News in April 2024

1. Mammography-based deep learning model for coronary artery calcification

Abstract

Aims

Mammography, commonly used for breast cancer screening in women, can also predict cardiovascular disease. We developed mammography-based deep learning models for predicting coronary artery calcium (CAC) scores, an established predictor of coronary events.

Methods and results

We evaluated a subset of Korean adults who underwent image mammography and CAC computed tomography and randomly selected approximately 80% of the participants as the training dataset, used to develop a convolutional neural network (CNN) to predict detectable CAC. The sensitivity, specificity, area under the receiver operating characteristic curve (AUROC), and overall accuracy of the model's performance were evaluated. The training and validation datasets included 5235 and 1208 women, respectively [mean age, 52.6 (±10.2) years], including non-zero cases (46.8%). The CNN-based deep learning prediction model based on the Resnet18 model showed the best performance. The model was further improved using contrastive learning strategies based on positive and negative samples: sensitivity, 0.764 (95% CI, 0.667–0.830); specificity, 0.652 (95% CI, 0.614–0.710); AUROC, 0.761 (95% CI, 0.742–0.780); and accuracy, 70.8% (95% CI, 68.8–72.4). Moreover, including age and menopausal status in the model further improved its performance (AUROC, 0.776; 95% CI, 0.762–0.790). The Framingham risk score yielded an AUROC of 0.736 (95% CI, 0.712–0.761).

Conclusion

Mammography-based deep learning models showed promising results for predicting CAC, performing comparably to conventional risk models. This indicates mammography's potential for dual-risk assessment in breast cancer and cardiovascular disease. Further research is necessary to validate these findings in diverse populations, with a particular focus on representation from national breast screening programmes.

2. Can machine learning predict cardiac risk using mammography?

The main purpose of breast screening programmes is to decrease mortality from breast cancer through early detection in asymptomatic women. Mammography reduces breast cancer mortality in women aged 50–74 years with smaller reductions in women aged under 50 years.1 The age and frequency of screening vary by country from annually from the age of 40–70 in the USA to every three years between the ages of 50 and 70 in the UK. Artificial intelligence algorithms have recently been developed to detect breast cancer and have been shown to be non-inferior to specialists and superior in cancer detection in combination with radiologists.2,3 The age range at which mammography is performed also coincides with the age range when statins might be prescribed for primary prevention if there are one or more cardiovascular disease (CVD) risk factors (i.e. dyslipidaemia, diabetes, hypertension, or smoking) and an estimated 10-year risk of a cardiovascular event of 10% or greater.4 Could there be a potential opportunity for opportunistic assessment of cardiovascular risk, as well as asymptomatic cancer, through novel analysis of mammographic images?

3. Long-Term Effect of Calcium and Vitamin D Supplementation on Mortality in Older Women

Calcium and vitamin D supplementation

This arm of the Women's Health Initiative (WHI) Study followed 36,282 postmenopausal women for a median of 22.3 years. The women were randomized to receive 1000 mg of calcium carbonate (400 mg elemental calcium) and 400 IU of vitamin D3 or placebo daily.

The primary outcomes were overall mortality and mortality from cancer and heart disease. The findings were mixed. There was a 7% reduction in cancer mortality and a 6% increase in mortality from heart disease; however, there was no difference in overall mortality.

What does this mean clinically?

Avoid calcium supplementation. There is significant evidence that suggests that calcium supplementation increases penetration into coronary arteries, particularly in diabetics.1 This can increase the risk of heart disease. Getting calcium slowly through the diet is ideal and has been associated with a reduced risk of colorectal cancer.

Foods rich in calcium:

Dark greens

Beans

Nuts and seeds

Fish with soft edible bones (sardines, salmon)

Dairy

Consider supplementing with vitamin D if serum levels are low. This study showed a greater reduction in cancer risk among women who had not

already been supplementing with vitamin D. This finding suggests that individuals with vitamin D deficiency had the greatest benefit. Analysis of the WHI and VITAL trial showed that vitamin D supplementation, without calcium supplementation was associated with a 13% to 17% reduction in cancer mortality.

Avoid giving calcium supplements with vitamin D. Vitamin D enhances the absorption of calcium, and if high doses of calcium are given at the same time, the body thinks it needs less calcium. This results in the body down-regulating the conversation of sunlight to vitamin D, reducing natural production.

The best advice has been handed down for centuries; enjoy multicolored whole foods and then go out into the sun and play!

4. Heart Transplant Offer Acceptance Highest for White Women

The cumulative incidence of heart transplant offer acceptance is highest for White women, according to a study published online March 25 in the Journal of the American Medical Association.

Khadijah Breathett, M.D., from the Krannert Cardiovascular Research Center at Indiana University in Indianapolis, and colleagues conducted a cohort study to examine whether race or gender of a heart transplant candidate is associated with the probability of a donor heart being accepted by the transplant center team using the United Network for Organ Sharing datasets.

There were 14,890 candidates listed for heart transplant; of these, 30.9 and 69.1 percent were Black and White, respectively, and 73.6 and 26.4 percent were men and women, respectively. The researchers found that the highest cumulative incidence of acceptance was seen for White women, followed by Black women, White men, and Black men. For the first offer through the 16th offer, the odds of acceptance were less for Black than White candidates (odds ratio, 0.76 for first offer). For the first through the sixth offer, the odds

of acceptance were higher for women than men (odds ratio, 1.53 for the first offer); the odds were lower for women for the 10th through the 31st offers.

"The cumulative incidence of donor heart offer acceptance by a transplant center team was consistently highest for White women followed by Black women, White men, and Black men," the authors write. "Further investigation is needed of the hospital-level decision-making process."

5. Successful Pregnancy After Cardiac Arrest in a Woman With Severe Coronary Vasospasm

We read with great interest the recently published paper by Ali Thara et al.1 In this paper, the authors describe an unplanned pregnancy in a patient who experienced a recent cardiac arrest in the setting of severe left anterior descending artery vasospasm. Following her cardiac event, she was discharged home with potentially teratogenic cardiovascular medications, but without discussion of contraception or pregnancy planning. We commend the authors for bringing attention to this gap in care, as well as the discussion of options for termination.

We would like to highlight the discussion regarding pregnancy prevention brought to light in the case report as commented on in Question 3. According to the U.S. Medical Eligibility Criteria (USMEC) for contraception, prolonged systemic use of progestins could be characterized as category III (theoretical or proven risks usually outweigh the advantages of using the method) for continued use after an ischemic cardiovascular event.2 The patient in this case did not have evidence of atherosclerosis, and ischemia was attributed to vasospasm, so the theoretical risk of systemic progestins is not likely directly applicable in this situation. However, even in the setting of atherosclerotic heart disease, levonorgestrel intrauterine devices (IUDs), which result in predominantly local rather than systemic effects, are considered category II (advantages of the method generally outweigh theoretical or proven risks) for initial use according to the USMEC.2 Notably, recent studies have identified that progestin-only contraceptive methods do

not carry significantly increased risk of venous or arterial thrombosis.3 As such, the American College of Obstetricians and Gynecologists currently recommends progestin-only pills, the subdermal implant, or the hormonal IUD for patients with a history of or at risk for venous thromboembolism, myocardial infarction, or stroke.4 Although a copper IUD would be also be a safe option for these patients (USMEC category I), it may be associated with increased menorrhagia in the setting of dual antiplatelet therapy or systemic anticoagulation.

6. Myocardial Strain Measurements Derived From MR Feature-Tracking: Influence of Sex, Age, Field Strength, and Vendor

Background

Cardiac magnetic resonance feature tracking (CMR-FT) is a novel technique for assessing myocardial deformation and dysfunction. However, a comprehensive assessment of normal values of strain parameters in all 4 cardiac chambers using different vendors is lacking.

Objectives

This study aimed to characterize the normal values for myocardial strain in all 4 cardiac chambers and identify factors that contribute to variations in FT strain through a systematic review and meta-analysis of the CMR-FT published reports.

Methods

The investigators searched PubMed, Embase, and Scopus for myocardial strains of all 4 chambers measured by CMR-FT in healthy adults. The pooled means of all strain parameters were generated using a random-effects model. Subgroup analyses and meta-regressions were performed to identify the sources of variations.

Results

This meta-analysis included 44 studies with a total of 3,359 healthy subjects. The pooled means of left ventricular global longitudinal strain (LV-GLS), LV global radial strain, and LV global circumferential strain (GCS) were −18.4% (95% CI: −19.2% to −17.6%), 43.7% (95% CI: 40.0%-47.4%), and −21.4% (95% CI: −22.3% to −20.6%), respectively. The pooled means of left atrial (LA)-GLS (corresponding to total strain, passive strain, and active strain) were 34.9% (95% CI: 29.6%-40.2%), 21.3% (95% CI: 16.6%-26.1%) and 14.3% (95% CI: 11.8%-16.8%), respectively. The pooled means of right ventricular (RV)-GLS and right atrial global longitudinal total strain were −24.0% (95% CI: −25.8% to −22.1%) and 36.3% (95% CI: 15.5%-57.0%), respectively. Meta-regression identified field strength ($P < 0.001$; $I2 = 98.6\%$) and FT vendor ($P < 0.001$; $I2 = 98.5\%$) as significant confounders contributing to heterogeneity of LV-GLS. The variations of LA-GLSactive were associated with regional distribution ($P < 0.001$; $I2 = 97.3\%$) and FT vendor ($P < 0.001$; $I2 = 97.4\%$). Differences in FT vendor were attributed to variations of LV-GCS and RV-GLS ($P = 0.02$; $I2 = 98.8\%$ and $P = 0.01$; $I2 = 93.8\%$).

Conclusions

This study demonstrated the normal values of CMR-FT strain parameters in all 4 cardiac chambers in healthy subjects. Differences in FT vendor contributed to the heterogeneity of LV-GLS, LV-GCS, LA-GLSactive, and RV-GLS, whereas sex, age, and MR vendor had no effect on the normal values of CMR-FT strain measurements.

