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# Heart failure in the elderly: ten peculiar management considerations

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**Abstract** Chronic heart failure (HF) is a disease with significantly higher prevalence in the elderly or patients older than 65 years old. Typically, older patients have more risk factors for HF, more comorbidities, and are more likely to have recurrent admissions for acute decompensations. With HF burden on health care systems primarily related to hospital and nursing home costs, it is critical that elderly patients are approached with a clear understanding of certain unique clinical, laboratory, imaging, and pharmacokinetic differences that can alter their management and outcomes. Psychosocial factors have major implications on adherence to therapy as well as decisions on advanced care for elderly HF patients. In this article, we highlight ten peculiar management considerations when approaching older patients with HF. We discuss issues related to epidemiology, diagnostic challenges, pharmacotherapy, and palliative care; all of which can impact this unique population and, more importantly, the disease burden as a whole.

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## Incidence and risk factors

The elderly are more susceptible to heart failure due to several morphological and physiological changes related to aging. More than 80% of individuals hospitalized for heart failure are over the age of 65 and 24% are 85 years or older [1, 2]. The annual rate of heart failure occurrence doubles in the age group of 75 to 84 as compared to 65 to 74 and more than quadruples in those over 85 years of age [3]. Increased incidence and improved survival have been noted over the last several years, particularly in elderly men with heart failure [4]. The elderly have variations at the cellular and the clinico-pathophysiological level that may interact with the lifelong exposure to cardiovascular risk factors and comorbidities leading to heart failure. Hypertension has historically been the most common risk factor in heart failure with coronary heart disease (CHD) being the most common etiology over the last few decades [3, 5]. It is important to note that most of this data has emerged from studies and registries conducted in the USA and Europe. In the Middle East Gulf region, two registries from seven countries showed that over 50% of patients admitted with acute heart failure had coronary artery disease as the main etiology [6, 7]. Heart failure is thought to be "superimposed on an ongoing aging process" and is sometimes described as "the end stage in the cardiovascular disease continuum" [8, 9]. Such statements are derived from the fact that the most common causes of heart failure (HF), namely, hypertension and CHD are also more common in the elderly. Moreover, with the continued growth of the elderly population, it is expected that the burden of HF in elderly men and women will continue to increase [8, 9].

Heart failure with preserved ejection fraction (HFpEF) is more common in the elderly with around 55% of elderly heart failure patients having normal left ventricular ejection fraction (LVEF) and 80% having normal or mildly reduced systolic function with LVEF of 45–55% [10]. Studies also show an association between female gender and preserved ejection fraction in elderly patients hospitalized with heart failure [11]. As a result, elderly patients, particularly elderly women with heart failure, end up being excluded from major trials of heart failure with reduced ejection fraction (HFrEF).

## Clinical assessment

Elderly patients may have more atypical presentations of heart failure, especially in more frail or cognitively impaired individuals, due to cognitive deficits, sedentary lifestyles or exercise limitations, and comorbid diseases. These factors may contribute to later onset of symptoms and complicate the presentation of dyspnea, fatigue, and lethargy. Infections, renal disease with fluid overload, anemia, and hypertension are among the comorbidities which can worsen or precipitate exacerbations of heart failure in the elderly. Recognizing subtle changes in the history or physical exam of an elderly patient may be the most important factor in evaluating and treating heart failure in these patients.

Elderly patients with heart failure are more likely to present with symptoms of decreased cardiac output, such as fatigue (most common), weakness, dizziness, and change in mental status. Exertional dyspnea may not be an early symptom in the elderly, namely, due to decreased exercise capacity from skeletal wasting; malnutrition; immobility; and iatrogenic factors, such as low salt diet and medications (e.g., digoxin toxicity). In about 14% of elderly patients, jugular venous distinction is absent, although it is the most specific sign to determine volume status [12]. Elderly patients may decrease their physical activities to compensate for a reduction in functional status, thereby delaying diagnosis and treatment further until they are in the more advanced stages of heart failure. Other comorbidities can complicate the presentation of heart failure in the elderly and include malnutrition from socioeconomic factors or medical illnesses, coexistent diseases (pulmonary disease, malignancies), confusion and memory changes, anxiety, insomnia, delirium, and psychosis. Iatrogenic heart failure resulting from overzealous hydration is a frequent complication in elderly patients, and treatment with diuretics can lead to delirium, electrolyte disturbances, and increased morbidity and mortality. A careful history inquiring about medication changes, recent hospitalizations, and changes in fluid intake can aid in diagnostic and therapeutic decision making.

