FEATURE

Managing resistant congestive cardiac failure in the elderly

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Congestive cardiac failure (CCF) in the elderly is a common management problem encountered by general practitioners and physicians. Elderly patients are at increased risk of developing resistant CCF, which can cause considerable management dilemmas in both the hospital and the community. This article discusses the management of resistant CCF in the elderly, highlighting the importance of identifying the precipitating and driving factors of decompensated CCF, and proposing strategies essential for achieving the main goal of optimising patient quality of life.

Key points

- **Elderly patients are at an increased risk of developing resistant congestive cardiac failure (CCF) and often pose considerable management dilemmas in both the hospital and the community.**
- **Age-related changes in physiology, as well as pharmacokinetic and pharmacodynamic changes in the elderly, pose additional challenges with drug therapy.**
- **Identification and management of precipitating factors for decompensated CCF, as well as optimisation of nonpharmacological and pharmacological management strategies, remain the focus of care in elderly patients with resistant CCF.**
- **Multidisciplinary holistic care is essential for achieving the main goal of optimising quality of life.**

CARDIOLOGY TODAY 2014; 4(4): 14-20

Congestive cardiac failure (CCF) remains an Australian national health priority, with high associated healthcare costs estimated at over AU$1 billion per year.[1,2] Over 10% of people aged 75 years and above have CCF.[3] Although many patients with CCF respond to conventional management strategies (Box 1),[4] a substantial proportion have a poor clinical response. Elderly patients are at increased risk of developing resistant CCF and often pose considerable management dilemmas in both the hospital and the community, with clinical courses characterised by lengthy hospital stays and frequent rehospitalisations despite the best efforts of general practitioners and cardiologists.

Why does CCF pose additional challenges in the elderly?

Age-related pharmacokinetic and pharmacodynamic changes pose additional challenges in drug therapy for patients with resistant CCF. Ageing is associated with impaired gastrointestinal absorption,

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reduced lean body mass and total body water, increased body fat, and reduced liver metabolism and renal clearance.[5] As a result, elderly patients are at an increased risk of medication-related side effects. Features of CCF in the elderly differ from those in younger age groups, as outlined in the Table. Ageing is also associated with hypertension and impaired left ventricular compliance and diastolic function,[6] resulting in heart failure with preserved ejection fraction (HFpEF), commonly referred to as diastolic heart failure. HFpEF is notoriously difficult to treat, and this is a major contributing factor to poor heart failure control in the elderly. Other important considerations as to why CCF poses additional challenges in the elderly are described below.

- **Renal function.** Elderly patients are at an increased risk of acute kidney injury following initiation or dose escalation of common medications for heart failure. Renal function should be closely monitored during periods of dose titration and after the patient has been discharged to ensure that renal function is stable on the new regimen. Acute renal failure is also common in elderly patients with limited mobility who are taking diuretics, some of whom overzealously fluid restrict themselves to avoid frequent mobilisations to the toilet.
- **Medication noncompliance.** Resistant CCF in the elderly is commonly due to noncompliance with medications and fluid restriction. This should be considered in patients who are easily stabilised on oral diuretic therapy while in hospital, but have early decompensation on discharge. Contributing factors include cognitive impairment and polypharmacy. Urinary incontinence is often exacerbated by diuretic therapy, and may therefore be a chief driving factor for noncompliance with diuretic therapy.
- **Malnutrition.** Elderly patients with CCF often have a reduced appetite. Hypoalbuminaemia may often precipitate or worsen peripheral oedema. Severe malnutrition may also result in anaemia, which may often exacerbate CCF.
- **Risk of hypotension and falls.** Care should be taken to avoid syncope and falls in elderly patients, resulting from hypotension associated with the use of ACE inhibitors, aldosterone antagonists and beta blockers, which are commonly used in patients with heart failure and reduced ejection fraction (HFrEF).

How to investigate elderly patients with resistant CCF

Heart failure resistant to optimal medical therapy in the elderly requires careful review of results of previous investigations and consideration of additional testing where appropriate (see Box 2). The following conditions should be considered.

