The Epidemiology of Congestive Heart Failure: Contributions from the Framingham Heart Study

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SUMMARY

In 1971, McKee et al. at the Framingham Heart Study published a seminal paper on the epidemiology of congestive heart failure. The authors proposed a set of standardized criteria for heart failure for use in research studies and described the risk factors for developing heart failure. Their data demonstrated the strong association between advanced age and increased incidence of heart failure and underscored the importance of hypertension as a precursor of heart failure in the community. The authors were also among the first to demonstrate the poor long-term outcomes of heart failure in the community, with 1 in 2 affected individuals dying within 5 years of the diagnosis. Subsequent Framingham studies have documented other predictors of new onset heart failure, including elevated plasma natriuretic peptide levels, asymptomatic left ventricular systolic dysfunction, and increased left ventricular diastolic dimension. These findings have highlighted potential opportunities for prevention based on the modification of risk factors such as hypertension, and they continue to provide a foundation for future investigations aimed at reducing the burden of heart failure.

The Framingham Heart Study was established in 1948, setting into motion over 6 decades of dedicated study of cardiovascular disease, including congestive heart failure (CHF). Indeed, one of the seminal papers describing the epidemiology of CHF arose out of Framingham. The 1971 paper by McKee et al. [1] described criteria for CHF that continued to be used to this day in clinical and epidemiologic studies, demonstrated that hypertension was an important precursor of CHF, and characterized the poor prognosis of individuals with CHF in the community. This paper briefly reviews the key findings from that paper and summarizes several contemporary Framingham publications on the topic.

CONGESTIVE HEART FAILURE: THE FRAMINGHAM CRITERIA

Until the 1960s, there were no standardized criteria for adjudicating CHF in clinical studies. McKee and colleagues recognized the need for such criteria to facilitate efforts to document the risk factors and natural history of CHF. As they wrote, "if preventive and prophylactic programs are to be developed, the identification of factors that predispose and influence the course of the disease become important" [1].

The criteria they proposed are shown in Table 1. Included in the list were physician's assessment of neck-vein distension, rales, S^3 gallop, venous pressure >16 cm of water, and hepatojugular reflux (major criteria). Weight loss of 4.5 kg in 5 days due to diuretic therapy was a major criterion only if it could not be attributed to a condition other than CHF, otherwise it was considered a minor criterion. Other minor criteria were ankle edema, night cough, dyspnea on exertion, hepatomegaly, tachycardia, and weight loss. "Definite CHF" was defined as having at least 2 major criteria, or 1 major criterion and 2 minor criteria, as long as the minor criteria could not be attributed to any other condition.

The emphasis in the criteria on symptoms and physical examination findings, rather than antecedent comorbidities or cardiac function assessment, underscored the fact that CHF is a clinical syndrome with many etiologies [2]. Today, the approach to detecting the clinical manifestations of CHF is largely unchanged, despite important advances in knowledge about the biology of cardiac remodeling since the early 1970s. Consequently, the Framingham criteria remain relevant in the 21st century and continue to be used in epidemiologic research.

The reliance on overt symptoms and signs of CHF in the Framingham criteria has occasionally led to the criticism that the criteria lack sensitivity, particularly for milder presentations of CHF. Sometimes, individuals will fail to fulfill an adequate number of major or minor criteria and will be regarded as having "probable" or "questionable" CHF. It is important to recognize the value in research of using diagnostic criteria that are highly specific, even at the expense of sensitivity. The number of CHF cases in any epidemiologic cohort will be far lower than the number of control cases. Consequently, misclassification of cases (as might occur with criteria lacking specificity) will cause greater problems than misclassification of control cases (as might occur with criteria lacking sensitivity).

EPIDEMIOLOGY AND NATURAL HISTORY OF CHF

Applying these new criteria, McKee and colleagues characterized the epidemiology of CHF in the Framingham cohort. They followed 5,209 men and women from the

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GLOBAL HEART

VOL. 8, NO. 1, 2013
ISSN 2211-8160/$36.00.
http://dx.doi.org/10.1016/j.gheart.2012.12.006

TABLE 1. Framingham criterion for congestive heart failure introduced in 1971

Major criteria
Paroxysmal nocturnal dyspnea or orthopnea
Neck-vein distension
Rales
Cardiomegaly
Acute pulmonary edema
S_3 gallop
Increased venous pressure >16 cm of water
Circulation time ≥25 s
Hepatojugular reflux
Minor criteria
Ankle edema
Night cough
Dyspnea on exertion
Hepatomegaly
Pleural effusion
Vital capacity ↓ 1/3 from maximum
Tachycardia (rate of ≥120/min)
Major or minor criterion
Weight loss ≥4.5 kg in 5 days in response to treatment

Adapted, with permission, from McKee et al. [1].

