ECCOA
Essentials of Cardiovascular Care in Older Adults

HEART FAILURE IN OLDER ADULTS

Case 3

A 79-year-old Caucasian man complains of orthopnea and paroxysmal nocturnal dyspnea. He has had a long history of exertional dyspnea that has recently worsened. He has no prior history of cardiovascular disease. Physical examination reveals a blood pressure of 110/70 mm Hg bibasilar pulmonary rales, jugular venous distention, a prominent third heart sound, and bilateral pedal edema. An echocardiogram shows global LV hypokinesis with an EF of 30%. His serum creatinine is 1.8 mg/dl (estimated glomerular filtration rate of 37 ml/min/1.73 m^2).

What are the goals of therapy for older adults with heart failure?

Goals of therapy in older adult HF patients include relief of symptoms, improvement in functional capacity and quality of life, reduction in hospital admissions, and survival. In older patients, preservation of independence and maintenance of a satisfactory quality of life may be more important than survival. Optimal management requires a systematic approach comprising: 1) diagnosis, 2) search for reversible or treatable etiology, 3) judicious use of medications, 4) management of risk factors, 5) patient and caregiver education, 6) enhancement of self-management skills, 7) coordination of care across disciplines, and 8) frequent and effective follow-up.

What therapies are effective for older adults with HFLEF?

Diuretics are necessary in most patients with moderate to severe HFREF since they usually have some degree of volume overload, however they can contribute to chronic activation of the renin-angiotensin system and adrenergic nervous system. In addition, older patients are at increased risk for diuretic-induced renal insufficiency and electrolyte disturbances. Therefore, the *lowest dose* capable of maintaining euvolemia should be utilized.

Several large- and small-scale clinical trials have demonstrated the beneficial effects of *ACE inhibitors* in patients with HFREF. However, no large-scale placebo-controlled clinical trial has published clinical outcome data specifically comparing older subgroups, nor have specific outcome trials been performed in the elderly. However, a meta-analysis of these trials with stratification for age (<55 years, 55-64 years, 65-74 years, >75 years) demonstrated no heterogeneity in the benefits of treatment for the combined outcomes of death or MI and death or readmission for HF, suggesting a consistent benefit even among those over the age of 75 years. The use of ACE inhibitors in older patients may be complicated by pre-existing renal dysfunction, renal artery stenosis, orthostatic hypotension, and increased susceptibility to side effects due to concomitant therapy with NSAIDs or other medications.

Angiotensin-receptor blockers (ARBs) are a reasonable alternative ACE inhibitors in chronic heart failure. ARBs are as likely to produce hypotension, worsening renal function, and hyperkalemia as ACE inhibitors, but angioedema is much less frequent with ARBs. Many older adults have low serum sodium, diabetes mellitus, and impaired renal function such that those on combined ACE/ARB therapy may merit more frequent surveillance during therapy.

The combination of *hydralazine* 75 mg four times daily *with isosorbide dinitrate* 40 mg four times daily has been shown to reduce mortality in HF patients ≤75 years of age not on an ACE inhibitor or beta-blocker, but the combination has an unfavorable tolerability profile and is less effective than ACE inhibitor for survival. Nonetheless, this combination can be used as an adjunct to ACE inhibitors or ARBs, or as an alternative in older patients with contraindications or intolerance to both ACE inhibitors and ARBs because of hypotension or renal insufficiency.

Several large randomized trials have shown that long-term treatments with *beta-adrenergic receptor antagonists* is beneficial in patients with HFREF. Patients up to the age of 80 have been included in these trials, and subgroup analyses indicate that beta-blockers are as effective in older as in younger adults. Older patients more often have co-morbidities that can pose relative contra-indications to beta blockers, such as bronchospastic COPD and severe peripheral vascular disease. However, those should be weighed with the robust mortality reduction due to BB therapy which occurs even on top of ACE-I and other therapy. Otherwise, guidelines for BB use should be similar in older as with younger patients though initiation may be more cautious.

The DIG study was one of the first large clinical HF trials with no age limit. In patients with symptomatic HFREF and sinus rhythm, the addition of *digoxin* to ACE inhibitor and diuretic therapy reduced HF symptoms but had no overall effect on mortality. Thus, this agent should be reserved for patients with persistent severe symptoms despite diuretics, ACE-I and BB. The effects of digoxin were similar in younger and older patients, however, the safety of digoxin in older adults has been questioned. The volume of distribution and renal clearance of digoxin decline with age, so that *lower doses* are needed to achieve a therapeutic effect in older adults. In a recent analysis from the DIG study, maximum benefit from digoxin was evident at serum digoxin concentrations of just 0.5-0.8 ng/ml, and digoxin levels ≥1.2 ng/ml were associated with *increased* mortality. A digoxin dose of 0.125 mg daily is adequate for most older adults with normal renal function, while in patients with significant renal dysfunction, 0.125 mg 1-3 times weekly is often sufficient.