7. Sex-Specific Genetic Architecture of Blood Pressure

The genetic and genomic basis of sex differences in blood pressure (BP) traits remain unstudied at scale. Here, we conducted sex-stratified and combined-sex genome-wide association studies of BP traits using the UK Biobank resource, identifying 1,346 previously reported and 29 new BP

trait-associated loci. Among associated loci, 412 were female-specific (Pfemale ≤ 5 × 10-8; Pmale > 5 × 10-8) and 142 were male-specific (Pmale ≤ 5 × 10-8; Pfemale > 5 × 10-8); these sex-specific loci were enriched for hormone-related transcription factors, in particular, estrogen receptor 1. Analyses of gene-by-sex interactions and sexually dimorphic effects identified four genomic regions, showing female-specific associations with diastolic BP or pulse pressure, including the chromosome 13q34-COL4A1/COL4A2 locus. Notably, female-specific pulse pressure-associated loci exhibited enriched acetylated histone H3 Lys27 modifications in arterial tissues and a female-specific association with fibromuscular dysplasia, a female-biased vascular disease; colocalization signals included Chr13q34: COL4A1/COL4A2, Chr9p21: CDKN2B-AS1 and Chr4q32.1: MAP9 regions. Sex-specific and sex-biased polygenic associations of BP traits were associated with multiple cardiovascular traits. These findings suggest potentially clinically significant and BP sex-specific pleiotropic effects on cardiovascular diseases.

8. Genetic Associations of Circulating Cardiovascular Proteins With Gestational Hypertension and Preeclampsia

IMPORTANCE

Hypertensive disorders of pregnancy (HDPs), including gestational hypertension and preeclampsia, are important contributors to maternal morbidity and mortality worldwide. In addition, women with HDPs face an elevated long-term risk of cardiovascular disease.

OBJECTIVE

To identify proteins in the circulation associated with HDPs.

DESIGN, SETTING, AND PARTICIPANTS

Two-sample mendelian randomization (MR) tested the associations of genetic instruments for cardiovascular disease-related proteins with gestational

hypertension and preeclampsia. In downstream analyses, a systematic review of observational data was conducted to evaluate the identified proteins' dynamics across gestation in hypertensive vs normotensive pregnancies, and phenome-wide MR analyses were performed to identify potential non-HDP-related effects associated with the prioritized proteins. Genetic association data for cardiovascular disease-related proteins were obtained from the Systematic and Combined Analysis of Olink Proteins (SCALLOP) consortium. Genetic association data for the HDPs were obtained from recent European-ancestry genome-wide association study meta-analyses for gestational hypertension and preeclampsia. Study data were analyzed October 2022 to October 2023.

EXPOSURES

Genetic instruments for 90 candidate proteins implicated in cardiovascular diseases, constructed using cis-protein quantitative trait loci (cis-pQTLs).

MAIN OUTCOMES AND MEASURES

Gestational hypertension and preeclampsia.

RESULTS

Genetic association data for cardiovascular disease-related proteins were obtained from 21 758 participants from the SCALLOP consortium. Genetic association data for the HDPs were obtained from 393 238 female individuals (8636 cases and 384 602 controls) for gestational hypertension and 606 903 female individuals (16 032 cases and 590 871 controls) for preeclampsia. Seventy-five of 90 proteins (83.3%) had at least 1 valid cis-pQTL. Of those, 10 proteins (13.3%) were significantly associated with HDPs. Four were robust to sensitivity analyses for gestational hypertension (cluster of differentiation 40, eosinophil cationic protein [ECP], galectin 3, N-terminal pro-brain natriuretic peptide [NT-proBNP]), and 2 were robust for preeclampsia (cystatin B, heat shock protein 27 [HSP27]). Consistent with the MR findings, observational data revealed that lower NT-proBNP (0.76- to 0.88-fold difference vs no HDPs)

and higher HSP27 (2.40-fold difference vs no HDPs) levels during the first trimester of pregnancy were associated with increased risk of HDPs, as were higher levels of ECP (1.60-fold difference vs no HDPs). Phenome-wide MR analyses identified 37 unique non-HDP-related protein-disease associations, suggesting potential on-target effects associated with interventions lowering HDP risk through the identified proteins.

CONCLUSIONS AND RELEVANCE

Study findings suggest genetic associations of 4 cardiovascular disease-related proteins with gestational hypertension and 2 associated with preeclampsia. Future studies are required to test the efficacy of targeting the corresponding pathways to reduce HDP risk.

9.Zipes Keynote to Examine Sex Differences in CV Research. Cardiovascular disease presents differently in women and men for a variety of biological reasons, but scientific research has traditionally considered men to be the gold standard, disregarding the potential for sex differences. With the dawn of precision medicine, researchers are increasingly recognizing the importance of investigating sex differences and including women in medical research. This topic will be explored during the Zipes Distinguished Young Scientist Awardee Keynote and its headline presentation from Emily S. Lau, MD, FACC, on "Overcoming the Male Bias: Why Sex Differences Matter."

"Women are consistently underrepresented across all stages of biomedical research, from cell line and animal studies to large randomized clinical trials," says Lau, an assistant professor of medicine at Harvard Medical School and director of the Cardiometabolic Health and Hormones Clinic in the Corrigan Women's Heart Health Program at Massachusetts General Hospital. "How can we provide the best care for our women patients if we don't understand the foundational principles that are driving disease and health in women?"

The Face of Heart Disease

While cardiovascular disease has historically focused on men, for Lau "the face of heart disease has always been a woman."

"Heart disease runs deep in my family, particularly in the women," she says. "My paternal grandmother died suddenly of a [myocardial infarction] and my maternal grandmother was repeatedly hospitalized for heart failure. My mother struggles with cardiometabolic disease and I personally experienced high blood pressure during my first pregnancy."

These experiences and family history with heart disease fueled her passion to study science and medicine and ultimately motivated her to pursue a career as a women's cardiovascular specialist. "I first began to ask the question, 'What makes men and women different?' after watching my parents experience very distinct medical journeys," Lau says. "My parents were both diagnosed with hypertension around the same time, but what meant popping a pill for Dad became a deluge of side effects, medication titrations and frustration for Mom."

The question "Why and how do men and women experience disease differently?" will be the focus of Lau's address.

"I will delve into the mechanisms, the biologic underpinnings that make heart disease so unique in women compared with men," Lau says. "I've done a lot of work specifically looking at sex differences in heart failure with preserved ejection fraction (HFpEF) and will use that as a case example. HFpEF is a type of heart failure that is much more prevalent among women compared with men and is one of the leading public health challenges that we face today."

The effort to learn more about biological sex differences has grown in recent years. It is now mandated for all studies funded by the National Institutes of Health to include sex as a biological variable, barring a strong justification for why only one sex should be evaluated. Even with this emphasis on inclusion, only 25-30% of participants in cardiovascular clinical trials are women.

"Heart disease is the leading cause of death in women, yet we don't fully understand what is unique about heart disease in women," Lau says. "Even in 2024 we are applying what we have learned from research conducted primarily in men to our women patients without actually knowing if that is the right thing to do."

Looking ahead, Lau notes that the future presents opportunities for clinicians to think creatively and innovate when approaching women's cardiovascular health. During her keynote address, she will also touch on work she has been doing with machine learning and how it can help support women's health issues.

The Zipes Keynote is also an opportunity for Lau, a young investigator, to speak about career pathways for women scientists.

"None of the physician-scientists that I knew looked like me. I didn't think this career path was possible for me, but I was lucky enough to have encountered a few mentors along the way who opened my eyes to the possibilities," she says. "I am hopeful I can open that dialogue for other young female trainees who are thinking about a career that bridges clinical medicine and investigation."

Moving the Field Forward

In addition to the Zipes Keynote, C. Noel Bairey Merz, MD, MACC, will build on the topic of women and heart disease with a presentation looking at "Where Are We Now: From WISE to CHEST PAIN Guidelines."

"[This is] the focused research study of women, not as a subgroup, or as compared to men, that has resulted after only two decades in evidence-based chest pain guidelines that improve the cardiovascular health of women (and some men)," she explains.

Garima Sharma, MBBS, FACC, will also provide insights into "Motherhood and Heart Health: Top 10 Breakthroughs in Cardiovascular Disease During Pregnancy and Postpartum." Specifically, her session will cover new guidance and treatments in cardiogenetics, peripartum cardiomyopathy, cardiovascular risk stratification in pregnancy, management of spontaneous coronary artery dissection, angina with nonobstructive coronary arteries and chest pain in women.

"Sex-specific risk enhancers and their unique pathways in cardiovascular disease remain an understudied part of cardiology," says Sharma. "Taking a tailored approach to management of heart disease in women, which focuses across the life course, is important."

10. ACC 2024: Uniform High-Sensitivity Cardiac Troponin I Threshold Safe, Effective for Ruling Out Myocardial Infarction in Men and Women

A uniform high-sensitivity cardiac troponin I rule-out threshold for myocardial infarction (MI) is safe and effective for identifying low-risk men and women presenting to the emergency department, according to a study published online March 25 in the Journal of the American College of Cardiology to coincide with the annual American College of Cardiology Scientific Session, held from April 6 to 8 in Atlanta.

Ziwen Li, Ph.D., from University of Edinburgh in the United Kingdom, and colleagues evaluated implementation of a uniform rule-out threshold (<5 ng/L with a high-sensitivity cardiac troponin I assay) in women and men with possible MI and derived and validated sex-specific thresholds. The analysis

included 16,792 patients presenting to the emergency department with possible MI.

The researchers found that the uniform threshold identified more female than male patients as low-risk (73 versus 62 percent). However, a similar proportion of low-risk patients were discharged from the emergency department (81 percent for both), with fewer than five patients (<0.1 percent) having a subsequent MI or cardiac death at 30 days. The authors observed that use of sex-specific thresholds would increase the proportion of female patients (61.8 versus 65.9 percent) and reduce the proportion of male patients (54.8 versus 47.8 percent) identified as low-risk compared with use of the uniform threshold.

“Compared to a uniform rule-out threshold, sex-specific rule-out threshold would reclassify four in 100 additional females and seven in 100 fewer males as suitable for safe early discharge, rendering the net benefit in effectiveness likely negligible,” senior author Dorien Kimenai, Ph.D., also from University of Edinburgh, told Elsevier’s PracticeUpdate. “We are hoping to send a clear message to our colleagues in the emergency department that a low, uniform rule-out threshold is effective and safe; but sex-specific rule-out thresholds should be considered where feasible.”

