New horizons in management of heart failure in older patients.

Submitted version

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Abstract

Heart failure has a high prevalence in older populations, is a common and growing cause for hospital admission and carries a high risk of morbidity and mortality. Important co-morbidities in older patients with heart failure include atrial fibrillation, renal impairment, hypertension and anaemia. Diagnosing and managing heart failure in older patients is complicated due to atypical presentations, co-morbidities and a relative lack of evidence for commonly used treatments in younger patients. The growing epidemic of heart failure is also under-recognised and resourced in most health systems. Despite potential differences, we recommend that the basic approach to management should be the same in older and younger heart failure patients with ejection fraction <40%. These treatments need to be started at low doses and titrated slowly along with management of co-morbidities. Older patients with ejection fraction 40-49% can be treated in a similar manner to those with <40%, while the treatment of those with ejection fraction ≥50% is pragmatic in nature based on symptom control and management of co-morbidities although the evidence base for these recommendations is lacking. Overall management must be holistic and continuous based on the patient's social circumstances and ongoing needs. Finally, there is an urgent need for more research, evidence and resources directed towards older populations with heart failure to improve their care and quality of life.

Key messages

1. Heart failure in older patients should be treated in a similar manner to younger patients taking into account co-morbidities and tolerance to treatment.
2. Heart failure with ejection fraction 40-49% can be treated in a similar manner to <40%.
3. Management of older patient with heart failure is associated with better outcomes in specialist, multidisciplinary units with experienced staff.

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Heart failure is a global epidemic that is impacting older populations [1]. There are major challenges to managing heart failure in older patients including generalising results of trials that have been mostly done in younger patients, presence of co-morbidities and high rates of atrial fibrillation. There is no definition of old as this is dependent on the context. In Western Europe and North America average life expectancy is about 83 years and therefore heart failure patients who are ≥75 years could reasonably be called “older patients”. This review explores current aspects of heart failure management in older patients.

Heart failure is a clinical syndrome characterised by breathlessness, fatigue, elevated natriuretic peptides and impaired cardiac function [2]. In younger patients the main problem is impaired left ventricular systolic function (often due to prior myocardial infarction or dilated cardiomyopathy) while in older populations systolic function appears “preserved” while diastolic function is impaired due to long-standing hypertension, concentric left ventricular hypertrophy and, in many cases, associated atrial fibrillation. Older patients can also present with atypical symptoms for heart failure for example confusion which can make diagnosis difficult [3]. The current classification of heart failure depends on the measurement of ejection fraction using transthoracic echocardiography. Heart failure with reduced, mid-range or preserved function correlates to ejection fraction ranges <40%, 40-49% and ≥50% [4]. There are potential limitations to these categories in older patients with heart failure. First, atrial fibrillation is common which makes ejection fraction measurement unreliable, and second ejection fraction ≥50% is usually associated with diastolic dysfunction which does not have a widely accepted definition.

Older populations with heart failure are characterised by higher proportions of women, atrial fibrillation, co-morbidities and preserved ejection fraction compared to younger populations [5]. Women may have a different ventricular remodeling response to hypertension compared to men with concentric hypertrophy, normal systolic function and diastolic dysfunction, whereas men are more prone to dilatation of the myocardium and decrease in systolic function [5]. Several hypotheses have been proposed to explain impaired cardiac function in the presence of preserved

ejection fraction including inflammation, multi-organ involvement, adverse myocardial signaling, myocardial fibrosis and microvascular dysfunction and it is likely that some or all of these factors play a role in individual patients [6]. Co-morbidities including hypertension, coronary heart disease, atrial fibrillation, diabetes, renal impairment, chronic lung disease and anaemia are common in older patients with heart failure, adversely affect cardiac function, and are associated with worse outcomes [7]. Co-morbidities also complicate the management of heart failure through polypharmacy and potential drug interactions. Cognitive decline and dementia are growing in frequency and make diagnosis and management more difficult due to potential difficulties in communication, self-care, compliance and dependence on others for activities of daily living.

A working concept is that older patients with preserved systolic function and impaired diastolic function are vulnerable to heart failure episodes in response to stress in the form of infections, renal impairment, anaemia, exacerbations of chronic obstructive pulmonary disease, atrial fibrillation, and poorly controlled hypertension and diabetes [8]. The logical interpretation of this is that careful control of these exacerbating factors, associated co-morbidities, good nutrition and supportive social environment could help to reduce the burden of heart failure in older patients although there is insufficient evidence for this.

