Failing ageing hearts

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Introduction

Chronic heart failure is a major and increasing cause of morbidity and mortality. Although it is widely recognized that chronic heart failure affects the elderly, little attention has been given to its study specifically in this patient group. For example, patients with chronic heart failure in clinical trials frequently have an average age of around 60 years, in comparison to one of nearer 80 years in epidemiological studies. The importance of examining the specific characteristics of chronic heart failure in older individuals is underlined by predictions of an ‘epidemic’ of chronic heart failure that will largely be driven by the combination of an ageing population (by 2030 it is projected that there will be 70 million adults in the United States alone greater than 65 years[1]) and improved survival following acute myocardial infarction. There is already evidence that the age of patients with chronic heart failure is increasing over time[2].

Epidemiology

Prevalence

It is clear from the major population-based epidemiological studies that the prevalence of chronic heart failure (Fig. 1) and left ventricular systolic dysfunction (Fig. 2) rises steeply with age[3–5]. In the Framingham study the prevalence of chronic heart failure was 0·8% in patients aged 50–59 years increasing to 9·2% in those aged 80–90 years, i.e. the prevalence approximately doubles with each decade[5]. Although several of these studies relied on non-specific and insensitive clinical criteria for case identification, the increasing prevalence of chronic heart failure with age has been confirmed by studies of population prevalence assessing symptoms in conjunction with left ventricular systolic function, measured by transthoracic echocardiography[4,6,7]. Overall, within the population, there are markedly more elderly than young people with left ventricular systolic dysfunction and heart failure[8–14].

Incidence

That the incidence of chronic heart failure also rises with age is illustrated in Fig. 3. In the Framingham study the incidence of chronic heart failure rose from 0·2% in persons 45 to 54 years to 4·0% in men 85 to 94 years[5]. Few of the very elderly were, however, included in the Framingham cohort. A more striking age difference was found in a recent study that combined clinical diagnosis of heart failure with transthoracic echocardiography from West London[15]. Incidence increased from 0·02 cases per 1000 population per year in those aged 25–34 years to 11·6 in those aged over 85 years. Median age at presentation was 76 years. In 1991 in Olmsted County, Minnesota, approximately 50% of incident cases of chronic heart failure were in patients aged greater than 80 years with 88% aged greater than 65 years[16]. Although a study in Eastern Finland only studied inhabitants aged between 45 and 74 years once again the greatest incidence was seen in the oldest group studied[9].

Risk factors/aetiology

Patients who develop chronic heart failure before the age of 75 years do not appear to have different aetiologies of chronic heart failure than those who develop chronic heart failure after this age[12].

Coronary heart disease

Coronary heart disease is the most common reported cause of chronic heart failure in all age groups[17–19]. Many investigators also found that more elderly than young patients develop chronic heart failure following a myocardial infarction: 47% of those aged greater than 75 years vs 23% aged less than 75 years, 65·2% aged greater than 80 years vs 29·3% aged 50–59 years[20–23]. Age is, in fact, an independent predictor of the development of heart failure post myocardial infarction[23].

Hypertension

Hypertension remains a major cause of heart failure in all age groups[17–19]. Although the relative risk of
chronic heart failure imparted by hypertension in the Framingham cohort was lower in elderly patients than their younger counterparts, the absolute risk was higher\cite{24}.

In clinical trials, elderly patients with hypertension appear to be more likely to develop chronic heart failure than their younger counterparts. In the Systolic Hypertension for the Elderly Program (SHEP) older patients were more likely to suffer fatal or non-fatal hospitalized chronic heart failure (age 60–69 years 1·43%; 70–79 years 2·97%; greater than 80 years 5·08%). The relative risk for those aged 80 years or older compared to those aged 60–79 years was 2·38 (95% CI, 1·60–3·55)\cite{25}. The SYST-EUR study has reported similar findings in patients with isolated systolic hypertension\cite{26}. The benefits of treating hypertension in preventing the onset of chronic heart failure are considered later (see Prevention).

**Diabetes mellitus**

As with hypertension, diabetes in the Framingham study imparted less relative risk but greater absolute risk of developing chronic heart failure in elderly patients than their younger counterparts\cite{24}. In a study from Connecticut, diabetes was an independent risk factor for the development of chronic heart failure in an elderly cohort (age greater than 65 years) (risk ratio 2·9; 95% CI 2·0–4·3).