It is paramount to establish a baseline for each patient through history and physical exam, including a mental status assessment and monitoring for any acute changes, as this may have important diagnostic and therapeutic implications. Upon examination, an elderly patient may not present in acute distress, but typically as pale, thin, and fatigued due to cardiac cachexia. They may not present in acute distress. Orthostatic changes in blood pressure and heart rate, assessment of nutritional status, risk of fall, and changes in activities of daily living (ADL) need to be assessed regularly, as subtle changes may be important determinants of progression of disease or the need for modifications in treatment. Deficiencies in language, cognition, and coordination may indicate cerebrovascular disease and need to be recognized early. Bilateral crackles and pleural effusions may be secondary to coexistent diseases and not exclusively heart failure, so alternate diagnoses may actually delay the diagnosis of heart failure. Most peripheral edema is due to venous insufficiency, not CHF [13]. With history taking, a review of the medications can guide further therapeutic decisions.

## Utility of brain natriuretic peptide

When using biomarkers, brain natriuretic peptide (BNP) and NT-proBNP were found to be very useful in the diagnosis of HF in the elderly when presenting to the emergency room with symptoms suspicious for HF. BNP of above 100 pg/mL has 90% sensitivity and 76% specificity in diagnosis of HF in patients presenting with HF symptoms [14]. BNP less than 50 pg/mL has a negative predictive value of 96%. BNP levels increase with age in normal individuals, but the increase is not as dramatic as in NT-proBNP, which has a longer half-life. One study found that in patients above 65 years old, the best cutoff value of BNP was greater than 250 pg/mL [15]. For NT-proBNP, a level above 1800 pg/mL in patients above the age of 75 years old has a 95% sensitivity and a 73% specificity in diagnosing HF in patients presenting with acute dyspnea [16]. However, the best utilization of these biomarkers is to rule out HF, since if NT-proBNP is less than 300 pg/mL, then HF is very unlikely with 99% sensitivity. Furthermore, it was also found that in the very elderly (above 80 years old), BNP may be a biochemical marker of an increased risk of cardiac morbidity and total mortality and therefore has a prognostic value [17].

## Echocardiographic differences

Echocardiogram is an essential diagnostic modality in the elderly due to its simplicity in use and that it carries almost no risk to the patient but may present technical limitations when performing on the elderly compared to younger individuals. Aging myocardium has an increase in myocyte size with reduction in number and degenerative changes. There is also an increase in fibroblast numbers, leading to an increase in collagen deposition and fibrosis and thus leading to atrial and ventricular stiffness that can lead to diastolic dysfunction [18–20].

We have to remember that changes related to normal aging can become pathological, at which point it can no longer be considered normal. It was demonstrated that the geometry of the heart changes with aging due to decreasing base-to-apex dimension, rightward shift, and dilatation of the aortic root. There is also a slight increase in the interventricular septal thickness. This can lead to the so called "sigmoid septum," which in some cases can cause left ventricular outflow tract obstruction [21].

Valvular heart disease is common in older population. Mitral annular calcification is very common in the elderly and can cause regurgitation and even stenosis; the latter can be distinguished from a rheumatic valve in that it spares the MV leaflets. Moreover, age-related degenerative changes in the aortic valve cause sclerosis, which can progress to aortic valve stenosis. The calcification can also be seen at the sinotubular junction. Degenerative changes due to wear and tear of the aortic valve can result in Lambl's excrescences and fibrous tags, which must be differentiated from infective endocarditis. Aging also changes normal values of Doppler indexes of left ventricular diastolic performance, making the diagnosis of diastolic dysfunction in the elderly more difficult [22].

## Comorbidities

Approximately 58% of elderly patients have five or more comorbidities [23]. Some of the most common comorbidities include hypertension, diabetes, chronic kidney disease, coronary heart disease, and chronic obstructive pulmonary disease [24]. In addition, some of the comorbidities that are more common with aging such as depression, frailty, and cognitive impairment might be underreported in the elderly [25]. Some of these illnesses including depression and functional and cognitive impairment have all been shown to increase mortality risk. Even mild functional impairment as reflected in a decline in the instrumental activities of daily living (IADL) but not ADL has been shown to be associated with increased mortality [23, 24]. The prevalence of some comorbidities in HF patients may also vary based on regional differences. For example, the prevalence of diabetes in the Middle East Gulf region is reported to be double the rate of that reported in Western HF registries [6, 7, 26].