Several large well-conducted randomised trials in heart failure have shown good evidence of benefit for angiotensin converting enzyme inhibitors (ACE-I), angiotensin receptor blockers (ARB), beta-blockers, aldosterone antagonists, biventricular pacing in patients with bundle branch block and the combination of sacubitril, a neprolysin inhibitor, and valsartan [4]. Evidence for anaemia correction through iron infusion is growing [9]. Although these therapies form the cornerstone of heart failure treatment and are incorporated into guidelines [4, 10] the populations studies have mean ages around 63 and almost all trials enrolled patients with ejection fraction <40%. This means that generalising results from these trials to older populations becomes difficult not only because older patients have higher rates of preserved ejection fraction and atrial fibrillation, but there could be important differences in efficacy, dosing requirements and safety aspects in older patients with heart failure [11]. One of the few trials to enroll older heart failure patients aged ≥70 years, including a

proportion with ejection fraction >40%, was SENIORS which evaluated the beta-blocker nebivolol and showed improvements in the composite outcome of all-cause mortality and cardiovascular hospital admission irrespective of ejection fraction [12]. A pooled analysis of individual patient data from the large randomised trials of beta-blockers in heart failure has shown large mortality reductions in patients with sinus rhythm and reduced systolic function, whereas there was little evidence of benefit of these agents in patients with atrial fibrillation although heart rate reduction was similar to those in sinus rhythm [13]. An analysis from the same database stratified by age and gender in heart failure patients has shown that beta-blockers have clear evidence of benefit in younger and older patients (mean age 75 years) in sinus rhythm and ejection fraction <40% and overall efficacy is similar in men and women [14].

At present there is limited evidence of benefit for conventional therapeutic agents in heart failure with ejection fraction >40%. The TOPCAT trial randomised patients with heart failure, elevated natriuretic peptides and mean ejection fraction 57% to spironolactone versus placebo and did not show an overall favourable effect for spironolactone although a subgroup analysis based on geographical area suggested a beneficial effect in North and South America but not in Russia or Georgia [15]. The I-Preserve trial of irbesartan versus placebo in 4128 patients with heart failure and mean ejection fraction 59% was also unable to show any beneficial effect of irbesartan [16]. The Beta-Blockers in Heart Failure Collaborative Group have shown potential for benefit of beta-blockers versus placebo in mid-range heart failure (ejection fraction >40-50%), but not in ejection fraction >50% in a pooled analysis although the numbers randomised in both of these subgroups are small [14]. The PARAGON trial of sacubitril/valsartan is investigating the effects of this agent in heart failure patients with mean ejection fraction 58% and is likely to report in 2019 [17].

Given the issues of increasing prevalence of heart failure in older patients, diagnostic challenges, co-morbidities and lack of evidence base for populations with preserved ejection fraction, what are the basic principles for managing older patients with heart failure (Figure 1)? First, we believe that heart failure care in older patients should be based on best practice and guidelines, including access to advanced therapies and

devices, derived from younger populations and applied appropriately for older patients. Second, heart failure care in older patients should be carried out by appropriately experienced multidisciplinary teams consisting at a minimum of specialist nurses, physicians, dieticians and social workers across the primary and secondary care interface using a holistic approach such as that being established in a network of Spanish centres [18]. Third, heart failure is a chronic condition that requires decisions to be made at each stage of care including provision of palliative care to keep patients comfortable when the condition progresses to a terminal stage.

A standard approach to diagnosis is needed including careful history and examination, routine blood tests for haematology, renal and liver function, natriuretic peptides (for example N-terminal pro-brain natriuretic peptide) and electrocardiogram (Figure 1) [19]. Echocardiography in the presence of elevated natriuretic peptides is essential to determine the extent and type of cardiac dysfunction, ejection fraction and any concomitant valve disease. Key aspects of assessment include documentation of heart rate and rhythm, cardiac function, fluid balance, renal function, relevant co-morbidities, functional capacity, cognitive function and social circumstances. Risk assessment can be carried out using established models, although most of the prognostic information can probably be achieved through heart rate and systolic blood pressure [20, 21]. Based on these findings a care package can be set up for individual patients and ideally this can be discussed at a multidisciplinary team meeting.