**Valvular heart disease**

That valvular heart disease remains an important cause of chronic heart failure in the elderly is evident in everyday clinical practice. The prevalence of chronic heart failure due to valvular disease (and the aetiologies of valvular disease) in different age groups has, however, not been reported\cite{19,27}.

**Systolic vs diastolic dysfunction**

In their 1995 review of diastolic heart failure Vasan et al. found that the prevalence of preserved vs impaired left ventricular systolic function differed according to age group\cite{28}. Out of 11 small studies, five found that increasing age was more likely to be associated with preserved left ventricular systolic function while six did not. In a recent report from Olmsted County of patients with a first diagnosis of chronic heart failure, only in those over 90 years was age an independent predictor of chronic heart failure with preserved left ventricular systolic function\cite{16}. While patients aged 60–69 years more often had impaired than preserved ventricular systolic function, those aged 70–89 years had similar rates of preserved and impaired ventricular function\cite{16}. A small study from the Framingham group found that patients with chronic heart failure and preserved left ventricular systolic function were slightly younger than those with chronic heart failure and impaired left ventricular systolic function (mean 72 ± 9 vs 74 ± 7 years)\cite{29}.

**Is there an interaction between the pathophysiological changes seen with ageing and those seen in chronic heart failure?**

Great advances have been made in our understanding of the pathophysiology of chronic heart failure and, in
parallel, in the physiology of ageing\textsuperscript{30,31}. What we do not know is how the pathophysiological changes seen in chronic heart failure interact with ageing i.e. how chronic heart failure in the elderly differs from chronic heart failure in their younger counterparts.

Cardiac changes do occur with age and these are discussed elsewhere\textsuperscript{32,33}. Whether or not ageing affects the cardiac changes seen in chronic heart failure has not been studied.

Neurohumoral changes are seen in the normal ageing population. Greater activation of the renin–angiotensin–aldosterone system is seen in healthy old subjects than in healthy young subjects\textsuperscript{34,35}. There are only limited data concerning ageing and neurohumoral activation in chronic heart failure. In a study of 40 patients with chronic heart failure aged over 75 years, plasma norepinephrine was higher and plasma atrial natriuretic peptide, renin and angiotensin II were lower in elderly than younger patients\textsuperscript{36}. This appears to suggest that the elderly with chronic heart failure have more activation of the sympathetic nervous system but less activation of the renin–angiotensin–aldosterone systems.

Ageing affects the kidney (e.g. decreased ability to excrete sodium\textsuperscript{37}) but whether an interaction between

\begin{figure}[h]
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\includegraphics[width=\textwidth]{figure2.png}
\caption{Prevalence of left ventricular systolic dysfunction.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure3.png}
\caption{Incidence of chronic heart failure.}
\end{figure}
chronic heart failure, ageing and the kidney occurs has not been investigated.

Likewise, both ageing[38] and chronic heart failure[39] are associated with changes in skeletal muscle but how skeletal muscle in the elderly chronic heart failure patients differs from their younger counterparts has not been studied. Weight loss seen in elderly heart failure patients may be due, at least partly, to malabsorption (particularly of dietary fats)[40].

Morbidity

Hospitalization

Patients admitted to hospital with chronic heart failure are old

Chronic heart failure is the most common cause of hospital admission in the elderly[41-43]. Moreover, the elderly make up the majority of patients admitted to hospital with heart failure[44,44,45]. In Scotland, 78% of chronic heart failure discharges are in persons aged 65 years and older[14]. In Birmingham, England, 53% of patients admitted with chronic heart failure were aged over 70 years[46]. In London, England, only 29 of 140 patients admitted with chronic heart failure were aged less than 65 years[47]. In the U.S.A. 75%–85% of hospitalizations with chronic heart failure are over 65 years[48–50] and 50% aged over 75 years[49]. In New Zealand, 75% of admissions are aged over 75 years and 62% of all bed days are occupied by patients over 75 years[51]. The average age of patients hospitalized for chronic heart failure is consistently above 70 and frequently over 80 in both Australia and the U.S.A.[52-54].

The increase in hospitalizations for chronic heart failure is mainly in the elderly

In the U.S.A. heart failure hospitalizations are rising in those aged over 65 years while remaining static in those aged 45–65 years[55]. The hospitalization rate (per 1000 population) for those aged greater than 85 years rose from 124–1 to 164–1 between 1985 and 1995, whereas it increased from only 4–2 to 4–9 in those aged 35–64 years[49]. In Spain the increase in hospitalizations between 1980–1993 was also confined to the elderly population[43]. In the Netherlands the increase in chronic heart failure hospitalizations was most marked in older age groups[56].

