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REVIEW
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Acute heart failure in elderly patients: a review of invasive and non-invasive management

Gregorio Tersalvi[1,*], Alessio Gasperetti[2,*], Marco Schiavone[2], Jeroen Dauw[3,4], Cecilia Gobbi[5], Marialessia Denora[2], Joel Daniel Krul[6], Giacomo Maria Cioffi[7], Gianfranco Mitacchione[2], Giovanni B. Forleo[2,✉]

1. Department of Internal Medicine, Hirslanden Klinik St. Anna, Lucerne, Switzerland; 2. Cardiology Unit, ASST-Fatebenefratelli Sacco, Luigi Sacco University Hospital, Milan, Italy; 3. Department of Cardiology, Ziekenhuis Oost-Limburg, Genk, Belgium; 4. Doctoral School for Medicine and Life Sciences, Hasselt University, Diepenbeek, Belgium; 5. Institut Cardiovasculaire de Caen, Hôpital Privé Saint Martin, Caen, France; 6. Division of Cardiology, Fondazione Cardiocentro Ticino, Lugano, Switzerland; 7. Division of Cardiology, Heart Center, Luzerner Kantonsspital, Lucerne, Switzerland

[*]The authors contributed equally to this manuscript

✉ Correspondence to: forleo@me.com

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ABSTRACT Acute heart failure (AHF) is a major cause of unplanned hospitalisations in the elderly and is associated with high mortality. Its prevalence has grown in the last years due to population aging and longer life expectancy of chronic heart failure patients. Although international societies have provided guidelines for the management of AHF in the general population, scientific evidence for geriatric patients is often lacking, as these are underrepresented in clinical trials. Elderly have a different risk profile with more comorbidities, disability, and frailty, leading to increased morbidity, longer recovery time, higher readmission rates, and higher mortality. Furthermore, therapeutic options are often limited, due to unfeasibility of invasive strategies, mechanical circulatory support and cardiac transplantation. Thus, the in-hospital management of AHF should be tailored to each patient's clinical situation, cardiopulmonary condition and geriatric assessment. Palliative care should be considered in some cases, in order to avoid unnecessary diagnostics and/or treatments. After discharge, a strict follow-up through outpatient clinic or telemedicine is can improve quality of life and reduce rehospitalisation rates. The aim of this review is to offer an insight on current literature and provide a clinically oriented, patient-tailored approach regarding assessment, treatment and follow-up of elderly patients admitted for AHF.

Heart failure (HF) is a growing health issue affecting around 2% of the adult population in developed countries.[1] HF predominantly concerns elderly patients, since its incidence doubles in men and triples in women with each decade after the age of 65 years.[2] HF is a common cause of hospitalisation, accounting for an estimated annual expense of at least 108 billion dollars in direct and indirect costs for health economies worldwide.[3] This disease may develop insidiously or presenting in an emergent fashion with rapidly progressive signs and symptoms, in the constellation of acute HF (AHF). Depending on the clinical profile, patients hospitalised with AHF may require loop diuretics to treat congestion, vasodilators, inotropic or vasopressor therapy, and non-invasive ventilation. Advanced interventions such as mechanical ventilation or mechanical circulatory support necessitate admission to an intensive care unit.[4,5] Since elderly patients with HF commonly differ from younger patients in terms of comorbidities, disability and drug therapy, they are often excluded from invasive and complex interventions, requiring tailored therapeutic pathways based on their clinical status and life expectancy. Furthermore, hospitalisation for AHF in the aged population is associated with higher rates of mortality, rehospitalisation, and decline in physical activity.[6–8] Earlier data suggested a 1-year all-cause mortality of 56% in patients aged > 75 years.[9] Finally, these patients have a greater symptom burden and a worse quality of life (QoL) than age-matched individuals with stable HF.[10]

Several attempts to improve the outcomes of geri-

atric patients have been done in the last years, although they are often excluded from HF clinical trials and underrepresented in clinical registries.[7,11] Thus, the information about the clinical profile and prognosis of patients hospitalised for AHF at extreme ranges of age is scarce. The purpose of this review is to offer an insight on current literature and provide a clinically oriented, patient-tailored approach regarding assessment, treatment and follow-up of elderly patients admitted for AHF.

CLINICAL PRESENTATION AND RISK STRATIFICATION

In the majority of patients, AHF results from the combination of an underlying pre-existing or newly diagnosed cardiac dysfunction and one or more precipitating factors, which may directly affect left ventricular (LV) or right ventricular (RV) function (e.g., myocardial ischaemia, arrhythmias) or may contribute to the development of congestion (e.g., infection, hypertension, scarce medication compliance).[12] Diastolic LV dysfunction in HF with preserved ejection fraction (HFpEF) or both diastolic and systolic LV dysfunction in HF with reduced ejection fraction (HFrEF) lead to pulmonary congestion, which contributes to RV dysfunction and systemic congestion. The latter, together with neurohumoral activation and inflammation, negatively affects ventricular function and further contribute to self-perpetuating congestion.[12] As a result, AHF often occurs without acute changes in cardiac function but is induced by fluid accumulation and/or redistribution, which results in systemic congestion, especially in the presence of an underlying diastolic dysfunction.[13] Diastolic abnormalities are common in the elderly, and usually can be identified in up to 54% of individuals > 65 years old in the general population.[14] As a consequence, elderly patients presenting with AHF more frequently have underlying HFpEF,[15] arterial hypertension,[16] atrial fibrillation (AF),[16] and an overall smaller left ventricle with increased wall thickness.[17] Since symptoms of reduced exercise tolerance are common in the elderly and have been shown to reflect normal physiological changes related to aging or could be related to non-cardiac aetiologies,[18,19] a transthoracic echocardiogram including complete diastolic function evaluation and the use of diagnostics tools such as the HFA-PEFF score from the European Society of Cardiology is recommended to postulate a first diagnosis of HFpEF.[20]