Evidence-based pharmacotherapy for heart failure may not have the same benefit-risk profile in older patients, given that these therapies are not well studied in the oldest of the elderly or those patients with multiple comorbidities, which is the norm rather than the exception in geriatric patients. As a result, when evidence-based medicine is extrapolated from trials to real-world clinical practice, the elderly can be the most vulnerable to side effects, drug disease, and drug-drug interactions [27]. Presence of comorbidities in elderly individuals with heart failure may lead to masking common symptoms such as cough, wheezing, shortness of breath, and fatigue, which may be attributed to other conditions such as lung disease or simply aging [28].

Dharmarajan et al. emphasized the importance of a holistic approach to the treatment of older patients with heart failure and multiple chronic conditions [29]. The authors identified the following five main recommendations for this patient population: first, treat the patient as a whole with a focus on general health-related outcomes rather than disease-specific outcomes; second, realize the significance of cognitive function in relation to patients' ability to self-care as this is an aspect that is sometimes overlooked; third, focus on non-pharmacologic treatments when possible to avoid side effects of medications in this particularly vulnerable group; and finally, minimize treatment burden and enhance care coordination where family support and multidisciplinary team approach come into play [29].

## Overprescribing vs underprescribing of medications and polypharmacy

The likelihood of an inappropriate medication increases with polypharmacy, even though more than five medications are often indicated by current guidelines if a patient has more than one chronic illness [30, 31]. Inappropriate prescribing in elderly patients, including misprescribing, underprescribing, and overprescribing, is difficult to assess due to complex medication needs for multiple comorbidities and the lack of easy-to-use generalizable criteria. The European Union Geriatric Medicine Society has adopted the Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP) and Screening Tool to Alert doctors to Right Treatment (START) criteria, a series of 87 drug-drug, drug-disease, and omission criteria organized by physiological system [32, 33]. These criteria have been shown to improve medication appropriateness, although data on avoidance of adverse events has yet to be documented [32]. The American Geriatric Society Beers Criteria for Potentially Inappropriate Medication (PIM) Use were recently updated to provide guidance on medications to avoid and now include a section on drug-drug interactions known to be highly associated with harm in older patients [34]. Heart failure therapies included in this new list of drug-drug interactions include ACE inhibitors administered with amiloride, triamterene, or lithium and loop diuretics administered with lithium or peripheral alpha-1 blockers [34]. Digoxin recommendations still advise to avoid as first-line therapy. However, these criteria provide no guidance on underprescribing or misprescribing, which are both common among older patients with heart failure. Table 1 summarizes the medication issues from the STOPP, START, and Beers criteria as they relate to use in elderly HF patients.

The OPTIMIZE-HF registry includes over 48,000 patients in the USA with a mean age of 73.2 years; 52.8% of whom were 75 or older. An analysis of recommended therapies for

