Editorial

Heart Failure: A Problem of Our Age

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With the advent of World Heart Day on 29th September 2011, it is timely to consider emerging global and local challenges in heart disease. Chief among these is the increasing incidence and prevalence of heart failure throughout most nations on earth. In the developed world increasing recognition of cardiovascular risk factors with falling smoking rates and the widespread partial success in treating hypertension, together with improved secondary treatment of, and survival with, coronary heart disease has reduced early cardiovascular morbidity and mortality (although a rising tide of obesity and diabetes may yet reverse these trends). Many have therefore been spared from early severe cardiac injury or death but as years of partially treated hypertension, ischaemia and/or diabetes take their toll, patients incur heart failure at a later age. At age 40 years, life-time risk of heart failure is approximately 20% for both genders in western society[1] with annual rates of new heart failure cases of 15, 32 and 65 per 1000 within age groups 65 to 74, 75 to 84 and over 85 years, respectively. In the developing world, increasing economic power and affluence are reflected in high smoking rates and rising rates of obesity, diabetes and hypertension with associated increases in early and late heart failure. In Singapore, which has enjoyed an unprecedented rate of development and increasing affluence over the last 50 years, age-adjusted heart failure admission rates rose 40% over 7 years from 1991 to 1998.[2] Currently, heart failure is the most common cardiac cause for admission to Singapore Hospitals accounting for approximately 25% of such hospital stays.

Despite improvements in outcome from treatment with neurohormonal blockade (angiotensin converting enzyme inhibitors [ACEIs], angiotensin 2 type one receptor blockers [ARBs], beta adrenoceptor antagonists [beta blockers] and mineralocorticoid receptor antagonists [MRAs]) the outlook for chronic heart failure remains threatening with over 60% mortality at 5 years after initial diagnosis. The incidence and prevalence of heart failure is strongly age-related and therein is the challenge for the future. The population in many parts of the world, including Singapore, is ageing. Some two thirds of people who have lived beyond 65 years of age are alive today. The median age of onset of heart failure is in the mid seventies with some inter-regional and inter-ethnic variations.

The efficacy of current pharmacotherapies for heart failure is best proven in relatively young patients with impaired systolic function and relative freedom from comorbidities. Unfortunately, we lack strong evidence that current treatments improve outcomes in those aged over 75 years, the demographic stratum in which a least half of heart failure occurs. Somewhere between 35% and 50% of such patients have left ventricular ejection fraction (LVEF) in excess of 45% and significant comorbidities are the rule rather than the exception. The elderly are under-represented in the existing evidence base which informs our use of ACEI's, ARB's, beta blockers and MR antagonists in HF.[3] In the elderly the burden of comorbidities is greater, renal function reduced and drug intolerance is more likely as is heart failure with preserved ejection fraction (HF-PEF) for which we have no proven therapy for any age group.

A metanalysis of ACEI efficacy in HF showed no mortality benefit in those over 75 years.[4] The PEP-CHF (Perindopril in Elderly People with Chronic Heart Failure) trial in the elderly failed to demonstrate a mortality benefit of perindopril therapy.[5] Trials of ARBs showed no difference in efficacy for those aged above and below 65 years but this does not inform us about benefit or lack of it in those over 75 years.[6,7] Two ARB trials aimed at those with preserved ejection fraction (CHARM-Preserved and I-PRESERVE) showed no overall mortality benefit irrespective of age. Participants in trials of beta blockade in heart failure averaged 60 to 65 years and although subgroup analysis has never shown an interaction between age and outcome, this may simply reflect lack of sample size in the over 75 years subgroup.[8] Notably, a beta blocker trial ("SENIORS") specifically aimed at older (>70 years) patients failed to show significant reduction in all-cause mortality.[9]

In MR antagonist trials RALES reported no difference

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in effect between those aged above and below 67 years but data on those over 75 years was limited.[10] EPHESUS trial participants averaged 64 years of age and this trial tells us little about effects in those over 75 years.[11]

However, trial results are not entirely devoid of encouraging findings. PEP-CHF did report improved NHYA functional class and a reduction in hospital admissions at least within the first year of treatment. In the CHARM-preserved (Candesartan in Heart Failure Assessment of Reduction in Mortality and Morbidity) trial, the addition of an ARB to standard therapy in HF-PEF significantly reduced the rate of cardiovascular events and hospital admissions for acute heart failure even though all-cause mortality was not significantly lowered. Most encouraging of all to date, in a subgroup analysis from the EMPHASIS trial of mineralocorticoid receptor antagonism with eplerenone in heart failure with reduced ejection fraction and mild symptoms, mortality was reduced significantly and equally well in those aged over 75 years as in younger patients.[12] We await the outcome of trials currently in progress to assess the efficacy of mineralocorticoid receptor antagonism in HF-PEF.[13,14]

To counter the epidemic of heart failure with prevention or effective treatment of new and existing cases, we require awareness and participation from primary and secondary sectors of the health care system and from patients themselves. Healthy levels of exercise, prudent diet and avoidance/cessation of smoking must be combined with consistent primary sector screening and effective treatment of hypertension. Successful management of hypertension and other risk factors places ongoing demands upon patients who need to adhere to life style and drug regimes in the long term.

Research is required to fully characterise the pathophysiology of heart failure including the full spectrum from preserved to reduced ejection fraction. An example of such epidemiological and pathophysiological work is the current "SHOP" (Singapore Heart Failure Outcomes and Phenotypes) trial which has engaged the participation of senior heart failure physicians from all the major public hospitals in Singapore and will study a large cohort of heart failure patients. Findings from research of this kind promise to inform subsequent trials of new treatment options which, together with appropriately targeted mineralocorticoid receptor antagonism and other established treatments, will improve survival and quality of life in the elderly with heart failure.

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