Regarding the clinical characteristics on admission, elderly patients present on average with lower heart rate and higher blood pressure, worse New York Heart Association (NYHA) functional class, significantly higher values of natriuretic peptides, worse renal function and lower haemoglobin levels compared to younger patients.[17,21] Individuals ≥ 80 years with AHF are more likely to be hospitalized compared to the population < 80 years old.[21] The decision to hospitalise a geriatric patient may be challenging, because of the other factors not directly related to AHF that may hamper successful home discharge (e.g., comorbidities, functional status, frailty).[22] In addition, the length of hospital stay should be as short as possible, to limit the negative impact of hospitalisation (i.e., physical deconditioning, iatrogenic complications).[23] Overall, AHF in the elderly population was associated with a 8%–10% mortality risk and up to 15%–30% risk of hospital readmission at 30 days.[23–25] The risk of 1-year all-cause mortality was shown to be 3.5-fold higher for patients ≥ 85 years compared to those < 65, and almost double when compared to those in between 74–85 years. Interestingly, a similar gradient of risk was found for HF-mortality.[17]

It is crucial to identify patients who are at risk of poor in-hospital outcomes at the earliest point possible, in order to tailor management and discuss treatment goals with the patient and their relatives. Clinical risk prediction in elderly patients can be difficult because of the presence of comorbidities. The use of standardised risk scores on top of clinical assessment may be considered (Table 1). Although most of them are not specifically validated in the geriatric population, the mean age of the cohorts mostly exceeds 75 years.[26–28] Notably, age is generally considered a variable of increased risk. As to the studies that assessed risk prediction in a selected geriatric cohort, the most important independent risk factors of in-hospital mortality included heart rate, hypertension, LVEF, NYHA class, pH value, anaemia, renal dysfunction (or use of haemodialysis/ultrafiltration), high levels of natriuretic peptides, use of inotropic agents, and length of ICU stay.[29–31]

Table 1 Scores for risk stratification in patients admitted for acute heart failure in the general and in the elderly population (integrated from Collins, *et al.*[147]).

	Year	*N*	Age	Variables	Outcome
General population					
Collins, *et al.*[114] STRATIFY	2015	1033	64.0 (53–75)	Demographics: age, BMI History: ACE-I use, supplemental oxygen use, dialysis Presentation: diastolic BP, respiratory rate, SaO_2 Lab: natriuretic peptides, BUN, Sodium, Troponin EKG: QRS duration	5- and 30-day hierarchical adverse events
Miro, *et al.*[27] MEESSI	2018	4897	79.7	Demographics: age Presentation: NYHA class at admission, respiratory rate, SaO_2, systolic BP, low-output symptoms, ACS Lab: natriuretic peptides, potassium, troponin, creatinine EKG: hypertrophy Other: Barthel index at admission	30-day mortality
Stiell, *et al.*[28] OHFRS	2017	1100	77.7 ±10.7	History: stroke or TIA, intubation for respiratory distress Presentation: tachycardia, low room air SaO_2 Lab: urea, serum CO_2, Troponin I or T, natriuretic peptides EKG: acute ischemic changes Other: desaturation or tachycardia during walk test or too ill to walk	30-day serious adverse events
Lee, *et al.*[26] EHMRG	2018	1983*	81.0 (71–87)	Demographics: age History: active cancer, metolazone use Presentation: arrival by ambulance, systolic blood pressure, heart rate, SaO_2 Lab: potassium, creatinine, troponin EKG: ST depression on 12-lead	7- and 30-day mortality
Elderly population					
Manzano, *et al.*[30] SENIORS	2011	728*	76.1 ± 4.6*	Demographics: BMI History: prior myocardial infarction Presentation: NYHA class Lab: uric acid Echocardiography: left atrial dimension	Time to first cardiovascular hospitalisation or all-cause mortality (21 months follow-up)
Jia, *et al.*[29]	2017	729*	75.4 ± 5.1*	Presentation: heart rate Lab: pH, eGFR, natriuretic peptides Echocardiography: left ventricular ejection fraction	In-hospital mortality
Gök, *et al.*[31] HF-TR	2020	346*	74.9 ± 6.9*	Demographics: age Presentation: uncontrolled hypertension Lab: anaemia Others: Inotrope use, haemodialysis/ultrafiltration, length of ICU stay	In-hospital mortality

ACE-I: angiotensin-converting enzyme inhibitors; ACS: acute coronary syndrome; BMI: body mass index; BP: blood pressure; BUN: blood urea nitrogen; CO2: carbon dioxide; eGFR: estimated glomerular filtration rate; EHMRG: Emergency Heart Failure Mortality Risk Grade; EKG: electrocardiogram; HF-TR: Patient Journey in Hospital with Heart Failure in Turkish Population; ICU: intensive care unit; MEESSI: Multiple Estimation of risk based on the Emergency department Spanish Score in patients with AHF; NYHA: New York Heart Association; OHFRS: Ottawa Heart Failure Risk Scale; SaO_2: oxygen saturation; SENIORS: Study of the Effects of Nebivolol Intervention on Outcomes and Rehospitalisation in Seniors with Heart Failure; STRATIFY: Improving Heart Failure Risk Stratification in the emergency department; TIA: transient ischemic attack. *Validation cohort.