**Table 1** Medication issues from the STOPP, START, and Beers criteria as they relate to use in elderly HF patients

| Criteria | Description | Items pertaining to HF |
|---|---|---|
| STOPP version 2, screening tool of older people's potentially inappropriate prescriptions [33] | 80 criteria addressing potentially inappropriate medications in persons over age 65<br>Developed by a panel of 19 experts<br>Organized by physiologic system | Inappropriate medication:<br>• Digoxin for heart failure with preserved systolic ventricular function<br>• Digoxin at a long-term dose >125 mcg/day with impaired renal function<br>• Use of diltiazem or verapamil with NYHA class III or IV heart failure<br>• Beta-blocker in combination with verapamil or diltiazem<br>• Beta-blocker with symptomatic bradycardia, type II heart block, or complete heart block<br>• Amiodarone as first-line antiarrhythmic therapy in supraventricular tachyarrhythmias<br>• Loop diuretic for dependent ankle edema without clinical, biochemical, or radiological evidence of heart failure, liver failure, nephrotic syndrome, or renal failure<br>• Thiazide diuretic with current significant hypokalemia, hyponatremia, hypercalcemia, or with a history of gout<br>• ACE inhibitors or angiotensin receptor blockers in patients with hyperkalemia<br>• Aldosterone antagonists with concurrent potassium-conserving drugs without monitoring of serum potassium<br>• Phosphodiesterase type-5 inhibitors in severe heart failure characterized by hypotension or concurrent daily nitrate therapy for angina<br>• Non-selective beta-blocker (oral or topical) with a history of asthma requiring treatment<br>• NSAID with severe hypertension or severe heart failure<br>• Vasodilator drugs with persistent postural hypotension<br>• Thiazolidinediones in patients with documented heart failure<br>• Beta-blockers in diabetes mellitus with frequent hypoglycemic episodes<br>• Acetylcholinesterase inhibitors with a known history of persistent bradycardia, heart block, or recurrent unexplained syncope or concurrent treatment with drugs that reduce heart rate such as beta-blockers, digoxin, diltiazem, and verapamil |
| START version 2, screening tool t o alert doctors to right treatments [33] | 34 criteria addressing medications that should be considered for patients 65 and older where no contraindication exists<br>Developed by a panel of 19 experts<br>Organized by physiologic system<br>Recommendations per medical condition | Consider starting<br>• ACE inhibitor with systolic heart failure and/or documented coronary artery disease<br>• Appropriate beta-blocker (bisoprolol, nebivolol, metoprolol, or carvedilol) with stable systolic heart failure |
| Beers criteria for potentially inappropriate medication use in older adults 2015 update [34] | 5 lists that identify over 40 medications or classes of medications that could be problematic for elderly patients<br>• In the general population<br>• With specific disease states<br>• And require special caution for use<br>• With renal dysfunction<br>• Leading to drug-drug interactions<br>Developed by a panel of 13 experts | • Avoid digoxin as first-line therapy for HF, avoid dose >0.125 mg/day<br>• Avoid amiodarone as first-line therapy for atrial fibrillation unless patient has heart failure<br>• Avoid NSAIDs and COX-2 inhibitors, non-dihydropyridine CCBs (rEF), thaizolidinediones, cilostazol, and dronedarone (severe or recently decompensated HF)<br>• Drug-drug interactions to avoid, ACEIs and amiloride, triamterene, and lithium; loop diuretics and lithium or peripheral alpha-1 blockers; and amiodarone and warfarin<br>• Avoid in creatinine clearance <30 mL/min amiloride, spironolactone, and triamterene |

HF in patients less than 75 compared with those 75 or older showed that statistically significant fewer eligible patients 75 years or older received prescriptions at discharge for ACE inhibitors, beta-blockers, or aldosterone receptor antagonists [35]. Another study in Europe compared 741 patients 80 years or older with 2836 younger patients (median age 68.4). This study also demonstrated a statistically significant lower rate of prescribing ACE inhibitors, beta-blockers, and spironolactone upon discharge but a significantly higher percentage of diuretic prescriptions [36]. Another study done in patients over the age of 75 with CHF showed that there was significantly lower use of recommended agents in this population, which led to a significantly greater amount of time in the hospital within 12 months [38]. In addition to the lack of prescribing, the dosages prescribed are often suboptimal even if the recommended agents are prescribed [36, 38]. This could be due to a perception of multiple comorbidities complicating therapy choices, a higher sensitivity to adverse effects from drugs, or the lack of data from key trials since elderly patients were mostly excluded from these trials [36, 38]. All guideline-based therapies without an absolute contraindication should be offered to these patients and titrated to goal doses as tolerated.

## Altered pharmacokinetics

Older patients face physiologic changes that make them more susceptible to adverse effects of medications. A full review of the pharmacokinetic and pharmacodynamic effects on cardiovascular medications was previously published, and general concepts will be discussed here [37]. Specifically for the cardiovascular system, the aorta and arterial system lose elasticity, leading to higher systolic arterial pressure and left ventricular hypertrophy. Myocardial relaxation is slowed, as is the heart rate and sinoatrial node conduction. Vasoconstrictor response to activation of the sympathetic nervous system is decreased, with beta-adrenergic receptors more affected than alpha receptors. Another striking difference is the change in adaptation to orthostasis. In younger patients, the heart rate increases to compensate for postural changes, but in older adults, stroke volume increases to compensate, which can lead to higher rates of orthostatic hypotension [39]. A decrease in hepatic blood flow of 20–50% and hepatic volume of 20–30% as well as renal mass reduction of 25–30% and renal blood flow of 1% per year after age 40 affect drug disposition in the body [40]. Hepatic first-pass metabolism is decreased, leading to higher bioavailability of drugs such as propranolol and labetalol, but pro-drugs which rely on this mechanism for activation such as enalapril and perindopril will see a decrease in availability. Absorption can be affected for some drugs, but there are conflicting data on the effects of aging on gastric acid secretion and gastric emptying, so the clinical significance of effect of aging on absorption is unclear but appears to be negligible for healthy older adults. As humans age, total body water and lean body mass decrease by 10–15% while body fat increases 20–40%, which affects the distribution of drugs [40]. Water-soluble drugs such as digoxin will have a smaller volume of distribution, leading to higher serum levels after one dose, meaning that loading doses must be decreased, while lipophilic drugs such as verapamil will have a higher volume of distribution in the older adult leading to a prolonged half-life. However, the decrease in half-life of water-soluble drugs is somewhat balanced by the decrease in clearance by the kidneys.

