

The importance of sex-specific strategies for prevention, treatment of heart failure in women

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There are many important differences between women and men with heart failure, highlighting the importance of sex-specific strategies for prevention and treatment, according to three papers publishing today in *JACC: Heart Failure*. This special focus issue will explore heart failure in women.

"Primary Prevention of Heart Failure in Women"

Men and women exhibit different [heart failure risk factors](#) and mechanisms, demonstrating the importance of sex-specific prevention strategies for [heart](#) failure. Unfortunately, women are frequently underrepresented in clinical trials for heart failure and data on the effectiveness of heart failure interventions in women are lacking. A review paper examines the different efforts that should be taken to prevent heart failure in women.

Women with heart failure are generally older, have a higher BMI and have a greater prevalence of hypertension, diabetes and kidney disease. Women are more likely to have heart failure with preserved ejection fraction (HFpEF), while men are more likely to have heart failure with reduced ejection fraction (HFrEF). Atrial fibrillation (AFib) has also been shown to have a sex-specific predictive value for the development of HFpEF in women. Interventions targeted at maintaining or achieving a health body weight and reducing risk factors, especially hypertension

and AFib, may help to lower the rates of heart failure in women. Additionally, pregnancy complications, breast cancer treatments and menopause can all increase the risk of heart failure in women.

"Women need to be adequately represented in [clinical research](#) and sex differences prospectively investigated," said Melissa A. Daubert, MD, cardiologist at Duke University and lead author of the paper. "In the meantime, incorporating specific recommendations for women into clinical guidelines when data are sufficient will likely improve heart failure outcomes and decrease health disparities in women."

"Is Cardiac Diastolic Dysfunction a Part of Post-Menopausal Syndrome?"

Postmenopausal women display an exponential increase in the incidence of HFpEF compared to men of the same age, indicating that hormonal changes may affect heart function. A review paper in this issue examines the involvement of estrogen on cardiac function in postmenopausal women.

"Estrogen deficiency influences both early diastolic relaxation via calcium regulation and late diastolic compliance associated with a thickening of the heart muscles," said Jagat Narula, MD, Ph.D., professor of medicine at Mount Sinai Hospital and senior author of the paper.

Changes in heart function and structure are often seen in older age in both men and women. These changes are more pronounced in postmenopausal women compared to premenopausal women, indicating that estrogen deficiency may be to blame.

"In women at a lower risk for heart failure, estrogen deficiency

combined with other risk factors such as hypertension, diabetes or obesity might lead to the development of full-blown clinical syndrome," Narula said.

Studies have inconclusively found that hormone replacement therapy could improve heart function in postmenopausal women, but more [clinical trials](#) and data are still needed.

"Long-term Risk of Heart Failure in Breast Cancer Patients After Adjuvant Chemotherapy With or Without Trastuzumab"

Trastuzumab treatment has been shown to significantly improve the outcomes of patients with a certain kind of breast cancer, but it is also associated with a two-fold increased risk of heart failure compared to other chemotherapy regimens, according to a study in this issue of *JACC: Heart Failure*.

Human Epidermal Growth Factor Receptor 2 (HER2) breast cancer is associated with a poor prognosis. While trastuzumab has significantly improved survival in these patients, previous studies have shown an increased risk in heart failure within the first two years after treatment. Long-term risks remain more uncertain.

This study included 8,812 patients scheduled for adjuvant therapy for early-stage breast cancer. A total of 2,117 had HER2 positive breast cancer and received both chemotherapy and trastuzumab, while 6,695 HER2 negative patients received chemotherapy only. The final cohort consisted of 8,611 patients who survived and did not develop heart failure within the first 18 months after treatment.

After a median follow-up period of 5.4 years, 2.7 percent of patients

who received trastuzumab developed new cases of heart failure compared to 0.8 percent who received chemotherapy only. The cumulative incidence of heart failure after nine years was 3.3 percent in the trastuzumab group compared to 1.3 percent in the chemotherapy only group. These results demonstrate a significant increase in both early and late heart failure among patients treated with both chemotherapy and trastuzumab compared to chemotherapy alone but with an overall low incidence.

"With many long-term survivors after modern breast cancer treatment, awareness of heart failure as a possible long-term consequence of trastuzumab treatment is important," said Ann Banke, MD, a researcher at Odense University Hospital in Denmark and the lead author of the study. "Even though overall risk of heart failure after trastuzumab treatment is low, it might be relevant to take this risk into consideration when planning the course of follow-up after HER2 positive breast cancer, especially in patients with other comorbidities, as this seems associated with a later diagnosis of heart failure."

In an editor's page publishing in the issue, JoAnn Lindenfeld, MD, and *JACC: Heart Failure* Editor-in-Chief Christopher O'Connor, MD, write that this issue demonstrates that, "there are important differences in clinical characteristics, comorbidities and overall characteristics of women with heart failure compared to men with heart failure. In addition, we described important differences in hospitalization rates, use of advanced heart failure therapies and mortality."

They add that the goals of this important issue of the journal are to increase awareness in these differences between heart failure in men and [women](#), to encourage research that looks at the outcomes by sex, and to provide patients with the information and knowledge needed to make informed decisions and be ensured they are receiving the best care.

Provided by American College of Cardiology

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