1. SEX-SPECIFIC VENTRICULAR ARRHYTHMIAS AND MORTALITY IN CARDIAC RESYNCHRONIZATION THERAPY RECIPIENTS

Abstract

Objectives

The study goal was to examine whether there are sex-related differences in the incidence of ventricular arrhythmias and mortality in CRT-defibrillator (CRT-D) recipients.

Background

Few studies have evaluated sex-related benefits of cardiac resynchronization therapy (CRT). Moreover, data on sex-related differences in the occurrence of ventricular tachyarrhythmias in this population are limited.

Methods

A multicenter retrospective study was conducted in 460 patients (355 male subjects and 105 female subjects) from the UMBRELLA (Incidence of Arrhythmia in Spanish Population With a Medtronic Implantable Cardiac Defibrillator Implant) national registry. Patients were followed up through remote monitoring after the first implantation of a CRT-D during a median follow-up of 2.2 ± 1.0 years. Sex differences were analyzed in terms of ventricular arrhythmia–treated incidence and death during the follow-up period, with a particular focus on primary prevention patients.

Results

Baseline New York Heart Association functional class was worse in women compared with that in men (67.0% of women in New York Heart Association functional class III vs. 49.7% of men; p = 0.003), whereas women had less ischemic cardiac disease (20.8% vs. 41.7%; p < 0.001). Female sex was an independent predictor of ventricular arrhythmias (hazard ratio: 0.40; 95% confidence interval: 0.19 to 0.86; p = 0.020), as well as left ventricular ejection fraction and nonischemic cardiomyopathy. Mortality in women was one-half that of men, although events were scarce and without significant differences (2.9% vs. 5.6%; p = 0.25).
Conclusions

Women with left bundle branch block and implanted CRT have a lower rate of ventricular tachyarrhythmias than men. All-cause mortality in patients is, at least, similar between female and male subjects.

2. PRAVASTATIN VS PLACEBO IN PREGNANCIES WITH HIGH PREECLAMPSIA RISK

BACKGROUND

Effective screening for term preeclampsia is provided by a combination of maternal factors with measurements of mean arterial pressure, serum placental growth factor and serum soluble fms-like tyrosine kinase-1 at 35 to 37 weeks of gestation, with detection rate of about 75%, at screen positive rate of 10%. However, there is no known intervention to reduce the incidence of the disease.

METHODS

In this multicenter, double-blind, placebo-controlled trial, we randomly assigned 1,120 women with singleton pregnancies at high-risk of term preeclampsia to receive pravastatin, at a dose of 20 mg per day, or placebo from 35 to 37 weeks of gestation until delivery or 41 weeks. The primary outcome was delivery with preeclampsia at any time after randomization. The analysis was performed according to intention-to-treat.

RESULTS

A total of 29 women withdrew consent during the trial. Preeclampsia occurred in 14.6% (80/548) participants in the pravastatin group and in 13.6% (74/543) in the placebo group. Allowing for the effect of risk at the time of screening and participating centre, the mixed effects Cox regression showed no evidence of an effect of pravastatin; hazard ratio (statin/placebo) 1.08 (95% confidence interval: 0.78, 1.49; p=0.65). There was no evidence of interaction between the effect of pravastatin, estimated risk of preeclampsia, previous pregnancy history, adherence and aspirin treatment. There was no significant between-group difference in the
incidence of any secondary outcomes, including gestational hypertension, stillbirth, abruption, delivery of small for gestational age neonates, neonatal death or neonatal morbidity. There was no significant between-group difference in the treatment effects on serum placental growth factor and soluble fms-like tyrosine kinase-1 concentrations 1 and 3 weeks after randomization. Adherence was good, with reported intake of 80% or more of the required number of tablets in 89% of participants. There were no significant between-group differences in neonatal adverse outcomes or other adverse events.

CONCLUSIONS

Pravastatin in women at high risk of term preeclampsia did not reduce the incidence of delivery with preeclampsia.

