Heart failure in older patients

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Abstract

As the population ages, so the prevalence of chronic heart failure (CHF) will rise. The majority of CHF patients in the future will be elderly, yet most of our current evidence for the management of this serious condition arises from trials that have largely excluded older patients. As a consequence, older patients who may derive the greatest benefit from treatments known to reduce morbidity and mortality in CHF, are often denied such treatments. The effects on quality of life of both the syndrome of CHF and its treatment in older CHF patients must be borne in mind, as must issues of compliance, prevalence of comorbidity, and requirement for physical and emotional support. We review the current epidemiology of CHF, and focus on the applicability and use of contemporary non-pharmacological and pharmacological therapy to older patients with CHF. The potential use of devices and surgery in older CHF patients is also discussed.

Key words: heart failure, older patients, epidemiology, under-use of evidence-based treatment.

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Introduction

Chronic heart failure (CHF) is a clinical syndrome that can result from any cardiac disorder that impairs the ability of the heart to deliver adequate cardiac output during exercise or rest. Whether it is defined as the symptomatic syndrome, or widened to incorporate asymptomatic left ventricular systolic dysfunction (LVSD), CHF is a growing clinical problem. The population is ageing – in 2000 it was estimated that more than 25% of the European population was older than 65 years, with significant increases in life expectancy noted at all ages (from 14.9–18.9 at 65 years, to 6.9–9.1 at 80 years).[1] With improved diagnosis and treatment of hypertension, and primary and secondary preventive treatment of ischaemic heart disease (IHD) – the two main precursors of CHF – the inevitable consequence will be increased numbers of elderly 'survivors' at risk of developing CHF. Most of the major clinical trials in CHF have excluded the very elderly, and application of current evidence to this population is fraught with difficulty. It is important to focus current thinking on older patients, as they will constitute the majority of our CHF patients in the future.

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Table 1. Prevalence of chronic heart failure (CHF) based on population surveys

Authors	Number of population screened	Prevalence of CHF	Prevalence of CHF in older age group
Droller and Pemberton (1953)	476	30/1000	30–50/1,000 (> 62 years)
Epstein *et al.* (1965)	8,641	5/1,000	13/1,000 (> 65 years)
Garrison *et al.* (1966)	1,840	21/1,000	35/1,000 (65–74 years)
McKee *et al.* (1971)	5,209	3/1,000	23/1,000 (60–79 years)
Ladahl *et al.* (1984)	973	3/1,000 (< 75 years)	80-170/1,000 (67–75 years)
Schocken *et al.* (1992) - NHANES data	14,407	20/1,000	80/1,000 (> 65 years)
Mair *et al.* (1996)	17,405	15/1,000	80/1,000 (> 65 years)

Data from Cowie *et al. Eur Heart J* 1999;**20**:421-8

Epidemiology: prevalence and incidence

There is currently much more information on the prevalence, as opposed to the incidence of, CHF. Despite differences in research methods and in study cohorts analysed, there is a definite increment in prevalence of CHF with age. Population studies based on clinical criteria include the Framingham study in which, after 34 years of follow-up of 5,209 persons, the prevalence of CHF in the age groups 50–59, 60–69, 70–79 and > 80 years was 0.8%, 2.3%, 4.9% and 9.1% respectively;[2] table 1 summarises such studies.

A small number of studies have reported on population prevalence of LVSD (and its association with age). In the largest

of these, an echocardiography-based study of 3,960 randomly-selected inhabitants of the West Midlands in England, the prevalence of LVSD (defined as an ejection fraction of < 40%) was 1.8% (72 persons); half were asymptomatic.[3] The prevalence rose with age from 0.3% in the 45–54 year age group to 3.6% in those over 75 years; it was also higher in men than in women. These findings are consistent with earlier population-based studies in Scotland, the Netherlands and Finland.

A significant proportion of people who suffer symptoms of CHF are found to have 'preserved' left ventricular systolic function at echocardiography. A recent epidemiological review suggests an approximate 50% prevalence of preserved systolic function among those with CHF and, furthermore, confirms that the prevalence of CHF with both preserved and reduced systolic function increases with age.[4]

The incidence of CHF also increases with age. Framingham data reveal an incidence of CHF in 45–54-year-olds of 0.2% that rises to 4% in 85–94-year-olds.[2] In a study from Minnesota just under 50% of incident cases of CHF occurred in those over 80 years (with 88% in those over 65 years).[5] Similar trends in incidence are seen in surveys of hospital admissions in Asia and Africa.[6,7] The incidence is generally higher in men than in women. The mean age at diagnosis in the UK is 74 years, and most of the burden of CHF lies within the older age groups.