11. Menopausal Hormone Therapy Use Beyond 65 Years Beneficial

Use of menopausal hormone therapy beyond age 65 years is associated with risk reductions in mortality as well as specific cancers and cardiovascular diseases, according to a study published online April 9 in Menopause.

Seo H. Baik, Ph.D., from the U.S. National Institutes of Health in Bethesda, Maryland, and colleagues examined the effects of different preparations of menopausal hormone therapy on all-cause mortality, five cancers, six cardiovascular diseases, and dementia using data for 10 million senior Medicare women.

The researchers found that the use of estrogen monotherapy beyond age 65 years was associated with significant risk reductions in mortality (19 percent), breast cancer (16 percent), lung cancer (13 percent), colorectal cancer (12 percent), congestive heart failure (CHF; 5 percent), venous thromboembolism (3 percent), atrial fibrillation (4 percent), acute myocardial infarction (11 percent), and dementia (2 percent) compared with never use or discontinuation beyond age 65 years. Both estrogen plus progestin and estrogen plus progesterone were associated with a 10 to 19 percent increased risk for breast cancer; use of low-dose transdermal or vaginal estrogen plus progestin could mitigate this risk. Significant risk reductions were seen in endometrial cancer, ovarian cancer, ischemic heart disease, CHF, and venous thromboembolism (45, 21, 5, 5, and 5 percent, respectively) with estrogen plus progestin, while risk reduction was only seen in CHF with estrogen plus progesterone (4 percent).

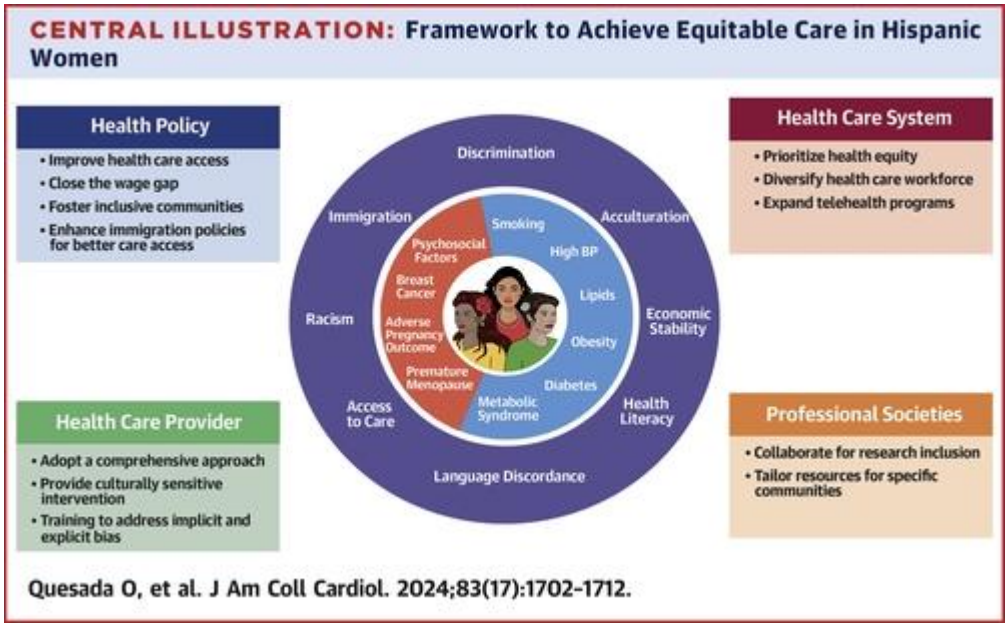
“This large observational study of women in Medicare provides reassurance regarding the safety of longer-term hormone therapy use and even potential benefits, particularly in women using estrogen alone,” Stephanie Faubion, M.D., medical director of The Menopause Society, said in a statement. “It also offers important insights into variations among different hormone therapy doses, routes of administration, and formulations that could facilitate individualization of treatment.”

12. Cardiovascular Disease in Hispanic Women: JACC Review Topic of the Week

Cardiovascular disease affects 37% of Hispanic women and is the leading cause of death among Hispanic women in the United States. Hispanic women have a higher burden of cardiovascular risk factors, are disproportionally affected by social determinants of health, and face additional barriers related to immigration, such as discrimination, language proficiency, and acculturation. Despite this, Hispanic women show lower rates of cardiovascular disease and mortality compared with non-Hispanic White women. However, this “Hispanic paradox” is challenged by recent studies that account for the diversity in culture, race, genetic background, country of origin, and social determinants of health within Hispanic subpopulations. This review provides a comprehensive overview of the cardiovascular risk factors in Hispanic women, emphasizing the role of social determinants, and proposes a multipronged approach for equitable care.

Highlights

- Hispanic women face disproportionate cardiovascular risk, although there is considerable heterogeneity among subpopulations.
- Social determinants of health influence cardiovascular risk in Hispanic women.
- A multipronged approach is needed to address social determinants of health and achieve equitable care for Hispanic women.



13. New light shed on Anderson–Fabry, peripartum, and early-onset cardiomyopathies

This Focus Issue on heart failure and congenital heart disease contains the State of the Art Review article 'Anderson–Fabry disease management: role of the cardiologist' by Maurizio Pieroni from the San Donato Hospital in Arezzo, Italy, and colleagues.1 The authors note that Anderson–Fabry disease (AFD) is a lysosomal storage disorder characterized by glycolipid accumulation in cardiac cells, associated with a peculiar form of hypertrophic cardiomyopathy (HCM). Up to 1% of patients with a diagnosis of HCM indeed have AFD. With the availability of targeted therapies for sarcomeric HCM and its genocopies, a timely differential diagnosis is essential. Specifically, the therapeutic landscape for AFD is rapidly evolving and offers increasingly effective, disease-modifying treatment options. However, diagnosing AFD may be difficult, particularly in the non-classic phenotype with prominent or isolated cardiac involvement and no systemic red flags. For many AFD patients, the clinical journey from initial clinical manifestations to diagnosis and appropriate treatment remains challenging, due to late recognition or utter neglect. Consequently, late initiation of treatment does not resolve cardiac involvement, representing the main cause of morbidity and mortality, irrespective of gender. Optimal management of AFD patients requires a dedicated multidisciplinary team, in which the cardiologist plays a decisive role, ranging from the differential diagnosis to the prevention of complications and the evaluation of timing for disease-specific therapies. This review aims to redefine the role of cardiologists across the main decision nodes in contemporary AFD clinical care and drug discovery.

Iron deficiency is becoming an important therapeutic target in the treatment of heart failure (HF).2–5 In a Clinical Research article entitled 'Intravenous iron for heart failure, iron deficiency definitions, and clinical response: the IRONMAN trial', John Cleland from the University of Glasgow in the UK, and colleagues evaluate what is the relationship between blood tests for iron deficiency, including anaemia, and the response to intravenous iron in patients with HF.6 In the IRONMAN trial, 1137 patients with HF, ejection fraction ≤45%, and either serum ferritin <100 μg/L or transferrin saturation (TSAT) < 20% were randomized to intravenous ferric derisomaltose (FDI) or usual care. Relationships were investigated between baseline anaemia severity, ferritin, and TSAT, and changes in haemoglobin from baseline to 4 months, Minnesota Living with HF (MLwHF) score and 6-min walk distance achieved at 4 months, and clinical events, including HF hospitalization (recurrent) or cardiovascular death. The rise in haemoglobin after administering FDI, adjusted for usual care, was greater for lower baseline TSAT (Pinteraction < .0001) and ferritin (Pinteraction = .028) and more severe anaemia (Pinteraction = .014). MLwHF scores at 4 months were somewhat lower (better) with FDI for more anaemic patients (overall Pinteraction = .14; physical Pinteraction = .085; emotional Pinteraction = .043) but were not related to baseline TSAT or ferritin. Blood tests did not predict difference in achieved walking distance for those randomized to FDI compared with controls. The absence of anaemia or a TSAT ≥20% was associated with lower event rates and little evidence of benefit from FDI. More severe anaemia or TSAT <20%, especially when ferritin was ≥100 μg/L, was associated with higher event rates and greater absolute reductions in events with FDI, albeit not statistically significant.

Cleland and colleagues conclude that this hypothesis-generating analysis suggests that anaemia or TSAT <20% with ferritin >100 µg/L might identify patients with HF who obtain greater benefit from intravenous iron. This interpretation requires confirmation. The contribution is accompanied by an Editorial by Peter van der Meer and Niels Grote Beverborg from the University Medical Center Groningen in the Netherlands.7 The authors note that while the field of iron deficiency holds promise, it has not fully met its anticipated potential. It still appears poised to significantly impact the prognosis of a substantial number of patients, yet the data are not as convincing as expected, and questions remain to be answered. The current study provides one step forward in solving the puzzle. Hopefully an individual patient data meta-analyses of all conducted trials can answer the question of whether we should treat patients with intravenous iron, and, perhaps even more importantly, which patients?There are no established clinical tools to predict left ventricular (LV) recovery in women with peripartum cardiomyopathy (PPCM).8,9 In a Clinical Research article entitled 'A novel score to predict left ventricular recovery in peripartum cardiomyopathy derived from the ESC EORP Peripartum Cardiomyopathy Registry', Alice Jackson from the University of Glasgow in the UK, and colleagues indicate that using data from women enrolled in the ESC EORP PPCM Registry, their aim was to derive a prognostic model to predict LV recovery at 6 months and develop the 'ESC EORP PPCM Recovery Score'—a tool for clinicians to estimate the probability of LV recovery.10 From 2012 to 2018, a total of 752 women from 51 countries were enrolled. Eligibility included (i) a peripartum state, (ii) signs or symptoms of HF, (iii) LV ejection fraction (LVEF) ≤ 45%, and (iv) exclusion of alternative causes of HF. The model was derived using data from participants in the registry and internally validated using bootstrap methods. The outcome was LV recovery (LVEF ≥50%) at 6 months. An integer score was created. Overall, 465 women had a 6-month echocardiogram. LV recovery occurred in 216 (46.5%). The final model included baseline LVEF, baseline LV end-diastolic diameter, human development index (a summary measure of a country's social and economic development), duration of symptoms, QRS duration, and pre-