Figure 1 summarize the most considered markers of poor outcome for patients presenting with AHF based on the risk scores currently available in literature.

IN-HOSPITAL MANAGEMENT

Elderly patients with AHF can be managed through different in-hospital care pathways. The choice of the right pathway (cardiology or geriatric ward vs coronary or intensive care unit, CCU–ICU) depends on the patient's clinical complexity, age, comorbidities and life expectancy. Interestingly, compared to studies involving younger patients, individuals with age > 65 years tend to receive less intensive treatment[32]. Furthermore, a "chaotic" in-

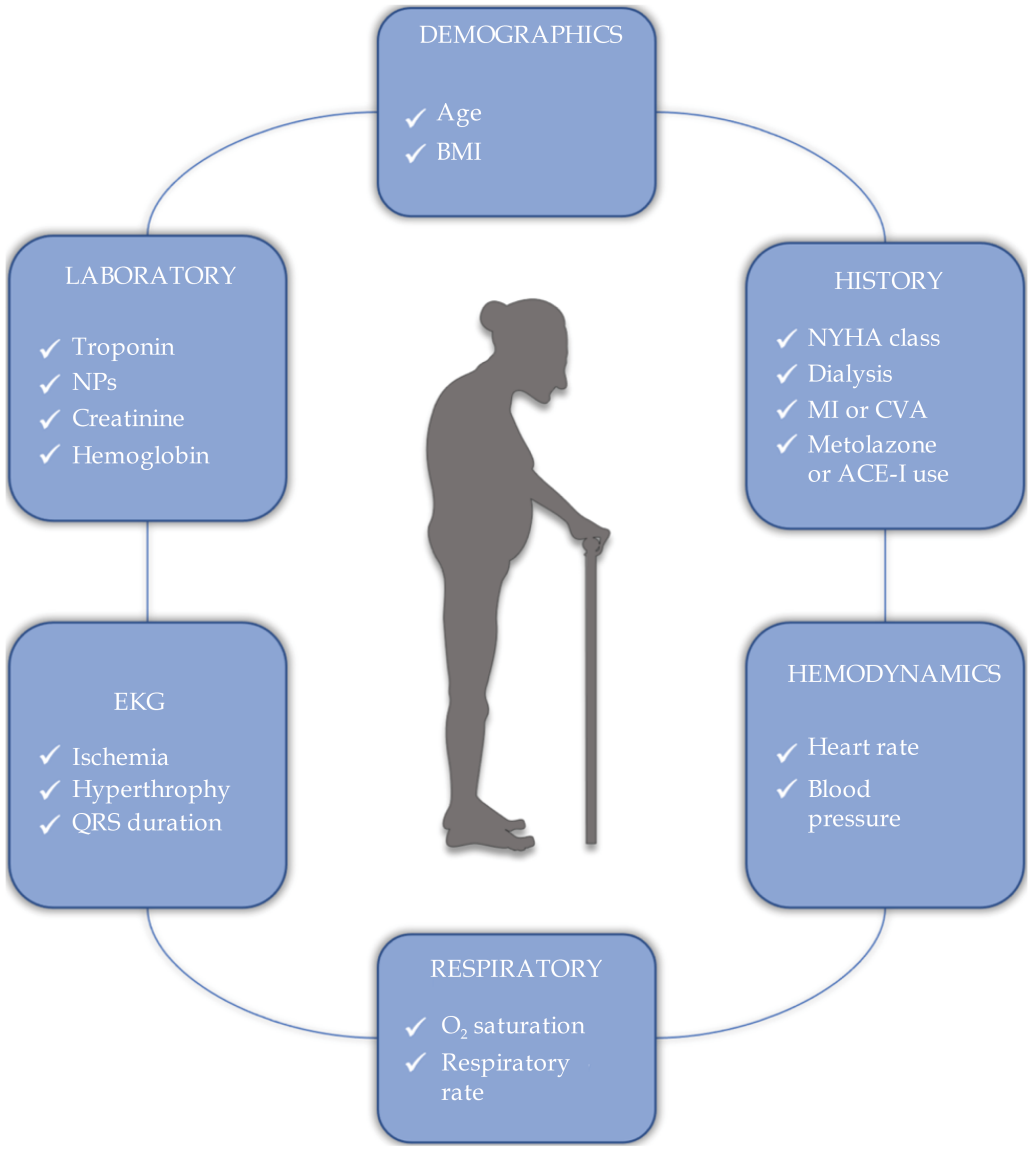

Figure 1 Risk stratification variables for patients presenting with AHF. ACE-I: angiotensin-converting enzyme inhibitors; AHF: acute heart failure; BMI: body mass index; CVA: cerebrovascular accident; EKG: electrocardiogram; MI: myocardial infarction; NPs: natriuretic peptides; NYHA: New York Heart Association. Modified from Servier Medical Art: licensed under a Creative Common Attribution 3.0 Generic License.