- **Atrial fibrillation.** New onset atrial fibrillation (AF) is a common precipitant of decompensated CCF. Chronic AF may also be a significant contributing cause of resistant CCF in the elderly.[7] Rate control remains the mainstay of treatment in elderly patients with CCF and AF, although rhythm control strategies may be offered to patients with paroxysmal AF and relatively normal-sized atria who have a reasonable chance of maintaining sinus rhythm.[4] Long-term anticoagulation is often required unless an easily reversible precipitating cause is found.
- **Myocardial ischaemia.** Myocardial ischaemia is an important precipitant of CCF in the elderly. Atypical presentations of myocardial ischaemia (e.g. exercise intolerance, vague gastrointestinal symptoms) are commonly missed in the elderly because of the presence of comorbidities such as diabetes and cognitive impairment.
- **Pulmonary hypertension.** This is more common in the elderly[8] and is often associated with signs of right heart failure, which may be resistant to oral diuretics because of impaired absorption. If severe pulmonary hypertension of unclear aetiology is present, investigations should be performed to exclude common treatable causes, such as pulmonary embolism and parenchymal lung disease.

1. Key recommendations from current Australian guidelines for management of heart failure[4]

- Realistic fluid restriction (e.g. 1.2 to 1.5 L per day)
- No added salt diet
- Strategies to encourage medication compliance (e.g. medication blister pack, dosette box)
- Physical activity and cardiac rehabilitation
- Referral and ongoing follow up with a community heart failure program

Pharmacological management of HFrEF

- ACE inhibitor/angiotensin receptor antagonist unless contraindicated
- Long-acting beta blockade after episode of acute decompensation, unless contraindicated or not tolerated
- Aldosterone antagonist (e.g. spironolactone in patients with class III and IV heart failure despite ACE inhibition; eplerenone for patients following acute myocardial infarction)
- Direct sinus node inhibitor (ivabradine for patients with sinus rhythm, ejection fraction ⩽35%, NYHA class II to IV, resting heart rate ⩾77 beats per minute)
- Iron replacement in patients with iron deficiency
- Polyunsaturated fatty acids
- Cardiac resynchronisation therapy in patients with normal sinus rhythm, QRS ⩾120 ms, ejection fraction ⩽35% and NYHA class III to IV symptoms despite optimum medical therapy

Pharmacological management of HFpEF

- No clinical trials have demonstrated that any of the drug classes effective in HFrEF are effective in HFpEF
- Risk-factor modification, including blood pressure reduction and improvement of glycaemic control

Abbreviations: HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; NYHA = New York Heart Association.

Table. Characteristics of heart failure in the elderly compared with young and middle-aged people

Feature	Elderly people	Young and middle-aged people
Prevalence	>10%	<1%
Sex	Female predominance	Male predominance
Aetiology	Multifactorial Chronic hypertension and heart failure with preserved ejection fraction plays an important aetiological role Atrial fibrillation is a common precipitant	Coronary artery disease Idiopathic dilated cardiomyopathy Severe valvular heart disease
Left ventricular systolic function	Often mildly reduced or preserved	Usually significantly impaired
Comorbidities	Multiple	Few

- **Cardiac amyloidosis, other causes of restrictive cardiomyopathy and pericardial constriction.** Although rare, cardiac amyloidosis is occasionally the cause of resistant CCF in the elderly. In addition to cardiac amyloidosis, other causes of restrictive cardiomyopathy and pericardial constriction should be considered in people with resistant CCF. Pericardial constriction should be considered in patients with a history of pericarditis, previous cardiothoracic surgery, radiotherapy or tuberculosis. Echocardiography is useful in detecting these conditions.

Managing resistant CCF in the elderly

As elderly patients often have reduced cardiovascular reserve, acute decompensation may reflect an underlying acute illness, such as a respiratory tract infection, occult gastrointestinal bleed and thyroid dysfunction. Identification and management of precipitating factors, as well as optimisation of nonpharmacological and pharmacological management strategies (see Box 3), remain the focus of care in elderly patients with resistant CCF because these patients are generally ineligible for heart transplantation and mechanical ventricular assist device implantation. Selected management options for elderly patients with resistant CCF are discussed in more detail below.

