Prevention or Procrastination for Heart Failure? Taking a Step Back to Move Forwards

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Brief Title:- Heart Failure: Why We Need a Universal Definition

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Perhaps everyone is destined to develop heart failure unless they die from something else first. Perhaps heart failure cannot be truly prevented unless the ageing process itself can be reversed or stopped. However, procrastination is a realistic and worthwhile objective. Heart failure is associated with a high mortality and substantial disability, which may be of even greater importance to both patients and society (1). Even if we cannot prevent heart failure, delaying its onset could improve the lives of billions of people for many years. Indeed, the principal reason for treating hypertension, hyperlipidaemia, diabetes mellitus, obesity, atrial fibrillation, myocardial infarction and perhaps chronic renal disease is to delay or prevent the development of the two most common cardiovascular reasons for chronic disability, heart failure and stroke. Treating risk factors has certainly postponed the average age at which heart failure and stroke occur, but age will eventually take its toll (2, 3). Nonetheless, health professionals and the population at large should not become despondent and should continue their efforts to procrastinate, even if prevention proves impossible. However, the resource requirements and economic consequences of procrastination are fundamentally different from those of prevention. Only if there is "compression" of morbidity and disability (ie:- fewer disability-adjusted life-years – DALYs), will procrastination reduce costs (4).

There are several complementary strategies, other than euthanasia (5), that might reduce DALYs due to heart failure. Increasing health education and awareness in the general population will reduce cardiovascular morbidity and consequently delay the onset of heart failure, although this strategy might be most effective for relatively affluent and well-educated people who have already reaped many such benefits. Indeed, the substantial age-gap between the most and least affluent people with heart failure is probably a good estimate of modifiable risk (3). Of note, the prevalence of heart failure is similar regardless of affluence; more affluent people just get heart failure at an older age. Another strategy is to identify and target individuals who are at high risk of developing heart failure in the next 5-10-years who

might benefit from further intervention beyond the routine management of problems such as hypertension and hyperlipidaemia. This requires the development of risk-prediction models. These must not only predict individuals at high risk but also a large proportion of those who develop heart failure. Identifying an individual-patient risk of 20% risk over 10 years that predicts only 10% of all cases might be an interesting academic exercise but will be of little help in designing an effective prevention strategy for a population. Alternatively, rather than prevent heart failure it might be better to manage it better once it develops, either by detecting and treating it before it causes substantial disability or by discovering more effective interventions after diagnosis. Ultimately, for a problem such as heart failure, all of the above may be required.

In this issue, Khan et al (6) describe the development of a 10-year model for incident heart failure. The study population comprised mainly (78%) white men and women drawn from six community-based cohorts of people from the United States of America and one from the Netherlands enrolled between 1985 and 2000; a time-frame that may no longer reflect contemporary clinical practice. Overall, 21,240 people (mean age ~52 years) were enrolled, of whom 2,552 (12%) developed heart failure in the following 10 years. Few people aged <60 years at baseline will have developed heart failure. Age was the strongest predictor of risk by a long-chalk for all groups except men of African-American origin, which may reflect the rather small sub-set (only 933 men in the derivation cohort of whom only 109 developed heart failure – about 10 cases per year and only 1,066 in the validation cohort of whom only 29 developed heart failure – about 3 cases per year) in which the predictive models were also weakest. A slightly higher proportion of men compared to women and “white” people rather than “black” people developed heart failure but after correction for age, the 10-year incidence was somewhat higher in black people. Other important predictors for some patients, grouped by sex and race, were not a surprise (7) and included hypertension (especially amongst

women), smoking (especially amongst white women) and obesity (especially white men and black women). The authors report a 10-year incidence of heart failure in people aged 50 years with a high-risk profile exceeding 20% for men and black women and 15% for white women, which looks impressive. However, the decile of patients at highest risk, which will mostly have included people aged >50 years, had an incidence of heart failure of only 12%. Accordingly, the very high-risk group in this report must apply to very, very few people indeed, which renders a strategy of targeted intervention based on this model unlikely to have much impact on the population-incidence of heart failure.

However, by far the most serious criticism of this analysis is the criteria for case-ascertainment which were heterogeneous, often subjective and lacked sensitivity. There is, as yet, no generally agreed definition of heart failure, which remains a diagnosis largely based on subjective criteria that are difficult to verify and validate in retrospect (3). A patient who is grossly overweight might say they are breathlessness climbing stairs and have fat ankles, but it is not clear that these problems are due to heart failure. Epidemiological work on heart failure is plagued by an obsession for specificity rather than sensitivity. Both specificity and sensitivity are important, and one should not always be preferred over the other. Clearly, applying a diagnosis of heart failure based on unverifiable subjective criteria is unhelpful but so is an obsession with specificity. Requiring overt evidence of clinical congestion before heart failure is diagnosed means that most patients are so sick at the point of first diagnosis that they need to be hospitalised (3, 8). Many people, who might otherwise fulfil all the criteria for heart failure, avoid provoking symptoms by adopting a sedentary life-style. On the other hand, amongst patients with cardiovascular disease, a substantial proportion have elevated plasma concentrations of natriuretic peptides, associated with an increasing prevalence of breathlessness and ankle swelling, high morbidity and a poor prognosis. What is this if not heart failure?

A Universal Definition of Myocardial Infarction based on troponin biomarkers is in its 4th iteration and increasingly accepted for epidemiological studies and clinical practice of acute coronary syndromes(9). Perhaps it is time to create a first Universal Definition of Heart Failure? The hallmark of a failing heart is congestion leading to a rise in plasma concentrations of natriuretic peptides and dilatation of the atria and great veins (10, 11). Some might argue that there are many reasons for increases in plasma concentrations of natriuretic peptides and atrial dilatation but, with rare exceptions, these are always associated with an increase in atrial and venous pressures, in other words congestion, and an adverse outcome. Congestion is a cardio-renal syndrome of water (with some salt) retention leading to increased secretion of natriuretic peptides, which may be viewed as a physiological attempt to control congestion. For some patients, congestion will be driven almost exclusively by cardiac dysfunction and for others almost exclusively by renal dysfunction, but most patients will sit somewhere on the spectrum between these extremes. When an increase in natriuretic peptides is associated with dilatation of the atria or great veins this may be considered 'congestive' heart failure (12). A Universal Definition of Heart Failure based on objective and verifiable measurements (biomarkers and imaging) that are deranged early in the course disease and dissociated from subjective criteria that such as symptoms and signs that only appear late will enable earlier intervention. We now need clinical trials to demonstrate that interventions based on the Universal Definition of Heart Failure in patients who have few or no symptoms improves outcomes. Such trials are underway(3).

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