hospital care pathway occurring in different wards (CCU, ICU, cardiology and/or geriatrics) has a significant impact on increasing the risk of one-year readmission for HF in older patients.[32]

Set Treatment Goals

To choose the right pathway of care before initiating treatment, it is important to set treatment goals early. In general, the goal in AHF treatment is to restore volume status and to improve the hemodynamic status on the short term and to improve hospitalisation-free survival on the long term. In elderly patients, the emphasis should be put on symptom control and QoL, more than on improving survival, as this is inherently impaired due to older age with lower life expectancy. Thus, treatment should be adjusted to these specific goals and can even differ more, e.g., in cases when palliative care is more reasonable and preferred by patients (see below).

Pharmacological Treatment

Diuretics

In patients with volume overload, loop diuretics are the cornerstone treatment and should be initi-

ated early, as this lowers in-hospital mortality.[33] Intravenous is preferred over oral administration, because bowel oedema can decrease intestinal absorption. In addition, dosing should be adequately high as polypharmacy and impaired renal function, which is often the case in elderly patients, might hamper diuretic response.[34]Current guidelines suggest using 1−2 times the home daily dose and this probably also applies to elderly patients.[4] Furosemide and bumetanide both have a short duration of action of around 6 h. Consequently, multiple dosing per day could improve diuretic response and decrease periods of post-diuretic sodium retention.[35] However, elderly patients are often more susceptible to volume shifts and can have lower plasma refill rates due to hypoalbuminemia and endothelial dysfunction.[36] Therefore, administrating multiple boluses per day should be done with caution in these patients or, alternatively, continuous infusion can be considered. Volume and diuresis assessment should be performed regularly in the first hours, in order to optimise loop diuretic dosing.[35] Urinary sodium measurement has been proposed as a useful parameter to tailor diuretic therapy in patients with AHF.[37] Importantly, worsening renal function on admission is often explained by venous congestion, which can be targeted by diuretics. Further, worsening renal function during diuretic treatment should not be of major concern and should not lead to withholding diuretic therapy by default because: (1) in case of a good diuretic response it is not associated with worse prognosis[38] or tubular injury;[39] (2) adequate diuresis improves symptoms, while worsening renal function does not necessarily increase symptom burden; and (3) worsening renal function does not reflect reaching euvolemia.[35] Moreover, worsening renal function without good diuretic response might reflect ongoing renal congestion and warrants loop diuretic escalation, rather than down-titration,[40] with a specific tailored treatment according to specific aetiology.

Vasodilators

In patients with volume redistribution, guidelines advise to use vasodilators to increase venous capacitance and lower vascular resistance.[4] However, these agents should be used cautiously in elderly patients. Due to aging and decreased compliance of the cardiovascular system, these patients can be more sensitive to nitrate treatment, leading to more pronounced drops in blood pressure and orthostatic hypotension. Excessive drops in blood pressure can lead to renal hypoperfusion and might hamper diuretic response. In addition, two recent randomised trials have challenged the routine use of nitrates in acute heart failure. In the Goal-directed Afterload Reduction in Acute Congestive Cardiac Decompensation Study (GALACTIC) trail, goal directed vasodilation including the use of nitrate did not improve long-term outcomes.[41] The Effect of an Emergency Department Care Bundle on 30-Day Hospital Discharge and Survival Among Elderly Patients With Acute Heart Failure (ELISABETH) trial investigated the effect of implementing a care bundle (including routine use of nitrate boluses) vs. usual care in 503 AHF patients aged 75 years and older.[25] One of the most striking differences was a 76% higher use of nitrates in the care bundle arm, but this did not result in a difference in 30-day hospital-free survival. Therefore, nitrate use in elderly patients should probably be limited to hypertensive patients with close monitoring of blood pressure and careful titration.

Morphine

Patients presenting with acute pulmonary oedema are often very anxious, further increasing the already high catecholamine levels. Although not supported by evidence, they are often treated with morphine, which decreases both anxiety and respiratory drive.[4] Benzodiazepines are considered as an alternative. The potential benefit of these drugs come with the advent of increased risk of delirium, for which elderly patients are more sensitive.[42] Often, other predisposing factors to delirium are also present such as bladder catheter insertion, ICU hospitalisation, relative immobilisation and serum electrolyte disturbances. Thus, use of these sedatives should prompt the treating physician to also take measures to prevent delirium (see below).

Inotropes

Inotropes increase cardiac output by increasing myocardial contractility and heart rate but also increase oxygen demand in an already stressed heart and increase the risk for ventricular arrhythmias. The use of inotropes has also been associated with increased mortality.[43]According to current guidelines, these agents are reserved for the treatment of cardiogenic shock and require ICU admission.[4] Overall, cardiogenic shock carries a poor prognosis with an in-hospital mortality of around 50%.[44] As elderly patients suffer from more comorbidities,

they are even at higher risk and ICU stay can often be traumatic for patients and families. Therefore, the initiation of inotropes should carefully be weight against the life expectancy and comorbidity burden in these patients. In certain cases, palliative care can be preferred in case of cardiogenic shock.