Diuretics

Oral dose escalation

Frusemide, a loop diuretic, acts on the Na-K-2Cl cotransporter on the luminal side of the ascending limb of the loop of Henle. Its secretion into the renal tubular lumen is impaired in patients with CCF and renal impairment because of diminished renal blood flow and competitive inhibition of its organic anion transporter in the presence of elevated organic anion plasma concentrations. Dose escalation may help overcome this. As frusemide is short acting, postdiuretic salt retention also contributes to diuretic resistance in patients on single-daily dosing, especially when salt intake is unrestricted. This can be prevented by increasing the dosing frequency, such as the addition of an afternoon dose, which may help avoid nocturnal pulmonary oedema.

Hospital admission for intravenous diuretics

Hospital admission for intravenous diuretic therapy often has the greatest benefit for people in the community who are resistant to oral diuretics. Intravenous administration overcomes impaired gastrointestinal absorption in patients with CCF. Intravenous doses are often uptitrated if diuresis is suboptimal (e.g. 40 mg daily, 40 mg twice daily, 80 mg twice daily, 80 mg three times daily). If patients fail to improve despite escalation of intermittent intravenous doses, and provided renal function has not deteriorated, continuous intravenous frusemide infusion (e.g. 240 mg over 24 hours) may improve diuresis by preventing postdiuretic salt retention.[9]

Aldosterone antagonists

Aldosterone antagonists may benefit some elderly patients who are resistant to loop diuretic monotherapy.[10] Their potassium sparing effect may help offset hypokalaemia caused by loop diuretics. Aldosterone antagonists should be commenced with caution (e.g. spironolactone 12.5 mg daily), then uptitrated if renal function and electrolytes are stable. They may not be appropriate for elderly patients with significant renal impairment (estimated glomerular filtration rate less than 40 mL/min/1.73 m^2) or hyperkalaemia.

Combination loop thiazide diuretic therapy

Thiazide diuretics (e.g. hydrochlorothiazide) are effective in patients who are resistant to high-dose loop diuretic monotherapy.[11] When used in this fashion, they should be administered 30 to 60 minutes before frusemide. Combination therapy should be commenced cautiously in the elderly because side effects such as hypokalaemia, hyponatraemia, hypovolaemia and renal failure are common. Elderly patients may need to commence combination therapy as an inpatient so that renal function and electrolytes can be closely monitored. Once target dry weight is achieved, the thiazide diuretic is often ceased to avoid the above side effects, but may need to be continued in patients who retain fluid when taking a loop diuretic as monotherapy.

2. Investigations for elderly patients with resistant congestive cardiac failure

Blood tests
Full blood count to exclude anaemia.
Measurement of electrolytes, urea, creatinine levels and liver function tests to exclude electrolyte abnormalities, renal dysfunction and hypoalbuminaemia.
Thyroid function, iron studies and measurement of vitamin D levels may help identify correctable abnormalities.

ECG
To look for atrial fibrillation, conduction disease, evidence of left ventricular hypertrophy (which may indicate longstanding hypertension or undiagnosed significant aortic stenosis) and evidence of myocardial ischaemia (Q waves, poor R wave progression, ST or T wave abnormalities).

Echocardiography
This should be reviewed to establish the presence of left and right ventricular systolic and/or diastolic dysfunction, significant pulmonary hypertension or new valvular abnormalities.

Ambulatory ECG
To identify paroxysmal atrial fibrillation, episodic ventricular tachyarrhythmia and significant bradyarrhythmia.

Coronary angiography or CT coronary angiography
This should be considered to exclude obstructive coronary artery disease as a cause of the patient's symptoms unless contraindicated (e.g. significant renal impairment, significant cognitive impairment, poor long-term prognosis).

Noninvasive functional imaging
This may be considered as a screening test prior to coronary angiography, or considered after coronary angiography if abnormalities are found on testing, to help justify future intervention.

Right heart catheterisation
Rarely indicated in the elderly but can be considered if significant pulmonary hypertension of unclear aetiology is found on echocardiography, or if there is concomitant significant valvular heart disease for which intervention is indicated.

Inotropic agents

Short-term dobutamine infusion (e.g. at 5 μg/kg/min) may be considered in select cases of resistant CCF in elderly people who are unresponsive to high-dose intravenous diuretics.[12] In the elderly, dobutamine increases stroke volume and cardiac output to a lesser degree than in younger patients.[13] Elderly patients are likely to be more prone to dobutamine-related tachyarrhythmias. Dobutamine infusion requires continuous telemetry in a coronary care unit, and should be reserved for refractory cases in patients with clearly reversible precipitants, no significant cognitive impairment and otherwise good quality of life. Levosimendan, a calcium-sensitiser used in the management of acute decompensated CCF, currently requires special access scheme approval for use in Australia and is rarely prescribed in the elderly.