eclampsia. The model was well calibrated and had good discriminatory ability (C-statistic 0.79). The model was internally validated (optimism-corrected C-statistic 0.78).Graphical summary of the main study findings. The human development index (HDI) is a summary measure (between zero and one) of a country's social and economic development and can be found at: https://hdr.undp.org/data-center/human-development-index#/indicies/HDI. CI, confidence interval; EORP, EURObservational Research Programme; ESC, European Society of Cardiology; LV, left ventricular: LVEF, left ventricular ejection fraction; PPCM, peripartum cardiomyopathy10The authors conclude that this study proposes a model which accurately predicts LV recovery at 6 months in women with PPCM. The corresponding ESC EORP PPCM Recovery Score can be easily applied in clinical practice to predict the probability of LV recovery for an individual to guide tailored counselling and treatment. The contribution is accompanied by an Editorial by Carmen Basic and Maria Schaufelberger from the University of Gothenburg in Sweden.11 The authors conclude their contribution by indicating that this is a call for action. Hopefully several research groups will test the model by Jackson and co-workers or further develop this predictive model to identify early those women with a low recovery probability in order to initiate appropriate actions, as this has an impact not only on the affected woman, but also on the child and her whole family. Finally, it is important to remember that prognostic models can only provide general guidance and should be interpreted in conjunction with the healthcare provider's clinical expertise.Childhood-onset cardiomyopathies are rare and poorly characterized.12–15 In a Clinical Research article entitled 'Cardiomyopathies in children and adolescents: aetiology, management, and outcomes in the European Society of Cardiology EURObservational Research Programme Cardiomyopathy and Myocarditis Registry', Juan Pablo Kaski from the University College London Institute of Cardiovascular Science and Great Ormond Street Hospital NHS Foundation Trust in London, UK, and colleagues examined the baseline characteristics and 1-year follow-up of children with cardiomyopathy in the first European Cardiomyopathy Registry.16 Prospective data were collected on individuals

aged from 1 up to 18 years enrolled in the European Society of Cardiology EURObservational Research Programme Cardiomyopathy and Myocarditis long-term registry. A total of 633 individuals with hypertrophic (HCM; 61%), dilated (DCM; 32%), restrictive (RCM; 4.4%), and arrhythmogenic right ventricular cardiomyopathy (ARVC; 1.6%) were enrolled by 23 referral centres in 14 countries. Median age at diagnosis was 4.0 years; 98% of patients were receiving cardiac medication; 13% had an implantable cardioverter-defibrillator; and 47% had familial disease. Genetic testing was performed in 68% of patients with a pathogenic or likely pathogenic variant reported in 60%. Rare disease phenocopies were reported in 28% of patients and were most frequent in patients under 10 years. Over a median follow-up of 12.5 months, 3.3% of patients died (2.6% from HCM, 3% from DCM, 16% from RCM). HF events were most frequent in RCM patients (36.0%).The findings confirm the heterogeneous aetiology of childhood cardiomyopathies and show a high frequency of familial disease. Outcomes differ by cardiomyopathy subtype, highlighting a need for disease-specific evaluation and treatment. This manuscript is accompanied by an Editorial by Jolanda Sabatino from the 'Magna Graecia' University of Catanzaro, Giovanni Di Salvo from the University of Padua, Italy, and Werner Budts from the University Hospitals Leuven in Belgium.17 The authors conclude by indicating that the establishment of the first European Paediatric Cardiomyopathy and Myocarditis Registry, as part of the EORP effort, signifies a relevant advancement in comprehending cardiomyopathies that occur in infancy. The insights from the registry have the potential to bring about a change in how paediatric cardiomyopathies are approached. This might lead to a new age where early detection becomes the crucial element for better outcomes, thereby guaranteeing the well-being of affected children and their families.The burden of congenital heart disease (CHD) keeps increasing thanks to a substantial prolongation of life expectancy generating new challenges.18–23 Cardiopulmonary fitness in CHD decreases faster than in the general population, resulting in impaired health-related quality of life (HRQoL). In a Clinical Research article entitled 'Early hybrid cardiac rehabilitation in congenital heart disease: the QUALIREHAB trial', Pascal

Amedro from the Bordeaux University Hospital in Pessac Cedex, France, and colleagues point out that as the standard of care seems insufficient to encourage and maintain fitness, an early hybrid cardiac rehabilitation programme could improve HRQoL in CHD.24 The QUALIREHAB multicentre, randomized, controlled trial evaluated and implemented a 12-week centre- and home-based hybrid cardiac rehabilitation programme, including multidisciplinary care and physical activity sessions. Adolescent and young adult CHD patients with impaired cardiopulmonary fitness were randomly assigned to either the intervention (i.e. cardiac rehabilitation) or the standard of care. The primary outcome was the change in HRQoL from baseline to 12-month follow-up in an intention-to-treat analysis. The secondary outcomes were the change in cardiovascular parameters, cardiopulmonary fitness, and mental health. The expected number of 142 patients were enrolled in the study (mean age 17.4, 52% female). Patients assigned to the intervention had a significant positive change in HRQoL total score (mean difference 3.8; P = .038), body mass index (mean difference −0.7 kg/m2, P = .022), level of physical activity (mean difference 2.5; P = .044, and disease knowledge (mean difference 2.7; P = .007). The per-protocol analysis confirmed these results with a higher magnitude of differences. Acceptability, safety, and short-term effects of the intervention were good to excellent.The long-term beneficial effect of the 12-week centre-based and home-based hybrid cardiac rehabilitation programme on adolescents and young adults with CHD was observed on HRQoL (primary outcome), BMI, physical activity, and disease knowledge, opening up the possibility for the QUALIREHAB programme to be rolled out to the adult population of CHD and non-congenital cardiac disease. BMI, body mass index; CHD, congenital heart disease; HRQoL, health-related quality of life.24The authors conclude that QUALIREHAB improves HRQoL, body mass index, physical activity, and disease knowledge in youths with CHD, opening up the possibility for this programme to be rolled out to the adult population of CHD and non-congenital cardiac disease. The contribution is accompanied by an Editorial by Keri Shafer and Anne Marie Valente from Harvard Medical School in Boston, MA, USA.25 The authors note that this study achieves an

important improvement in HRQoL in patients with CHD characterized by severe physical limitations. Perhaps by focusing on the improvement made in social functioning and disease knowledge we can better understand the benefits. Each subject was provided with multiple opportunities to connect and inquire about their heart condition, a unique aspect of this trial. Additionally, social determinants of health were addressed by reducing transportation insecurity and improving access to care, i.e. the fitness programme came to them. Similar to the Black Barbershop study, this study design met patients in their own communities. By doing so in all aspects of CHD care, we have an opportunity to see improvements in many other areas of health. Using these data, future research could focus both on higher intensity exercise training programmes together with a comprehensive approach to supporting CHD patients in their fitness and health improvement. Interventions that couple patient education and social support may be especially useful in this cohort. The authors are congratulated on accomplishing just that in this important and often overlooked population.

The issue continues with a Rapid Communications contribution entitled 'Hepatocellular carcinoma in survivors after Fontan operation: a case–control study', by Yuli Kim from the Hospital of the University of Pennsylvania in Philadelphia, PA, USA, and colleagues.26 The authors point out that liver injury is universal in patients who have undergone Fontan palliation for complex congenital heart disease and results in fibrosis and cirrhosis. Fontan-associated liver disease (FALD) can be rarely complicated by hepatocellular carcinoma (HCC), the risk factors for which are not fully elucidated. The authors aim to identify clinical characteristics associated with the development of HCC in adult single ventricle patients with Fontan circulation. Out of a total of 3251 adult Fontan patients followed across all 18 centres, the estimated prevalence of HCC was 1.8%. Median age of HCC diagnosis was 31 years. One-year survival after HCC diagnosis was 81%. Desaturation [adjusted odds ratio (aOR) 2.4, P = .02], history of Fontan revision (aOR 2.3, P = .02), and thrombocytopenia (aOR 2.3, P = .02) were associated with increased odds of HCC.

The authors conclude that hepatocellular carcinoma is diagnosed in up to 2% of adult Fontan patients. Those with more advanced Fontan-associated liver disease represented by abnormal liver biochemistries and signs of circulatory failure may be at increased risk. Until more clearly defined risk factors are identified, the authors recommend abdominal ultrasounds and alpha-foetoprotein determination every 6 months for adult Fontan patients in accordance with guidelines for HCC screening.

Systemic right ventricular (sRV) dysfunction is highly prevalent and is associated with substantial morbidity and mortality in patients with complete transposition of the great arteries with atrial switch surgery (D-TGA/AS) and in those with congenitally corrected transposition of the great arteries (ccTGA). In a Rapid Communications contribution 'Angiotensin receptor–neprilysin inhibitor vs. placebo in congenital systemic right ventricular heart failure: the PARACYS-RV trial', Marie-A. Chaix from the Université de Montréal in Canada, and colleagues note that there is no recommended evidence-based therapy proven to halt disease progression or improve survival for sRV dysfunction. Recent open-label studies support the safety of sacubitril combined with valsartan in this setting, and highlight the need for randomized trials.27 In their contribution, Chaix et al. present the results of the Prospective comparison of Angiotensin Receptor-neprilysin inhibitor vs. plAcebo in patients with Congenital sYStemic Right Ventricular heart failure (PARACYS-RV) trial. This randomized, double-blind, placebo-controlled, crossover trial was designed to compare sacubitril/valsartan with placebo in adults (≥18 years) with moderate to severe sRV dysfunction, biventricular physiology, and New York Heart Association (NYHA) functional class II–III symptoms. The study protocol (NCT05117736) was previously published. The trial was prematurely interrupted upon a unanimous decision by the steering committee owing to the high rate of worsening HF events. Analysis of unblinded data revealed a clear association between these events and interruption of sacubitril/valsartan, either after the run-in phase was followed by placebo or during the 2-week sacubitril/valsartan washout period prior to crossover to placebo.

The authors conclude that premature interruption of PARACYS-RV precludes firm conclusions regarding the efficacy of sacubitril/valsartan in patients with sRV dysfunction and NYHA Class II–III symptoms. Despite the small sample size, sacubitril/valsartan was associated with favourable trends regarding the two primary outcomes (maximal total exercise duration and N-terminal probrain natriuretic peptide). These promising results, along with encouraging observational studies, support the need for conclusive trials. Future trials should avoid crossovers to placebo and discontinuation of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers without substitution.