Guideline-based medical therapy

For patients with HFrEF, the use of a beta-blocker, a blocker of the renin-angiotensin-aldosterone system (i.e., Angiotensin-converting enzyme inhibitors [ACEI], angiotensin II receptor blockers [ARBs], or angiotensin-receptor-neprilysin inhibitors [ARNI]) and a mineralcorticoid-receptor antagonist (MRA) constitute the mainstays of guideline-based medical therapy (GDMT).[4] Decisions to initiate, continue, switch, or withdraw HFrEF medications during a hospitalisation for AHF are complex, often based on multiple factors and at the discretion of the treating physician.[45] However, clinical treatment guidelines, hospital performance measures, and ongoing quality improvement initiatives all strongly emphasize prescription of these medications by time of hospital discharge,[4,46] as it showed association with improved outcomes.[47] Since randomised data for GDMT in patients ≥ 80 years old are scarce, observational data represent the main lines of evidence supporting similar treatment benefits in older patients with HFrEF.[48] Generally, target doses for GDMT should be attempted in older patients, with close surveillance for any adverse drug reactions; however, the pharmacokinetic profile for GDMT as a function of age is not known, and higher risks of adverse events have been described in older populations.[49] Accordingly, optimal doses for older patients may be lower than those studied in trials or tolerated in younger patients. As we stated before, QoL is of primary importance in this population, and it comes before mere long-term prognosis. As such, decisions regarding up-titration of GDMT should be discussed with patient and their environment and be made in a holistic context. In frail patients, guidelines suggest to up-titrate GDMT only if symptomatic, to consider reducing dose of beta-blockers if fatigue is an issue, and to avoid hypotension that may exacerbate risk of falls at home.[50]

Non-pharmacological Treatment

Acute heart failure is often combined with respiratory failure due to pulmonary oedema. In case of increased work of breathing or pulse oxygen saturation below 90%, oxygen therapy is indicated.[4] Non-invasive ventilation is also often used, especially in case of more severe respiratory failure (high respiratory rate despite oxygen therapy, hypercapnia or severe hypoxemia). Non-invasive ventilation does not only treat respiratory failure, but by decreasing preload and afterload it can improves the hemodynamic status in patients with AHF.[51] High-flow nasal cannula can be used as an alternative but cannot treat hypercapnia in contrast to non-invasive ventilation. Given its non-invasive nature and the often only short term necessity of its use, non-invasive ventilation and high-flow nasal cannula are good options to treat more severe respiratory failure in the elderly and might help to avoid invasive mechanical ventilation.[52,53] However, in some non-invasive strategies can fail. In these cases, the decision to initiate invasive mechanical ventilation should be judged carefully, according to the condition and wishes of each individual patient.

Ultrafiltration is a technology that allows isotonic fluid removal from the blood compartment in a controlled continuous way. This is in contrast with loop diuretics that remove hypotonic fluid and have a peak response and subsequent drop in urine output, when given as a bolus. Despite its advantages, ultrafiltration did not result in a better decongestion in patients with worsening HF and a median age of 69 years in the Cardiorenal Rescue Study in Acute Decompensated Heart Failure (CARRESS-HF) trial.[54] Guidelines recommend to reserve ultrafiltration for patients with refractory congestion, with insufficient response to diuretics and to use renal replacement therapy in case of combination with acute kidney injury.[4]

Precipitating Causes and Underlying Disease

Besides the acute treatment of respiratory failure and/or volume overload, it is important to look for and treat precipitating factors. AHF occurs in a subject with an underlying disease entity and is often triggered by a dislodging event. Common triggers for AHF are cardiac arrhythmia (40%, that in the elderly are often underestimated and misdiagnosed),[55] ischemia (30%), infections (20%), hypertension (16.5%), anaemia (15.7%) and therapy incompliance (5.8%).[56] These triggers should be iden-

tified and treated to avoid recurrence of the AHF event.

Specific Treatments in the Elderly

Due to their higher burden of comorbidities and higher frailty, elderly patients often face specific problems that are not common in other patient populations (Table 2).

Polypharmacy

Older adults with HF contend with multiple chronic conditions which contribute to a high medication burden in addition to HF itself.[57,58] Polypharmacy, most commonly defined as use of ≥ 5 medications daily,[59] is associated with several adverse outcomes, such as falls,[60] disability,[61] and hospitalisations.[62] In a recent multicentre study in the US on patients with HF, the vast majority of participants (84% at admission and 95% at discharge) had more than five medications, and 42% at admission and 55% at discharge more than 10.[57]

Particular attention should be paid to (1) medications that could exacerbate HF (e.g., NSAIDs, verapamil, diltiazem, thiazolidinediones);[63,64] (2) long-term use of no longer indicated medications (e.g., antibiotics); and (3) unnecessary medications and/or herbal supplements.[65] For example, proton pump inhibitors (PPI) is the most frequently prescribed non-cardiovascular medication overall and often without a mandatory indication.[57] In cardiovascular patients, indications of long-term PPI is often the reduction of gastrointestinal bleeding risk in the setting of antiplatelet or anticoagulant therapy.[66] In absence of strict long-term indication, PPI should be stopped, since a prolonged use is associated with osteoporotic fractures, vitamin B12 deficiency, pneumonia, Clostridium difficile infection, kidney disease, and dementia.[67]