Clearance of many medications is affected by the change in renal function, although there is some evidence that renal function might not deteriorate as much as previously thought in healthy older patients [40]. Medications with extensive renal clearance and a narrow therapeutic index such as digoxin should be monitored closely, and loop diuretics should be used cautiously when appropriate to avoid overdiuresis leading to dehydration, renal failure, and electrolyte derangements. Among the beta-blockers used for heart failure, metoprolol does not appear to be affected by changes in renal function, while studies have shown reduced clearance of carvedilol [39]. Dihydropyridine calcium channel blockers as well as verapamil have demonstrated a prolonged half-life, while diltiazem has shown conflicting effects. Among the ACE inhibitors, enalapril, perindopril, and lisinopril did show decreased clearance, causing higher blood pressure-lowering effects with enalapril and perindopril but not lisinopril [37]. However, older patients are more susceptible to renal function compromise when any ACE inhibitor is started in the presence of NSAID and diuretic use, so caution and discontinuation of NSAIDS is advised if possible [39]. Angiotensin II receptor blockers (ARBs) irbesartan and valsartan are only slightly affected by changes in renal function. Both ACE inhibitors and ARBs have been shown in subgroup analyses of most of the major trials in heart failure patients to be beneficial in older patients, so these agents should remain a cornerstone of treatment [39]. Table 2 summarizes the dose adjustments for common HF drugs in elderly patients and the associated safety and pharmacokinetic concerns in this patient population [41, 42].

## Adherence to therapy

Another major issue in treatment effectiveness is patient adherence to therapy. A recent position paper on measuring adherence in elderly patients estimates the adherence in this population to be less than 45% on average and that one third of hospital admissions were attributable to non-adherence [43]. Polypharmacy contributes to non-adherence, with a non-adherence rate of 35% in patients taking four or more medications in one study [44]. Non-adherence with drug or diet therapy in CHF was the precipitating factor in decompensation for 42% of the patients in another study [45]. However,

**Table 2** Common HF drugs in elderly patients: dose recommendations and associated safety and pharmacokinetics concerns