Why does CHF affect older patients?

The most common causes of CHF in the developed world in all age groups are coronary heart disease (CHD) and hypertension; indeed, more than 75% of elderly patients with CHF have coexisting CHD and/or hypertension.[1] Age is also an independent risk factor for the development of CHF post-myocardial infarction (MI).[8] Other causes, many of which are more common in developing countries, include arrhythmias, valvular heart disease, alcohol, infection, infiltrative diseases, endocrinopathies, inherited disorders and idiopathic dilated cardiomyopathy.

Why does CHF affect older people in particular? There are two main reasons. First, CHD and hypertension increase in incidence with age. Second, there are both structural and functional changes that occur within the heart and vascular tree with healthy ageing which may result in greater susceptibility to this condition. These include hypertrophy of myocytes with progressive loss of myocyte numbers, gradual accumulation of interstitial connective tissue within the myocardium (including amyloid) causing increased left ventricular wall thickness and stiffness independent of blood pressure;[9] fibrosis and calcification of valves; loss of cells in the sinus node and conducting system, which can lead to conduction abnormalities and impairment of myocardial contractility.[1] There is relative activation of the renin-angiotensin-aldosterone system (RAAS) and reduced beta-receptor responsiveness in healthy older individuals,[10] and CHF is, of course, associated with chronic activation of the renin-angiotensin-aldosterone system (RAAS) and sympathetic nervous system. All these factors can influence the manifestations and treatment of CHF in older people.

Table 2. New York Association (NYHA) classification for heart failure

NYHA class	Exercise tolerance	Symptoms
I	No limitation	No symptoms during usual activity
II	Mild limitation	Comfortable with rest or with mild exertion
III	Moderate limitation	Comfortable only at rest
IV	Severe limitation	Any physical activity brings on discomfort and symptoms occur at rest

Morbidity

Quality of life

CHF significantly reduces quality of life: the further a patient progresses through the New York Heart Association (NYHA) grading from I to IV, the further the reduction in quality of life (table 2). Although it seems likely that older, frailer CHF patients might have more impairment of quality of life than their younger, and otherwise fitter, counterparts, there are few studies that directly examine this. There is evidence, however, of a profound reduction in quality of life in older populations with CHF.[11]

One small study of women with CHF showed that age alone did not affect quality of life.[12] This may be because older patients have a lower expectation of quality of life in general and, hence, under-report reductions in quality of life. A more likely explanation, however, is that quality of life is more dependent on co-morbidity rather than age alone.

Co-morbidity

Older CHF patients are more likely to have concomitant medical conditions than younger patients. Indeed, the majority of elderly CHF patients have between three and five additional conditions.[13] Moreover, treatment of these other conditions, with non-steroidal anti-inflammatory drugs, for example, may also precipitate or exacerbate CHF. Renal dysfunction remains highly prevalent in the elderly, affecting up to 20%.[14] Anaemia in CHF has recently come under the spotlight, with several studies showing that anaemia is associated with poorer quality of life, exercise tolerance and higher mortality.[15] Cognitive dysfunction may also be more common in older CHF patients, resulting in difficulties in history taking, comprehension of self-management programmes, and compliance with the polypharmacy that is now recommended. Co-morbidity is also important because it increases hospitalisations, length of stay and mortality.[16]

Hospitalisation

CHF is the most common cause of hospital admissions in the elderly; the majority of in-patients with CHF are over 65 (varying from 53% to well over 75% in studies from Britain, the US, Australia and New Zealand).[17] In-patient stays are frequently of longer duration in older patients, who are also more likely to

require long-term care than younger CHF patients. Readmission rates are also higher in older CHF patients.[17]

Mortality

It has been suggested that mortality from CHF is comparable to that from cancer in the western world. A number of studies, including the Framingham group, have shown that CHF mortality increases with age.[2,18,19] Indeed, elderly patients within the SOLVD (Studies Of Left Ventricular Dysfunction) trial registry exhibited an increased total and one-year (specifically related to heart failure) mortality compared to younger patients.[18] In Scotland, mortality rate per 1,000 population is much higher in older age groups (49.16 in those > 85 years) than younger age groups (0.36 in those < 65 years) with CHF.[20] Diagnosis of CHF is associated with roughly 60% mortality rate within five years.[21] One study from the 1980s suggested that one-third of patients aged > 65 years and hospitalised for the first time with CHF died within one year, followed by an annual mortality approaching 10%.[22]

Diagnosis and investigation

Diagnosis can be difficult as many of the clinical features are not specific to CHF and may be caused by other conditions: dyspnoea, fatigue, ankle oedema and reduced exercise capacity are often of non-cardiac aetiology. Symptoms may not be reported as they may be perceived by patients to be inevitable consequences of ageing. As discussed earlier, the higher prevalence of cognitive decline may make it difficult to elicit an accurate history.