Digoxin

The Digitalis Investigation Group (DIG) study found that although digoxin had no effect on mortality in patients with heart failure, it reduced heart failure-related hospitalisations, an effect which was also found in the elderly subgroup.[14] There was also weak evidence that digoxin reduced heart failure hospitalisations in patients with HFpEF, a result which was not statistically signifcant.[15]

Digoxin is often useful in elderly patients, although it should be avoided in those with severe renal impairment or conduction disease. Patients with a glomerular filtration rate of 30 to 45 mL/min/1.73 m^2 and otherwise difficult to control heart failure symptoms may tolerate low-dose digoxin. Regular monitoring of plasma digoxin levels is required. Patients, family members and clinicians should be vigilant for symptoms of digoxin toxicity (e.g. nausea, gastrointestinal symptoms, visual disturbances, confusion).

Nitrates

Nitrate options include oral isosorbide mononitrate, transdermal glyceryl nitrate patch and nicorandil (which also has potassium-channel activating properties together with its nitrate effect). Nitrates are useful in patients with both heart failure and myocardial ischaemia owing to their venous vasodilating properties, which reduce preload and myocardial oxygen demand. Nitrates may be particularly useful in normotensive or hypertensive elderly patients with relatively preserved left ventricular systolic function. Nocturnal dosing may help reduce the risk of early morning acute pulmonary oedema. Side effects such as headache and hypotension are common in the elderly. Nitrates are generally avoided in elderly patients with low systolic blood pressure and severely impaired left ventricular systolic function.

Sinus node inhibitors

Ivabradine has been shown to be effective in reducing cardiovascular death and heart failure-related hospital admissions in patients with symptomatic HFrEF with a left ventricular ejection fraction of 35% or less normal sinus rhythm and a resting heart rate of 77 beats per minute or more. However, its beneficial effect was not as pronounced among older age groups compared with younger age groups.[16] Nevertheless ivabradine remains an option for patients with severe HFrEF, normal sinus rhythm and high resting heart rate, especially if they are intolerant of beta blockade.

Biventricular pacing

Biventricular pacing may help alleviate heart failure resulting from dyssynchronous right ventricular pacing in elderly patients with HFrEF. Elderly patients with normal sinus rhythm, QRS of

120 ms or more, an ejection fraction of 35% or less and New York Heart Association class III to IV symptoms despite optimum medical therapy may benefit from cardiac resynchronisation therapy. Elderly patients with significant pacing requirements, deterioration of heart failure symptoms during prolonged periods of right ventricular pacing and echocardiographic evidence of cardiac dyssynchrony may be suitable candidates for cardiac resynchronisation therapy.

Managing specific cardiac causes of CCF in the elderly

Valvular heart disease

In patients with resistant CCF in association with severe valvular abnormalities, correction of these abnormalities may improve control of heart failure. Many elderly patients, however, are unsuitable for surgery because of advanced age, cognitive impairment and significant comorbidities.

Treatment options are available for elderly patients with severe aortic stenosis, provided they have reasonable cognitive function and quality of life. Transcutaneous aortic valve implantation remains a suitable option for patients with prohibitive cardiothoracic surgical risk. Surgical aortic valve replacement has also been performed in carefully selected elderly patients with good postoperative results. The inpatient hospital mortality in a case series of 87 patients aged 80 years or above undergoing aortic valve replacement at our institution between 2000 and 2009 was 3.4%, with one-year, three-year and five-year survival of 93%, 87% and 75%, respectively.[17]

Functional mitral regurgitation can occur in association with ventricular dilatation and poor ventricular function, and may fluctuate in severity depending on the volume status of the patient, thus complicating decisions regarding whether intervention is necessary. The MitraClip device is a percutaneous mitral valve intervention developed for patients with severe mitral regurgitation who are ineligible for conventional surgery. Several new percutaneous mitral valve replacement devices are currently being investigated in clinical trials.

Myocardial ischaemia

Age alone is not a contraindication for percutaneous coronary intervention or coronary artery bypass surgery. In elderly patients with coronary artery lesions who are unsuitable for percutaneous or surgical intervention, or those with significant comorbidities precluding intervention, escalation of medical antianginal therapy should be considered. In addition to antiplatelet therapy and nitrates, two management options are described below.