Once hospitalized, not surprisingly, more elderly than younger chronic heart failure sufferers are discharged to long-term care and this number is increasing[49].

It is reasonable to extrapolate from the foregoing that elderly chronic heart failure patients are responsible for a large percentage of the estimated annual inpatient expenditure on chronic heart failure of $8 billion in the United States[57] and £215 million in the U.K.[58].

Length of hospital stay

As well as being admitted more frequently, elderly patients with chronic heart failure spend longer in hospital during each admission. In Scotland chronic heart failure patients aged 45–64 years stayed an average of 11-5 days compared to 26-3 days for those over 75 years[14]. In New Zealand, patients over 75 years stayed an average 19 days compared to 11 days for those under 75 years[51].

Readmissions

All-cause readmission rates in elderly patients with chronic heart failure range from 25% to 47% within 3 months[59–62], and 33%–54% within 6 months[59–63]. In one study, 69% of patients were readmitted over a mean of 1-6 years of follow-up[53]. In another report, not surprisingly, 80% of elderly patients admitted with heart failure had been admitted before[18].

Indeed, age is the most powerful predictive factor for readmission in previously hospitalized patients with chronic heart failure[69]. Many chronic heart failure readmissions can be attributed to behavioural and social factors rather than to deteriorating cardiac function or an intercurrent cardiac event. Such factors include: non-adherence to medications and diet, inadequate discharge planning or follow-up, failed social support system, failure to seek medical support promptly when symptoms recurred[19,63,68,70,71]. In one study it was estimated that 62% of admissions of elderly chronic heart failure patients were precipitated by one of these factors[19]. As well as patient-related factors, suboptimal management can lead to readmission e.g. omission (or submaximal dosing) of ACE inhibitors or undesirable concomitant pharmacotherapy (e.g. co-prescription of a non-steroidal anti-inflammatory agent). It has been estimated that 50% of hospital admissions among older individuals with chronic heart failure are preventable[72]. That readmissions account for 41% of the total cost of hospitalization emphasizes the importance of this problem[68].

Quality of life

Although there are many studies documenting the profound effect of chronic heart failure on quality of life[73,74], there are sparse data reporting the effect of age on quality of life in chronic heart failure. Reports in solely elderly populations[75–77] confirm that chronic heart failure has a marked effect on quality of life. However, in one small study of women with chronic heart failure, age itself did not affect quality of life[78]. A report from the Framingham study found that chronic heart failure was more strongly related to disability in younger women than in other age and sex groups[79].

Older patients hospitalized with severe chronic heart failure are less likely to want to be resuscitated than their younger counterparts, although, interestingly, the majority of elderly patients do express a preference for resuscitation[80].

Co-morbidity

Few elderly chronic heart failure patients present with heart failure as an isolated medical problem[18,19,63]. One
study reported that three quarters of elderly patients with chronic heart failure have been found to have three or more secondary diagnoses[63]. Another hospital-based study of elderly patients with chronic heart failure found that the diagnosis of chronic heart failure was associated with an average of five unrelated diseases[10]. Common co-morbidities in the elderly are diabetes, chronic renal failure and chronic pulmonary disease. Diabetes is present in between 28% and 37%[81,82], chronic renal failure in around 20%[53] and chronic pulmonary disease in between 10% and 20%[53,81] of elderly patients hospitalized with chronic heart failure. In a cohort of elderly patients, 34% had severe renovascular disease as assessed by magnetic resonance angiography[83]. Those chronic heart failure patients with renovascular disease were older than those without. Not only can other conditions coexist, but they can also precipitate admission. Both cardiac (e.g. atrial fibrillation) and non-cardiac conditions (renal failure and anaemia) can lead to hospitalization with worsening chronic heart failure[19]. Up to 38% of elderly patients with heart failure have been found to have atrial fibrillation[18], while atrial fibrillation has been found to cause 16% of admissions with chronic heart failure[19].

Mortality

**In-hospital case fatality**

At least one study shows that in-hospital mortality rates are strongly age related[86].