The issue is also complemented by two Discussion Forum contributions. In a commentary entitled 'The obesity paradigm on outcome in heart failure with reduced ejection fraction', Wolfram Doehner from the Charité-Universitätsmedizin Berlin, Germany and colleagues comment on the recent publication 'Anthropometric measures and adverse outcomes in heart failure with reduced ejection fraction: revisiting the obesity paradox' by Jawad H. Butt from the University of Glasgow, UK, and colleagues.28,20 Butt et al. respond in a separate comment.30

The editors hope that this issue of the European Heart Journal will be of interest to its readers.

Dr. Crea reports speaker fees from Abbott, Amgen, Astra Zeneca, BMS, Chiesi, Daiichi Sankyo, Menarini outside the submitted work.

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14. A novel score to predict left ventricular recovery in peripartum cardiomyopathy derived from the ESC EORP Peripartum Cardiomyopathy Registry

There are a number of established risk models and tools for predicting morbidity and mortality in people with chronic heart failure.1,2 They facilitate prediction of events within a specific population by utilizing characteristics to estimate the risk of an event occurring. Accurate quantification of risk for a particular individual, based on that individual's own characteristics, allows a

clinician to tailor counselling and treatment. There are currently no clinical tools that can be used to predict outcomes for women with peripartum cardiomyopathy (PPCM), a type of de novo heart failure which develops in approximately 1–100 in 1000 pregnancies.3,4 It is characterized by relatively frequent recovery of left ventricular (LV) function, when compared to dilated cardiomyopathy more generally.5,6 Although the definition of LV recovery used in studies varies, it is usually considered to be an improvement in LV ejection fraction (LVEF) to above a threshold of either 50% or 55%6–9. Estimating the propensity for LV recovery in PPCM is important and underpins a number of clinical decisions, such as recommending an implantable cardioverter defibrillator (ICD).

The European Society of Cardiology (ESC) EURObservational Research Programme (EORP) PPCM Registry is the largest prospective study of PPCM.7 Using patient-level data from women in the ESC EORP PPCM Registry, a prognostic model to predict LV recovery at 6 months was derived, internally validated and a 'PPCM Recovery Score' was generated—a tool for clinicians to estimate the probability of LV recovery at 6 months in this patient group.

Methods

Registry design

Registry design, patient selection and data collection have been published previously.7,10 Briefly, women who were diagnosed with PPCM within the preceding 6 months were prospectively enrolled into an observational registry. Inclusion criteria were: (i) a peripartum state, (ii) signs and/or symptoms of heart failure, (iii) a LVEF ≤45%, and (iv) the exclusion of alternative causes of heart failure. A total of 752 women from 51 countries were originally enrolled into the Registry (2012–2018). Core clinical data, such as data from the electrocardiogram and echocardiogram, were centrally validated by a data monitor who contacted the sites. LV recovery was defined as a LVEF ≥50% on the 6 month follow-up echocardiogram. Comorbidities, including diabetes, pregnancy-induced hypertension and pre-eclampsia, were clinician-recorded.

Health expenditure (HE) is the share of gross domestic product within a country and was defined as low (<5%), medium (5%–8%) and high (>8%). Human development index (HDI) is a summary measure (between zero and one) of a country's social and economic development, encompassing three domains—life expectancy, education, and standard of living. Human development index was defined as low (<0.550), medium (0.550–0.699), and high (≥0.700). Participating centres managed the approvals of national or regional ethics committees or institutional review boards according to local regulations. Locally appointed ethics committee approved the research protocol and informed consent was obtained from participants or a legally authorized representative.

Statistical methods

The main analysis included patients with complete data. Multiple imputations were used as a sensitivity analysis for model derivation. Patient characteristics were compared according to recovery status using Pearson's chi-squared tests, two sample t-tests and Wilcoxon rank-sum test as appropriate. A total of 20 variables known or suspected to be prognostically significant in PPCM were included as candidate variables and are listed in the Appendix. Highly skewed data were log transformed. A logistic regression prediction model for LV recovery at 6 months was built using a backward selection process including all potential predictor variables, with a two-sided P-value of <.05 as the initial significance level. All selected variables were then examined for interactions, with a two-sided P-value threshold of <.05 considered to be statistically significant. The final predictor variables in the model were converted from continuous to categorical forms to allow clinical applicability of the model. Clinically relevant categories were determined by systematically assessing different cut-offs and identifying those resulting in a model with optimal discriminatory ability.

Model calibration was assessed by comparing predicted probability of LV recovery, estimated by the final model, with observed probability in deciles and the comparison was displayed graphically with a lowess smoother line using the 'pmcalplot' package in Stata. As a secondary measure of model

calibration, a Hosmer–Lemeshow chi-squared goodness-of-fit test was performed. The discriminatory ability of the model was assessed using the C-statistic, which is equivalent to the area under the receiver operating characteristic curve; a value below 0.5 indicates a poor model, a value of 0.5 indicates that the model is no better at predicting the outcome than chance, and a value of 1 means that the model perfectly predicts individuals who will and will not experience the outcome. The model was internally validated using 1000 bootstrap samples. Bias-corrected 95% confidence intervals (CI) were obtained from bootstrap samples. The optimism-corrected C-statistic, which provides a measure of the extent to which the original model is too optimistic, or overfits the data, was calculated by generating the difference between the original C-statistic and the C-statistic obtained from each bootstrap sample, taking this difference from the original C-statistic and averaging this across the bootstrap samples. A PPCM recovery score was generated by converting the variable coefficients to corresponding integer points, by multiplying the coefficient by 1.75.

A number of sensitivity analyses were conducted:

Women who died were categorized as 'unrecovered' and a new model derived and performance assessed.

Model performance was assessed in a complete dataset using multiple imputation by chained equations according to Rubin's rules.

Model-building was approached using alternative methods: forward selection (including all potential predictor variables, with a two-sided P-value of <.05 as the initial significance level) and stepwise selection (forward and backward, removing terms with P-value ≥.1 and adding those with a P-value of <.05).

Analyses were conducted using Stata SE v16.1 (StataCorp). The transparent reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) guidelines were followed.11

Results

Patient characteristics

In total, LVEF was available in 465 women at 6 months and LV recovery occurred in 216 (46.5%). The mean change in LVEF from baseline to 6 months was 15% (±13); 8% (±10) in women without recovery, and 24% (±12) in women with recovery.

Compared to unrecovered women, women with LV recovery were more often White, less often Black and Middle Eastern, and were more often from the highest HDI and HE categories (Table 1). They had a shorter median duration between symptom-onset and diagnosis, more frequently had pregnancy-induced hypertension and pre-eclampsia, had higher baseline systolic blood pressure and lower heart rate, and had a higher white blood cell count and serum sodium level. They also had a shorter QRS duration, higher baseline LVEF, smaller LV end diastolic and systolic diameter, smaller left atrial diameter, and less frequent right ventricular impairment and mitral regurgitation (moderate or worse). The extent of missing data is shown in Supplementary data online, Table S1. Characteristics are also presented by displaying proportions according to the characteristic, rather than recovery status, in Supplementary data online, Table S2.

Table 1

Characteristics in patients with and without left ventricular recovery

	All (n = 465)	Unrecovered (n = 249)	Recovered (n = 216)	P-value
Age, years	31 ± 6	31 ± 6	31 ± 6	.30
Region				<.001
Africa	141	88 (35.3)	53 (24.5)	

	All (n = 465)	Unrecovered (n = 249)	Recovered (n = 216)	P-value
	(30.3)			
Asia-Pacific	75 (16.1)	28 (11.2)	47 (21.8)	
Europe	171 (36.8)	76 (30.5)	95 (44.0)	
Middle East	78 (16.8)	57 (22.9)	21 (9.7)	
Ethnicity				.002
White	149 (33.3)	63 (26.2)	86 (41.3)	
Black	132 (29.5)	84 (35.0)	48 (23.1)	
Asian	100 (22.3)	54 (22.5)	46 (22.1)	
Middle Eastern	49 (10.9)	32 (13.3)	17 (8.2)	
Other	18 (4.0)	7 (2.9)	11 (5.3)	
HDI category				<.001
Low	93 (20.1)	62 (25.0)	31 (14.5)	

	All (n = 465)	Unrecovered (n = 249)	Recovered (n = 216)	P-value
Medium	175 (37.9)	103 (41.5)	72 (33.6)	
High	194 (42.0)	83 (33.5)	111 (51.9)	
Health expenditure				.038
Low	159 (34.5)	98 (39.7)	61 (28.5)	
Medium	142 (30.8)	72 (29.1)	70 (32.7)	
High	160 (34.7)	77 (31.2)	83 (38.8)	
Body mass index kg/m2	26 ± 6	26 ± 6	26 ± 6	.84
Parity ≥2	221 (74.7)	127 (75.1)	94 (74.0)	.82
Postpartum diagnosis	396 (89.6)	212 (89.8)	184 (89.3)	.86
Postpartum	278	151 (68.9)	127	.70

	All (n = 465)	Unrecovered (n = 249)	Recovered (n = 216)	P-value
symptom-onset	(68.1)		(67.2)	
Duration o symptoms,days	11 (3–34)	17 (5–53)	7 (1–22)	<.001
Family history o heart failure o sudden death	70 (15.2)	34 (13.8)	36 (16.8)	.37
Diabetes	15 (3.3)	10 (4.0)	5 (2.3)	.31
Smoking (current/former)	68 (15.3)	28 (11.7)	40 (19.4)	.024
HIV Status	19 (6.6)	15 (9.3)	4 (3.1)	.035
Pregnancy-induced hypertension	182 (39.9)	83 (34.2)	99 (46.5)	.007
Pre-eclampsia	119 (26.1)	51 (21.0)	68 (31.9)	.008
Prior PPCM	23 (7.7)	15 (8.9)	8 (6.2)	.40
Systolic blood pressure, mmHg	119 ± 23	116 ± 22	123 ± 24	<.001

