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Risk Factors for Heart Failure: A Population-Based Case-Control Study

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ABSTRACT

BACKGROUND: The relative contribution of risk factors to the development of heart failure remains controversial. Further, whether these contributions have changed over time or differ by sex is unclear. Few population-based studies have been performed. We aimed to estimate the population attributable risk (PAR) associated with key risk factors for heart failure in the community.

METHODS: Between 1979 and 2002, 962 incident heart failure cases in Olmsted County were age and sex-matched to population-based controls using Rochester Epidemiology Project resources. We determined the frequency of risk factors (coronary heart disease, hypertension, diabetes mellitus, obesity, and smoking), odds ratios, and PAR of each risk factor for heart failure.

RESULTS: The mean number of risk factors for heart failure per case was 1.9 ± 1.1 and increased over time ($P < .001$). Hypertension was the most common (66%), followed by smoking (51%). The prevalence of hypertension, obesity, and smoking increased over time. The risk of heart failure was particularly high for coronary disease and diabetes with odds ratios (95% confidence intervals) of 3.05 (2.36-3.95) and 2.65 (1.98-3.54), respectively. However, the PAR was highest for coronary disease and hypertension; each accounted for 20% of heart failure cases in the population, although coronary disease accounted for the greatest proportion of cases in men (PAR 23%) and hypertension was of greatest importance in women (PAR 28%).

CONCLUSION: Preventing coronary disease and hypertension will have the greatest population impact in preventing heart failure. Sex-targeted prevention strategies might confer additional benefit. However, these relationships can change, underscoring the importance of continued surveillance of heart failure.

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KEYWORDS: Epidemiology; Heart failure; Risk factors

Population-based studies have investigated the heart failure epidemic. In the Framingham Heart Study[1] and in Olmsted County,[2] the incidence of heart failure has remained stable or decreased over time while survival improvements were limited and diverged by sex, with greater survival gains in men than women. The explanations for these disparities are lacking and could be related to differences in the risk factors for development of heart failure.

The relative contribution of various risk factors to the development of heart failure remains controversial and has seldom been investigated in population-based studies.[3-7] In the Framingham Heart Study, hypertension contributed a large portion of heart failure cases, particularly in women.[6] Further, obesity was associated with a doubling of the risk of heart failure and was responsible for an estimated 14% of heart failure cases in women and 11% in men.[7] However, data from the National Health and Nutrition Epidemiologic Survey (NHANES) suggested that coronary heart disease had the largest impact on the development of heart failure and might be responsible for more than 60% of cases. These

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important findings were derived from Framingham and NHANES participants enrolled starting in the 1970s. Consequently, these data might not be applicable to different cohorts or time periods when the burden of risk factors can differ. This underscores the importance of examining the risk of heart failure conferred by various conditions among different populations, including more contemporary cases.

We aimed to address these gaps in knowledge and to evaluate the contribution of coronary disease, hypertension, diabetes mellitus, obesity, and smoking to heart failure. This population-based case-control study was undertaken to determine the frequency of risk factors for heart failure among incident cases, to determine how these frequencies may have changed over time, and to estimate the population attributable risk (PAR) for each risk factor for heart failure.

CLINICAL SIGNIFICANCE

- The number of risk factors diagnosed per patient before the development of heart failure has increased over time.
- Coronary heart disease and hypertension are responsible for the largest proportion of new heart failure cases in the population.
- Coronary heart disease, hypertension, diabetes mellitus, obesity, and smoking are responsible for 52% of incident heart failure cases in the population.

MATERIALS AND METHODS

Study Population

Olmsted County, Minnesota, has an estimated population of 137,521 (2006 US Census); 50.4% are female. Epidemiologic research is possible because the county is isolated from other urban centers, and medical care is delivered to local residents by few providers.[8] Through the Rochester Epidemiology Project, the medical records from all sources of care used by the population are linked, providing a unique infrastructure to analyze disease determinants and outcomes. This study was approved by the Mayo Clinic and Olmsted Medical Center Institutional Review Boards.

Selection of Cases and Controls

Case subjects were Olmsted County residents with a first diagnosis of heart failure from 1979 to 2002. Potential case subjects were identified by International Classification of Diseases, Ninth Revision code 428 (heart failure). A subset was randomly selected for validation and data abstraction. The index date was defined as the first evidence of heart failure in the medical record. Cases were validated using methods previously described.[2] Briefly, nurse abstractors reviewed records to ensure each met Framingham criteria[9] and had a physician's diagnosis of heart failure. When this method was used previously,[2] missing data were minimal and Framingham criteria could be applied in 98% of cases. The inter-abstractor agreement was 100%, indicating these methods are highly reproducible.

Control subjects were selected from the Olmsted County population. In any 3-year period, more than 90% of residents are seen at Mayo Clinic.[8,10] Thus, the Rochester Epidemiology Project provides a virtually complete enumeration of the population from which we selected controls. Information on exposures before the index date was obtained from the medical record. This approach avoids many biases common with case-control studies, including differential recall, non-response bias, and survivor bias.

Control subjects were matched to each case subject by age (±3 years) and sex. The index date for the control corresponds to the incidence date of the matched heart failure subject. Among eligible controls, we selected those with the closest clinic registration numbers to the cases, which matches them for their medical record duration to ensure similar opportunities for care. Control subjects were sampled without replacement. Controls with heart failure before the index date were excluded.

Risk Factors

The occurrence of each risk factor (coronary disease, hypertension, diabetes, obesity, smoking) was collected from age 18 years (or date of emigration to Olmsted County thereafter) until the date of incident heart failure or index date for controls. Myocardial infarction was ascertained using standardized criteria.[11] Coronary disease was defined as a prior myocardial infarction or revascularization (coronary bypass surgery or angioplasty). Hypertension was defined by physician diagnosis or systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg. Diabetes was defined by fasting blood glucose levels or use of insulin or oral hypoglycemic medications. Body mass index (kilograms/meters squared) was calculated using the weight and earliest adult height. Obesity was defined as a body mass index of 30.0 kg/m^2 or greater. The date when patients first fulfilled criteria for the diagnoses of coronary disease, hypertension, diabetes, or obesity was used as the diagnosis date. Smoking status was defined as "never" or "ever"; heavy smoking was defined as >20 pack-years.

Statistical Analysis

Differences in the prevalence of risk factors by sex were examined using a chi-square test; trends over time were compared by year of heart failure diagnosis (1979-1984, 1985-1990, 1991-1996, 1997-2002) with the Mantel–Haenszel chi-square test. Differences in the time from onset of risk factor to heart failure by sex were tested using linear regression adjusting for age.

To account for the case-control design, a matched analysis was performed with conditional logistic regression. A model was developed to estimate the odds ratio (OR) of heart failure associated with each risk factor. To determine whether risk of heart failure differed by sex, an interaction