia (6.8% vs. 4.5%; p=0.001), and more vascular complications persisted in women vs. men after propensity score matching (10.4% vs. 7.4%; p=0.06).

The authors write, "We have reported one of the largest contemporary analyses of real-world registry data on the characteristics and outcomes of women vs. men with CS, with a focus on patients with AMI-CS and HF-CS."

In an accompanying editorial comment, **Sara Kalantari, MD**; Chair of the Critical Care Section Leadership Council **Robert O. Roswell, MD**, **FACC**, and **Jonathan Grinstein, MD, FACC**, write "The results of the CSWG analysis provide valuable information about gender-related inequality in care and outcomes in the management of cardiogenic shock, although the exact mechanisms driving these observed differences still need to be elucidated. Broadly speaking, barriers in the care of women with heart failure and cardiogenic shock include a reduced awareness among both patients and providers, a deficiency of sex-specific objective criteria for guiding therapy, and unfavorable t-MCS devices with higher rates of hemocompatibility-related complications in women."

16. **Increasing left ventricular mass and mortality in 303,548 men and women investigated with echocardiography**

Background and Aims

Left ventricular hypertrophy (LVH) categories are based on left ventricular mass index (LVMi). This study aimed to generate sex-stratified, statistically-

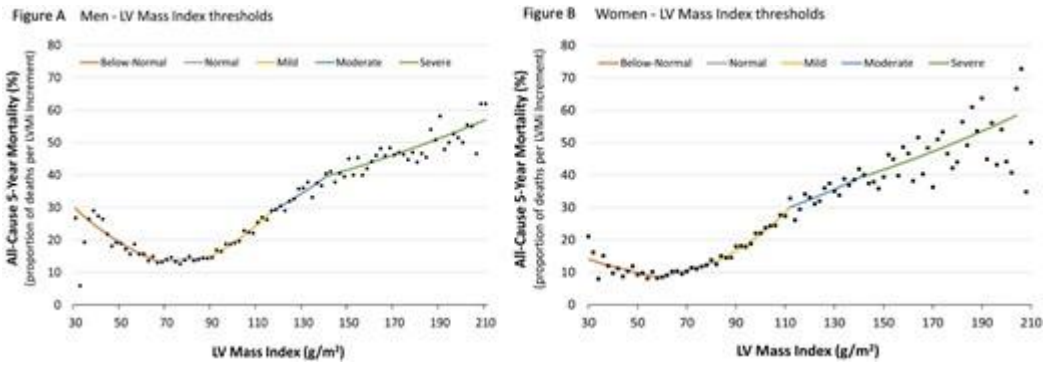
derived thresholds of mortality according to LVMi within a large, real-world patient cohort.

Methods and Results

Echocardiographic and linked mortality data were extracted from the National Echocardiography Database of Australia. LVH categories were first defined according to American Society of Echocardiography (ASE) criteria in 303,548 adults comprising 155,668 men (aged 61.3±17.3 years) and 147,880 women (61.8±18.3 years). Sex-specific mild to severe thresholds of increasing 5-year mortality based on LVMi increments were generated. Overall, 36,198 men (23.3%) and 38,898 women (26.3%) had LVH. Actual 5-year mortality rose from 16.9%-38.3% and 11.9%-31.2% in men and women with no LVH versus LVH, respectively. The statistical threshold at which LVMi was associated with increased mortality was lower than traditional LVH criteria in both men (Figure A, ≥88g/m2 versus ≥115g/m2) and women (Figure B, ≥82g/m2 versus ≥95g/m2). For men versus lowest-risk LVMi, the fully adjusted risk of 5-year mortality was 14% (95%CI 1.03-1.25) and 68% higher (95%CI 1.49-1.90) when LVMi levels were mildly (88 to <116) to severely (≥140g/m2) increased, respectively. In women, the equivalent LVMi thresholds of 82 to <112 and ≥140g/m2 were associated with a 13% (95%CI 1.03-1.24), and 81% higher (95%CI 1.58-2.08) 5-year mortality risk.

Conclusion

A high proportion of men and women have LVMi levels associated with elevated mortality risk that are lower than those traditionally used to diagnose or manage LVH. Such individuals may benefit from more proactive recognition and clinical management.