**Long-term follow-up**

Many studies have found that age adversely affects long-term prognosis. Mortality in the Framingham study increased with advancing age[24,55]. In men, the increase was 27%/decade of age (95% CI 9% to 47%). In women, the mortality rate increased by 61%/decade of age (95% CI 37% to 90%)[24]. Few patients with chronic heart failure in the Framingham study over the age of 80 survived more than 5 years[84].

Elderly patients in the SOLVD registry had an increased total mortality and mortality related to heart failure at 1 year when compared to their younger counterparts[54].

Further evidence from the U.S.A. supports the effect of age on prognosis from chronic heart failure. In Minnesota, age was found to be an independent predictor for survival for chronic heart failure patients[2]. Gillum found that chronic heart failure mortality rates from chronic heart failure are strikingly age-dependent[85]. A study in the 1950’s reported that 80% of men aged more than 65 years had died within 3 years of follow-up[86]. In the 1980’s one third of patients aged more than 65 and hospitalized for the first time with chronic heart failure died within 1 year[87].

More than 90% of deaths in the U.S.A. from chronic heart failure occur among adults 65 years and older[88]. Very elderly patients with chronic heart failure have a very high mortality. Patients over the age of 80 hospitalized in the Philadelphia Geriatric Centre for chronic heart failure had a 1 year mortality of 63%[89].

In New Zealand, of approximately 850 heart failure deaths each year, two thirds occur in patients over 75 years of age[51]. In Scotland, mortality is strikingly higher in older age groups[90]. The mortality rate per 1000 population is 49-16 in patients aged greater than 85 years, 18-77 in those aged 75-84 years, 6-31 in those aged 65-74 years and only 0-36 in those aged less than 65 years[90].

Although overall mortality from chronic heart failure seems to be decreasing in Spain, this does not seem to be the case for patients aged over 80 years[43].

**Diagnosis/investigation**

**Diagnosis**

It is a widely accepted that a clinical diagnosis of heart failure is less reliable in elderly patients although there are only sparse data addressing this issue. In a recent study of the elderly with chronic heart failure the strongest predictors of the presence of chronic heart failure were a history of myocardial infarction or angina[7]. The most sensitive physical sign was basal crepitations (sensitivity 44%, 95% confidence interval 32% to 56%) and the most specific physical sign was a raised jugular venous pressure >5 cm (specificity 97%, 95% confidence interval 95% to 98%)[71]. In Glasgow, clinical assessment in an elderly population with a diagnosis of chronic heart failure proved sensitive (93%) but lacked specificity (32%)[91].

**Hospital referral and inpatient care**

Whether there is an age bias in referral to outpatient or inpatient hospital care has not been studied. Once hospitalized, elderly patients are less likely to receive care from a cardiologist than their younger counterparts[92,93].

**Patient investigation**

The elderly are less likely to have a transthoracic echocardiogram to assess left ventricular function following a diagnosis of chronic heart failure in the community[90]. In observational, hospital-based, studies of elderly patients with chronic heart failure, 39%–75% had undergone echocardiography or assessment of left ventricular function[16,85,96].

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Treatment

Aims of treatment

The aims of treatment of heart failure are usually stated as relieving symptoms, preventing hospital admission and improving survival. The importance of reducing mortality in the elderly has, however, been questioned. Nevertheless, recent data from the SUPPORT study show that the majority (69%) of elderly patients hospitalized with severe heart failure express a preference for active resuscitation, suggesting improved survival is still important to this age group [88,97,98].

Diuretics

Both age and heart failure affect the pharmacokinetic and pharmacodynamic responses to frusemide and bumetanide. Renal clearance of frusemide is reduced in the elderly [89,100]. Absorption of frusemide and bumetanide is delayed in chronic heart failure [101,102]. Less is known of the effect of ageing and heart failure on thiazide therapy and on potassium sparing diuretics.

Adverse effects of diuretics

The elderly have a reduced dietary intake of potassium, decreased body stores and less effective renal conservation of potassium [103,104]. Chronic heart failure is associated with reduced total body potassium [105]. Elderly patients with chronic heart failure are therefore particularly prone to hypokalaemia [106].

Clinical trials of other drugs for chronic heart failure

There is a striking paucity of elderly patients in clinical trials of heart failure (Table 1). Whether or not this is due to an unwillingness of investigators to recruit and follow-up these patients, or to other factors, is unclear. The design of many studies, with exclusion criteria related to age and co-morbidity, and the setting of an upper limit for left ventricular ejection fraction, undoubtedly mitigates against inclusion of the elderly. Similarly, the common requirement in trials to perform an exercise test prior to randomization frequently prevents the inclusion of frail, infirm and elderly patients. A consequence of the exclusion of elderly patients from trials of chronic heart failure treatments is a low percentage of women. Table 2 illustrates that trials that include greater numbers of elderly patients also have greater numbers of females.