Framingham cohort for up to 16 years. Eliminated from the analysis were 17 subjects who had a diagnosis of CHF at the time of Framingham recruitment. Subjects were assessed every 2 years with vital signs, electrocardiogram (ECG), chest x-ray, urinalysis, vital capacity on pulmonary function testing, and blood work. Only 2% of subjects were completely lost to follow-up [3]. A total of 142 individuals developed "definite" CHF according to the Framingham criteria. The rate of CHF per person-year rose more than 10-fold between the age of 29 to 39 years (0.6 to 0.8 cases/1,000 years) and 70 to 74 years (8.7 cases/1,000 years).

The longitudinal design of the cohort facilitated the characterization of antecedent comorbidities in the 142 individuals with CHF (Fig. 1). Definite hypertension, defined using criteria employed at the time (systolic blood pressure ≥160 mm Hg or diastolic blood pressure ≥95 mm Hg), was present in 75% of cases. This was typically accompanied by evidence of cardiomegaly on chest x-ray or ECG. Coronary heart disease was present in approximately one-half of the individuals with hypertension. Conversely, coronary heart disease without hypertension was present in only 10% of individuals with CHF.

Prior to the advent of modern therapies, treatment of CHF primarily involved diuresis and digoxin. Clinical perceptions of survival were based on relatively limited experiences in the hospital setting. Thus, a key contribution of McKee and colleagues was to document the poor prognosis of individuals with CHF in the community. They examined the outcomes of individuals meeting criteria for definite, probable, or questionable CHF. As seen in Figure 2, approximately 1 in 2 subjects with CHF died within 5 years of the initial diagnosis. Among men, the mortality rate was substantially higher than that observed in Framingham individuals with myocardial infarction (approximately 30% at 5 years). This difference was even more pronounced a decade after the index event: roughly 4

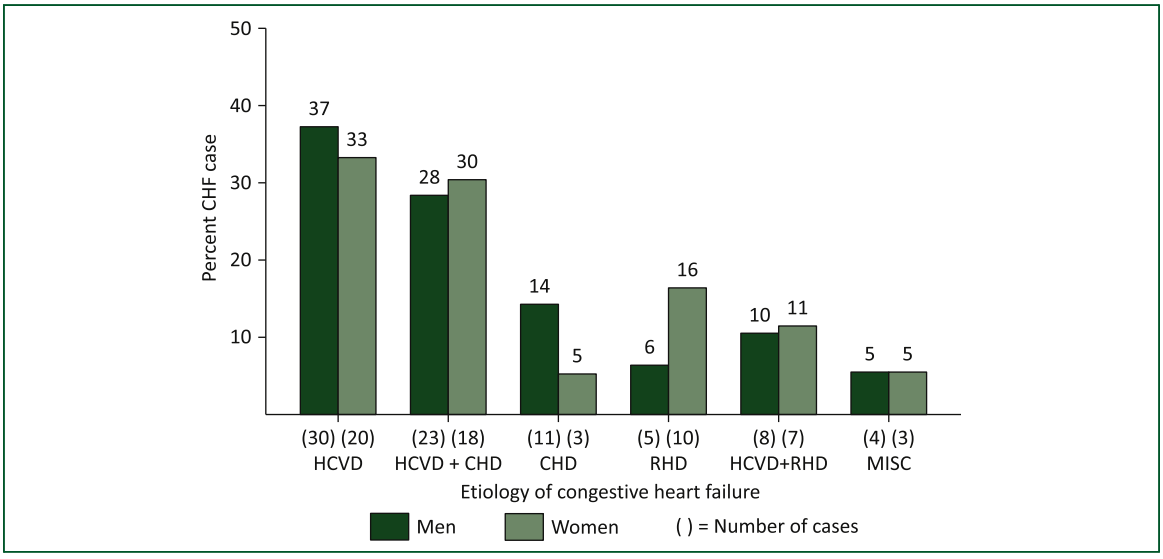

FIGURE 1. Risk factors seen in patients who developed congestive heart failure during 16 years of follow-up. CHD, coronary heart disease; HCVD, hypertensive cardiovascular disease; RHD, rheumatic heart disease. Adapted, with permission, from McKee et al. [1].