17. Standardized longitudinal strain curves stratified by age and sex in healthy individuals: The Copenhagen City Heart Study

Introduction

Speckle-tracking echocardiography has gained widespread use, and strain parameters such as global longitudinal strain (GLS) and strain rates are strongly associated with risk of heart failure and cardiovascular death. Such strain measures, however, only represent limited features of the complete longitudinal strain (LS) curve. Thus, interpretation of entire curves might provide additional insight.

Purpose

To establish normal standardized LS curves over an entire heart cycle for healthy subjects stratified by age and sex. Furthermore, to assess how these curves vary with age and to compare this with conventional strain measures.

Methods

The study population consisted of 1790 healthy subjects free of cardiovascular disease and risk factors including diabetes mellitus and hypertension at baseline. Subjects were stratified by sex and further by age in groups as defined in the SCORE risk chart. Subjects underwent echocardiography, and LS curves from the apical four-chamber view were derived and standardized in length using linear interpolation. Terms to describe qualitative findings in the standardized strain curves were established (Figure 1). Early diastolic strain (EDS) was defined as the difference in strain from peak LS to maximal curvature after early diastolic filling, while late diastolic strain (LDS) was defined as the difference in strain from the plateau phase in late passive diastole to maximal curvature in active diastole. Conventional strain measures included GLS, systolic strain rate (SRS), early diastolic strain rate (SRE), and late diastolic strain rates (SRA). The association between these and age group were investigated using univariable linear regression for each sex.

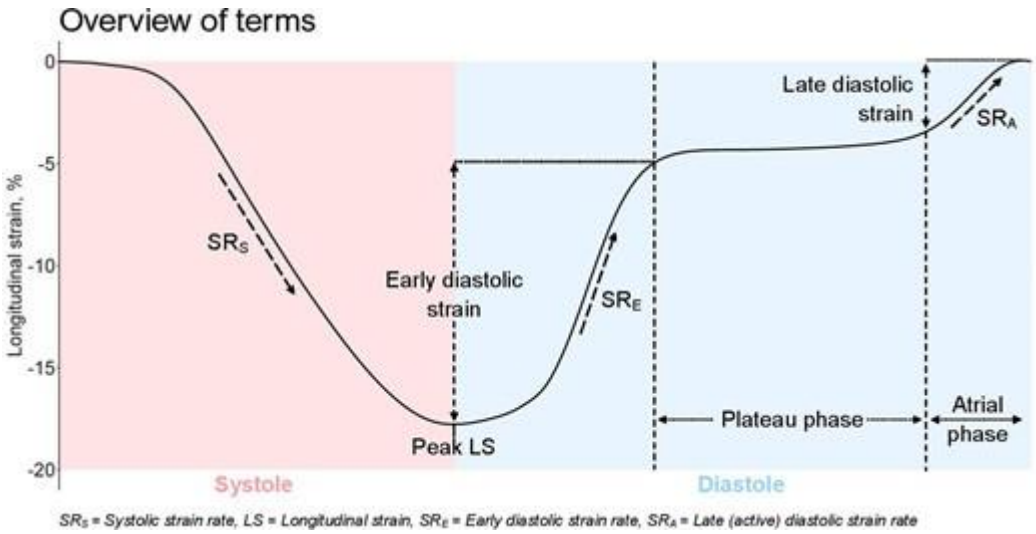
Results

In the study population, 1101 (61.5%) subjects were female. The standardized strain curves (Figure 2) showed that aging primarily manifested in the diastolic part of the strain curve. Decreasing EDS was associated with increasing age group, while the opposite was true for LDS. In linear regression, both SRE (female: beta=-0.13; p<0.001, male: beta=-0.1; p<0.001) and SRA (female: beta=0.09; p<0.001, male: beta=0.09; p<0.001) were associated with age group for both sexes. Peak LS did not change notably with age, and in linear regression, GLS and SRS were only significantly associated with age for women (GLS: beta=0.12; p<0.001, SRS: beta=0.01; p<0.001).

Conclusion

We derived normal standardized LS curves for healthy individuals stratified by age and sex, which can serve as normal values in future studies. In addition, these showed that age was primarily associated with changes in the diastolic part of the strain curve in both sexes, which was consistent with conventional strain measures.