Trials with angiotensin converting enzyme (ACE) inhibitors in heart failure

ACE inhibitors are widely used in the management of heart failure in both men and women. The large multicentre trials that have reported mortality and morbidity benefit have, however, contained only a small proportion of elderly subjects. The average age of patients in CONSENSUS I was 70 years and enalapril significantly reduced mortality and the number of days patients spent in hospital. NYHA class was also significantly reduced mortality and the number of days patients spent in hospital. Nevertheless, recent data from the SUPPORT study have shown that the majority (69%) of elderly patients hospitalized with severe heart failure express a preference for active resuscitation, suggesting improved survival is still important to this age group [88,97,98].

In a meta-analysis of the ACE inhibitor trials, the survival benefit with active therapy was greater in those less than 60 (OR 0.72, 95% CI 0.59–0.89) than in those greater than 60 years of age (OR 0.94, 95% CI 0.78–1.13) [110]. By contrast, active therapy had a comparable effect on the combined end-point of total mortality and hospitalizations in those aged less than 60 years (OR 0.71, 95% CI 0.59–0.86) and those aged greater than 60 years (0.79, 95% CI 0.66–0.95).

Table 1 Mean age and proportion of elderly patients in large heart failure trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Mean age</th>
<th>% &gt;70 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>V-HeFT I [123]</td>
<td>58</td>
<td>—</td>
</tr>
<tr>
<td>V-HeFT II [122]</td>
<td>61</td>
<td>—</td>
</tr>
<tr>
<td>CONSENSUS II [108]</td>
<td>71</td>
<td>50*</td>
</tr>
<tr>
<td>SOLVD-T [109]</td>
<td>61</td>
<td>15</td>
</tr>
<tr>
<td>ELITE [106]</td>
<td>73</td>
<td>70</td>
</tr>
<tr>
<td>ELITE-III [161]</td>
<td>71</td>
<td>NA</td>
</tr>
<tr>
<td>PROVED [112]</td>
<td>64</td>
<td>—</td>
</tr>
<tr>
<td>RADIANCE [162]</td>
<td>60</td>
<td>—</td>
</tr>
<tr>
<td>DIG [114]</td>
<td>63</td>
<td>27</td>
</tr>
<tr>
<td>MDC [163]</td>
<td>49</td>
<td>—</td>
</tr>
<tr>
<td>CIBIS II [164]</td>
<td>59</td>
<td>—</td>
</tr>
<tr>
<td>US carvedilol trial [115]</td>
<td>58</td>
<td>—</td>
</tr>
<tr>
<td>A-NZ carvedilol trial [118]</td>
<td>67</td>
<td>—</td>
</tr>
<tr>
<td>MERIT-HF [117]</td>
<td>64</td>
<td>—</td>
</tr>
<tr>
<td>ATLAS [111,114a]</td>
<td>64</td>
<td>31</td>
</tr>
<tr>
<td>CIBIS II [165]</td>
<td>61</td>
<td>—</td>
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<tr>
<td>RALES [106]</td>
<td>61</td>
<td>NA</td>
</tr>
<tr>
<td>DIAMOND-CHEF [167]</td>
<td>70</td>
<td>NA</td>
</tr>
</tbody>
</table>

*Based on mean age of 70 years. NA=not available.

Table 2 Age–sex interactions in chronic heart failure

<table>
<thead>
<tr>
<th>Trial</th>
<th>&gt;70 years (%)</th>
<th>Female (%)</th>
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</thead>
<tbody>
<tr>
<td>ELITE-I [160]</td>
<td>70</td>
<td>33</td>
</tr>
<tr>
<td>CONSENSUS-II [108]</td>
<td>50</td>
<td>30</td>
</tr>
<tr>
<td>DIAMOND-CHEF [167]*</td>
<td>50</td>
<td>27</td>
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<tr>
<td>MERIT-HF [117]</td>
<td>32</td>
<td>23</td>
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<tr>
<td>DIG [114]</td>
<td>27</td>
<td>22</td>
</tr>
<tr>
<td>SOLVD-T [109]</td>
<td>15</td>
<td>20</td>
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</table>

*Based on mean age of 70 years.
Recently the ATLAS study reported a comparison of high dose (32.5–35 mg) vs low dose (2.5–5.0 mg) lisinopril in patients with chronic heart failure. The average age was 64 years. There was no significant difference between doses for the primary end-point of all-cause mortality, although the principal secondary composite end-point of all-cause death or all-cause hospitalization, was significantly reduced by high dose compared to low dose lisinopril. The relative risk reduction for this secondary end-point with high dose treatment was similar in those greater than 70 years and those less than 70 years old\textsuperscript{113}.