| Drugs used in HF [30, 31, 41, 42] | HF dose recommendations [41, 42] | Dose adjustments in elderly [41, 42] | Significant safety concerns in elderly patients [9, 39] |
|---|---|---|---|
| Angiotensin-converting enzyme inhibitors (ACEIs) | | | |
| *Benazepril* | n/a | None in HF, consider lower initial doses in HTN | Increased orthostatic hypertension<br>• Take before bedtime<br>• Decrease diuretic dose<br>More susceptible to renal dysfunction<br>• Monitor closely (serum creatinine, potassium)<br>• Limit NSAID use<br>• Use caution if supplementing potassium<br>Target dose unachievable/drug class avoided<br>• Give maximum tolerated dose<br>• Use even in patients with comorbidities for mortality benefit but monitor closely |
| **Captopril***^ | Initial 6.25 mg three times daily, maximum 50 mg three times daily | None in HF, consider lower initial doses in HTN | |
| **Enalapril***^ | Initial 2.5 mg twice daily, maximum 10–20 mg twice daily | None | |
| **Fosinopril*** | Initial 5–10 mg daily, maximum 40 mg daily | None | |
| **Lisinopril***^ | Initial 2.5–5 mg daily, maximum 20–40 mg* (20–35 mg)^ daily | None in HF, consider lower initial doses in HTN | |
| Moexipril | n/a | None | |
| *Perindopril** | Initial 2 mg daily, target 8–16 mg daily | None in HF, consider lower initial doses in HTN | |
| **Quinapril*** | Initial 5 mg twice daily, maximum 20 mg twice daily | None | |
| **Ramipril***^ | Initial 1.25–2.5 mg* (2.5 mg^) daily, maximum 10 mg daily | Adjust for renal function in elderly | |
| **Trandolapril***^ | Initial 1 mg* (0.5 mg^) daily, maximum 4 mg daily | None | |
| Angiotensin II receptor blockers (ARBs) | | | |
| Azilsartan | n/a | None | No unique safety concerns, similar to ACEIs |
| **Candesartan***^ | Initial 4–8 mg daily, maximum 32 mg daily | None but higher AUC and $C_{max}$ observed | |
| *Eprosartan* | n/a | None in HF, consider lower initial doses in HTN | |
| Irbesartan—LVH | n/a | None | |
| *Losartan**^ | Initial 12.5–50 mg* (50 mg^) daily, maximum 50–150 mg* (150 mg^) daily | None | |
| Olmesartan | n/a | None in HF, consider lower initial doses in HTN | |
| Telmisartan—LVH | n/a | None | |
| **Valsartan***^ | Initial 20–40 mg* (40 mg^) twice daily, maximum 160 mg twice daily | None | |
| Beta-adrenergic receptor antagonists (beta-blockers) | | | |
| **Bisoprolol***^ | Initial 1.25 mg daily, maximum 10 mg daily | None | Fluid retention<br>• Monitor daily weight<br>• Adjust diuretic dose<br>Increased risk for hypotension and bradycardia<br>• Start with low dose and titrate slowly<br>• Ensure adequate hydration<br>Increased fatigue<br>• Improves with time<br>• Consider other causes of fatigue, e.g., anemia and sleep medications |
| **Carvedilol***^ | IR initial 3.125 mg twice daily, maximum 50 mg twice daily<br>ER initial 10 mg daily, maximum 80 mg daily | None in HF, consider lower initial doses in HTN | |
| **Metoprolol** succinate*^ | Initial 12.5–25 mg daily, maximum 200 mg/day | None in HF, consider lower initial doses in HTN | |
| *Nebivolol*^ | Initial 1.25 mg daily, target 10 mg daily | None | |
| Aldosterone receptor antagonists | | | |
| **Eplerenone***^ | Initial 25 mg daily, maximum 50 mg daily*; 12.5–50 mg + ACEI/ARB, 50–200 mg/day −ACE/ARB^ | None | Increased risk of hyperkalemia and renal dysfunction<br>• Monitor serum creatinine and potassium level |
| **Spironolactone***^ | Initial 12.5–25 mg daily, maximum 25–50 mg/day*; 12.5–50 mg + ACEI/ARB, 50–200 mg/day −ACE/ARB^ | None | |
| Loop diuretics | | | |
| **Bumetanide*** | Initial 0.5–1 mg once or twice daily, maximum 10 mg/day* (usual 1–5 mg/day^) | None | Increased risk for fluid imbalances and electrolyte disturbances<br>• Monitor closely |
| **Furosemide*** | Initial 20–40 mg once or twice daily, maximum 600 mg/day* (usual 40–240 mg/day^) | Initial 20 mg daily | |
| **Torsemide***/ **torasemide**^ | Initial 10–20 mg* (5–10 mg^) once daily, maximum 200 mg/day* (usual 10–20 mg/day^) | None | |
| Thiazide diuretics | | | |
| Bendroflumethiazide^ | Initial 2.5 mg/day, usual 2.5–10 mg/day | n/a | Monitor fluid status and electrolytes |
| Chlorothiazide* | Initial 250–500 mg daily BID, maximum 1000 mg/day | Start at low end of dosing range | |
| Chlorthalidone* | Initial 12.5–25 mg daily, maximum 100 mg daily | None in HF, consider lower initial doses in HTN | |
| Hydrochlorothiazide*^ | Initial 25 mg daily BID, maximum 200 mg/day* (usual 12.5–100 mg/day^) | Initial 12.5–25 mg with slower titration | |