Figure 1:



18. Clinical Outcomes by Sex After Pulsed Field Ablation of AF

Study Questions:

What are the sex differences in patients undergoing pulsed field ablation (PFA) for atrial fibrillation (AF) in the MANIFEST-PF (Multinational Survey on the

Methods, Efficacy, and Safety on the Postapproval Clinical Use of Pulsed Field Ablation) registry?

Methods:

The authors analyzed clinical data from the MANIFEST-PF registry of all consecutive patients who underwent first-ever PFA for paroxysmal or persistent AF.

Results:

The study included a total of 1,568 patients (male, 65%). Female patients, as compared with male patients, were older (age 68 vs. 62 years), had more paroxysmal AF (70% vs .62%), and had fewer comorbidities. Pulmonary vein isolation was performed in 99.8% of female and 98.9% of male patients. Additional ablation was performed in 22% of female and 23% of male patients. The 1-year freedom from atrial arrhythmia was similar in male and female patients (79% vs. 76%). There was no significant difference in acute major adverse events between groups (male 1.5% vs. female 2.5%).

Conclusions:

The study included a total of 1,568 patients (male, 65%). Female patients, as compared with male patients, were older (age 68 vs. 62 years), had more paroxysmal AF (70% vs .62%), and had fewer comorbidities. Pulmonary vein isolation was performed in 99.8% of female and 98.9% of male patients. Additional ablation was performed in 22% of female and 23% of male patients. The 1-year freedom from atrial arrhythmia was similar in male and female patients (79% vs. 76%). There was no significant difference in acute major adverse events between groups (male 1.5% vs. female 2.5%).

Perspective:

MANIFEST-PF demonstrated similar clinical effectiveness with PFA in both male and female individuals for both paroxysmal and persistent AF. This is the first study examining PFA for AF, which reported clinical outcomes

according to sex. Prior studies of traditional radiofrequency ablation and cryoablation showed variable outcomes across gender, and some of them reported a higher risk of procedure-associated complications such as cardiac tamponade, stroke/transient ischemic attack, vascular complications, and major bleeding in female patients compared with male patients. The absence of sex differences for major adverse events in the present study suggests improved safety of AF ablation in part due to advanced “single-shot” PFA technology that minimizes catheter manipulation in the left atrium.

19. Sex differences in symptoms of anxiety, depression, post-traumatic stress disorder, and cognitive function among survivors of out-of-hospital cardiac arrest

Aims

Anxiety, depression, and post-traumatic stress disorder (PTSD) among out-of-hospital cardiac arrest (OHCA) survivors may impact long-term recovery. Coping and perception of symptoms may vary between sexes. The aim was to explore sex differences in psychological consequences following OHCA.