As in younger patients, a normal resting 12-lead ECG virtually excludes significant heart failure.[1] The most useful diagnostic test for CHF is two-dimensional echocardiography with Doppler colour flow mapping. Historically, in some series, older patients were much less likely to be scanned.[23] The importance of ensuring equitable access to echocardiography is obvious.

Elevated circulating levels of B-type natriuretic peptide (BNP) may also assist in the exclusion of CHF in older individuals but are less specific, particularly in older females, who have higher circulating BNP levels in health; sequential BNP measurements may be helpful in monitoring management of those with established CHF.

Management of CHF

Since CHF is a syndrome that affects not only physical health but also quality of life, the goals of therapy for each individual patient require careful consideration. Maintenance or improvement in quality of life may be more valuable than prolonging survival.

Non-pharmacological management

The European Society of Cardiology guidelines stress the importance of general lifestyle measures, which are likely to be of similar benefit in the elderly.[24] Although regular aerobic exercise should be encouraged as it may improve skeletal muscle function and exercise capacity in patients with CHF, it needs to be tailored for older patients with co-morbidity. Bed rest is discouraged in the elderly as the risks of complications such as thromboembolism, de-conditioning and pressure-area problems outweigh any benefits. Fluid and salt restriction are important components of CHF management programmes, but require careful instruction. Older people often reduce their oral intake when ill, increasing the risk of significant dehydration. Daily monitoring of weight and reporting of significant weight gain is standard care among CHF community services but may be difficult in some older patients. Enlisting the assistance of a carer can be a useful strategy. The effects of cardiac cachexia on a frequently undernourished individual may be profound, and nutritional supplementation may be required.

Pharmacological management

Loop and thiazide diuretics

CHF is a condition associated with episodes of decompensation interspersed with periods of relative stability. Loop diuretics are often needed although there are no randomised controlled trials assessing their effect on survival. Diuretics are the most effective means of relieving fluid overload, providing rapid symptomatic improvement. The dose of loop diuretic necessary to produce adequate diuresis is frequently higher in the elderly consequent to the age- and CHF-related reduction in glomerular filtration rate (GFR). In those resistant to increasing doses of loop diuretic, a thiazide such as metolazone (at doses of 2.5–5 mg daily) or bendrofluazide (at doses of 2.5–5 mg daily) may be introduced for brief periods as they have a synergistic effect with loop diuretics. Usually no more than three doses of metolazone 2.5 mg/day in a single week should be used. Close monitoring of serum urea and electrolytes in elderly patients on diuretics (particularly on combinations of diuretics) is mandatory, particularly as the clinical features of dehydration may be non-specific.

The effect of diuretics on lifestyle must also be considered: modifying timing of doses may reduce inconvenience. Diuretic therapy may precipitate or exacerbate urinary incontinence, and the minimum sufficient dose of diuretic should be used for each individual patient.

Angiotensin-converting enzyme inhibitors

Angiotensin-converting enzyme (ACE) inhibitors reduce the production of the potent vasoconstrictor angiotensin II and, by inhibiting the enzyme kininase II, block the breakdown of the powerful vasodilator bradykinin. They cause a variety of effects including reduced sympathetic tone, reduced systemic vascular resistance and attenuation of left ventricular remodelling, and have been shown to reduce morbidity and mortality in all grades of CHF in two major trials – CONSENSUS (Co-operative North Scandinavian Enalapril Survival Study) and the treatment arm of SOLVD (SOLVD-T).[25,26]