**Table 2** (continued)

| Drugs used in HF [30, 31, 41, 42] | HF dose recommendations [41, 42] | Dose adjustments in elderly [41, 42] | Significant safety concerns in elderly patients [9, 39] |
|---|---|---|---|
| **Indapamide***^ | Initial 2.5 mg daily, maximum 5 mg daily* (usual 2.5–5 mg/day^) | None (Canada 1.25 mg daily) | |
| **Metolazone***^ | Initial 2.5 mg daily, maximum 20 mg daily* (usual 2.5–10 mg/day^) | None | |
| Potassium-sparing diuretics (see also aldosterone receptor antagonists) | | | |
| **Amiloride***^ | Initial 5 mg daily, maximum 20 mg daily*; 2.5–10 mg + ACEI/ARB, 5–20 mg/day −ACE/ARB^ | Decreased clearance, use with caution | Decreased renal clearance<br>• Avoid use or start with low dose<br>• Monitor serum creatinine and potassium |
| Triamterene*^ | Initial 50–75 mg twice daily, maximum 200 mg/day*; 25–100 mg + ACEI/ARB, 50–200 mg/day −ACE/ARB^ | None in HF, consider lower initial doses in HTN | Increased risk of hyperkalemia, monitor closely |
| Other agents used in HF | | | |
| **Digoxin***^ | 0.125–0.250 mg daily | If >70 years old, impaired renal function, or low lean body mass, use low doses (0.125 mg daily<br>or every other day) | Volume of distribution decreased<br>• Loading dose unnecessary<br>Decreased renal clearance<br>• Monitor digoxin levels<br>• Use low doses<br>Monitor closely for drug-drug interactions (e.g., verapamil, amiodarone, other drugs affecting heart rate) |
| **Hydralazine/isosorbide dinitrate***^ | Initial hydralazine 25–50 mg three to four times daily/ID 20–30 mg three to four times daily, maximum hydralazine 300 mg/day/ID 120 mg/day | None for hydralazine, use lowest recommended isosorbide dose initially | Monitor for hypotension |
| **Sacubitril/valsartan***^ | Initial sacubitril 24 mg/valsartan 26 mg* (49/51 mg^) twice daily, target sacubitril 97 mg/valsartan 103 mg twice daily | None | No difference in safety in elderly patients, monitor renal function, potassium levels |
| **Ivabradine***^ | Initial 2.5–5 mg (5 mg^) twice daily, maximum 7.5 mg twice daily | None in HF, consider lower initial doses in stable angina | Limited data over age 75, monitor for rhythm disorders |

Items in bold: FDA approved for heart failure; italic: off-label indication for heart failure; others: other agents in class with no FDA indication for heart failure

*n/a* no dosing for heart failure available

*Included in AHA/ACC/HFSA 2016 heart failure guidelines update

^Included in ESC 2016 heart failure guidelines

adherence is a complex interplay of factors both within and beyond the patient's control. The effect of age itself is unclear with a review of studies showing conflicting conclusions, although the number of medications is unequivocally associated with worsening adherence, as well as cost of treatment [46]. Drug-related factors such as adverse effects and complexity of the treatment regimen contribute to non-adherence, but less tangible factors such as patient's perception of the necessity of treatment as well as health literacy level also affect adherence rates. Including the patient as the central point in all medical decisions creates a partnership that allows for open communication and trust which can lead to stronger commitment to the care plan.

## Adverse events and drug-drug interactions

Adverse events due to medication use are a serious issue in older adults. A recent article reported statistics from several studies showing that older adults are twice as likely to be hospitalized due to an adverse drug reaction as younger patients. The article goes on to state that over 50% of hospitalizations from adverse drug reactions are avoidable, mostly due to diuretics, NSAIDs, antiplatelet, anticoagulant, and antidiabetic drugs [47]. Polypharmacy contributes to adverse events and hospitalization, with rates of 41.4 and 67% of elderly patients taking greater than five medications at hospital discharge in studies in the USA and Italy, respectively. In a US survey of nursing homes in 2004, 39.7% of patients were taking nine or more medications [44]. The risk of drug-drug interactions increases with the number of medications taken, with a 50% risk when taking between 5 and 9 medications and 100% risk if taking 20 or more medications [44]. Figure 1 summarizes some of the issues and considerations surrounding medication use in elderly heart failure patients.

## Palliative care

Palliative care should be instituted in elderly heart failure patients when it has been determined that they have incurable disease and aggressive treatment is deemed ineffective. This usually involves a multidisciplinary approach and a team consisting of the main physician, nursing team, pastoral care/bereavement support, and other support staff. The aim is to provide the highest quality of life to the patient for as long as possible. For this reason, palliative interventions should not be withheld until the final stages of life.