Methods and results

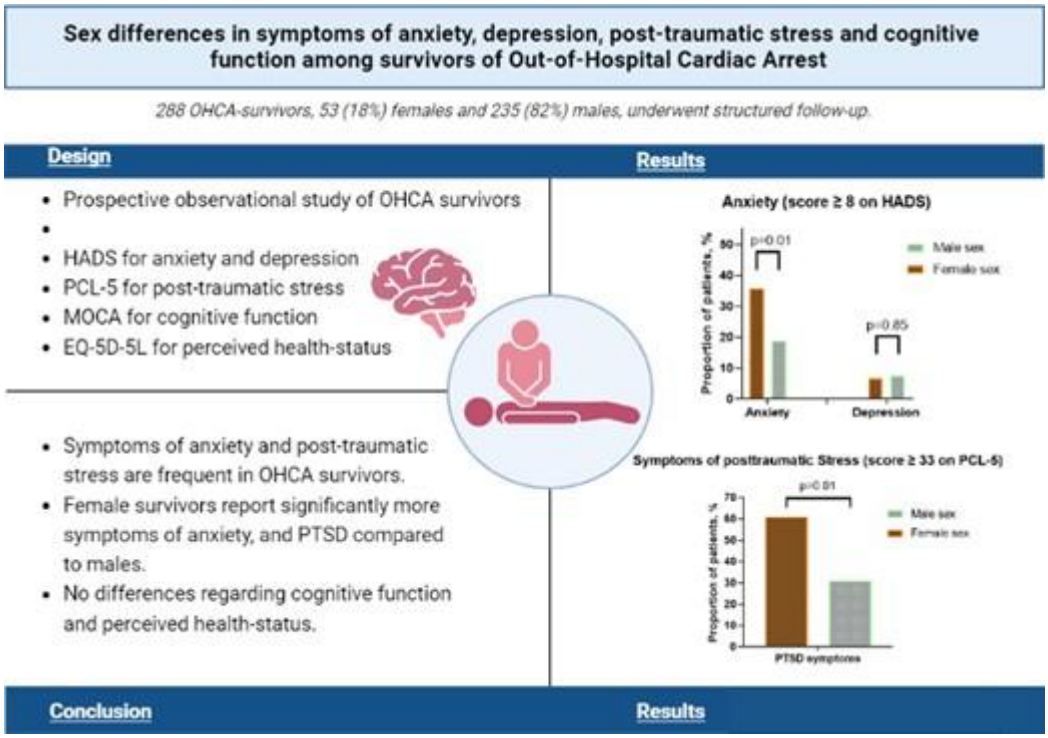
This was a prospective observational study of OHCA survivors who attended a structured 3-month follow-up. Symptoms of anxiety/depression were measured using the Hospital Anxiety and Depression Scale, range 0–21, with a cut-off score of ≥8 for significant symptoms; PTSD was measured with the PTSD Checklist for DSM-5 (PCL-5), range 0–80. A score of ≥33 indicated PTSD symptoms. Cognitive function was assessed by the Montreal Cognitive Assessment. From 2016 to 2021, 381 consecutive comatose OHCA survivors were invited. Of these, 288 patients (76%) participated in the follow-up visit [53 (18%) females out of 80 survivors and 235 (82%) males out of 300 alive at follow-up (78%)]. Significant symptoms of anxiety were present in 47 (20%) males and 19 (36%) females (P = 0.01). Significant symptoms of PTSD were present in 30% of males and 55% of females (P = 0.01). Adjusting for pre-specified covariates using multivariable logistic regression, female sex was significantly associated with anxiety [odds ratio (OR): 2.18, confidence interval

(CI): 1.09–4.38, P = 0.03]. This difference was especially pronounced among young females (below median age, $OR_{adjusted}$: 3.31, CI: 1.32–8.29, P = 0.01) compared with young males. No significant sex difference was observed for depression or cognitive function.

Conclusion

Symptoms of anxiety and PTSD are frequent in OHCA survivors, and female survivors report significantly more symptoms of anxiety and PTSD compared with males. In particular, young females were significantly more symptomatic than young males.

Graphical Abstract



20. **Higher cardiovascular risk for women throughout the glycaemic spectrum: only a question of sex?**

- This is an observational, cohort study, based on data from the UK Biobank and funded by Diabetes UK and British Heart Foundation, aimed at assessing sex-specific risk for cardiovascular disease (CVD) across the whole glycaemic spectrum and characterizing the contribution of clinical and lifestyle factors to sex-related differences.1

- From 2006 to 2010, a total number of 502 398 subjects aged 40–69 were recruited across England, Scotland, and Wales and followed through 2021. Every participant underwent baseline assessment for sociodemographic, clinical, and lifestyle characteristics and blood sampling for biomarker measurement. Based on glycated haemoglobin (HbA1c) levels, participants were categorized as (i) low-normal (<35 mmol/mol or <5.5%, including 47% of the entire population), (ii) normal (35–41 mmol/mol or 5.5%–5.9%, including 44% of the entire population), (iii) pre-diabetes (42–47 mmol/mol or 6.0%–6.4%, including 3% of the entire population), (iv) undiagnosed diabetes (≥48 mmol/mol or ≥6.5%, including 1% of the entire population), and (v) diagnosed diabetes (based on medical history and use of glucose-lowering medications, including 4% of the entire population).
- Outcomes included coronary artery disease (CAD), atrial fibrillation, deep vein thrombosis, pulmonary embolism, stroke, and heart failure, as well as a composite outcome of any CVD on its first occurrence. For the analysis of any CVD, individuals who had any CVD prior to baseline were excluded. Similarly, for the analysis of each outcome, individuals who had the respective event prior to baseline were excluded.
- Covariates were selected based on known determinants of HbA1c levels and CVD and included sociodemographic factors (i.e. age, sex, ethnicity, and index of multiple deprivation), mostly self-reported lifestyle [i.e. smoking status, alcohol consumption, physical activity, body mass index (BMI), waist–hip ratio, and dietary intake], and clinical characteristics (i.e. total cholesterol, serum creatinine, C-reactive protein, diagnosed hypertension, use of antihypertensive drugs or statins, and family history of CVD).
- The final analysis included 427 435 participants, of whom 195 752 (45.8%) men and 231 683 (54.2%) women. Both men and women in higher HbA1c categories had higher BMI, poorer renal function, greater prevalence of hypertension, and use of antihypertensive medications or statins compared with their counterparts with low-normal or normal HbA1c levels. Over a median 12-year follow-up, age-standardized

