News in February 2022

1. Importance of sex and gender in ischaemic stroke and carotid atherosclerotic disease

Stroke is a leading cause of death and disability worldwide. Women are disproportionately affected by stroke, exhibiting higher mortality and disability rates post-stroke than men. Clinical stroke research has historically included mostly men and studies were not properly designed to perform sex- and gender-based analyses, leading to under-appreciation of differences between men and women in stroke presentation, outcomes, and response to treatment. Reasons for these differences are likely multifactorial; some are due to gender-related factors (i.e. decreased social support, lack of stroke awareness), yet others result from biological differences between sexes. Unlike men, women often present with ‘atypical’ stroke symptoms. Lack of awareness of ‘atypical’ presentation has led to delays in hospital arrival, diagnosis, and treatment of women. Differences also extend to carotid atherosclerotic disease, a cause of stroke, where plaques isolated from women are undeniably different in morphology/composition compared to men. As a result, women may require different treatment than men, as evidenced by the fact that they deriving less benefit from carotid revascularization than men but more benefit from medical management. Despite this, women are less likely than men to receive medical therapy for cardiovascular risk factor management. This review focuses on the importance of sex and gender in ischaemic stroke and carotid atherosclerotic disease, summarizing the current evidence with respect to (i) stroke incidence, mortality, awareness, and outcomes, (ii) carotid plaque prevalence, morphology and composition, and gene connectivity, (iii) the role of sex hormones and sex chromosomes in atherosclerosis and ischaemic stroke risk, and (iv) carotid disease management.

2. GDM May Up Risk for Range of Later Cardiovascular Conditions

Gestational diabetes mellitus (GDM) is associated with an increased risk for diverse cardiovascular outcomes later in life, according to a study presented at the annual meeting of the Society for Maternal-Fetal Medicine, held virtually from Jan. 31 to Feb. 5.

Seung Mi Lee, M.D., from the Seoul National University College of Medicine in South Korea, and colleagues examined whether women with a history of GDM have an increased risk for long-term overall cardiovascular outcomes. The analysis included 219,330 women who reported at least one live birth.

The researchers found that women with a history of GDM had an increased risk for total cardiovascular outcomes. Among women with a history of GDM, there was an
increased risk for the new occurrence of coronary artery disease (hazard ratio [HR], 1.330), myocardial infarction (HR, 1.678), ischemic stroke (HR, 1.696), peripheral artery disease (HR, 1.064), heart failure (HR, 1.426), mitral regurgitation (HR, 2.276), and atrial fibrillation/flutter (HR, 1.474) when adjusting for confounding variables. Subsequent overt diabetes explained 23 percent of the association between GDM and overall cardiovascular outcome, while hypertension explained 11 percent and dyslipidemia explained 10 percent of the association.

"This research shows us the extent of heart health problems that can arise long after someone has given birth," Lee said in a statement. "The next step is to look at what kind of preventative measures can be taken during pregnancy to hopefully prevent cardiovascular disease from developing later in life."

3. SCAI Statement Seeks to Delineate Sex-Based Differences in Revascularization

Current practice guidelines do not address sex-based differences in treatment for and outcomes in myocardial revascularization between women and men, according to an expert consensus statement released Friday by the Society for Cardiovascular Angiography & Interventions (SCAI).

Alexandra Lansky, MD, of the Yale School of Medicine, Suzanne Baron, MD, MSc, of Lahey Hospital and Medical Center, Burlington, Massachusetts, and colleagues, wrote the paper, which was published in the Journal of the Society for Cardiovascular Angiography & Interventions.

Cardiovascular disease claims the lives of nearly 8.5 million women worldwide every year. But the consensus statement found that “access and timely delivery of optimal treatment for women lags significantly behind men.”

Based on their review of literature and data from clinical trials, utilization of common cardiovascular procedures, like percutaneous coronary intervention (PCI) and mechanical circulatory support, is “far lower in women compared with men,” the authors wrote.

An accompanying press release from SCAI detailed the paper’s areas of interest.

“The paper explores gaps in evidence in several areas including the epidemiology of ischemic heart disease, diagnostic tools to guide coronary revascularization,
revascularization for chronic coronary syndromes, revascularization for non-ST-elevation myocardial infarction (MI) and ST-elevation MI, and revascularization consideration for specific patient populations, vascular access in women,” the press release says.