**Trials of digoxin**

Trials of digoxin in heart failure have not reported subgroup analyses by age\textsuperscript{112–114}.

**Trials of beta-blockers**

The US carvedilol group found that the statistically significant reduction in death was similar for those younger and older than 59 years (hazard ratios: 0.30 (0.11–0.80) vs 0.38 (0.19–0.77)\textsuperscript{119}). The reduction of cardiovascular hospitalization was also not dependent on age. The only other large trial of beta-blockers to report the effect of age on treatment was the MERIT-HF trial\textsuperscript{116–118}. Although slightly less benefit was seen in the upper age tertile, this was not significant and a beneficial treatment effect was still seen. The average age of patients in MERIT-HF was 64 years; 37% of patients were aged 40–60 years, 37% aged 61–70 years and 28% were greater than or equal to 71 years.

**Spiranolactone**

The RALES trial randomized NYHA Class III and IV patients with a median age of 67 years. Low dose spironolactone (average dose 26 mg), added to full conventional therapy (including an ACE inhibitor), decreased mortality, reduced hospital admissions and improved NYHA Class. The reduction in mortality was similar in patients greater than or equal to, or less than, 67 years\textsuperscript{119}.

**Angiotensin II receptor antagonists**

ELITE II randomized 3152 patients aged 60 years of age or older (85% greater than 65 years) to the same two treatment regimens\textsuperscript{120}. The average age of patients enrolled was 71.5 years. The hazard ratio for all-cause mortality with captopril vs losartan was 0.93 in those aged greater than 71 and 0.84 in those aged 71 years (i.e. there was a trend for better outcome with captopril in patients above and below the median age). There was no significant age treatment interaction. ELITE II confirmed that losartan was better tolerated than captopril. Several other large trials examining the relative merits of ACE inhibitors and angiotensin II receptor antagonists are still underway.

**Hydralazine plus isosorbide dinitrate**

The V-HeFT-I trial, showing a mortality benefit with the vasodilating combination of isosorbide dinitrate and hydralazine, recruited few elderly patients and did not report the effect of age on treatment effect\textsuperscript{121}. Likewise, V-HeFT-II has not reported an elderly subgroup analysis\textsuperscript{122}.

**Other issues related to pharmacological therapy in the elderly**

**Under-prescribing of ACE inhibitors in the elderly with heart failure and left ventricular systolic dysfunction**

ACE inhibitors are generally under-prescribed in chronic heart failure but this is particularly the case in the elderly\textsuperscript{123}. An early study found that 30% of chronic heart failure patients aged 65 or over were prescribed ACE inhibitors\textsuperscript{124}. More recently, 57% of patients discharged from an acute geriatric unit were on an ACE inhibitor\textsuperscript{97}. In the United States, one study showed that 25% of elderly patients with chronic heart failure (mean age 85) admitted to long-term care facilities in the United States were prescribed an ACE inhibitor\textsuperscript{125}. Prescription of ACE inhibitors for chronic heart failure in the Cardiovascular Health Study of patients greater than 65 years increased by 10% (26%–36%) between 1989 and 1990 and 1994 and 1995\textsuperscript{126}. Perhaps more disappointing than both the modest increase over time and rates of ACE prescription was the observation that the treatment of incident cases had actually slightly declined over this period. Only one study has found reasonable rates (86%) of prescribing although only 14% were receiving target doses\textsuperscript{96}.

A recent analysis of the use of ACE inhibitors post-myocardial infarction in patients over 65 years found that only 45% of those with echocardiographic ejection fractions less than 40% post infarct with no contraindications to therapy received ACE inhibitors\textsuperscript{127}.

A further study has found that the elderly are less likely to be prescribed target doses of ACE inhibitors (21.4% vs 66.8%, \textit{P}=0.0136)\textsuperscript{128}.

