JACC: HEART FAILURE
VOL. 4, NO. 12, 2016

ISSN 2213-1779/$36.00
http://dx.doi.org/10.1016/j.jchf.2016.10.003

EDITORIAL COMMENT

Living Without Heart Failure

Contemporary Concepts in Prevention*

Thomas J. Wang, MD

In the past several decades, randomized trials have established the life-prolonging benefit of selected therapies for chronic systolic heart failure. Nonetheless, prognosis after the onset of this condition remains poor, worse than that of many common cancers. Outcomes are nearly as poor for individuals with heart failure with preserved ejection fraction, a fact that is compounded by the complete lack of proven therapies in that condition.

Given the suboptimal outcomes for individuals with diagnosed heart failure, it is clear that clinical approaches must emphasize prevention in addition to treatment. An important shift occurred 15 years ago, when the American College of Cardiology/American Heart Association practice guidelines introduced a 4-stage classification system for heart failure that included 2 preclinical stages (1). Stage A describes individuals who are at high risk for heart failure by virtue of having 1 or more risk factors, such as hypertension or diabetes. Stage B consists of individuals with structural heart disease but no overt symptoms. Stages C and D include individuals with symptomatic heart failure.

To leverage this classification at the patient level, it is important to know both the likelihood of developing disease and the timing. Risk calculators, particularly ubiquitous for atherosclerotic disease, typically focus on medium-term cardiovascular risk. However, the benefits of therapy may accrue over periods of time that far exceed the time interval for medium-term prediction. Heart failure is a case in point. The syndrome of heart failure is the culmination of a disease process that begins with etiologic risk factors, progresses through asymptomatic left ventricular dysfunction, and finally ends in overt heart failure. This process may take place over decades, as illustrated by the fact that stage A risk factors typically appear in middle age, whereas the average age of onset of heart failure is in the 70s. Thus, the absolute risk of heart failure in middle-aged individuals is almost uniformly low over the short and medium term. A 55-year-old man with no risk factors has an estimated 10-year heart failure risk of 1.1% (2). Even with multiple risk factors, including hypertension and diabetes, a 55-year-old man has a 10-year risk of only 2.7%. Over this time frame, most pharmacological interventions would not be viewed as cost-effective.

Examining lifetime risk and the related outcome of heart failure-free survival provides an alternate perspective. In 2002, Lloyd-Jones et al. (3) published the earliest large study of the lifetime risk of heart failure, using data from the Framingham Heart Study. They estimated that the risk of developing heart failure was about 20%, a figure that was similar for men and women and also across different baseline ages. Thus, an individual at age 40 years has a 1 in 5 chance of developing heart failure over his or her remaining lifetime, the same as an individual at age 80 years (because the higher incident risk for the 80-year-old is offset by the shorter remaining lifespan).

Given the moderate size of most individual cohorts, collaborative studies are required to obtain estimates of long-term risk in different subgroups. The Cardiovascular Lifetime Risk Pooling Project is an impressive initiative that draws upon internal and public-use data from 20 U.S.-based epidemiological cohorts to generate such estimates. The study by

*Editorials published in *JACC: Heart Failure* reflect the views of the authors and do not necessarily represent the views of *JACC: Heart Failure* or the American College of Cardiology.

From the Division of Cardiovascular Medicine and the Vanderbilt Translational and Clinical Cardiovascular Research Center, Vanderbilt University Medical Center, Nashville, Tennessee. Dr. Wang has reported that he has no relationships relevant to the contents of this paper to disclose.

Ahmad et al. (4) in this issue of *JACC: Heart Failure* leverages this unique resource. The investigators examined 4 National Institutes of Health–supported cohorts with available data for incident heart failure. Two of the cohorts were multiethnic. The analysis contained 19,429 individuals at age 45 years and 23,915 individuals at age 55 years, permitting relatively robust estimates of the effect of baseline risk factor status on cumulative risk.

SEE PAGE 911

The investigators estimated that 45-year-old individuals without hypertension, obesity, or diabetes had 73% (in men) to 85% (in women) lower risks of developing heart failure over their lifetimes, compared with individuals with all 3 risk factors. The reduction in risk was even greater for black participants, who had an 88% lower risk of heart failure when risk factors were absent. These estimates underscore the stark differences in heart failure risk in those with and without cardiometabolic disorders. Such differences are not easy to appreciate in analyses with short time horizons, highlighting 1 of the advantages of thinking about cumulative risk over longer periods.

The investigators used the same methods to calculate heart failure–free survival, or years lived free from heart failure, a useful measure of "healthy longevity" (5). At age 45 years, individuals without risk factors lived 10.6 years (men) to 14.9 years (women) longer free of heart failure than individuals with all 3 risk factors. This 10- to 15-year disease-free interval is significant, considering that the average remaining lifespan for 45-year-old individuals in the study sample ranged from 25 to 35 years.

