1 CHAPTER 1

Epidemiology of heart failure: progression to pandemic?

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Introduction

Congestive heart failure (CHF), traditionally considered an edematous disorder, was described hundreds of years ago. Hypertension and valvular heart disease were the most frequent co-morbidities [1]. Physicians could only attempt to control pulmonary and peripheral congestion with diuretic therapy. Heart failure was a progressive disease culminating in biventricular dysfunction, anasarca, and finally organ failure due to hypoperfusion. Symptomatic heart failure in the 21st century is most often characterized by effort intolerance (dyspnea) and fatigue. CHF is growing at epidemic proportions, particularly in the elderly, consuming significant health-care dollars and resulting in disability and premature death. Common illnesses, including coronary artery disease, hypertension, and diabetes mellitus, are the major etiologic risk factors. In the United States, heart failure incidence is twice as common in hypertensives and five times greater in persons who have had a myocardial infarction (http://www.nhlbi.nih.gov/health/public/heart/other/CHF.htm) [2]. The National Heart, Lung and Blood Institute (NHLBI) estimates that 75% of heart failure cases have antecedent hypertension. Major advances in the treatment of coronary artery disease and acute ischemic syndromes that have saved countless lives have resulted in a growing population of chronic patients with left ventricular dysfunction that may develop clinical heart failure. The NHLBI estimates that 22% of male and 46% of female myocardial infarction victims will develop heart failure within 6 years (Figure 1.1). Heart failure is the most common indication for hospitalization in the United States in patients over 65 years of age. It is estimated that about one-half of patients with heart failure are greater than or equal to 65 years old. Finally, it is now recognized that the syndrome of heart failure may also occur as a consequence of diastolic dysfunction. Recent reports have shown that 40–50% of patients hospitalized with heart failure have normal ejection fractions.

The mainstay of heart failure therapy today is "treatment" for established and symptomatic diseases. The public health impact of heart failure for our society will continue to grow until effective primary and secondary prevention strategies are adopted and employed. The recent heart failure guidelines now define patients at risk of heart failure (ACC Stage A) as a high priority for preemptive therapy. Patients with advanced heart failure, ACC Stage D (www.acc.org/guidelines/heart failure) represents almost 10% of the total heart failure population, have the highest short-term mortality and consume the greatest percentage of resources [3]. The cost of treating advanced symptomatic heart failure is a growing economic burden for industrialized nations. An analysis of six countries revealed that 1–2% of total health-care expenditures were for heart failure and about 70% of the total heart failure cost was consumed for hospital costs [4]. The rapidly increasing prevalence of heart failure clearly represents the most important public health problem in cardiovascular medicine [1,4,5].