3. IS IT TIME FOR SEX-SPECIFIC GUIDELINES FOR CARDIOVASCULAR DISEASE?

The importance of sex-specific research regarding all aspects of cardiovascular disease (CVD)—from risk stratification to treatment—has received increasing recognition in recent years. Sex differences in pathophysiology influence the risk of heart failure (HF), arrhythmias, coronary artery disease (CAD), and stroke (1). However, current cardiovascular society guidelines rarely propose sex-specific recommendations or sex-specific levels of evidence unless the diagnosis is specific to women or occurs during pregnancy and lactation. Recommendations are often made across subgroups of patients who may have been under-represented in primary research. In this viewpoint, we discuss the current landscape of sex-specific research and endorse the role of sex-specific guidelines, particularly for CVD prevention.

4. MATERNAL DIABETES LINKED WITH ADVERSE DISEASE CHARACTERISTICS AND COMPLICATIONS AMONG YOUTH WITH TYPE 2 DIABETES

The presence of maternal diabetes among youth with type 2 diabetes is associated with accelerated progression of disease and complications, according to an analysis of the findings of the Treatment Options for type 2 Diabetes in Adolescents and Youth (TODAY) study, presented at the 81st Scientific Sessions of the American Diabetes Association, held virtually from June 25 to 29.

“In participants with youth-onset type 2 diabetes that were followed over 10 years, we saw that a maternal history of diabetes was associated with accelerated loss of glycemic control, impaired beta cell function, and an increased incidence of renal hyperfiltration and unfavorable vascular indices,” said coauthor Rachana D. Shah, MD, of the Children’s Hospital of Philadelphia, during her presentation of the data. “Both maternal and parental diabetes were associated with baseline HbA1c and oral disposition index.”

TODAY was a multicenter, randomized trial of 699 youth aged 10 to 17 years who had a recent onset of type 2 diabetes. From 2004 to 2011, these patients were randomized to one of three treatment regimens: metformin, metformin plus rosiglitazone, or metformin plus lifestyle modification. From 2011 to 2014, patients were off randomized treatment but continued to receive care from the study team. From 2014 to 2020, patients transitioned to community care.
Patients were followed for an average of 10.2 years overall. This included annual vital sign assessments, physical examinations, and laboratory tests. Bone density scans and oral glucose tolerance testing was conducted at select study visits. Fundus photography and vascular studies were conducted at two timepoints. Information on diabetes diagnosis of biological parents was also included in the analysis.

Of the study cohort, 158 youths did not have a parent with diabetes, 177 had a mother with diabetes, 72 had a father with diabetes, and 79 had two parents with diabetes. There was no significant difference in age, sex, and race or ethnicity among the four groups. More youth with both parents with diabetes came from households with an income of $25,000 or less. Youths of parents who were both diabetic or whose mother was diabetic had higher birth weights, compared with those who had a father with diabetes or when both parents were non-diabetic.

Mean glycated hemoglobin (HbA1c) was lower among youths whose parents did not have diabetes, compared with youths for whom both parents had diabetes or the mother had diabetes (5.8% vs 6.2% and 6.1%, \( P < .0001 \)). Similarly, mean C-peptide index was higher among those whose parents did not have diabetes than those whose parents or mother had diabetes (0.115 vs 0.063 and 0.066 ng/mL per mg/dL, \( P < .0001 \)).

Loss of glycemic control was more common among those with maternal diabetes occurring during pregnancy (88.2%) or after pregnancy (87.2%), compared with those whose mothers never had diabetes (70.9%). It was also more common among those for whom both parents had diabetes (90.4%) and those whose mothers had diabetes (85.5%), compared with those whose fathers had diabetes (69.2%) or for whom neither parent had diabetes (70.4%). Greater HbA1c and insulin sensitivity as well as lower C-peptide index were significantly linked with maternal diabetes before pregnancy and diabetes in both parents. Insulin sensitivity and C-peptide index but not HbA1c were also linked with parental diabetes after pregnancy.