	All (n = 465)	Unrecovered (n = 249)	Recovered (n = 216)	P-value
Diastolic blood pressure, mmHg	78 ± 16	77 ± 16	79 ± 16	.20
Heart rate, b.p.m.	99 ± 21	101 ± 21	96 ± 22	.016
NYHA class				.23
I	39 (8.5)	18 (7.3)	21 (9.8)	
II	122 (26.5)	69 (28.0)	53 (24.8)	
III	159 (34.6)	92 (37.4)	67 (31.3)	
IV	140 (30.4)	67 (27.2)	73 (34.1)	
S3 gallop	198 (44.3)	116 (48.7)	82 (39.2)	.044
Elevated jugular venous pressure (>6 cm)	183 (41.3)	106 (45.1)	77 (37.0)	.084
Peripheral oedema	267 (57.5)	147 (59.3)	120 (55.6)	.42

	All (n = 465)	Unrecovered (n = 249)	Recovered (n = 216)	P-value
Pulmonary rales	276 (60.7)	147 (61.0)	129 (60.3)	.88
Serum creatinine, μmol/L	70 (58-87)	71 (59–88)	67 (57-82)	.21
Hemoglobin, g/L	115 (105–129)	114 (104-127)	115 (105-130)	.47
White blood cells ×10^9/L	9 (7–12)	9 (6–11)	10 (7–13)	.004
Platelets, ×10^9/L	266 (219–354)	263 (221-344)	268 (212-354)	.86
Sodium, mmol/L	138 (136–141)	138 (135-140)	139 (136-141)	.029
Potassium, mmol/L	4 (4–4)	4 (4–4)	4 (4–4)	.60
QTc duration, ms	461 ± 71	461 ± 76	461 ± 66	.99
QRS duration, ms	89 ± 20	92 ± 22	84 ± 17	<.001
Left bundle	32 (7.1)	25 (10.5)	7 (3.3)	.003

	All (n = 465)	Unrecovered (n = 249)	Recovered (n = 216)	P-value
branch block				
Atrial fibrillation/flutter	7 (1.6)	7 (2.9)	0 (0.0)	.012
LV ejection fraction, %	31 ± 10	29 ± 9	34 ± 10	<.001
LV end diastolic diameter, mm	59 ± 7	62 ± 7	56 ± 7	<.001
Indexed to body surface area, mm/m2	35 ± 5	36 ± 5	33 ± 5	<.001
LV end systolic diameter, mm	49 ± 8	52 ± 7	46 ± 7	<.001
Indexed to body surface area, mm/m2	29 ± 5	31 ± 5	27 ± 5	<.001
Left atrial diameter, mm	40 ± 7	41 ± 7	38 ± 7	.002
Right ventricular impairmenta	153 (37.3)	101 (45.7)	52 (27.5)	<.001

	All (n = 465)	Unrecovered (n = 249)	Recovered (n = 216)	P-value
≥ Moderate mitral regurgitation	159 (43.8)	95 (50.3)	64 (36.8)	.010

Data are presented as n (%), mean ± standard deviation, or median (interquartile range).

HDI, human development index; HIV, human immunodeficiency virus; PPCM, peripartum cardiomyopathy; NYHA, New York Heart Association; LV, left ventricular.

aQualitatively assessed; function recorded by the investigator as normal, mildly impaired, or severely impaired.

Medical therapy

The proportions of women treated with an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, a beta-blocker and bromocriptine were similar irrespective of whether or not LV recovery occurred. Women with LV recovery were less often on a mineralocorticoid receptor antagonist, diuretic, digoxin, and anticoagulant (see Supplementary data online, Table S3).

Model derivation, performance and validation

A total of 20 potential predictor variables were included in a backward selection process and are listed in the Appendix. The final multivariable predictors of LV recovery were the following: LVEF, LV end diastolic diameter, HDI, duration of symptoms, QRS duration, and pre-eclampsia (n = 351 in the final model) (Table 2). No significant interactions were identified. Clinically applicable categorical thresholds were determined as follows: LVEF >35% and ≤35%; LV end diastolic diameter <53 mm, 53–61 mm, and ≥62 mm (as per international categorizations12); duration of symptoms ≤10 days and >10 days; QRS duration ≤80 ms, 81–109 ms, and ≥110 ms (the model performed

less well when bundle branch block vs. no bundle branch block, i.e. QRS durations <120 ms vs. ≥120 ms, was included instead). Predicted and observed probabilities of LV recovery were plotted according to decile of probability and are shown in Figure 1. Overall, the model was well-calibrated (Hosmer–Lemeshow chi2 goodness-of-fit test P = .87). The discriminative ability of the model was good, with a C-statistic of 0.79 (95% CI 0.74–0.83). The optimism-corrected C-statistic through internal validation by bootstrapping 1000 samples was 0.78 (95% CI 0.73–0.82).

Predicted and observed probability of left ventricular recovery according to decile of probability. The probabilities presented are those for each group of patients and the plot is a calibration plot of observed against expected probabilities. The dotted line represents perfectly matching predicted and observed probabilities, the green circles and extended lines represent the actual data point per decile with 95% confidence intervals and the blue line represents the lowess (locally weighted scatterplot smoothing) line, which is a smooth line through the scatterplot points

Final multivariable prediction model for left ventricular recovery

	Odds ratio	Bias-corrected 95% CI	Coefficient
LV ejection fraction			
≤35%	1.00		
>35%	1.85	1.09–2.96	0.61
LV end diastolic			

	Odds ratio	Bias-corrected 95% CI	Coefficient
diameter			
≥62 mm	1.00		
53–61 mm	1.69	0.94–2.88	0.52
<53 mm	8.43	3.34–19.18	2.13
Human development index			
Low	1.00		
Medium	0.97	0.49–1.92	−0.03
High	2.27	1.01–4.95	0.82
Duration o symptoms			
>10 days	1.00		
≤10 days	1.81	1.04–3.25	0.60
QRS duration			

	Odds ratio	Bias-corrected 95% CI	Coefficient
≥110 ms	1.00		
81–109 ms	3.98	1.64–14.57	1.38
≤80 ms	5.93	2.42–23.26	1.78
Pre-eclampsia			
No	1.00		
Yes	1.98	1.12–3.32	0.69

N = 351 in final model.

PPCM recovery score

A score was generated to allow calculation of an individual's predicted probability of LV recovery at 6 months (Figure 2). Variable coefficients were converted to integer points. The highest possible score was 11. Those with a score of 0 or 1 and of 10 or 11 were categorized as ≤1 or ≥10, respectively, due to small numbers with extremes of scores. The predicted probability of LV recovery was estimated for each integer score. The predicted and observed probabilities of LV recovery according to score are shown in Figure 3.

Integer score for left ventricular recovery and predicted probability of left ventricular recovery for each score. Human development index (HDI) is a summary measure (between zero and one) of a country's social and economic development and can be found at: https://hdr.undp.org/data-center/human-development-index#/indicies/HDI

Predicted and observed probabilities of left ventricular recovery according to score. The mean predicted probability of recovery for all patients within an integer score group is presented against the proportion of observed recovery within that group

Sensitivity analyses

As a sensitivity analysis, women who died were included and categorized as 'unrecovered'. Patient characteristics are shown in Supplementary data online, Table S4. Backward selection using the same 20 candidate variables was performed. Results were similar, with the only difference being the removal of pre-eclampsia from the model (n = 384 in final model) (see Supplementary data online, Table S5). This model was well-calibrated (Hosmer–Lemeshow chi2 goodness-of-fit test P = .88) and demonstrated good discriminative ability (C-statistic 0.79, 95% CI 0.75–0.84).

In a further sensitivity analysis, model performance was assessed in a complete dataset using multiple imputation (n = 465 in final model with ×10 imputations). The mean C-statistic for the model across the imputed datasets was 0.79 (95% CI 0.75–0.84) (see Supplementary data online, Table S6).

In order to evaluate different methods of model-building, forward selection and stepwise selection (both forward and backward) were used. Using forward selection, the final variables included in the model were the same, with the exception of pre-eclampsia which was replaced with pregnancy-induced hypertension. The final variables included in the model were unchanged using stepwise selection.

Discussion

A prognostic model for LV recovery in women with PPCM in the ESC EORP PPCM Registry was derived, internally validated and an integer score generated (Structured Graphical Abstract). A small number of studies have investigated factors associated with LV recovery, but this is the first prospective study to systematically assess model calibration and

discrimination, and to provide validation. Factors most strongly associated with LV recovery in this global registry were LVEF, LV end diastolic diameter, HDI, duration of symptoms, QRS duration and pre-eclampsia.

Higher LVEF and lower LV end diastolic diameter at baseline have previously been shown to be associated with more frequent LV recovery.6,8,9,13,14 In the IPAC (Investigations of Pregnancy-Associated Cardiomyopathy) study, which prospectively recruited 100 women with PPCM in North America, 86% of women who had recovered by 12 months (defined as LVEF >50%) had a baseline LVEF ≥30%.6 Moreover, LV recovery occurred in 91% of women in the IPAC cohort with a baseline LVEF ≥30% and LV end diastolic diameter <6 cm. Pre-eclampsia has also been shown to be associated with approximately two-times greater a likelihood of LV recovery, even after adjusting for baseline LVEF.15 The reasons for more frequent LV recovery in patients with pre-eclampsia may be related to the different pathophysiological mechanisms through which women with gestational hypertensive disorders develop heart failure, compared to women with a genetic cardiomyopathy for example. This may also, in part, explain why the New York Heart Association (NYHA) functional class was not independently predictive of LV recovery in this cohort, since it has previously been shown that women with PPCM with pre-eclampsia have more severe symptoms (i.e. higher NYHA class) than those without pre-eclampsia but have a higher rate of LV recovery despite this.15