incidence rates for any CVD were 16.9 and 9.1 events/1000 person-years for men and women, respectively. Both men and women with pre-diabetes, undiagnosed diabetes, and, more markedly, diagnosed diabetes had higher CVD rates than those with normal HbA1c. In contrast, CVD rates were lower in those with low-normal HbA1c compared with normal HbA1c. The relative associations between diagnosed diabetes and any CVD were more pronounced in women than in men: age-adjusted hazard ratios (HRs) were 1.55 [95% confidence interval (CI), 1.49–1.61] in men and 2.00 (95% CI, 1.89–2.12) in women (P for interaction <.0001). Compared with those with normal HbA1c, the risk of CVD was also higher in pre-diabetes and undiagnosed diabetes groups, with age-adjusted HRs ranging from 1.30 to 1.47, with relative increases higher for women. In addition, both women and men with low-normal HbA1c were at decreased risk of CVD (HR 0.86, 95% CI, 0.84–0.98 and 0.86, 0.84–0.88, respectively).

- These associations attenuated after additional adjustment for clinical and lifestyle factors, particularly BMI, waist–hip ratio, and antihypertensive or statin use. However, the increased risk of CVD remained higher in both sexes with diagnosed diabetes (fully adjusted HR: 1.06, 95% CI, 1.02–1.11 for men and 1.17, 1.10–1.24 for women; P for interaction = .0387).

21. Cardiac Remodeling After Hypertensive Pregnancy Following Physician-Optimized Blood Pressure Self-Management

Hypertensive pregnancy disorders are associated with adverse cardiac remodeling, which can fail to reverse postpartum in some women. The Physician Optimized Postpartum Hypertension Treatment trial demonstrated improved blood pressure control, while the cardiovascular system recovers postpartum, associates with persistently reduced blood pressure. We now report the impact on cardiac remodeling.

METHODS

In this prospective, randomized, open-label, blinded endpoint trial, in a single UK hospital, 220 women were randomly assigned 1:1 to self-monitoring with research physician-optimized antihypertensive titration, or usual postnatal care from primary care physician and midwife. Participants were aged 18 years or over, with pre-eclampsia or gestational hypertension, requiring antihypertensives on hospital discharge postnatally. Pre-specified secondary cardiac imaging outcomes were recorded by echocardiography around delivery, and again at blood pressure primary outcome assessment, around nine months postpartum, when cardiovascular magnetic resonance was also performed.

RESULTS

187 women (101 intervention; 86 usual care) underwent echocardiography at baseline and follow up, at a mean 258+/-14.6 days postpartum, of which 174 (93 intervention; 81 usual care) also had cardiovascular magnetic resonance at follow up. Relative wall thickness by echocardiography was 0.06 (95% CI0.07 to 0.05, P=<0.001) lower in the intervention group between baseline and follow up, and cardiovascular magnetic resonance at follow up demonstrated a lower left ventricular mass (-6.37g/m2 (95% CI -7.99 to -4.74, P<0.001), end diastolic volume (-3.87ml/m2, 95% CI -6.77 to -0.98, P=0.009) and end systolic volume (-3.25ml/m2, 95% CI 4.87 to -1.63, P <0.001) and higher left and right ventricular ejection fraction by 2.6% (95% CI 1.3 to 3.9, P<0.001) and 2.8% (95% CI 1.4 to 4.1, P<0.001) respectively. Echocardiography assessed left ventricular diastolic function demonstrated a mean difference in average E/E' of 0.52 (95% CI -0.97 to -0.07, P=0.024), and a reduction in left atrial volumes of -4.33ml/m2 (95% CI -5.52 to -3.21, P=<0.001) between baseline and follow up, when adjusted for baseline differences in measures.