The incidence of renal hyperfiltration progressively increased with age from birth in the youth with type 2 diabetes in the 10-year follow-up. The cumulative incidence when maternal diabetes occurred during or after pregnancy was 57.2% and 54.2%, respectively, compared with 37.1% in the absence of maternal diabetes. The cumulative rates over the same length of time were 60.2% when both parents had diabetes and 55.2% when only the mother had diabetes, compared with 37.2% when only the father had diabetes and 38.6% when neither parent had diabetes.

No significant effects of parental diabetes were evident concerning retinopathy or arterial stiffness. Youths with no parental history of diabetes had significantly lower 5-year drops in heart rate variability, compared with those with a mother and/or father with diabetes.

“Parental diabetes is associated with adverse diabetes characteristics and accelerated onset of complications in youth with type 2 diabetes,” concluded Dr. Shah. “Further studies on the mechanisms of prenatal exposures are needed with the ultimate goal of preventing adverse impacts.”

5. SEVERE ABNORMAL UTERINE BLEEDING RISK WITH ANTICOAGULANT THERAPY EXAMINED

Rivaroxaban may increase the risk of severe abnormal uterine bleeding compared with other direct oral anticoagulants (DOACs) or warfarin, according to the findings of a retrospective study recently published in Drug Safety.

To assess whether anticoagulant therapy increases the risk of severe abnormal uterine bleeding, study authors utilized the FDA’s Sentinel System (10/2010-09/2015) to obtain data
on females over 18 years old with a history of venous thromboembolism or atrial flutter/fibrillation who had recently initiated a DOAC or warfarin.

“We followed women from dispensing date until the earliest of transfusion or surgery following vaginal bleeding, disenrollment, exposure or study end date, or recorded death,” the authors explained. “We estimated hazard ratios (HRs) using Cox proportional hazards regression via propensity score stratification.” Additionally, the authors conducted 4 pairwise comparisons for each intervention.

Study findings revealed an increased risk of surgical intervention in women exposed to rivaroxaban compared with those exposed to dabigatran (HR, 1.19; 95% CI, 1.03-1.38), apixaban (HR, 1.23; 95% CI, 1.04-1.47), and warfarin (HR, 1.34; 95% CI, 1.22-1.47). For the dabigatran/apixaban comparisons, no difference was observed when assessing the risk of surgical intervention. It was noted that the risk of transfusion was only found to be increased when comparing rivaroxaban and dabigatran (HR, 1.49; 95% CI, 1.03-2.17).

Exposure to rivaroxaban was also associated with an increased risk of surgical intervention in patients without underlying gynecological conditions when compared with dabigatran (HR, 1.22; 95% CI, 1.05-1.42), apixaban (HR, 1.25; 95% CI, 1.04-1.49), and warfarin (HR, 1.36; 95% CI, 1.23-1.50).

Based on their findings, the authors concluded that women of reproductive age on anticoagulant therapy should be made aware of the potential risk of severe abnormal uterine bleeding.

6. COVID-19 Vaccine Effectively Reduces Infection in Pregnant Women

The Pfizer-BioNTech COVID-19 vaccine is associated with a significantly lower risk for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in pregnant women, according to a study published online July 12 in the *Journal of the American Medical Association*.

Inbal Goldshtein, Ph.D., from Maccabi Healthcare Services in Tel Aviv, Israel, and colleagues used data from a pregnancy registry (including 7,530 vaccinated and 7,530 matched unvaccinated women) to assess the association between receipt of the BNT162b2 mRNA vaccine and the risk for SARS-CoV-2 infection among pregnant women.

The researchers noted 118 SARS-CoV-2 infections in the vaccinated group and 202 in the unvaccinated group. In the vaccinated group, 83.8 percent were symptomatic versus 83.2 percent in the unvaccinated group (P ≥ 0.99). However, in the 28 to 70 days of follow-up, there were 10 infections in the vaccinated group and 46 in the unvaccinated group, yielding hazards of infection of 0.33 and 1.64 percent, respectively (absolute difference: 1.31 percent; adjusted hazard ratio, 0.22). Sixty-eight patients reported vaccine-related adverse events, including headache (0.1 percent), general weakness (0.1 percent), nonspecified pain (<0.1 percent), and stomachache (<0.1 percent); no severe reactions were reported.