Focused treatment of specific symptoms can help alleviate discomfort in end-of-life heart failure patients. Severe dyspnea can be alleviated through a combination of vasodilators, diuretics as tolerated, and thoracentesis (for pleural effusion) [48]. Simple maneuvers, such as encouraging an upright position and increasing airflow with a fan or oxygen treatment, may help alleviate breathlessness as well [49]. Anxiety and depression can be treated with SSRIs and spiritual support to both the patient and family and can be very beneficial in this period. Targeted treatment of specific symptoms, such as pain, constipation, diarrhea, sleep disorders, ulcers, and anorexia, can make the terminal stages of the disease more comfortable and should be sought and treated [50]. Though dyspnea and fluid overload can be symptoms often troubling end-of-life heart failure patients, many succumb to death from metabolic disturbances, coma, or sudden death.

In the last moments of life, treatment should be focused on maximizing patient comfort. Medications should aim at alleviating symptoms with the goal of eliminating unnecessary medications. Pain and anxiety should be adequately managed through the use of narcotics, benzodiazepines, and sedatives, and this is a vital aspect of end-of-life care [51]. While many patients prefer to die in the comforts of their own home, and this is in fact advisable if family and medical support is

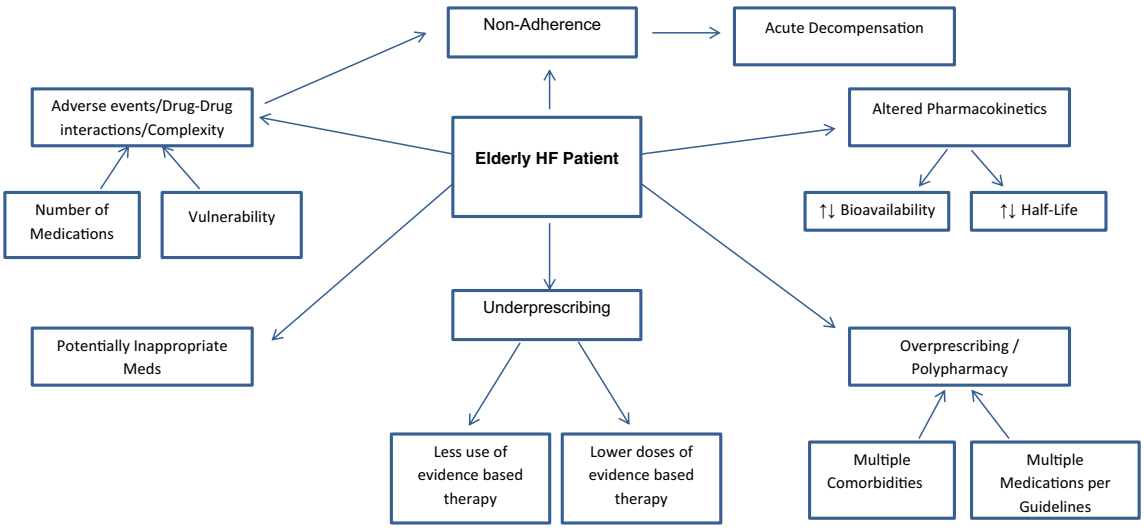


**Fig. 1** Issues and considerations surrounding medication use in elderly heart failure patients

available, many heart failure patients end up dying in the hospital setting. It is imperative that the palliative care physicians and the health care team involve family members in decision making. Family members are the "hidden patients" who provide for and observe the care of the patient and receive counseling and assistance from the health care team, yet can be dramatically affected personally with feelings of guilt and regret that can ultimately impact their psychological and physical well-being [52]. Hospice services can be instituted earlier to avoid aggressive and often times futile and uncomfortable interventions in this critical stage of life. Providers should have an open dialog with the family and patient until it is no longer feasible, limiting unnecessary treatments and interventions if risks outweigh benefits and ultimately continuing bereavement support to the family after the patient has passed away [53].

## Conclusion

Heart failure is particularly common in the elderly. Certain clinical, structural, biochemical, and psychosocial factors are unique to that patient population. Better understanding of these factors and tailoring management accordingly may result in better outcomes and less burden on health care systems worldwide.

### Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

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