Deprescribing can improve clinical care and enhance QoL in older adults.[68] Thus, AHF hospitalisation should be seen as an opportunity to review the whole pharmacological therapy of the patient and eventually stop dangerous or unnecessary drugs.[69,70] A stepwise approach and the use of specific tools (e.g., the STOPP/START criteria) can facilitate the process.[68,69]

Psychiatric diseases and delirium

Psychiatric conditions such as anxiety, depression, cognitive impairment and dementia are common in elderly patients with HF and are related to worse clinical outcomes.[71] Delirium, an acute confusional state evident as inattention and global cognitive dysfunction, has been reported in 17%–35% of patients admitted with AHF, and associated with worsening HF during hospitalisation, increased length of stay and readmission rates, and greater short and long-term mortality.[72,73] Therefore, it is important to immediately institute preventive measures, such as good orientation of the patient with clocks and calendars, sufficient cognitive stimulation, and avoiding unnecessary procedures or catheters. In selected patients, use of antipsychotic agents such as haloperidol can be considered with careful monitoring of the electrocardiogram, as these can prolong the QT-interval.

Table 2 Common challenges in treating elderly patients with acute heart failure.

Specific issues	Potential causes	Potential solutions
Hypotension	Nitrates Large volume shifts	Low dose nitrates only in selected patients Single LD boluses or continuous infusion Stop antihypertensives without benefit in HF
Polypharmacy	Multiple comorbidities Harmful drugs Unnecessary drugs	Accurate checking of medications Deprescribing
Delirium	Bladder catheter Sedatives Electrolyte disturbances Immobilisation ICU admission Non-invasive ventilation	Avoid bladder catheter Careful use of sedatives Diagnose and treat electrolyte disturbances Early mobilisation Carefully weigh risk vs. benefits regarding ICU admission and non-invasive ventilation Use specific anti-psychotics in selected patients
Sarcopenia, cachexia, frailty	Chronic HF Multiple comorbidities Immobilisation Malnutrition	Optimise HF therapy Treat comorbidities accordingly Early mobilisation and exercise Nutritional advice, supplementation

HF: heart failure; ICU: intensive care unit; LD: loop diuretics.

Sarcopenia, cachexia and frailty

The imbalance between anabolic and catabolic state in HF often exacerbates the decline in muscle mass and strength, favouring the occurrence of sarcopenia and cachexia.[74] In particular, respiratory muscle weakness can contribute to persisting dyspnoea in these patients.[75] Cachexia is often present in patients with advanced HF and it might result in a loss of plasma proteins, reducing plasma oncotic pressure, hampering plasma refilling from the interstitium, thus complicating the maintenance of a euvolemic state.[76] So far, no drug therapy has been shown to reverse either sarcopenia or cachexia complicating HF. Exercise training programs have shown beneficial effects in limiting muscle loss,[77] and nutritional supplementation may also be helpful.[78]

Frailty is considered a state of increased vulnerability to endogenous and exogenous stressors, due to age-related declines in physiologic reserve and function across multiple physiologic systems.[40] Patients with HF are up to six times more likely to be frail, especially patients with HFpEF; this is possibly related to the greater burden of cardiac and non-cardiac comorbidities in HFpEF.[79] Frailty accelerates the progression of HF, contributes to a higher risk of mortality, increased HF hospitalisations with longer hospital stay, and a decreased 10-year survival.[80] Although frailty can be experienced also by younger (< 60 years) patients with HF, its prevalence increases with age. The recognition of frailty is the first step for an accurate risk stratification and planning a tailored therapeutic plan and an early discharge, also to avoid delays in referral to rehabilitation if needed.[81]A multimodal approach aimed at improving appetite, reducing the inflammatory response, provision of additional calories, and exercise training to improve exercise capacity and QoL is a potential therapeutic strategy both in frailty and sarcopenia/cachexia.[82] Thus, a multidisciplinary rehabilitation program can be of specific benefit and in some, it can be necessary to include patients in a longer-term rehabilitation unit after the AHF event has been treated.[23]

Management of Arrhythmias and Device Therapy

AF represent a common trigger of AHF and is present in around 40% of all patients admitted with AHF.[56] In the elderly, AF is the most common arrhythmia and may lead to a significant LV dysfunction and worse outcomes,[83] especially the setting of AHF in which AF is associated with longer hospitalisation, higher rehospitalisation rate and mortality at 30 days.[84,85] According to European Guidelines,[86] prompt restoration of sinus rhythm is highly recommended when tachycardiomyopathy is suspected, regardless of patients symptoms, to reverse LV dysfunction in AF patients. Specifically, catheter ablation (CA) is known to be an effective first-line rhythm control strategy to improve outcomes and induce LV function improvement for isthmus-dependent atrial flutter, which is a rare but well-established cause of tachycardiomyopathy in the elderly, leading to AHF.[87] As for AF, latest evidence advocate the same role for CA in tachycardiomyopathy setting as a class I recommendation.[86]