CONCLUSIONS

Short-term postnatal optimization of blood pressure control following hypertensive pregnancy, through self-monitoring and physician-guided antihypertensive titration, associates with long term changes in

cardiovascular structure and function, in a pattern associated with more favorable cardiovascular outcomes.

22. AHA: Self-Monitoring, Remote Physician-Guided Titration Aids Postpartum BP Control

The combination of self-monitoring and physician-guided titration of antihypertensive medications is associated with lower postpartum blood pressure following a hypertensive pregnancy compared with usual postnatal outpatient care, according to a study published online Nov. 11 in the Journal of the American Medical Association to coincide with the American Heart Association Scientific Sessions 2023, held from Nov. 11 to 13 in Philadelphia.

Jamie Kitt, D.Phil., from the University of Oxford in the United Kingdom, and colleagues assessed whether remote self-monitoring and physician-guided titration of antihypertensive medications using a Bluetooth-enabled app provides better long-term blood pressure control than usual outpatient care during the first nine months postpartum. The analysis included 200 participants randomly assigned following a hypertensive pregnancy.

The researchers found that the 24-hour mean diastolic blood pressure, measured at 249 days postpartum, was 5.8 mm Hg lower in the intervention group (71.2 versus 76.6 mm Hg) than in the control group (between-group difference, −5.80 mm Hg). Similar results were seen for 24-hour mean systolic blood pressure (114.0 versus 120.3 mm Hg; between-group difference, −6.51 mm Hg).

"An intervention that lowers blood pressure by 5 mm Hg would be expected to delay progression to hypertension by many years and, over a lifetime, reduce risk of cardiovascular or cerebrovascular events," the authors write.

23. Maternal Depressive Symptoms May Start at Pregnancy

Maternal depressive symptoms probably start at or before pregnancy, with trajectories that remain stable across the perinatal into the postnatal period, new research suggests.

The analysis of more than 11,000 pregnant women with depressive symptoms from seven prospective cohorts in Canada, the United Kingdom, and Singapore suggests that depressive symptoms (low, mild, or high levels) start sooner and last longer than is commonly thought.

The term "postnatal depression" is "at odds with existing scientific literature and the experience of clinicians who treat mental disorders in the context of obstetric practice," said Michael J. Meaney, PhD, professor at McGill University, Montreal, Quebec, and director of the Translational Neuroscience Program at the Agency for Science, Technology and Research (A*STAR), Singapore.

"Although we anticipated that the prenatal period would be the primary time of onset and that symptom levels would be largely stable, I was nevertheless surprised at how this pattern was so universal across so many studies," he said, speaking to Medscape Medical News. "In truth, we saw very little evidence for a postnatal onset."

This suggests that depressive symptoms start earlier than previously thought, and "that the relevant clinical settings for prevention are those treating women in routine health care, including family medicine," he added.

Start Screening Sooner

The investigators examined the course and stability of self-reported depressive symptoms at multiple time points across the perinatal period among 11,563 pregnant women in seven cohorts from the United Kingdom, Canada, and Singapore. Participants' mean age was 29 years; 87.6% were White, 4.9% were East Asian, and 2.6% were Southeast Asian.

The analysis tracked depressive symptoms from preconception through pregnancy to 2 years after childbirth. Three groups of mothers were identified in each cohort on the basis of their level of depressive symptoms (low, mild, or high) as assessed by the Edinburgh Postnatal Depression Scale (EPDS) or the Center for Epidemiological Studies Depression (CES-D).

The team found that all mothers within and across all cohorts had stable trajectories of maternal depressive symptoms from pregnancy onward. Trajectories for mothers who passed clinically validated cutoffs for "probable" depression also showed stable trajectories from pregnancy into the postnatal period.

"Taken together, these findings suggest that maternal depressive symptom levels in community-based cohort studies are apparent during pregnancy and remain stable into the postnatal period," the authors write. "The results point to the early antenatal period as a timepoint for the identification of stable trajectories of maternal depressive symptoms. Public health policies should emphasize the early antenatal period as the optimal timing for interventions targeting maternal depressive symptoms."

The findings, they note, "underscore the American Psychiatric Association's recent approach in renaming postpartum depression as peripartum depression."