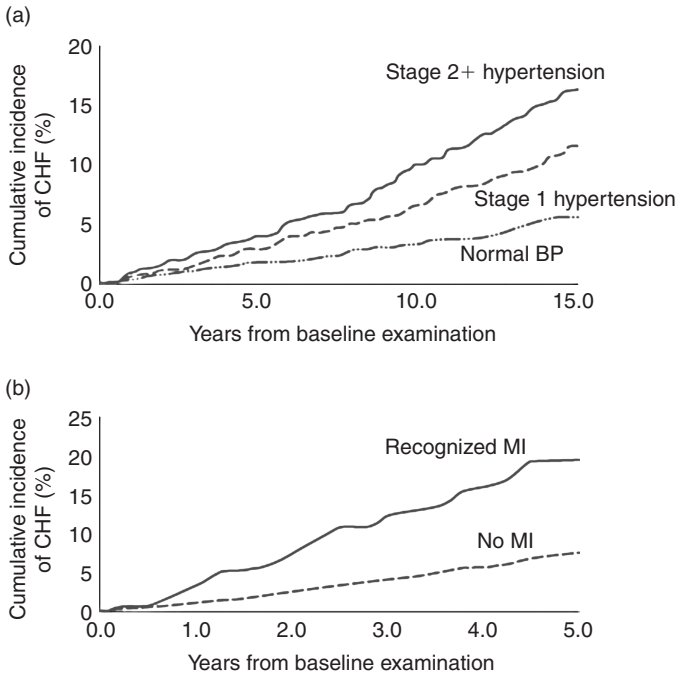

Figure 1.1 (a) Incidence of heart failure in men and women age 50–79 years by hypertension status. Stage 1 hypertension is defined as a systolic BP of 140–159 mmHg or diastolic BP of 90–99 mmHg in people not receiving antihypertensive medication; Stage 2 or greater is defined as systolic BP of 160 mmHg or greater, diastolic BP of 100 mmHg or greater, or current use of antihypertensive medication (adapted from [2]). *Source*: Framingham Heart Study, National Heart, Lung, and Blood Institute. (b) Incidence of heart failure by myocardial infarction status (adapted from [2]). *Source*: Cardiovascular Heart Study, National Heart, Lung, and Blood Institute.
CHF: congestive heart failure; BP: blood pressure; MI: myocardial infarction.

Epidemiology

An epidemic is described as affecting or tending to affect a disproportionately large number of individuals within a population, community, or region at the same time (excessively prevalent). Pandemic refers to a disease occurring over a wide geographic area and affecting an exceptionally high proportion of the population. Heart failure is a worldwide phenomenon that is indeed pandemic. Heart failure affects approximately 2–4 million Americans and over 15 million people worldwide [5]. The American Heart Association estimates there are 4.9 million Americans alive in 2002 with CHF (http://www.americanheart.org). Based on the 44-year follow-up of the NHLBI's Framingham Health Study, heart failure incidence approaches 10 per 1000 population after 65 years of age. Despite declining mortality rates for cardiovascular disease in the United States, hospitalizations for heart failure have increased substantially. Hospital discharges for CHF in the United States rose from 377,000 in 1979 to 999,000 in 2000, a 165% increase (http://www.americanheart.org).

The criteria for the diagnosis of the syndrome of CHF are not standardized, hence population estimates may underestimate the extent of heart failure. Measures used in population-based studies and cardiovascular drug research rely on a composite of signs, symptoms, and diagnostic findings. Attempts to validate the Framingham Clinical Heart Failure Score against a measure of ejection fraction showed that, in patients with a low left ventricular ejection fraction (LVEF <0.40), 20% met none of the criteria for CHF. A cohort of 2000 persons aged 25–74 years living in Scotland underwent a detailed assessment of cardiac status including echocardiography [4]. The overall prevalence of left ventricular systolic dysfunction (ejection fraction 30%) was 2.9%;

concurrent symptoms of heart failure were found in 1.5%, while the remaining 1.4% were asymptomatic. Prevalence was greater with age and in men, reaching 6.4% in men aged 65–74 years. Therefore, population estimates of heart failure have many pitfalls, and utilization of death rates and hospitalizations likely grossly underestimate the true magnitude of the heart failure pandemic. An analysis using administrative data sets to create a definition of heart failure using diagnosis codes (REACH Study) confirmed the heart failure epidemic in the United States [6]. The authors concluded that International Classification of Diseases, Clinical Modification (ICD-9-CM) codes and automated sources of data can be used within health systems to describe the epidemiology of heart failure. Newer modalities such as the brain natriuretic peptide assay may enable investigators to interrogate populations to determine the incidence of subclinical ventricular dysfunction, hence diagnosing and perhaps treating asymptomatic patients and ultimately improving long-term outcomes.

Incidence and prevalence

Incidence refers to the number of new cases observed in a year in a defined population. Prevalence refers to the number of cases observed at a specified point in time in a defined population. The crude incidence of heart failure (unadjusted for age) ranges from one to five cases per 1000 population per year, and increases sharply with advancing age to as high as 40 cases per 1000 population over 75 years in some studies [7]. A reflection of the incidence of heart failure in the US is made from the Framingham Study and the Framingham Offspring Study, representing a population of over 10,000 [8]. The incidence of heart failure raises with age in both men and women as shown in Figure 1.2. The incidence of CHF after adjustment for age is one-third lower in women than in men. Based on the increasing age of the US population and improved survival, it is estimated that the CHF prevalence will nearly double to 5.7 million cases by the year 2030 [9].