**Adverse effects with ACE inhibitors and age**

In the 40 month follow-up of the Studies of Left Ventricular Dysfunction, older patients taking enalapril were more likely to report adverse events than younger patients\textsuperscript{129}. In the age tertiles, less than 56.4, 56.4 to 65.1 and greater than 65.1, adverse events were reported in 18.6%, 21.2% and 26.2% of patients (\textit{P}<0.001). This increased risk with age was seen for symptoms attributed to hypotension, azotaemia, gastrointestinal symptoms, cough, hyperkalaemia and leukopaenia. A more recent report from the Studies of Left Ventricular Dysfunction found that older age was associated with an increased risk of developing worsening renal function. While this was true in both placebo and treatment
groups, deteriorating renal function was more marked in the group taking enalapril (enalapril–risk ratio 1.42 per 10 years [95% CI 1.32–1.52]; placebo–risk ratio 1.18 per 10 years [95% CI 1.12–1.25]). In CONSENSUS-I age was an independent determinant of deterioration in renal function (mean age 70) [130].

Encouragingly, a study of ACE initiation in 97 elderly patients (mean age 84) found that there was little in the way of symptomatic first dose hypotension [131].

Recently, the ATLAS investigators reported slightly, but not significantly, higher adverse event rates in older (≥70 years), compared to younger, patients in both the high and low dose lisinopril treatment groups [131a]. Remarkably, only 2.3% of those aged 70 years or over withdrew from high dose therapy because of an adverse event (compared to 1.5% of those aged <70 years). The equivalent withdrawal rates in the low dose group were 0.8% and 1.2% [131a].

**Adherence to prescribed therapy**

Non-compliance with prescribed medication is suspected to be an important cause of treatment failures in chronic heart failure [70,71,132,133]. Compliance in the elderly with chronic heart failure has been assessed by monitoring prescriptions of newly prescribed digoxin in a population of elderly (aged 65 to 99 [mean age 77]) chronic heart failure patients. On average patients were without digoxin or an alternative for 111 days out of 365, while only 10% had sufficient medication for the entire year’s follow-up [134]. Patients greater than 80 years had better compliance. Naylor found that compliance was improved following education and follow-up in the over 70’s [135]. Stewart et al. have found that a nurse-led home-based intervention both reduces the number of unplanned readmissions caused by poor non-compliance and improves medication-related knowledge in elderly patients [141].

**Polypharmacy/drug interactions**

In the SOLVD registry, patients older than 70 years of age were on more medication than those younger than 50 years of age [137].

Non-steroidal antiinflammatory drugs (NSAIDs) are widely used in the elderly. The use of NSAIDs in patients aged over 55 years old taking diuretics is associated with a 2-fold increased risk of hospitalization for chronic heart failure [138].

**Non-pharmacological aspects of management**

**Nurse-led intervention to prevent readmission in the elderly with chronic heart failure**

In a landmark study Rich et al. addressed several of the potentially remediable factors that precipitate readmissions in the elderly. A randomized, nurse-led multidisciplinary study was undertaken in the over 70’s with chronic heart failure [139]. Intervention included patient and family education, dietary intervention, social service planning on discharge, medication review and close post discharge follow-up (which involved home visits). In the 90-day follow-up period the intervention group showed a significant reduction in readmissions for all causes (P=0.02), a reduction in admissions for chronic heart failure (P=0.04), improved chronic heart failure specific health-related quality of life, together with markedly reduced costs. On 1 year’s follow-up of this group (with no further intervention after the first 90 days) a strong trend towards a reduction in chronic heart failure readmissions persisted.

Other randomized trials have reported similar findings. Stewart randomized hospitalized chronic heart failure patients (mean age 75) to usual care or nurse-led home based intervention [140]. Intervention resulted in fewer readmissions, fewer days hospitalized and fewer multiple readmissions for chronic heart failure. A further study from the same group reported a reduction in the combined end-point of unplanned readmission plus out-of-hospital death within 6 months of hospital discharge [141]. Cline randomized 206 patients (aged 65–74) to intervention by specialist nurses or usual care. Time to readmission was 33% longer in the intervention group [142]. Most recently Jaarsma in a similar randomized nurse-based intervention programme (mean age 73) found a borderline statistical reduction in the number of patients readmitted within 9 months of follow-up [143].