Furthermore, a recent paper of the group's findings details that depressive symptoms may often predate conception.

"Our findings should serve to universally align practice to prenatal screening," even though depression screening often takes place in a mid-gestational visit during the second trimester, Meaney said. "Our findings and those on the effects on child development strongly suggest the timing of the screening must be advanced into the first confirmation of pregnancy."

Depression Is Likely Worse in the United States

Catherine Monk, PhD, who is chief of the Division of Women's Mental Health and professor of medical psychology at Columbia University Vagelos College of Physicians and Surgeons in New York, commented on the study for Medscape Medical News.

"The results of this well-conducted and important study amplify similar research findings and the experience of most perinatal clinicians: depression is stable from pregnancy onwards," said Monk, who was not involved in the research. "As the authors note, the common focus on postpartum depression misses the months of prior suffering and an opportunity for earlier intervention."

Monk would have liked the results to have been examined further by race and ethnicity and socioeconomic factors, she noted. "Also, the combined sample does not include a US cohort. This is significant as the US has the highest maternal morbidity and mortality rate of developed nations, and some reports identify mental health factors as the number-one cause of maternal mortality."

"Given the tremendous economic, racial, and ethnic inequities in healthcare — the lack of any kind of health justice — it is quite possible that in the US, depression that starts in pregnancy worsens over time, at least for some demographic groups," she said. "Rates of depression, levels of depression, and the course of it during the peripartum period may be even more dire [in the US] than what is represented in this article."

"What should be practice-changing about this article, and so many others demonstrating the persistent, and often high levels of life-threatening depression during pregnancy, is the need for mental health providers to advocate for changes to the low rates of insurance reimbursement that push providers away from accepting insurance and into private practice, making access to affordable mental care nearly impossible for most," she concluded.

24. Better Postpartum BP Control With Self-Monitoring: POP-HT

Self-monitoring blood pressure (BP) during the early postpartum period may take advantage of a "critical window" when better BP monitoring could prevent later cardiovascular events in women who have hypertensive pregnancies, new research suggests.

In a randomized trial of 220 women with preeclampsia or gestational hypertension, those who took daily postpartum BP readings and received clinician-guided advice for titrating antihypertensives had a 5 mm Hg lower average diastolic BP at 9 months, compared with those receiving usual care.

Jamie Kitt, DPhil, from the University of Oxford, Oxford, England, presented these findings from the Physicians Optimized Postpartum Hypertension Treatment (POP-HT) clinical trial at the American Heart Association (AHA) 2023 Scientific Sessions. The study was simultaneously published online in JAMA, and a cardiac imaging substudy was published online in Circulation.

"This trial identifies a potential need for a paradigm shift in the way women affected by hypertensive pregnancy are managed postnatally," Kitt said. "If a 5 mm Hg improvement in BP is maintained longer term, it can result in about a 20% reduction in lifetime cardiovascular risk."

The imaging substudy suggests that short-term postnatal optimization of BP control following hypertensive pregnancy through self-monitoring and physician-guided antihypertensive titration is linked with better cardiac remodeling changes seen by cardiovascular magnetic resonance and echocardiography.

POP-HT "proves for the first time that the first few weeks after delivery are a critical time that can determine the long-term cardiovascular health of the mother," senior author Paul Leeson, PhD, also from the University of Oxford, who presented the findings in a press briefing, told theheart.org | Medscape Cardiology.

"Interventions during this period can have long-term beneficial impacts on cardiovascular health," he said. "These findings rewrite the textbook on our

understanding of how and why hypertensive pregnancies associate with later cardiovascular disease in the mother."

Next, Leeson said, "We need to work out the best ways to implement these interventions "at scale. Then we can ensure all women who have hypertensive pregnancies can get access to the long-term cardiovascular benefits we have demonstrated are possible through improving postpartum cardiac care," he said, adding that "this is entirely achievable using current available technologies."

Hypertension in Pregnancy

About 1 in 10 pregnant women develop hypertension in pregnancy (preeclampsia or gestational hypertension), and 1 in 3 such women go on to develop chronic hypertension within 10 years, "when they are usually still in their 30s or 40s," Leeson said.

During pregnancy, the heart remodels to cope with pregnancy and it undergoes more severe changes if BP is high. Then during the 6 weeks after giving birth, this remodeling rapidly reverses.