A recent analysis of the Framingham Heart Study cohort demonstrated over the past 50 years that the incidence of heart failure has declined among women, but not men; however, survival after the onset of heart failure has improved in both sexes [10].

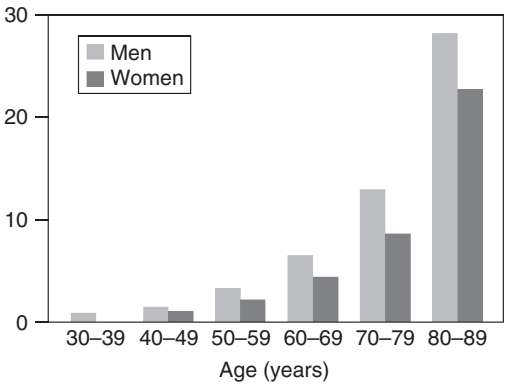

Figure 1.2 The annual incidence of congestive heart failure is shown by population age/decade in men and women among The Framingham Heart Study subjects (adapted from [8], with permission from the American College of Cardiology Foundation).

When established clinical criteria are used to define heart failure, the lifetime risk for heart failure is one in five for both men and women [11]. Both hypertension and antecedent myocardial infarction significantly impact the lifetime risk for heart failure between ages 40 and 80 years in both men and women. These findings highlight the importance of risk factor modification to reduce ischemic heart disease and the potential impact of antihypertensive therapy to reduce the development of overt clinical heart failure.

Mortality

Since 1968, heart failure as the primary cause of death has increased fourfold [8]. The most dismal prognosis for patients with severe symptoms (New York Heart Association Class IV) and coronary artery disease was a 43% and 18% survival rate at 1 and 3 years, respectively [12]. Symptomatic patients with dilated nonischemic cardiomyopathy who are with medical therapy have a better prognosis compared to patients with underlying coronary artery disease [12].

Survival in patients with heart failure has improved over the past 50 years. The 30-day, 1-year, and 5-year age-adjusted mortality among men declined from 12%, 30%, and 70% from 1950 through 1969 to 11%, 28%, and 59% in the period from 1990 through 1999. In women, the corresponding rates were 18%, 28%, and 57% for the period 1950 through 1969, and 10%, 24%, and 45% from 1990 through 1999 [10].

Overall there was an improvement in survival rate after the onset of heart failure of 12% per decade, a significant reduction in both men ($P = 0.01$) and women ($P = 0.02$). The explanation for this is purely speculative; however, the improved survival was temporally associated with the use of both angiotensin-converting enzyme inhibitors (ACEIs) and beta blockers. Another analysis examined the short- and long-term mortality of patients after initial hospitalizations for heart failure using a cohort of 38,702 consecutive patients from April 1994 through March 1997 in Ontario, Canada. The crude 30-day and 1-year mortality rates were 11.6% and 33.1%, respectively [13]. Complex interactions among age, sex, and co-morbidities impacted short- and long-term survival. In the oldest co-morbidity-laden subgroup, 30-day and 1-year mortality were 23.8% and 60.7%, respectively. A subgroup analysis from the Digitalis Investigation Group (DIG) study showed that, in ambulatory patients with CHF, estimated creatinine clearance predicts all-cause mortality independently of established prognostic variables [14]. In Cox regression analyses, independent predictors of mortality were estimated creatinine clearance, 6-min walk distance ⩽262 m, ejection fraction, recent hospitalization for worsening heart failure, and need for diuretic treatment. It is obvious that, as a population ages, heart failure becomes more prevalent and the mortality raises, especially in patients with compromised renal function and co-morbidities. It has been recognized that elderly persons have a substantial risk for death after a diagnosis of heart failure with normal left ventricular systolic function. A longitudinal population based in 5888 persons of at least 65 years of age revealed that 4.9% had CHF, and ejection fraction was normal in 63%, borderline decreased 15% or impaired in 22%, and determined by a core echocardiographic laboratory [15]; 45% of those with heart failure and 16% without heart failure died within 6–7 years [15]. A cross-sectional survey was performed in Olmsted County, Minnesota to determine the prevalence of diastolic and systolic dysfunction, and if diastolic dysfunction was predictive of all-cause mortality [16]. A cohort of 2042 randomly selected residents of Olmsted County aged 45 years or older were surveyed between June 1997 and September 2000. The prevalence of heart failure was 2.2% with 44% having an ejection fraction >50%. Among those with moderate or severe diastolic or systolic dysfunction, <50% had recognized heart failure. Both mild and moderate or severe diastolic dysfunction were predictive of all-cause mortality (hazard ratio for severe diastolic dysfunction: 10.17; $P < 0.001$).