A number of other prognostic factors were identified. First, a longer median time between symptom-onset and diagnosis predicted a lower likelihood of LV recovery. In the ESC EORP PPCM Registry, median delay to diagnosis was 10 days.7 Delay to diagnosis and later presentation of PPCM (e.g. >1 month postpartum) have been shown to be associated with a greater frequency of adverse cardiovascular events and lower rates of LV recovery.16,17 Conversely, the timing of diagnosis (pre- vs. postpartum) was not an independent predictor of LV recovery in the current study. Second, a greater QRS duration predicted a lower likelihood of LV recovery. QRS duration has been shown to be associated with a greater degree of LV dilatation.18 Bundle branch block could reflect a subgroup of people with

conduction delay due to specific genetic variants, or with fibrosis affecting the conduction system. Genetic data and data on fibrosis on cardiac magnetic resonance imaging were not available in the ESC EORP PPCM Registry to confirm or refute these hypotheses. In PPCM, women without gestational hypertensive disorders have a higher prevalence of bundle branch block than those with gestational hypertensive disorders, and these women tend to have a phenotype more compatible with a persistent, dilated cardiomyopathy.15 Third, higher HDI predicted a greater likelihood of LV recovery. The ESC EORP PPCM Registry is the only global cohort of women with PPCM and the first to describe socioeconomic factors as determinants of outcomes. In an analysis of country-level (HDI, HE and GINI coefficient) and individual-level (educational attainment and income) factors, low HDI and HE were associated with less frequent recovery of LV function.19 HDI is a summary measure of average achievement in three aspects of human development—life expectancy, education, and standard of living.20 It is a more widely encompassing marker of disparity than factors such as ethnicity, education or income alone and, indeed, was a more robust predictor of LV recovery than ethnicity. Whether or not HDI also represents better access to heart failure treatments is uncertain, but there did not appear to be an association between treatment and LV recovery in the current study. In fact, fewer women with LV recovery than without were on a mineralocorticoid receptor antagonist at 6 months, which suggests that these women had less severe disease at presentation. Only a small number of patients in the ESC EORP PPCM Registry received bromocriptine, which was given a IIb recommendation in the ESC guidelines on cardiac disease in pregnancy in 2018, 6 years after the ESC EORP PPCM Registry began enrolling patients.21 The efficacy of bromocriptine with respect to LV recovery in women with PPCM is currently being studied in a prospective randomized controlled trial.22

Understanding the individualized chance of recovery is important to guide tailored counselling, risk stratification, more timely optimization of medical therapy, referral to specialist services, and to inform decisions about certain

treatments such as an ICD.23 Early implantation of an ICD is generally not advised in women with PPCM because of a higher propensity for recovery relative to that seen in patients with other types of cardiomyopathy. In some places, wearable cardioverter defibrillators are used in the early phase.23,24 International guidelines suggest that ICD implantation should be considered in patients who have a LVEF <35% despite optimal medical therapy for at least 3 months.25 In patients with cardiomyopathy, ventricular arrhythmias are more likely to occur with impaired LVEF and this is also true in PPCM.26 Although the majority of women who recover will do so within the first 6 months, it has been shown that recovery can occur beyond this time in women with PPCM.27 Being able to predict more accurately who will go on to normalize LVEF may prevent unnecessary implantation of a primary prevention ICD or, conversely, identify those at greatest risk of persisting LV dysfunction who warrant closer follow-up, more timely optimization of therapies and early involvement of advanced heart failure teams. In the future, comprehensive phenotyping of women with LV dysfunction around the time of pregnancy is required to identify those with specific genetic variants or those with acquired cardiotoxic mechanisms that result in different rates of LV recovery.

Prediction tools are also necessary to provide women with tailored counselling regarding a subsequent pregnancy. These risks are largely based on LVEF prior to the subsequent pregnancy, though all subsequent pregnancies carry a degree of risk.21,28 Discussions about subsequent pregnancies have been underpinned by data from small studies including patients with vastly different demographics. Applicability of these data on a wider scale is limited. Relapse is thought to occur in around 30% of subsequent pregnancies (approximately one in five when there has been recovery of cardiac function following the index pregnancy and just under half without recovery of cardiac function).29–31 All reported deaths associated with a subsequent pregnancy have occurred in women without recovery (equivalent to one in seven women without recovery). While this model concerns prediction of LV recovery after an index presentation of PPCM, and cannot be used to predict outcomes

associated with a subsequent pregnancy, more reliable prediction of LV recovery at the time of initial presentation with PPCM will allow counselling with respect to future pregnancies earlier in the patient journey.

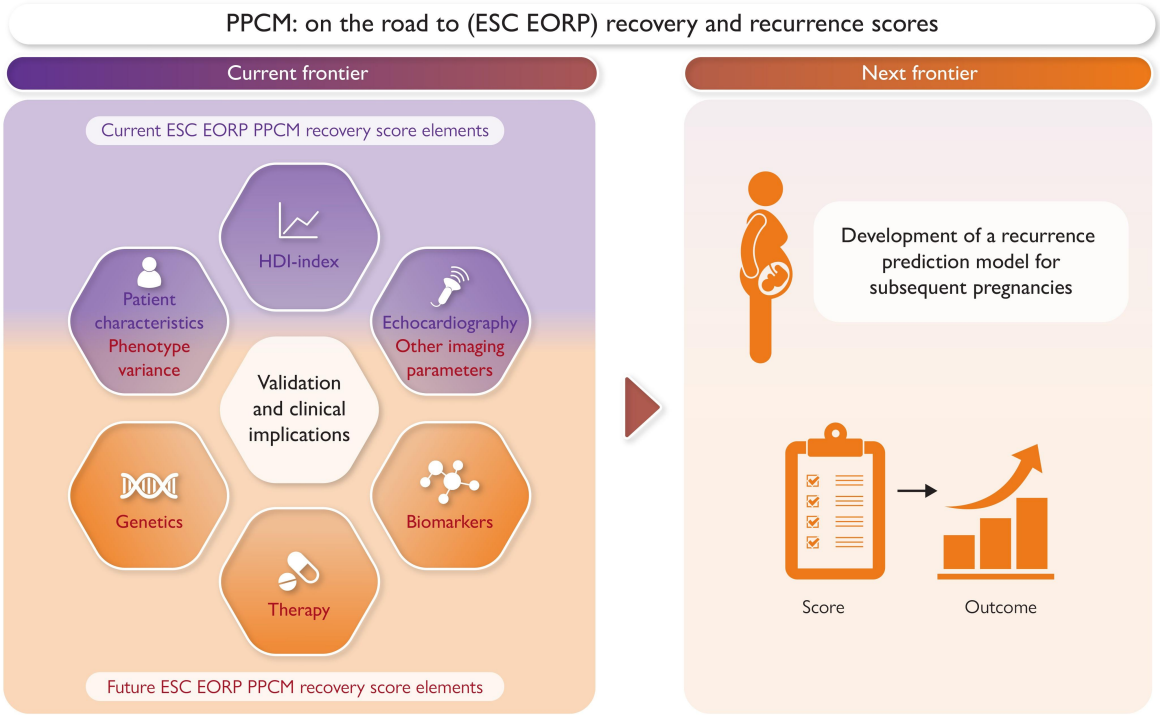
Strengths of the model are derivation in a large, global cohort, with inclusion of easily accessible clinical data. Applicability is not limited only to regions where more advanced and costly tests are routinely performed, such as cardiac magnetic resonance imaging or genetic or biomarker testing. The model was internally validated. The model was derived in a cohort receiving contemporary guideline-recommended heart failure therapies; in the ESC EORP PPCM Registry, 85% were prescribed angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, 81% were prescribed beta-blockers, and 45% were prescribed mineralocorticoid receptor antagonists.7 Heart failure therapies were not included at the model-building stage to avoid confounding by indication and to allow the tool to be used at the point of diagnosis, rather than after a period of up-titration of medication. A further strength is the generation of clinical useful score which can be quickly calculated to estimate probability of LV recovery.

Limitations of the study include the inability to include certain variables in model-building, either due to missing data or due to a low prevalence of the characteristic. Validation was done internally using accepted methods, but not externally, due to the lack of other large, prospective cohorts of women with PPCM with similar data capture (e.g. duration of symptoms). The score could not be validated in subgroups of patients with different phenotypes and, although many important variables were included in the model, calibration and precision could vary by phenotype. The model cannot be used to predict LV recovery following a subsequent pregnancy. Generating an integer score from 1–10 is less precise than using original coefficients, but produces a score which is simple and easy to use. Other limitations of the study are shared with many global registries, including lack of genotyping and more detailed cardiac imaging beyond echocardiography, lack of consecutive recruitment, and lack of biomarker measurement in all individuals; these are all difficult to

achieve in a registry performed mostly in low GDP countries without payment to sites.

In summary, this model accurately predicts LV recovery at 6 months in women with PPCM. It relies on accessible, readily available data and includes a simple integer score which can be easily applied in clinical practice to predict the probability of LV recovery for an individual at the point of presentation. Better prediction of those who will and will not recover can guide information-giving and tailored counselling, referral to specialist services, more timely optimization of treatments when appropriate, and avoidance of unnecessary treatments when inappropriate.

15. Peripartum cardiomyopathy: the challenge of predicting cardiac function recovery



Predicting recovery from PPCM: future perspectives. Except the variables in the prediction model ESC EORP PPCM Recovery Score, variables that may be included in future predictive models at 6 and 12 months follow-up are genetics, biomarkers, cardiac magnetic resonance imaging, phenotype variance, and therapy. External validation of the ESC EORP PPCM Recovery Score is of importance, as well as recommendations on how the outcome should be interpreted in the clinic.

Variables included in the prediction model ESC EORP PPCM Recovery Score by Jackson and co-workers comprise: LV ejection fraction ≤35%, LV end-diastolic diameter, high human developmental index, duration of symptoms ≤10 days, QRS duration, and pre-eclampsia. Future perspectives in development of the ESC EORP PPCM Recovery Score; variables that may be included in future predictive models at 6 and 12 months follow-up. Actions needed: external validation of the model in different populations and defining of clinical implications of the score sum of the ESC EORP PPCM Recovery Score.

16. ACC: Coronary Artery Calcium Progression May Accelerate After Menopause

Postmenopausal changes may accelerate coronary artery calcium (CAC) progression in women, according to a study presented at the annual meeting of the American College of Cardiology, held from April 6 to 8 in Atlanta.

Ella Ishaaya, M.D., from Harbor-UCLA Medical Center in Torrance, California, and colleagues compared CAC progression between postmenopausal women and age-matched men with equivalent statin therapy and coronary artery disease risk factors to determine if postmenopausal changes contribute to faster CAC progression. The analysis included 579 postmenopausal women on statin therapy who underwent baseline and follow-up CAC scans at least one year apart, as well as male patients, matched (1:1) for age, race, statin use, hypertension, and diabetes mellitus.