The concept of heart failure–free survival adds another dimension to lifetime risk estimates by taking into account the timing of disease onset. Because healthy individuals live longer overall, they have more years exposed to the possibility of getting heart failure, which may increase lifetime risk estimates. However, when heart failure does occur in such individuals, it typically does so at a later age. The ability to enjoy more years free of disease is more important for many individuals than simply living longer.

Interestingly, although healthy individuals got heart failure at later ages, they experienced *shorter* survival with the disease compared with individuals at higher baseline risk. The explanation is not entirely clear. A diagnosis of heart failure at a later age could be associated with worse outcomes due to the presence of other comorbidities, less physiological tolerance, and/or diagnosis of more advanced disease. It is important to note that the shorter survival after heart failure did not offset the improved overall survival conferred by the avoidance of metabolic risk factors.

One important consequence of longer overall survival but shorter disease-related survival is the "compression of morbidity" at the end of life, a concept first proposed by Fries (6) in 1980. Indeed, in the data of Ahmad et al. (4), individuals without metabolic risk factors spent a much lower proportion of their lifespan in heart failure. For instance, women at age 45 years with 3 risk factors spent an average of 10.2% of their remaining lifespan in heart failure, compared with only 2.1% for women with no risk factors. The shorter disease-related survival was particularly prominent for individuals without obesity or diabetes. Lean individuals who developed heart failure had shorter survival than obese individuals (1.50 years vs. 0.98 year for men and 2.06 years vs. 0.90 year for women). This is reminiscent of the "obesity paradox" in heart failure that has been well documented in the published data (7). The finding raises the possibility that, for some individuals, the "compression of morbidity" phenomenon contributes to the obesity paradox.

Several limitations of the present study should be noted. As the authors acknowledge, the methods for ascertaining heart failure varied. The Chicago Heart Association study relied on hospital discharge diagnoses from Medicare data, whereas the other studies obtained data from several sources and performed central committee-adjudication. Second, the authors did not distinguish between heart failure with reduced ejection fraction and heart failure with preserved ejection fraction. Although these conditions share certain clinical features, the underlying pathophysiology differs. Although obesity, hypertension, and diabetes are risk factors for both types of heart failure, the strengths of association and the underlying biological mechanisms differ. Last, information on longitudinal changes in risk factor status was not available. Given the high incidence of metabolic traits in adults, it is likely that many individuals developed 1 or more risk factors after age 45 or 55 years.

The present findings reinforce the contribution of obesity, hypertension, and diabetes to heart failure risk, and highlight new ways of thinking about this risk. Such a perspective is particularly valuable when one considers another result embedded in the data: for almost all of the clinical subgroups, the interval between heart failure diagnosis and death was very

short (≤2 years). Although advancing the care of patients with established heart failure remains an important objective, figuring out how to maximize the number of years free of disease is just as critical. As the study by Ahmad et al. (4) nicely emphasizes, delaying the onset of heart failure should involve not only arresting disease pathogenesis in its early stages (primary prevention), but also preventing the development of key risk factors in the first place (primordial prevention).

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Thomas Wang, Division of Cardiovascular Medicine, Vanderbilt University Medical Center, 2220 Pierce Avenue, PRB 383, Nashville, Tennessee 37232. E-mail: thomas.j.wang@vanderbilt.edu.

REFERENCES

1. Hunt SA, Baker DW, Chin MH, et al. ACC/AHA guidelines for the evaluation and management of chronic heart failure in the adult: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1995 Guidelines for the Evaluation and Management of Heart Failure). J Am Coll Cardiol 2001;38:2101–13.

2. Agarwal SK, Chambless LE, Ballantyne CM, et al. Prediction of incident heart failure in general practice: the Atherosclerosis Risk In Communities (ARIC) study. Circ Heart Fail 2012;5:422–9.

3. Lloyd-Jones DM, Larson MG, Leip EP, et al. Lifetime risk for developing congestive heart failure: The Framingham Heart Study. Circulation 2002;106:3068–72.

4. Ahmad FS, Ning H, Rich JD, Yancy CW, Lloyd-Jones DM, Wilkins JT. Hypertension, obesity, diabetes, and heart failure-free survival: the Cardiovascular Disease Lifetime Risk Pooling Project. J Am Coll Cardiol HF 2016;4:911–9.

5. Wilkins JT, Ning H, Berry J, Zhao L, Dyer AR, Lloyd-Jones DM. Lifetime risk and years lived free of total cardiovascular disease. JAMA 2012;308:1795–801.

6. Fries JF. Aging, natural death, and the compression of morbidity. N Engl J Med 1980;303:130–5.

7. Wang TJ. The obesity paradox in heart failure: weighing the evidence. J Am Coll Cardiol 2014;64:2750–2.

KEY WORDS epidemiology, heart failure, prevention