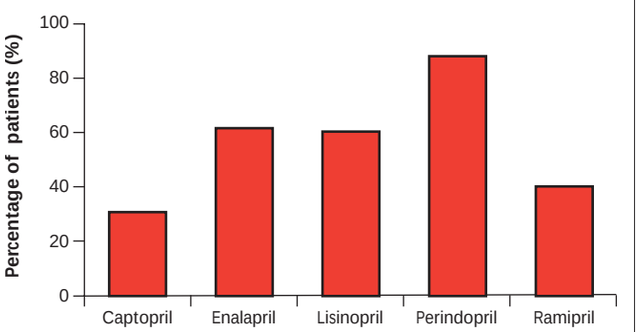
The CONSENSUS trial is of particular relevance in that it examined an older cohort than most of the other ACE inhibitor trials (mean age 71 years). Although enalapril was shown to reduce significantly mortality and duration of hospital admission in those under 65 years, the mortality results in those over 65 years did not reach statistical significance, there being a trend only towards lower mortality, although this is likely to be a consequence of reduced statistical power related to the small num-

Table 3. Directions for use of ACE inhibitors in the elderly

- Mortality benefit in elderly (> 80 years) patients is comparable to that in younger (≤ 60 years) patients[(a)]
- ACE inhibitors are often underprescribed in the elderly due to perceived cautions/relative contraindications[(b)]
- Start at low dose
- Gradual up-titration with close monitoring of renal function
- Target doses are the same as for younger patients

Data from: [(a)] Garg R, Yusuf S. *JAMA* 1995;**273**:1450-6; [(b)] Ahmed *et al. J Am Geriatr Soc* 2002;**50**:1659-66

Figure 1. Percentage of patients receiving ACE inhibitors at or above target CHF doses (data from IMPROVEMENT-HF survey[28])



Key: ACE = angiotensin-converting enzyme; CHF = chronic heart failure

bers in this group.[25] Although SOLVD-T showed that the addition of enalapril to conventional treatment significantly reduced mortality and hospitalisations for heart failure in those with CHF and reduced ejection fractions (predominantly in NYHA class II-III symptoms) in a study population of mean age 61 years, it did not report on the effect of age on outcome.[26]

The ATLAS (Assessment of Treatment with Lisinopril And Survival) trial showed that high doses compared to low doses of lisinopril reduced the risk of major clinical events in those with CHF (NYHA class II-IV symptoms) of mean age 64 years but somewhat surprisingly there was no difference between the two groups in all-cause mortality (the primary end point). The reduction in the combined risk of death and all-cause hospitalisation did reach significance in the higher dose group, and this was borne out in both the < 70 and the > 70 years age groups.[27] The oldest patients in this study tolerated the high-dose lisinopril rather poorly. The evidence base for the use of ACE inhibitors, particularly target doses in advanced age, is therefore rather limited. Standard current practice is to aim for doses used in the major trials; the more robust older patients will tolerate these well. However, for many frailer patients the maximum tolerated dose may fall far short of ideal.

In general, ACE inhibitors should be introduced at a low dose, then gradually up-titrated with close monitoring of renal function. Although there is a lack of population-based studies of renal artery stenosis, the prevalence of atherosclerotic renovascular disease rises with age,[28] and occult renovascular disease may result in unexpected deterioration in renal function. Despite a meta-analysis of 32 clinical trials demonstrating mortality benefit of ACE inhibitor therapy that was similar in older (> 80 years) and younger (≤ 60 years) patients (table 3), ACE inhibitors are still underprescribed in older patients. This was highlighted in the IMPROVEMENT-HF study (Improvement Programme Evaluation and Management of Heart Failure) a survey of 11,062 patients with CHF.[29] The percentage of patients receiving an ACE inhibitor at (or above) target CHF doses in this survey fell significantly short of 100% in most cases (figure 1), and was lower still in the older subgroup. ACE inhibitors are frequently underprescribed in older patients due to perceived rather than absolute contraindications; one interesting study of 295 hospitalised older patients with CHF showed significant survival benefit of ACE inhibitors in both those with and without perceived cautions/relative contraindications, such as a systolic blood pressure < 90 mmHg, creatinine > 200 µg/L, serum potassium > 5.5 mmol/L or severe aortic stenosis (table 3).

The finding that the average age of subjects in the major ACE inhibitor clinical trials is relatively low (71, 61 and 64 years for CONSENSUS, SOLVD and ATLAS respectively, for example) highlights that older patients are frequently excluded from such trials; clearly there is a need for large trials which specifically address these problems in older patients as they will make up the bulk of the CHF population in years to come. PEP-CHF (Perindopril for Elderly People with Chronic Heart Failure), examining perindopril in the very elderly, is one such study, due to report in 2006. At the time of writing, ACE inhibitors should certainly be considered as first-line therapy for older patients with CHF.