The results of these five randomized studies are consistent with those of other non-randomized studies of similar strategies targeting older, hospitalized chronic heart failure patients. Kornowski reported that an intensive home-based intervention by physicians was associated with reduced hospitalization rates and better quality of life in such patients [140]. West found that an intensive physician supervised, nurse-mediated, home-based system for heart failure management is associated with improved functional status and exercise capacity and reduced hospitalization rates among both previously hospitalized and clinic-managed chronic heart failure patients [145].

**Exercise training**

While now established as a beneficial intervention in chronic heart failure, this has only been studied in elderly patients in two small studies [146,147]. Encouragingly similar results were achieved.

**Immunization**

Administering influenza A vaccine to patients over 64 years old with chronic heart failure during the 1991–1992 influenza epidemic resulted in a 37% reduction in the rate of hospitalizations for heart failure [149]. There was an associated reduction in costs of 43% for
admissions in 1990–1991. The percentage of patients with chronic heart failure appropriately vaccinated is unknown.

**Emotional support**

Fifty to 58% of elderly patients hospitalized with chronic heart failure are depressed\[18,190\]. Depression is more common in chronic heart failure than in other chronic illnesses\[190\]. Lack of emotional support in patients aged 65 or older who are hospitalized with chronic heart failure is associated with an increased risk of fatal and non-fatal cardiovascular events at 1 year (odds ratio, 3.2; 95% confidence interval, 1.4 to 7.8)\[151\].

**Heart transplantation**

The lack of availability of donor organs means that only those expected to gain maximal benefit are offered the opportunity of cardiac transplantation. One group has found that patients aged over 60 have a worse prognosis following transplantation\[152\] while another has found that survival rates were not significantly different in patients over 60 when compared to younger recipient\[153\].

**Prevention of chronic heart failure**

*Post myocardial infarction studies*

A recent meta-analysis of the results of the SAVE, AIRE, TRACE and SOLVD studies (of the use of ACE inhibitors in patients with post myocardial infarction left ventricular systolic dysfunction) has again emphasized the lack of elderly patients included in clinical trials\[154\]. The numbers of patients aged less than 55, 55–64, 65–75 and over 75 years of age were 3165, 4315, 4194 and 1066, respectively. The treatment effects of ACE inhibitors in those age quartiles less than 75 years of age were similar, while the benefit of treatment in those aged above 75 years of age was not as pronounced. The odds ratios of deaths in the above age groups were 0.76 (95%CI 0.62–0.93), 0.84 (0.73–0.97), 0.75 (0.66–0.86) and 0.95 (0.74–1.22), respectively. Corresponding odds ratios for the combined end-point of death/readmission for decompensated chronic heart failure/myocardial infarction were 0.77(0.66–0.91), 0.71(0.62–0.81), 0.67(0.59–0.76) and 0.89(0.69–1.13).

**Treatment of hypertension**

The importance of treating hypertension in the elderly as a means of preventing chronic heart failure was emphasized by a recent meta-analysis; treating hypertensive patients aged over 80 reduces the development of heart failure by 39%\[155\]. In the Swedish Trial of Old Patients (STOP) the risk of developing chronic heart failure was reduced by 51% (P<0.01) with active therapy\[156\]. STOP-2 showed that ACE inhibitors were better at reducing the risk of developing heart failure than calcium channel blockers\[157\].

**ACE inhibitors in patients with vascular disease or diabetes mellitus**

The HOPE study randomized patients over 55 years with vascular disease (coronary, peripheral or cerebrovascular) and high risk diabetics (hypertension, cigarette smoking, dyslipidaemia or microalbuminuria) to placebo or ramipril 10 mg per day. There were striking and significant reductions in death and cardiovascular morbidity. The risk of developing heart failure was reduced by 23%. The overall benefit of ramipril was at least as large in those aged greater than or equal to 65 as it was in patients aged less than 65 years\[158\].

**Summary**

Heart failure in the elderly is common and disabling but largely remains a neglected area of study. The elderly differ in many aspects from their younger counterparts. Interaction of the physiological processes of ageing with the pathophysiological processes of chronic heart failure may explain some of these differences. Elucidation of the basis of the age differences in the pathophysiology and treatment response in chronic heart failure is urgently required. This will require a greater awareness of and a greater effort to address the problem of heart failure in the elderly. It is still, sadly, the case that very few clinical trials are currently addressing the issue of chronic heart failure in the elderly in chronic heart failure\[159,160\].

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**References**


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