Despite medical advances, heart failure remains a lethal illness. Heart failure in the elderly has the

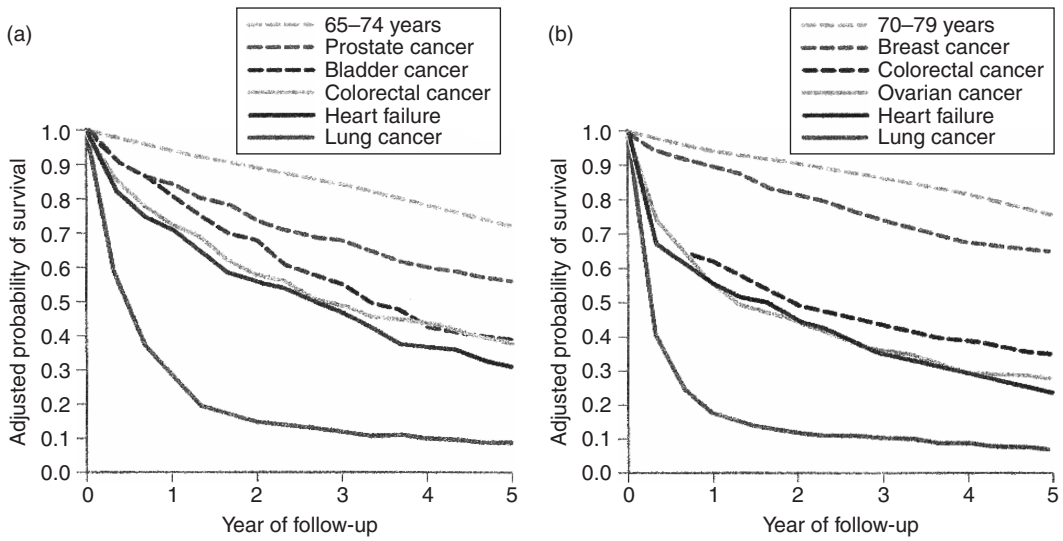

Figure 1.3 Five-year age-adjusted, survival curves following an incident admission for heart failure versus common types of cancer in age-matched patients. (a) Scottish men and (b) Scottish women (adapted from [17] with permission from the European Society of Cardiology). *Source*: Adapted with permission from [32].

highest mortality. Heart failure with preserved systolic function is a growing concern and carries an ominous prognosis. Mortality from heart failure is high, and most patients and families are uninformed and unprepared for the risk of death and need to make end-of-life decisions. A recent Scottish analysis showed that the 5-year age- and sex-adjusted mortality for heart failure is worse than common forms of cancer [17] as depicted in Figure 1.3.

Reasons for increasing prevalence

The prevalence of heart failure increases with age. Furthermore, advances in the pharmacologic and surgical management of coronary artery disease, arrhythmias, valvular heart disease, and hypertension have resulted in an ever-enlarging aging pool of patients who are likely to develop worsening systolic or diastolic function and pathologic ventricular remodeling leading to irreversible heart failure. Effective medical and surgical interventions have resulted in a reduction in mortality. However, the prevalence of heart failure is rising because predisposing conditions (coronary artery disease and diabetes mellitus) are palliated but not cured. The use of implantable cardiac defibrillators (ICDs) will reduce the incidence of sudden cardiac death but does not change the natural history of heart failure/pump dysfunction.