Beta blockers

Although their anti-ischaemic effects are well known, treatment with beta blockers has been shown to lead to regression of eccentric hypertrophy and reduction in left ventricular dimensions, suggesting attenuation of the ventricular remodelling process. There is now strong evidence of their benefit in CHF. CIBIS-II (Cardiac Insufficiency Bisoprolol Study II) and MERIT-HF (Metoprolol CR/XL Randomised Intervention Trial in Heart Failure) suggested survival benefit of bisoprolol and metoprolol CR/XL respectively in patients with NYHA class II-III CHF.[30,31] This was extended to include those with more severe NYHA class IV symptoms using carvedilol in the COPERNICUS (Carvedilol Prospective Randomised Cumulative Survival trial).[32] The average age of patients in these trials was 61, 64 and 58 years respectively; indeed CIBIS-II and MERIT-HF excluded persons over 80 years old and although slightly less benefit in MERIT-HF was seen in the upper age tertile, this was not significant and beneficial effect of treatment was seen. The very recent SENIORS (Study of the Effects of Nebivolol Intervention on Outcomes and

Rehospitalisation in Seniors) trial has confirmed the benefit of nebivolol.[33] In SENIORS, a trial of 2,128 subjects, the mean age was 76 years, and most patients were treated with ACE inhibitors. There was a significant 14% relative risk reduction in the primary end point of death or cardiovascular hospitalisation with the addition of nebivolol (mean daily maintenance dose 7.7 mg). These data are reassuring and suggest that age is not a contraindication to beta blocker therapy.

Beta blockers are less commonly prescribed in elderly CHF patients than their younger counterparts.[22] Moreover, it is common for beta blockers to be stopped in an elderly person with non-specific 'collapse' or 'blackout' despite the lack of definite evidence of bradyarrhythmia and, once stopped, these agents are not re-instituted.

That bad experiences with beta blocker initiation may lead to failure to re-challenge (particularly older) CHF patients underlines the importance of appropriate starting doses and up-titration regimes. Clinical stability is a prerequisite for beta blocker commencement in CHF. The starting dose, derived from the aforementioned clinical trials of beta blockers in CHF, is typically low. Assuming patients tolerate beta blocker initiation both symptomatically and haemodynamically, the dose should be slowly increased at intervals of no less than two weeks towards the target dose. Recommended starting, incremental and target doses are shown in table 4. A policy of 'start low, go slow' should be adopted in the use of beta blockers in CHF.

Not all CHF patients can tolerate beta blocker initiation, and many fail to reach target dose. Beta blockers should not be commenced if resting heart rate is less than 60 beats per minute and/or systolic blood pressure is < 90 mmHg; likewise, if a patient's heart rate and blood pressure fall to these levels while on a beta blocker, further up-titration is not indicated. The SENIORS trial protocol involved monitoring all patients for two hours after up-titration but this is neither economically nor temporally feasible in the community in general.[33]

Recently, COMET (Carvedilol Or Metoprolol European Trial) compared carvedilol with a once-daily metoprolol preparation in CHF patients. There was a 17% reduction in all cause mortality with carvedilol over metoprolol, but the preparation of metoprolol used was different to that in MERIT-HF.[34]

Bisoprolol, carvedilol and nebivolol are licensed for CHF use in the UK. Patients with CHF on other beta-blockers should be switched to these agents. For younger patients with heart failure, the ESC guideline of 2005 recommends that beta-blockers should be tried in all symptomatic patients with CHF.[24] Up to around 85% of CHF patients will tolerate these drugs. They should certainly be tried in older individuals.

Table 4. Starting doses, recommended increments and target doses of beta blockers in chronic heart failure patients

Beta blocker	Starting dose	Increments	Target dose
Metoprolol CR/XL	12.5–25 mg once daily	25 mg, 50 mg, 100 mg, 200 mg	200 mg once daily
Bisoprolol	1.25 mg once daily	2.5 mg, 3.75 mg, 5 mg, 7.5 mg, 10 mg	10 mg once daily
Carvedilol	3.125 mg twice daily	6.25 mg, 12.5 mg, 25 mg, 50 mg b.d.	25–50 mg b.d.
Nebivolol	1.25 mg once daily	2.5 mg, 5 mg, 7.5 mg, 10 mg	10 mg once daily

Angiotensin II type 1 receptor blockers

Angiotensin II type 1 receptor blockers (ARBs) are newer drugs that specifically block angiotensin II type 1 receptors, resulting in blockade of both ACE- and non-ACE-generated angiotensin II and, by avoiding the ACE inhibitor-induced accumulation of kinins, avoid the cough caused by ACE inhibitors.