In the RALES trial, the addition of an a*ldosterone antagonist* (spironolactone 12.5-50 mg daily) to standard therapy reduced mortality by 30% in patients with NYHA class III or IV HF symptoms who were already receiving ACE inhibitors and diuretics. Aldosterone antagonism also significantly reduced hospitalizations and improved quality of life. Subgroup analysis showed a similar relative risk reduction of death in the elderly cohort (RR 0.68), ≥67 years of age compared with the younger cohort (RR 0.74) <67 years of age. The main potentially serious adverse effect is hyperkalemia, which occurs in <2% of patients in randomized clinical trials, but in a larger percentage of older adult prescribed spironolactone in usual care settings. Thus, older adult patients should be closely monitored for side effects, most notably renal impairment and hyperkalemia.

Case 3 (continued)

The patient is admitted to the hospital with decompensated HF. His diet has been high in sodium and he has consumed 3-4 liters of fluid daily due to excessive thirst. He is treated with Lasix 80 mg IV daily over 48 hours and has a marked diuresis. He loses 5 kg and is ambulating without symptoms and feels markedly improved. His creatinine rises from 2.0 mg/dl to 2.8 mg/dl during the hospitalization. His physician stops the IV diuretics and resumes his preadmission medications and releases him from the hospital. The patient is readmitted to the hospital 2 weeks later with a 10 kg weight gain.

What could have been done to prevent the patient's readmission?

Prior to discharge, the patient, family, and caregivers must understand the medical regimen and diet, especially sodium restriction. Each HF patient should have a scale, record *daily weights*, and know what steps to take if weight increases beyond a prespecified range. Nurses can perform diuretic adjustments over the telephone, and in some cases, patients themselves can manage their diuretic dosages using individualized algorithms. Older HF patients should be encouraged to undertake moderate *physical activity*, and they may benefit from medically supervised exercise conditioning programs.

Case continued

The patient is placed on a regimen for heart failure that includes aspirin, carvedilol 50 mg bid, captopril 50 mg tid, spironolactone 25 mg qd, digoxin 0.125 mg qd, and furosemide 80 mg bid. With a multidisciplinary disease management program and current therapy, he is not hospitalized for two years. He now represents with NYHA class IV symptoms to your office accompanied by his daughter. His most recent MI was 5 years ago, and he underwent CABG at age 74. His LVEF is 20% by recent echocardiography. His ECG shows sinus rhythm and anterior Q waves, with a QRS width of 100 msec. His daughter has done a lot of reading, is very worried about the risk of sudden cardiac death, and wants everything done including an ICD and or biventricular pacemakers.

What is the role of AICDs in older adults with advanced heart failure?

Device therapies such as biventricular pacer and ICDs have been demonstrated in randomized clinical trials to improve symptoms and prolong life. However, very few of these trials have included older adults (e.g., >75 years of age), and thus, the benefits of such therapy in this population are unknown. Accordingly, the decision process for these interventions requires a comprehensive approach directed not only at physiologic benefits and potential clinical risks, but attention to psychosocial and ethical issues. ICDs are not indicated in patients with class I or IV HF, or in patients with life-expectancy less than 12 months per national guidelines, and thus, this patient is clearly not a candidate for an ICD.

Therapy for advanced HFREF (Stages C and D) has progressed considerably in the last few years with the biventricular pacing, automatic implantable defibrillators, and LV assist devices; very few clinical trials have included older adults (e.g., >75 years of age). Accordingly, the decision process for these interventions requires a comprehensive approach directed not only at physiologic benefits and potential clinical risks, but attention to psychosocial and ethical issues.

Cardiac Resynchronization Therapy (e.g., Biventricular Pacers)

More than 4,000 patients with HFREF and ventricular dyssynchrony have been evaluated in randomized controlled trials of optimal medical therapy alone versus optimal medical therapy plus cardiac resynchronization therapy (CRT) with or without an ICD. These studies show improved symptoms, exercise capacity, quality of life, LVEF, and survival and decreased hospitalizations in patients with persistently symptomatic HFREF undergoing optimal medical therapy with a prolonged QRS duration.

In a meta-analysis of several CRT trials, including almost 5,000 patients (age 65 ± 11 years), HF hospitalizations were reduced by 32% and all-cause mortality by 25%. In properly selected candidates, benefits have been reported in octogenarians.

Defibrillators

Guidelines for the use of ICDs in patients with HF have been developed based on the results of several randomized clinical trials. Subgroup analyses of the available trials have demonstrated a similar benefit for elderly and younger patients using age cut-offs of 60, 65, or 70 years. Unfortunately, HF patients ≥75 years, octogenarians, or patients with more severe comorbidities have been either under-represented or excluded in ICD intervention trials. Therefore, it is currently not possible to draw any firm conclusions with regard to the risk/benefit ratio in the older adult (e.g., ≥75 years) population.

With 1-year mortality rates as high as 25-50%, HF can be considered a terminal illness in older patients with advanced symptoms, yet end-of-life care is often inadequately addressed, and pain, dyspnea, and anxiety are often untreated. This discussion should include end-of-life planning and palliative approaches, including the possibility of ICD inactivation during the process of dying once end-stage HF has occurred. Patients should be encouraged to develop a living will and to assign durable power of attorney. End-of-life preferences should be discussed periodically and whenever there has been a significant change in clinical status.

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