Treatment of older patients with heart failure is mainly guided by fluid and haemodynamic status, ejection fraction, and renal function. Excess fluid needs to be managed by loop diuretics such as frusemide or bumetanide with careful monitoring of renal function. Patients with ejection fraction <40% can be treated in a conventional manner with initial low doses of beta-blockers and ACE-I/ARB titrating up as tolerated [22, 23]. Spironolactone or eplerenone can also be added in a phased manner in patients with reasonable blood pressure and renal function with review of potassium levels. The use of newer agents such as sacubitril/valsartan instead of ACE-I/ARB can be considered in patients with ejection fraction ≤35%. Patients with systolic dysfunction and bundle branch block can be considered for cardiac resynchronisation (biventricular pacing) if they do not respond to

conventional therapy in a manner consistent with younger patients if there is a reasonable expectation of a good quality of life. Heart failure management in older patients needs to be based on a holistic approach with careful appraisal and management of major co-morbidities, nutritional status, fluid balance, sodium intake and improvement in social circumstances where possible. Older heart failure patients with mid-range ejection fraction (40-49%) in general can be managed as for patients with ejection fraction <40%. The formal evidence base for this is lacking but reasonable extrapolation from existing data from large trials suggest that this is a reasonable approach [14]. The evidence base for improvements in outcomes is lacking in older heart failure patients with ejection fraction ≥50%, and the approach to management is more pragmatic based on fluid status and careful management of co-morbidities (Figure 1). Older heart failure patients can experience lack of continuity of care after discharge, and even if provided with information regarding community care, a significant proportion feel insecure returning home [24]. According to the National Institute for Health and Care Excellence patients with heart failure should receive a specialist assessment within 2 weeks of hospital discharge [10], however the proportion of older patients seen within the recommended 2 weeks of discharge is only about 2% [25]. A key part of managing heart failure in older patients is through specialised units for inpatient and outpatient management with easy access to experts in the field [18].

From this brief overview there are challenges in managing heart failure in older populations mainly related to the lack of evidence base of benefit for treatments in patients with preserved systolic function, presence of co-morbidities and lack of resources to manage the high rates of heart failure in this patient group. Much more research targeted specifically at older patients with heart failure is needed as well as recognition among health care providers that this is an area that needs substantial investment to improve quality of care and patient outcomes.

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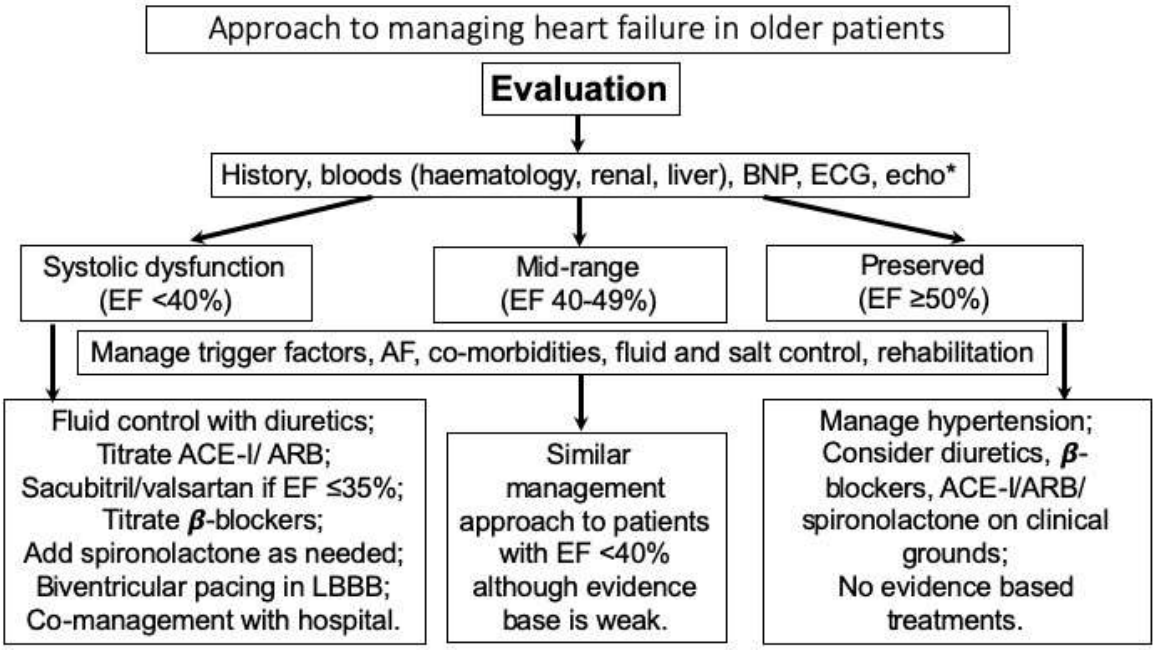
Figure 1.

A schematic approach to managing heart failure in older patients.



*Indicated in the setting of elevated natriuretic peptides; BNP = brain natriuretic peptide; ECG = electrocardiogram; echo = echocardiogram; EF = ejection fraction; AF = atrial fibrillation; ACE-I = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; LBBB = left bundle branch block.