There have been three major clinical trials using ARBs in CHF. The ELITE-II (Evaluation of Losartan In The Elderly II) study (one of the very few heart failure trials in the elderly) failed to confirm its hypothesis that losartan was superior to captopril in reducing mortality in elderly patients of a mean age of 71 years with CHF, the outcome in both groups was similar.[35] Rather than comparing ACE inhibitors with ARBs, Val-HeFT (Valsartan Heart Failure Trial) analysed whether adding valsartan to patients already on conventional CHF treatment (including ACE inhibitors in 93%, diuretic in 86% and beta blockers in 35%) improved outcome.[36] Although there was no reduction in mortality in patients with CHF and LVSD following the addition of valsartan, there was a significant reduction in combined mortality plus non-fatal morbid events – driven by a reduction in hospital readmissions – by 13%. Val-HeFT did, however, lead to observations that the benefit was greater in the 7% of patients not on ACE inhibitors.

The CHARM (Candesartan in Heart failure – Assessment of Reduction of Mortality and morbidity) programme examined the effect of candesartan (mean dose 24 mg daily) in 7,601 CHF patients of mean age 66 years (and of whom 23% were $\geq$ 75 years) enrolled in three component trials: those with LVSD intolerant of an ACE inhibitor (CHARM Alternative); those with LVSD already taking an ACE inhibitor (CHARM Added); and those with preserved left ventricular systolic function (CHARM Preserved). Overall, there was a trend towards reduction in all-cause mortality and a significantly lower incidence of cardiovascular death/CHF admissions with candesartan in both the Alternative and Added studies; a significant reduction in hospitalisation was seen in the Preserved group although there was no effect on all-cause or cardiovascular mortality. Candesartan is therefore the first ARB to improve survival rates in patients with CHF, independently of left ventricular function. The results are summarised in table 5.[37-39]

Aldosterone antagonists

RALES (Randomised Aldactone Evaluation Study) showed that low-dose spironolactone (mean 26 mg daily) added to an ACE inhibitor and standard diuretic therapy in patients with NYHA class III-IV CHF resulted in improved symptoms, decreased mortality, reduced hospitalisation rates and improvement in NYHA class.[40] This reduction

Table 5. The effect of candesartan on major end points in the three CHARM trials[37,39]

End point	CHARM Alternative (n = 2,028)	CHARM Added (n = 2,548)	CHARM Preserved (n = 3,025)
All-cause mortality	Trend to benefit	Trend to benefit	No effect
CV death/CHF hospitalisation	Significant benefit	Significant benefit	Trend to benefit
CV death	Significant benefit	Significant benefit	No effect
CHF hospitalisation	Significant benefit	Significant benefit	Significant benefit

Key: CV = cardiovascular; CHF = chronic heart failure

in mortality was similar in patients greater than, equal to or less than the mean age, which was 67 years. Elderly patients given spironolactone in addition to an ACE inhibitor require close monitoring of potassium. It is the authors' experience that hyperkalaemia is more common in general clinical practice than was reported in the RALES trial, presumably related to the stricter monitoring of serum electrolytes in the setting of a drug trial.

Digoxin

Digoxin has an important role in the symptomatic treatment of patients with CHF and atrial fibrillation, although there is no evidence that it improves survival in patients in sinus rhythm.[41] It may reduce the risk of hospital admission, but its toxicity must be considered, especially in the elderly who are more prone to its toxic effects. Its use in patients with CHF in sinus rhythm is declining in the UK, except as a last resort. A plasma level of about 1.0 mmol/L is sufficient.

Other vasodilators

The major vasodilator trials have excluded the elderly, e.g. V-HeFT-1, which showed a mortality benefit of hydralazine plus isosorbide dinitrate over the alpha-blocker prazosin in men with CHF.[42] More recently, the combination has been shown to reduce mortality by 40% in black American men with CHF, in a study where most of the patients were prescribed ACE inhibitors.[43] In general, there is no place for alpha blockers in the routine management of CHF.

Other issues in elderly CHF patients

While the evidence mounts for the use of various drugs in treating CHF, do elderly people take them? It has been shown that the elderly make their choices about their drugs on the basis of factors such as cost, side effects and perceived efficacy. Quality of life issues also arise – adjustment of dosing regimes may be necessary to allow attendance at special events; the elderly may become isolated through fear of a sudden episode of dyspnoea or an episode of incontinence from the effects of diuretic therapy. A lack of rapid improvement in symptoms may lead to cessation of a tablet, while the combination of polypharmacy and the increased prevalence of cognitive dysfunction in the elderly may promote under-compliance in this subgroup. The advent of multi-disciplinary management programmes has been shown to reduce CHF hospitalisation rates and total number of CHF hospitalisations in pooled small trial data.[44] Of interest, CHF patients in such trials tend to be substantially older than their counterparts in the large pharmacotherapeutic trials discussed earlier.