- **Perhexiline.** This reduces tissue oxygen requirements in areas of ischaemic myocardium by inhibiting myocardial fatty acid metabolism and improving glucose metabolism. Plasma level monitoring is required. It should not be used in elderly patients with poor renal or liver function, and should only be used with great caution in patients with diabetes who are taking insulin or oral hypoglycaemics because of the increased risk of hypoglycaemia. As nausea, liver dysfunction and neurological side effects, such as ataxia and peripheral neuropathy, are very common, this drug is reserved for patients with refractory angina.
- **Ivabradine.** Although this agent has also been prescribed for patients with chronic stable angina and normal sinus rhythm, the recent study on effects of ivabradine in patients with stable coronary artery disease without clinical heart failure (SIGNIFY) found that ivabradine was associated with a slightly increased incidence of death from cardiovascular causes or nonfatal myocardial infarction in patients with activity-limiting angina.[18]

3. Management strategies for resistant cardiac failure in the elderly (mnemonic: DREAM)

Diagnosis
- Assess left ventricular systolic and diastolic function, and investigate for the presence of valvular heart disease

Rule out/Exclude
- Exclude atrial fibrillation (often paroxysmal)
- Exclude pulmonary hypertension and right heart dysfunction (e.g. concomitant chronic obstructive pulmonary disease or pulmonary embolism)
- Identify correctable causes (e.g. myocardial ischaemia, valvular heart disease, drug interactions, iron deficiency, endocrine disorders)
- Identify medications that exacerbate heart failure (e.g. NSAIDs)

Assist long-term goals
- Ensure multidisciplinary management with close collaboration between the specialist, heart failure nurse and general practitioner
- Medication compliance may be improved with a medication blister pack

Management
- Set a realistic fluid restriction target
- Encourage a 'no-added salt' diet
- Optimise diuretic therapy: this may require hospitalisation for intravenous diuresis; in resistant cases, the cautious addition of a thiazide diuretic with careful monitoring of renal function and electrolytes may be helpful
- Optimise heart rate control
- Consider early palliative care involvement if appropriate

Importance of a team-based approach

Elderly patients with CCF often benefit from the close involvement of a community heart failure service. These programs help to identify and treat early decompensation upon discharge, and assist with long-term health maintenance. The WHICH (Which Heart Failure Intervention is Most Cost-effective and Consumer Friendly in Reducing Hospital Care) study, an Australian examination of

home-based care compared with hospital-based specialist care, showed lower rehospitalisation rates and overall health costs with community heart failure programs.[19]

In light of the ageing population, collaboration with community heart failure nurses is indicated in most patients with CCF. There is no substitute for regular clinical review by a general practitioner, who is often the health professional most attuned to the patient's individual circumstances. Frequent communication between the cardiologist, general practitioner and community heart failure team is vital to optimal care and management in elderly patients with CCF.

End of life discussion and palliative care referral

Elderly patients with CCF have a poor prognosis with a one-year mortality rate of 30% or greater after a first hospital admission for heart failure in those aged 67 years or above.[20] The clinical course of CCF in the elderly usually involves progressive stepwise deterioration in physical condition. As a result, elderly patients with CCF may eventually require residential care placement.

Advanced directives and clarification of wishes regarding cardiopulmonary resuscitation should be discussed with the patient and/or family. In cases of severe refractory CCF, the patient should be referred to palliative care services because early involvement may help mobilise additional resources to support the psychosocial needs of the patient and family.[21] This can initially be provided as an outpatient. Patients with advanced resistant CCF who are unable to be discharged home may benefit from transfer to a hospice or palliative care facility.

Conclusion

CCF in the elderly is a common management dilemma facing general practitioners and physicians. Many elderly patients with CCF will progress to a stage where they are no longer stable on standard oral therapies. Subsequent treatment decisions should be made with open discussion between the patient, family, general practitioner and hospital treating team. Multidisciplinary holistic care is essential for achieving the main goal of optimising quality of life. **CT**

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COMPETING INTERESTS: Dr Wang: None. Professor Hayward has served on the advisory board or received honoraria from Menarini, HeartWare, Novartis and AstraZeneca.