JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
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PUBLISHED BY ELSEVIER INC.

VOL. 66, NO. 2, 2015
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2015.04.062

ORIGINAL INVESTIGATIONS

Ventricular Ectopy as a Predictor of Heart Failure and Death

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ABSTRACT

BACKGROUND Studies of patients presenting for catheter ablation suggest that premature ventricular contractions (PVCs) are a modifiable risk factor for congestive heart failure (CHF). The relationship among PVC frequency, incident CHF, and mortality in the general population remains unknown.

OBJECTIVES The goal of this study was to determine whether PVC frequency ascertained using a 24-h Holter monitor is a predictor of a decrease in the left ventricular ejection fraction (LVEF), incident CHF, and death in a population-based cohort.

METHODS We studied 1,139 Cardiovascular Health Study (CHS) participants who were randomly assigned to 24-h ambulatory electrocardiography (Holter) monitoring and who had a normal LVEF and no history of CHF. PVC frequency was quantified using Holter studies, and LVEF was measured from baseline and 5-year echocardiograms. Participants were followed for incident CHF and death.

RESULTS Those in the upper quartile versus the lowest quartile of PVC frequency had a multivariable-adjusted, 3-fold greater odds of a 5-year decrease in LVEF (odds ratio [OR]: 3.10; 95% confidence interval [CI]: 1.42 to 6.77; $p = 0.005$), a 48% increased risk of incident CHF (HR: 1.48; 95% CI: 1.08 to 2.04; $p = 0.02$), and a 31% increased risk of death (HR: 1.31; 95% CI: 1.06 to 1.63; $p = 0.01$) during a median follow-up of >13 years. Similar statistically significant results were observed for PVCs analyzed as a continuous variable. The specificity for the 15-year risk of CHF exceeded 90% when PVCs included at least 0.7% of ventricular beats. The population-level risk for incident CHF attributed to PVCs was 8.1% (95% CI: 1.2% to 14.9%).

CONCLUSIONS In a population-based sample, a higher frequency of PVCs was associated with a decrease in LVEF, an increase in incident CHF, and increased mortality. Because of the capacity to prevent PVCs through medical or ablation therapy, PVCs may represent a modifiable risk factor for CHF and death. (J Am Coll Cardiol 2015;66:101-9)

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This work was made possible by grants 12GRNT11780061 from the American Heart Association and the Joseph Drown Foundation to Dr. Marcus, and grant R01HL116747 to Dr. Sotoodehnia from the National Heart, Lung, and Blood Institute (NHLBI); contracts HHSN268201200036C, HHSN268200800007C, N01 HC55222, N01HC85079, N01HC85080, N01HC85081, N01HC85082, N01HC85083, N01HC85086, and grant HL080295 from the NHLBI, with additional contribution from the National Institute of Neurological Disorders and Stroke. Additional support was provided by AG023629 from the National Institute on Aging. A full list

ABBREVIATIONS AND ACRONYMS

2D = 2-dimensional
AF = atrial fibrillation
BMI = body mass index
CAD = coronary artery disease
CHF = congestive heart failure
CI = confidence interval
ECG = electrocardiography
HR = hazard ratio
IQR = interquartile range
LV = left ventricular
LVEF = left ventricular ejection fraction
MI = myocardial infarction
NPV = negative predictive value
OR = odds ratio
PPV = positive predictive value
PVC = premature ventricular contraction
VT = ventricular tachycardia

The effect of premature ventricular contraction (PVC) frequency on left ventricular (LV) systolic function, incident congestive heart failure (CHF), or mortality in the general population remains unknown. Because the diurnal distribution of ectopic beats can vary, 24-h Holter monitoring is essential to accurately assess periodic events that contribute to the true burden of PVCs (1,2). Because of the pervasiveness of PVCs in the general population and the number of "idiopathic" CHF patients who contribute to significant health care resource use (3,4), it is important to understand the association between PVC frequency and myocardial function in the general population. Therefore, we sought to investigate PVC frequency ascertained using a 24-h Holter monitor as a predictor of a decrease in the left ventricular ejection fraction (LVEF), incident CHF, and death in a population-based cohort study.

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METHODS

STUDY DESIGN. The Cardiovascular Health Study (CHS) is a prospective, community-based cohort study sponsored by the National Heart, Lung, and Blood Institute. Details regarding eligibility, enrollment, and follow-up have been previously published (5–7). Briefly, 5,201 subjects 65 years of age or older were recruited between 1989 and 1990 from a random sample of Medicare beneficiaries by 4 academic centers (Johns Hopkins University, Wake Forest University, University of Pittsburgh, and University of California, Davis). An additional 687 black patients were recruited between 1992 and 1993. All participants underwent a medical history, physical examination, laboratory testing, and 12-lead electrocardiography (ECG) at enrollment. Participants were then followed with annual clinic visits and semi-annual telephone contact for 10 years, with telephone contact continued every 6 months thereafter.

STUDY COHORT. Our analysis was restricted to the subset of 1,429 subjects who were randomly assigned to 24-h ambulatory ECG (Holter) monitoring during their initial assessment and who were part of the initial recruitment cohort (those recruited between 1989 and 1990). Patients without a normal LVEF, as determined by the baseline echocardiogram, or with prevalent CHF were excluded from the study cohort.

HOLTER ASSESSMENT. Holter data were analyzed at the Washington University School of Medicine Heart Rate Variability Laboratory using a MARS 8000 Holter scanner (GE Medical Systems, Milwaukee, Wisconsin), and all PVC, atrial fibrillation (AF), and ventricular tachycardia (VT) episodes were identified. The results were then manually reviewed to ensure accuracy. The percentage of PVCs was determined by dividing the total number of ventricular ectopic beats by the total number of beats recorded during Holter monitoring.

ECHOCARDIOGRAPHIC EVALUATION. The echocardiographic assessment of participants in the CHS were previously described (8). In brief, 2-dimensional (2D) echocardiography, 2D targeted M-mode, and Doppler imaging were performed on each participant at baseline using Toshiba SSH-160A echocardiographic machines (Toshiba Medical Systems, Tustin, California), equipped with 2.5- and 3.75-MHz transducers. Imaging was performed at the highest megahertz that provided adequate tissue penetration for 2D imaging. Images were recorded and stored on Super-VHS videotape at the recruitment sites and then transferred to the University of California, Irvine, for central interpretation. LV function was qualitatively assessed from the 2D imaging views, where at least 80% of the myocardium was visualized. Function was subjectively categorized as normal, borderline, or abnormal, with 94% interreader agreement and 98% intrareader agreement of paired studies (9). LV end-diastolic diameter and LV mass were derived from M-mode measurements, using leading-edge-to-leading-edge methodologies per American Society of Echocardiography standards (10). LV mass was calculated using the Devereux formula and indexed by dividing by the body surface

of principal CHS investigators and institutions can be found at CHS-NHLBI.org. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. Dr. Psaty has served on the Data and Safety Monitoring Board for a clinical trial of a device funded by Zoll (LifeCor); and is on the Steering Committee of the Yale Open Data Access Project funded by Medtronic. Dr. Marcus has received research support from Gilead Sciences and Medtronic. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.
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Manuscript received October 15, 2014; revised manuscript received April 29, 2015, accepted April 30, 2015.