The researchers found that for a baseline CAC level of 1 to 99, women had significantly higher CAC progression versus men (8 versus 4 points). Annualized median CAC change for a baseline CAC of 100 to 399 was 31 versus 16 points for women versus men. When CAC was >400, there was no significant difference observed in annualized progression by gender.

"This is a unique study cohort of only postmenopausal statin users that signals that postmenopausal women may have risk of heart disease that is on par with males," Ishaaya said in a statement. "Women are underscreened and undertreated, especially postmenopausal women, who have a barrage of new

risk factors that many are not aware of. This study raises awareness of what those risk factors are and opens the door to indicating the importance of increased screening for coronary artery calcium."

16. Cardiovascular Disease in Hispanic Women: JACC Review Topic of the Week

Cardiovascular disease affects 37% of Hispanic women and is the leading cause of death among Hispanic women in the United States. Hispanic women have a higher burden of cardiovascular risk factors, are disproportionally affected by social determinants of health, and face additional barriers related to immigration, such as discrimination, language proficiency, and acculturation. Despite this, Hispanic women show lower rates of cardiovascular disease and mortality compared with non-Hispanic White women. However, this “Hispanic paradox” is challenged by recent studies that account for the diversity in culture, race, genetic background, country of origin, and social determinants of health within Hispanic subpopulations. This review provides a comprehensive overview of the cardiovascular risk factors in Hispanic women, emphasizing the role of social determinants, and proposes a multipronged approach for equitable care.

Highlights

- Hispanic women face disproportionate cardiovascular risk, although there i considerable heterogeneity among subpopulations.

- Social determinants of health influence cardiovascular risk in Hispani women.

- A multipronged approach is needed to address social determinants of healtl and achieve equitable care for Hispanic women.

17. Pregnancy Complications Impart Higher Death Risk for Decades

omen who experience adverse pregnancy outcomes (APOs) face an increased likelihood of death decades later, according to an observational study of more than 2 million Swedish women.

Investigators looked at several APO types—gestational diabetes, preterm delivery, small for gestational age, other hypertensive disorders, and preeclampsia—and several different causes of death.

“It was striking that all five adverse pregnancy outcomes were independently linked with increased mortality risks even more than 40 years after delivery,” lead investigator Casey Crump, MD, PhD (University of Texas Health Science Center, Houston), told TCTMD in an email. These increases, though not all statistically significant over the longest time frame, extended to the various causes of death as well, “suggesting that there are multiple different underlying pathways,” he said. “Additional research is needed to delineate the underlying mechanisms, which may reveal new targets for intervention.”

Natalie Bello, MD, MPH (Smidt Heart Institute, Cedars-Sinai Medical Center, Los Angeles, CA), commenting on the study for TCTMD, said its results are the most recent confirmation that complications during pregnancy can have long-lasting fallout for female patients and even their children. Yet, these risks continue to be underappreciated.

“Primary prevention guidelines for cardiovascular disease do consider adverse pregnancy outcomes as a risk enhancer,” knowledge that can inform decisions on preventive measures like whether to start statin therapy, Bello explained.

It’s important for patients, if they’re not asked directly, to “bring up their pregnancy history when they’re meeting with all of their care team to discuss their personal risk” so that other factors, such as blood pressure and cholesterol, can be tracked, she said. “Our care is very fragmented in this country—you see an OB who delivers your child and if you’re lucky that’s in an integrated healthcare system where [clinicians] can see that, but often we may not be going back to those records.”

Understandably, these conversations can get skipped over, because “primary care doctors are really busy,” Bello noted. “They’re doing depression screening and [addressing] domestic violence: all these things are on their plates.” Pregnancy, she added, can fit in with that routine as part of medical history taking.

Women who experience adverse pregnancy outcomes need close follow-up with their primary care physician, starting soon after delivery, for regular preventive care.Casey Crump

For their paper, published online recently in JAMA Internal Medicine, Crump and colleagues looked at data on 2,195,667 Swedish women who gave birth during the years 1973 to 2015. Thirty percent had at least one APO and 8% had at least two, though not necessarily in the same pregnancy. The most common of these outcomes were delivery of an infant small for gestational age and preterm delivery.

The women were followed to a median age of 52, with the dataset reaching a total of 56 million person-years of follow-up by the end of 2018. Four percent of the women died, and the median age at death was 59 years. The most common cause of death was cancer (49%), followed by "other" causes (32%), cardiovascular disease (14%), respiratory disorders (4%), and diabetes (1%).

Each of the five APOs considered in the study were linked to all-cause mortality risk.

All-Cause Mortality Risk by Adverse Pregnancy Outcome

	Adjusted HR	95% CI
Gestational Diabetes	1.52	1.46-1.58
Preterm Delivery	1.41	1.37-1.44
Small for Gestationa Age	1.30	1.28-1.32
Other Hypertensiv Disorders	1.27	1.19-1.37
Preeclampsia	1.13	1.10-1.16

Women with APOs continued to have elevated risk even 30 to 46 years after delivering their babies: the associations were statistically significant for preterm delivery (HR 1.35), small for gestational age (HR 1.23), and gestational diabetes (HR 1.38).

Regarding cause-specific mortality, the likelihood of CV death was higher with each of the APOs. For cancer and respiratory death, risks were significantly elevated with preterm delivery and small for gestational age. Diabetes-related deaths were increased with preterm delivery, preeclampsia, and gestational diabetes.

To bolster their findings, the researchers also did an analysis that compared the female study participants with their siblings, which offered a way to control for unmeasured genetic or environmental factors that could be shared determinants of pregnancy complications and premature death. While this somewhat attenuated the associations, the added risk with each of the APO types remained significant.

For Crump, pregnancy is a time of “opportunity to identify high-risk women and start interventions earlier in life, before other health problems develop.

“Women who experience adverse pregnancy outcomes,” he continued, “need close follow-up with their primary care physician, starting soon after delivery, for regular preventive care to help reduce these risks and protect their long-term health.”

18. Hypertensive Disorders of Pregnancy Raise Risk for Postpartum Mortality for One Year

Hypertensive disorders of pregnancy (HDPs) are strong risk factors for pregnancy-associated mortality due to cardiovascular disease (CVD) at delivery through one year postpartum, according to a study published online in the March issue of Paediatric and Perinatal Epidemiology.

Rachel Lee, from the Rutgers Robert Wood Johnson Medical School in New Brunswick, New Jersey, and colleagues evaluated the association between HDP (chronic hypertension, gestational hypertension, preeclampsia, eclampsia, and superimposed preeclampsia) and pregnancy-associated mortality rates from all causes and CVD-related causes both at delivery and within one year following delivery. The analysis included roughly 33.4 million hospital deliveries identified from the Nationwide Readmissions Database (2010 to 2018) among females (15 to 54 years old).

The researchers found that the rate of HDP was 11.0 percent, and the pregnancy-associated mortality rate from CVD was 6.4 per 100,000 delivery hospitalizations (2,141). CVD-related pregnancy-associated mortality rates increased with HDP severity, reaching more than 58-fold higher for eclampsia patients. Risk was higher for stroke-related (1.2 to 170.9) than heart disease-related (0.99 to 39.8) mortality across all HDPs. The increased risks for CVD mortality were evident at delivery and persisted to one year postpartum for all HDPs except for gestational hypertension.

"While absolute pregnancy-associated mortality rates are low, this study supports the importance of extending postpartum care beyond the traditional 42-day postpartum visit for people whose pregnancies are complicated by hypertension," the authors write.

19. Keeping Systolic BP Below 130 May Help Women Live Into Their 90s: WHI Data

Maintaining a systolic blood pressure below 130 mm Hg may increase the probability of survival to age 90 in healthy older women, with or without BP-lowering medications, data from the Women's Health Initiative (WHI) suggest.

The apparent protective effect of a systolic BP in the range of 110 to 130 mm Hg was consistent across sociodemographic and lifestyle factors, with those aged 65 to 75 displaying the strongest association with respect to survival to age 90 when systolic BP was kept in that range.

"These findings should encourage primary care physicians, policymakers, and other stakeholders to ensure adequate blood pressure management even at older ages," lead author Bernhard Haring, MD, MPH (Saarland University, Homburg, Germany), said in an email. "Preventive measures and risk factor control, and if necessary, initiation of blood pressure medication to ensure a systolic blood pressure level following guideline recommendations even at higher age, are therefore warranted."

The study population consisted of 16,570 participants (6% Black) who were enrolled in the Women's Health Initiative at a mean age of 70.6 years between 1993 and 1998. Participants were generally healthy and postmenopausal at the time of enrollment and were part of the WHI's randomized clinical trials portion, which involved annual BP measurements.

Compared with those who did not survive to age 90, people who did were slightly older at enrollment and more likely to be non-Hispanic white, married, or a college graduate and to have a higher income. They were also more likely to be overweight or obese, never smokers, current alcohol users, and physically active and more apt to report healthier diets. Survivors to age 90 were less likely than those who died at younger ages to have a history of hypertension or use of antihypertensives at baseline.

At ages 65, 70, 75, and 80, there was a consistent trend toward increased probability of survival to age 90 with a systolic BP of 110 to 130 mm Hg. For 80-year-old women with a systolic BP 110 mm to 130 mm Hg, for example, the probability of reaching age 90 was 79% if they were not on an antihypertensive medication and 72% if they were. With diastolic BP, the highest probability of surviving to age 90 years occurred in those who maintained a range of 70 to 80 mm Hg.

When the researchers included the possibility of disease-free survival to age 90, a target systolic BP below 130 mm Hg was associated with better odds of CVD-free survival.

“Our findings are in line with results from the Blood Pressure Lowering Treatment Trialists’ Collaboration showing that BP medication should be viewed as an effective tool for preventing cardiovascular disease when an individual’s cardiovascular risk is elevated,” Haring and colleagues write.

While the harms of too-tight BP control also are an important consideration in elderly patients with limited life expectancy, Haring said the women in the study reflect “a very large part of the population for which the benefits of maintaining a systolic blood pressure level below 130 mm Hg clearly outweigh the risks.”

Since the study consisted of women in generally good health and with no history of severe illnesses such as cancer, he added that the findings may not be generalizable to women with a high chronic disease burden.