Economics of heart failure

Recent estimates of total annual health-care expenditures for heart failure in Americans have ranged from $10.3 to $37.8 billion [18,19]. The disparity of these figures demonstrates the lack of available accurate economic data, but the cost to American society per year is at least $10 billion and may be as high as $40 billion. The American Heart Association estimates $21.0 billion for direct and indirect costs of CHF in the United States in 2001 [20]. The breakdown includes: $14.3 billion hospitals/nursing homes, $1.5 billion physicians/professionals, $1.6 billion medications, $1.5 billion home health care, and $1.6 billion for lost productivity/mortality. Hence, 68% of the total expense is for inpatient care, very similar to the estimates consumed on inpatient care (73% and 62%) in the other two reports [18,19]. Considering the rates of hospitalization (including readmissions) for heart failure, it is not surprising that 1–2% of the total health-care expenditures is consumed for heart failure in a number of industrialized countries [4].

The frequency of hospitalizations for CHF accounts for much of the economic burden. A conservative estimate of cumulative care costs during hospitalization ranges from $6000 to $12,000 per admission. Approximately, 35% of the diagnosed heart failure population become hospitalized on an annual basis [5]. Multiple hospitalizations, particularly of elderly patients with multiple co-morbid conditions (50% have three or more), are especially common. Indeed, it has been found that the 3-month readmission rate after an index hospitalization for CHF was as high as 47% of discharges [21]. Many factors are related to the high rates of hospitalization for heart failure, including progression of underlying disease, inappropriate treatment plans, lack of patient compliance with prescribed regimens or diet or both, and use of detrimental drug therapy in certain heart failure settings. There are many patient- and physician-specific issues that contribute to "heart failure decompensation" which are potentially reversible [22]. An analysis in Germany of 179 patients admitted to the hospital with acute decompensation of pre-existing heart failure concluded that 54% of admissions could be regarded as preventable [23]. Noncompliance with drugs or diet was the leading cause of acute decompensation, present in 42%. Practitioners should utilize pharmacologic agents, proven to be effective in multicenter clinical trials, at target doses when managing chronic heart failure.

Interventions to reduce the high frequency and acuity of hospitalization, prolonged length of hospital stays and frequent emergency room visits are essential to attenuate costs. Outpatient care is less costly. Thus, the costs to intensify the outpatient delivery of care are trivial and are offset by the major reduction in total health-care costs if hospital days are reduced. One goal should be to improve the "effectiveness" of inpatient stays such that the readmission rate declines. Up to 25% of Medicare expenditures for hospitalizations are for readmissions [24]. Thus, in heart failure, improving the "quality of the hospitalization" may be most

cost-effective. Reduction in length of stay initiatives are important but should not compromise efforts to decrease the risk of hospital readmission.

Severity of heart failure and resource utilization

Patients with advanced heart failure represent about 10% of the total heart failure population, experience the highest short-term mortality and consume tremendous resources. With improved pharmacotherapy and management, an increasing pool of patients are expected to survive with severe left ventricular dysfunction who will ultimately die from refractory heart failure. Patients with refractory heart failure are the consumers of expensive technologic-sophisticated therapies, including cardiac transplantation, mechanical circulatory assist devices, automatic ICDs, biventricular pacemakers, outpatient intravenous inotropic therapy, and frequent high-acuity admissions (intensive care unit stays and hemodynamic monitoring). A European analysis has shown that it is more expensive to treat severe heart failure than mild heart failure, primarily due to the high rate and costs of hospitalization over a 6–12-month period prior to dying [25]. An admission for cardiac transplantation and postoperative care averages $303,400. Cost for implantation and care associated with a left ventricular assist device averages $175,000, and implantation of a cardiac defibrillator $50,000. Specialized regional heart failure centers will play a critical role in the delivery of cost-effective high-quality care to this group of patients. The proper use of sophisticated therapies, including ventricular assist devices, biventricular pacemakers/ICDs, outpatient infusion therapies, and high-risk surgical procedures (coronary artery bypass grafting (CABG), mitral valve repair, and Dor procedure) can improve outcomes and reduce costs.