Instead, when AF triggers or aggravates pre-existing HF, different strategies may be used to control ventricular rate or restore sinus rhythm. In common clinical practice, rate control is usually preferred over rhythm control in the elderly,[88,89] also since they are often unsuitable for CA, thereby limiting the available options to achieve durable sinus rhythm. In general, beta-blockers and diltiazem/verapamil are preferred over digoxin due of their rapid onset of action and their better safety profile in the elderly with AF, but care should be taken in the AHF setting and in case of reduced EF, since verapamil/diltiazem are contraindicated. In AF patients presenting with marked congestion and pulmonary edema, initial treatment with digoxin or amiodarone might be preferred to control heart rate.[90] In the elderly, a decreased volume of digoxin distribution and an age-related worsening of renal function may contribute to increase the incidence of digoxin toxicity. Nevertheless, digoxin toxicity more often occurs in case of a chronic use of this drug, still causing a significant number of emergency department and subsequent rehospitalisations.[91] Thus, while the short-term use of digoxin in AHF is supported by European guidelines[92] in case of new-onset rapid AF and appears safe in a controlled environment (e.g., ICU), a revaluation of home-therapy after the resolution of the acute event is required. If AF triggers hemodynamic compromise, urgent electrical cardioversion is recommended to restore sinus rhythm. In all other cases, rhythm control strategies should preferentially involve amiodarone over flecainide or propafenone that are not recommended when LV function is reduced.

In elderly patients with HFrEF, there is a recog-

nised role for atrioventricular (AV) node ablation with cardiac resynchronisation therapy (CRT), especially if medical therapy fails, and neither rhythm nor rate control is achievable with beta-blockers, CA with or without amiodarone[93] and other drugs. As highlighted in a randomised trial and its relative follow-up,[94,95] *ablate-and-pace* strategy has been shown to improve QoL with respect to medical therapy in patients with a median age of 74 ± 7.5 years. Besides QoL, this strategy may also improve ventricular function, exercise duration, and healthcare use.[96] In particular, AV junctional ablation may provide the greatest benefit in the elderly with HFrEF and AF with uncontrolled ventricular rates, which do not represent good candidates for catheter ablation or may have undergone failed previous ablation attempts. This benefit is also maintained in patients with HFrEF and QRS ≤ 110 ms, as described in the APAF-CRT trial,[97] which found this strategy to be superior to medical therapy in improving QoL and reducing HF hospitalisation among elderly patients with permanent AF. In case of first diagnosed AF during the AHF hospitalisation, starting and managing oral anticoagulant (OAC) therapy in geriatric patients is not as straightforward as in the young, due to the higher risk of bleeding, related to comorbidities and the potential risk of falls. Thus, older patients are unlikely to always receive OACs,[98] with the lowest rates recorded among frail elderly[99] or older patients with major comorbidities. Nevertheless, several randomised trials and meta-analyses have shown that the use of OACs is supported in these patients,[100,101] even if their role has been questioned after successful CA,[102] thereby advocating an even more important role of this procedure in the elderly. It should also be underlined that a non-justified dose reduction might be less effective[103] and that avoiding OACs in older patients having a higher risk of falls is not reasonable.[104] Besides stroke prevention, OACs have shown a benefit against dementia, preserving progressive cognitive impairment among old patients with AF.[105,106]

Finally, ventricular arrhythmias and rarely bradyarrhythmias may be associated with AHF in the elderly. In all cases, ischemic etiology should be excluded and a thorough electrocardiographic and echocardiographic assessment evaluating intraventricular conduction and LVEF should be made, in order to choose the most appropriate device therapy. As reported in a large European survey,[107] up to 63.5% of Centers involved reported to have no age limits for CA, which is known to be particularly beneficial in treating selected patients with monomorphic ventricular tachycardia. As for drug therapy, beta-blockers should be preferred to amiodarone, since the latter has not shown to decrease mortality in elderly patients with HF and ventricular arrythmias, as well as having a wider spectrum of side effects.[108]

Palliative Care and Ethical Challenges

Throughout the chronic HF trajectory, AHF hospitalisations represent inflection points with a negative impact on general prognosis and, if clustered, may indicate the terminal phase of the disease. Furthermore, the stressors of the acute care environment can exacerbate physical and psychological impairments and lead to further declines in QoL. Thus, in geriatric patients presenting with AHF and clinical characteristics of poor prognosis,[109] palliative care (PC) should be considered at an early stage, in order to avoid unnecessary and harmful diagnostics and treatments. PC is usually provided by an interdisciplinary team, with the aims of relieving symptoms, particularly pain and dyspnoea, and offering psychological support to patients and caregivers to improve QoL.[110]

Hospital admission has been specifically cited as an opportunity to integrate PC, but incorporating PC as standard care in patients with AHF remains difficult. Involvement of PC during an unplanned hospitalisation is exceptional, being documented at only 3%-4% of patients admitted with AHF, increasing to 7.3% following readmission.[111,112] A major issue for physicians to consider PC in AHF is the prognostication of the HF trajectory. Although multivariate risk scores for AHF populations have been developed,[26,113,114] these are not validated in selected elderly population, thus prognostic judgment on the single patient remains challenging. Importantly, early transfer to a dedicated palliative care unit and delivery of the appropriate symptomatic treatment are associated with improved patient and family satisfaction. As showed by a recent review, the topics emerging as determinants of a "good death" in HF patients were effective communication between patients, families and healthcare providers, good clinical navigation through the terminal phase, avoidance of futile invasive interventions,

good symptom control, timely access to specialist PC, and achieving the preferred place of care and death.[115]