Emotional support is underemphasised – in a study of 292 elderly hospitalised CHF patients, the absence of emotional support pre-admission was found to be a strong independent predictor of the recurrence of fatal and non-fatal cardiovascular events in the year after admission.[45] Depression, often under-diagnosed in the elderly, was found to be an independent risk factor for heart failure arising in elderly women (not men) in a 14-year follow-up study of 2,501 elderly individuals in the US.[46]

Devices and surgery

There have been major recent developments in the device-led treatment of CHF. Implantable cardioverter-defibrillator (ICD) insertion into mild/moderate CHF patients (NYHA class II-III, left ventricular ejection fraction [LVEF] ≤ 35%), caused a significant mortality reduction in SCD-HeFT (Sudden Cardiac Death in Heart Failure Trial)[47] comparable to that observed in MADIT-II (Multicentre Automatic Defibrillator Implantation Trial),[48] where ICD insertion into patients with severe LVSD (LVEF 30%) at least one month post-MI reduced risk of death by 31%. Importantly, both ischaemic and non-ischaemic cardiomyopathies were included in SCD-HeFT, and there was no difference in treatment effect observed.

At least 25% of CHF patients have some degree of intraventricular conduction delay (IVCD) resulting in ventricular dyssynchrony. The concept of cardiac resynchronisation therapy (CRT) has come to the fore with the publication of COMPANION (Comparison of Medical Therapy, Pacing and Defibrillation in Chronic Heart Failure)[49] and CARE-HF (Cardiac Resynchronisation in Heart Failure Study).[50] The former proved that CRT and CRT with ICD reduced the combined risk of all-cause death and first hospitalisation in severe CHF patients (NYHA III-IV, LVEF < 35%) with evidence of IVCD; CRT with ICD significantly reduced mortality. CARE-HF confirmed that CRT prolongs survival in advanced CHF. Patients in NYHA III-IV with LVEF ≤ 35%, with prolonged QRS ± echocardiographic evidence of dyssynchrony survive longer with fewer hospitalisations for any cardiovascular event with CRT compared to best medical treatment. Improvements in symptoms and objective markers of left ventricular function were also seen.

The mean age of patients in MADIT-II and SCD-HeFT was 64 and 67 years, respectively, similar to the median ages in COMPANION (60 years) and CARE-HF (67 years). MADIT-II reported no significant effect of age on outcome in the ICD group; the remaining trials failed to report on significant differences in outcome between those < 65 years and those > 65 years. Clearly, as

Table 6. ESC guidelines for consideration of CRT and ICD in CHF[24]

- CRT can be considered if:
  - reduced LVEF and QRS width ≥ 120 ms
  - symptomatic despite optimal medical therapy to reduce symptoms, hospitalisations and mortality
- ICD insertion:
  - is reasonable in selected patients with LVEF < 30–35%, not within 40 days of MI, on optimal background medical therapy (including ACE inhibitor, ARB, beta blocker and aldosterone blocker, where appropriate) to reduce sudden death
  - is recommended to improve survival in patients who are survivors of cardiac arrest, or who have had sustained ventricular tachycardia (either poorly-tolerated or associated with left ventricular systolic dysfunction)
- ICD in combination with CRT can be considered in
  - patients who remain symptomatic with severe CHF (NYHA III-IV, with LVEF ≤ 35% and QRS ≥ 120ms) to improve morbidity and mortality

Key: ESC = European Society of Cardiology; CRT = cardiac resynchronisation therapy; ICD = implantable cardioverter-defibrillator; CHF = chronic heart failure; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NYHA = New York Heart Association

Key messages

- Chronic heart failure (CHF) is increasing in prevalence, and will continue to increase as the population ages
- Many of the landmark CHF trials excluded older patients, in whom evidence-based therapies are under-utilised. The prognosis remains poor in older patients with CHF
- Under-diagnosis (and thus under-treatment) of left ventricular dysfunction, particularly asymptomatic, is common in older patients
- CHF with preserved left ventricular systolic function is common in the elderly
- While trials assessing the benefits of the standard evidence-based treatment specifically targeting older patients are much needed, the use of beta blockers, ACE inhibitors and other contemporary CHF medication is indicated in older patients, and efforts should be made to ensure such patients are treated with the maximal tolerated doses of these drugs

the population ages, more elderly CHF patients will be considered for devices, although cost implications may restrict their use to younger patients who may derive more prolonged benefit. Current ESC guidelines[24] on eligibility for CRT/ICD are shown in table 6.