Heart failure guidelines

Clinical practice guidelines have been developed by carefully evaluating the world's literature with emphasis on well-controlled randomized clinical trials of solid scientific validity and expert opinion from prominent clinicians. Consensus guideline documents for the evaluation and management of heart failure have been published [3,26]. Heart failure experts believe that the pharmacologic treatment of patients remains suboptimal and that both beta blockers and ACEI are underutilized. The guidelines emphasize the importance of appropriate pharmacologic therapy (target doses and ACEI use for asymptomatic left ventricular dysfunction) and nonpharmacologic treatment (counseling, education, and lifestyle modifications) in the management of heart failure. The economic and quality of care ramifications related to the adoption and improved adherence of heart failure guidelines are enormous. The advent of published guidelines has led to the development of disease care management algorithms that can be implemented within healthcare systems [27,28].

Educational programs can improve quality of life for the patient and reduce hospitalization. Multidisciplinary interventions designed to improve dietary compliance and reduce hospital admissions in heart failure patients have been found to be highly effective. A multidisciplinary heart failure disease management program is employed at the Cleveland Clinic Health System [27]. The cornerstone of a heart failure disease management program is to employ pharmacologic therapy in compliance with evidence-based heart failure guidelines and to develop a mechanism to monitor compliance both for patients and physicians. Elderly, socially deprived, recently hospitalized heart failure patients are at increased high risk for readmission and likely will derive the greatest benefit from disease management programs [29,30].

The future and the heart failure epidemic

Many heart failure patients are treated suboptimally with pharmacotherapy [26,31,32]. A US survey showed that cardiologists are more likely to prescribe ACEIs than are general practitioners and internists [38]. A survey comparing the practice patterns between cardiologists and heart failure specialists showed general conformity but concluded that a portion of heart failure patients may be better managed by heart failure specialists [33]. Few data are currently available to prove that heart failure specialists provide superior care for heart failure patients. Perhaps the greatest impact of heart failure specialists is to evaluate patients with cryptogenic heart

failure with the goal to find treatable components that have precipitated the heart failure syndrome (i.e. surgical coronary and/or valvular disease, dysynchrony responding to resynchronization therapy, ablation for tachycardia-induced cardiomyopathy). A recent study concluded that cardiology participation in outpatients with new-onset heart failure was associated with improved guideline adherence and a reduction in the composite endpoint of death plus cardiovascular hospitalization [34]. Specialized centers for heart failure can treat severe decompensated patients, often resulting in prolonged stabilization and improved quality of life in patients originally referred expecting cardiac transplantation was the only option [35].

Strategies to attack the epidemic of heart failure should include the following initiatives:

(a) reduction of inpatient costs;
(b) investment in outpatient care and development of chronic disease management programs;
(c) reduce admissions (more important than reduction in length of stay);
(d) focus efforts/resources on the "high-risk" patient (history of frequent readmissions);
(e) utilization of specialized "heart failure providers" (physicians, nurses, dietitians, rehabilitation specialists);
(f) extensive patient education.

Dedicated "specialized heart failure centers" should include the following mandates to help achieve these initiatives:

(a) detailed patient evaluation to "stage" disease and ensure appropriate diagnosis and treatment;
(b) close patient monitoring at intervals tailored to the individual patient's needs;
(c) immediate access to "heart failure team" staff and timely responses to patient needs;
(d) patient education concerning heart failure.

Specialized heart failure centers can provide expertise in the medical and surgical management of heart failure [36]. Surgical therapy for heart failure (high-risk standard cardiac surgical procedures, transplantation, mechanical circulatory assist devices, ventricular remodeling procedures (partial left ventriculectomy, Dor procedure, Acorn device®, Myosplint®), transmyocardial laser revascularization, etc.) has become an essential component and now extends far beyond transplantation [37]. Many high-risk patients will benefit from standard surgical procedures with a safety net of mechanical support and transplantation available at specialized heart failure centers.

Primary prevention is the solution to heart failure. However, secondary prevention strategies to alleviate morbidity and reduce mortality are the immediate focus to reduce the burden of this global pandemic.

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