For example, under the sub-heading “Invasive IVUS and OCT Imaging,” the authors noted that while women have smaller heart sizes and coronary arteries than men, there are no sex-specific recommendations for optimal computer tomography or intravascular ultrasound guidance of PCI. The authors added that intravascular imaging could be more useful in detecting and managing stent edge dissections in women than in men, as stent edge dissections are often more common and complex in women.

The authors also offered strategies, guidelines, and suggestions for clinicians to use when treating women cardiovascular patients.

While evaluating women for myocardial ischemia, physicians should take care to limit ionizing radiation, as the risk for cancer is 38% higher in women compared to men, the authors noted. Cardiac magnetic resonance stress imaging should be used for its “superior diagnostic accuracy” and equal diagnostic performance in both men and women without exposure to ionizing radiation.

Additionally, the authors tackled the difference in clinical outcomes from a fractional flow reserve strategy versus an instantaneous wave-free ratio strategy in men and women. The data, they found, is similar in both women and men, and supports using either method to guide revascularization. While current data does not support sex-specific cut-offs for invasive functional assessments, the authors did cite research that showed how lesions of similar angiographic severity were less likely to be ischemia-producing in women.

Using data from the SYNTAX, SYNTAX II, and EXCEL clinical trials, the authors said women with multivessel disease (MVD) and left main disease (LMD) might benefit more from coronary artery bypass graft surgery (CABG) than PCI compared with men. With that, the authors emphasized the need for contemporary studies that perform a randomized evaluation of CABG versus PCI in women with MVD, as well as in women with LMD.

The consensus statement also includes information and guidance on coronary revascularization for chronic coronary syndromes, ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction.
The authors reiterated that being a woman presenting with STEMI has been associated with delays to intervention, which they say is attributable, at least in part, to atypical symptoms and slower presentation compared to men.

“These delays and disparities in care have contributed to worse in-hospital mortality in women presenting with STEMI, particularly in younger women,” the authors wrote.

The authors emphasized the need to develop sex-specific algorithms for the management of cardiogenic shock in women, as well as identifying sex-specific pathogenesis and risk factors that are associated with recurrence of spontaneous coronary artery dissection (SCAD) and takotsubo cardiomyopathy. Even though it accounts for less than 1% of all acute myocardial infarctions, the authors noted, approximately 90% of patients with SCAD are women between 47 and 53 years old.

“This consensus is an international collaborative effort that highlights the knowns, the gaps and ambiguities in evidence related to sex-specific revascularization,” Lansky said in the press release. “It will inform clinicians on best practices most relevant to our female patients and [draw] attention to areas in need of additional evidence.”

4. Association Between Menstrual Cycle Length and COVID-19 Vaccination

OBJECTIVE

To assess whether coronavirus disease 2019 (COVID-19) vaccination is associated with changes in cycle or menses length in those receiving vaccination as compared with an unvaccinated cohort.

METHODS

We analyzed prospectively tracked menstrual cycle data using the application "Natural Cycles." We included U.S. residents aged 18-45 years with normal cycle lengths (24-38 days) for three consecutive cycles before the first vaccine dose followed by vaccine-dose cycles (cycles 4-6) or, if unvaccinated, six cycles over a similar time period. We calculated the mean within-individual change in cycle and menses length (three prevaccine cycles vs first- and second-dose cycles in the vaccinated cohort, and the first three cycles vs cycles four and five in the unvaccinated cohort). We used mixed-effects models to estimate the adjusted difference in change in cycle and menses length between the vaccinated and unvaccinated cohorts.

RESULTS
We included 3,959 individuals (vaccinated 2,403; unvaccinated 1,556). Most of the vaccinated cohort received the Pfizer-BioNTech vaccine (55%) (Moderna 35%, Johnson & Johnson/Janssen 7%). Overall, COVID-19 vaccine was associated with a less than 1-day change in cycle length for both vaccine-dose cycles compared with prevaccine cycles (first dose 0.71 day-increase, 98.75% CI 0.47-0.94; second dose 0.91, 98.75% CI 0.63-1.19); unvaccinated individuals saw no significant change compared with three baseline cycles (cycle four 0.07, 98.75% CI -0.22 to 0.35; cycle five 0.12, 98.75% CI -0.15 to 0.39). In adjusted models, the difference in change in cycle length between the vaccinated and unvaccinated cohorts was less than 1 day for both doses (difference in change: first dose 0.64 days, 98.75% CI 0.27-1.01; second dose 0.79 days, 98.75% CI 0.40-1.18). Change in menses length was not associated with vaccination.

CONCLUSION

Coronavirus disease 2019 (COVID-19) vaccination is associated with a small change in cycle length but not menses length.