Interventional and surgical procedures (ranging from revascularisation to valve repair and replacement) are less likely to be undertaken in the elderly – mainly due to the presence of co-morbid conditions. Cardiac transplantation – the ultimate treatment – is possible but is limited by the lack of organs (although the number of referrals has dropped substantially with contemporary medical and device-led therapy). Quite rightly, the few hearts available for transplantation are given to those who will derive most benefit – younger patients.

CHF with preserved left ventricular systolic function

As mentioned earlier, up to 50% of patients with clinical CHF are found on echocardiography to have preserved left ventricular systolic function.[4] Such patients are found to have smaller cardiac dimensions on echocardiography than those with LVSD,[51,52] and are more commonly older and female.[53]

The aetiology of this condition is unclear. While there is the possibility that some may have experienced transient myocardial ischaemia leading to transient LVSD (and hence clinical features of CHF), MI and indeed any evidence of CHD has been shown to be much less common in CHF patients with preserved left ventricular systolic function compared to those with LVSD.[52,54] In contrast, systemic hypertension (especially when associated with LVH) is more common in CHF patients with preserved left ventricular systolic function; while atrial fibrillation is common, it has yet to be shown convincingly to be more common in this condition.[52,53] The influence of valvular disease on CHF with preserved left ventricular systolic function has yet to be defined. While "diastolic dysfunction" remains a controversial term, and echocardiographic measurements of this condition tend to correlate poorly with the incidence of CHF with preserved left ventricular systolic function,[55] there probably are a few patients who do possess abnormal myocardial relaxation during passive ventricular filling, leading to clinical features of CHF but preserved left ventricular systolic function on echocardiography.

Evidence from clinical trials is lacking. We have seen from the CHARM Preserved trial that candesartan did not reduce the risk of cardiovascular death in these patients but did reduce the rate of hospitalisations for CHF (table 5). More information will become available when the results of the I-PRESERVE (Irbesartan in Heart Failure with Preserved Systolic Function) and PEP-CHF trials are reported, examining the effects of irbesartan and perindopril, respectively, on CHF patients including, specifically, those with preserved left ventricular systolic function. At present it would seem reasonable to prescribe blood pressure-lowering therapy (particularly in those with left ventricular hypertrophy) such as candesartan, together with agents that promote myocardial relaxation and prolong diastolic filling, such as beta blockers and rate-limiting calcium channel blockers, but clearly more evidence on definite treatment options for this condition should become available over the next few years.

Conclusions

CHF is a major clinical problem and will continue to increase as the population ages. There are deficiencies in both the investigation and management of CHF in elderly patients, not least because they have generally been excluded from the large clini-

cal trials. Elderly patients with CHF are less likely to receive evidence-based treatment, less likely to be considered for interventional/surgical procedures, and consequently have a poorer prognosis. Moreover, the syndrome of CHF in those with preserved left ventricular systolic function – more common in older than younger CHF patients – is still a grey area with respect to treatment options (although studies are ongoing). Unrecognised (and therefore untreated) LVSD is common in the elderly.[56] In addition to the need for trials in the elderly of the major drugs commonly used in CHF treatment, the importance of the non-pharmacological, emotional, psychological and social management of CHF in the elderly should not be understated. These must be borne in mind in years to come.

Conflict of interest

None declared.

Editors' note

This is the eighth article in our clinical cardiology series. Previous articles include: the future of cardiology – heart disease in older patients (*Br J Cardiol* 2003;**10**:45-8); heart disease in older patients – myocardial infarction (*Br J Cardiol* 2003;**10**:123-7); thrombolytic therapy for acute ischaemic stroke (*Br J Cardiol* 2003;**10**:197-205); percutaneous coronary intervention in the elderly (*Br J Cardiol* 2003;**10**:293-6); atrial fibrillation in the elderly (*Br J Cardiol* 2003;**10**:373-8), bradycardia and tachycardia occurring in older people – an introduction (*Br J Cardiol* 2004;**11**:61-4); and bradycardia and tachycardia occurring in older people: investigations and management (*Br J Cardiol* 2004;**11**:224-8).

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