Optimising care at the end of life requires re-examination of the utility of previously prescribed medication and any implanted device therapy, the benefits or burdens of invasive measures to support hydration or nutrition, and the appropriateness of intensive care.[116] Switching to PC in patients with HFrEF does not automatically imply the discontinuation of GDMT. On the contrary, GDMT helps maintain ventricular function, renal function, blood pressure targets, reducing dyspnoea, arrhythmias and risk of symptomatic deterioration. However, down-titration of GDMT in case of adverse effects (e.g., symptomatic hypotension), as well as deprescription of long-prescribed drugs (e.g., statins) may be reasonable.[68] Patients with advanced HF may receive continuous inotropic therapy as a form of palliation.[117] While inotropes can be administered at home, this may be impractical for some, obliging them to stay in hospital, and this therapy may be disallowed in those transitioning to hospice care.[116] Finally, in patients with an implantable cardioverter-defibrillator, device deactivation should be considered.[118]

In summary, physician treating elderly patients with AHF should assess need for PC plan already in the first phases of hospitalisation, eventually referring the patient to the specialist after discharge to revaluate treatment goals, symptom control, and to discuss with the patient and their family further planning of care.

FOLLOW-UP AND REHABILITATION

Outpatient Clinic

The days that immediately follow discharge are a vulnerable period due to the addition of therapies or changes to existing medical therapy that may worsen clinical status, especially in individuals with more comorbidities and frailty as the elderly. In these patients, a rapid up-titration of GDMT during the days of hospitalisation for AHF is challenging and often not possible, because of higher incidence of hypotension and low tolerability.[119] For this reason, a strict follow-up plan should be organised when the patient is still hospitalised, including a first ambulatory visit in the first 5–7 days, or earlier in case of advanced HF, for volume assessment and eventually optimisation of oral loop diuretics and GDMT.[4,120] Moreover, the first follow-up visit is also an opportunity to reassess the patient's functional status, QoL, therapy adherence, and to discuss with the patient and their environment about future treatment goals.[120] Importantly, early follow-up visits after discharge for AHF is associated with a lower risk of 30-day readmissions.[121]

Telemedicine

Out-of-hospital care and follow-up might also be provided through a structured telemedicine program.[122] Telemonitoring studies have used various interventions, such as telephone consultations with medical providers, recording of vital signs (via implantable or non-invasive sensors) with results collected at a central monitoring station, and video consultations.[122] Especially during the actual Coronavirus Disease 2019 (COVID-19) pandemic, which has seen a dramatic reduction of HF hospitalizations,[123] in order to keep HF patients safe from infection risk and equally continuing with strict monitoring and follow-up, various strategies of telemedicine and remote monitoring were developed rapidly and implemented widely.[124] This strategy has been of the outmost importance during the pandemic, since several links between COVID-19, cardiovascular diseases and hypercoagulability have been highlighted,[125–128] and the elderly themselves with a higher number of comorbidities, were at the highest risk of developing myocardial involvement and acute hypoxemic respiratory failure, often triggering AHF. Due to the critical care and medical ward increasing demand during COVID-19 outbreak, that forced clinician to home-manage a relevant number of patients, telemonitoring offered a reliable way to monitor home-treated patients, that were often managed with QT-prolonging drugs (i.e., hydroxychloroquine and/or azithromycin[129,130]), potentially leading to serious cardiovascular consequences, such as cardiac arrhythmias.[131] This experience demonstrated that targeting telemedicine to the elderly could therefore be useful, but also a great challenge, since older patients may be unable to utilise the required devices because of poor hearing, cognitive dysfunction or poor technology expertise.[124,132] Thus, physicians and healthcare providers should tailor telemedicine to the single patient, exploring different modal-

ities such as telephone support, videocalls, device-based or app-based monitoring.[133,134] The choice should be based on the patient's preferences and their helping environment, knowing that they may require the assistance of a family member or caregiver.[124,134]

Rehabilitation

Exercise-based cardiac rehabilitation (CR) is recommended by HF guidelines to improve exercise capacity and to reduce the frequency of hospital readmission.[4,135,136] Moreover, exercise training has shown benefits also in specific issues that are peculiar in the elderly, such as QoL, depression, sarcopenia, and frailty.[77,137–140]Applying CR to older adults is often limited by issues of access, the specific needs of vulnerable patients, and common comorbidities that further reduce exercise capacity (i.e., cerebrovascular and peripheral artery disease, diabetes, musculoskeletal disorders, renal and pulmonary disease, and cognitive dysfunction).[141,142] As a result, utilisation of CR continues to remain low (< 10%) in the older population after AHF hospitalisation.[143,144] A recent study on Japanese elderly patients showed that eGFR at hospitalisation and walking level before hospitalisation are independent factors delaying patient progress in early rehabilitation.[145] More evidence will be available after completion of the ongoing Rehabilitation Therapy in Older Acute Heart Failure Patients (REHAB-HF) trial, designed to assess the utility of exercise therapy after AHF hospitalisation among older adults.[146]

CONCLUSION

Elderly patients carry a higher burden of comorbidities, frailty, polytherapy, and special needs. Although the overall AHF management guidelines also apply to these patients, a tailored approach should be pursued (Figure 2), starting from the first

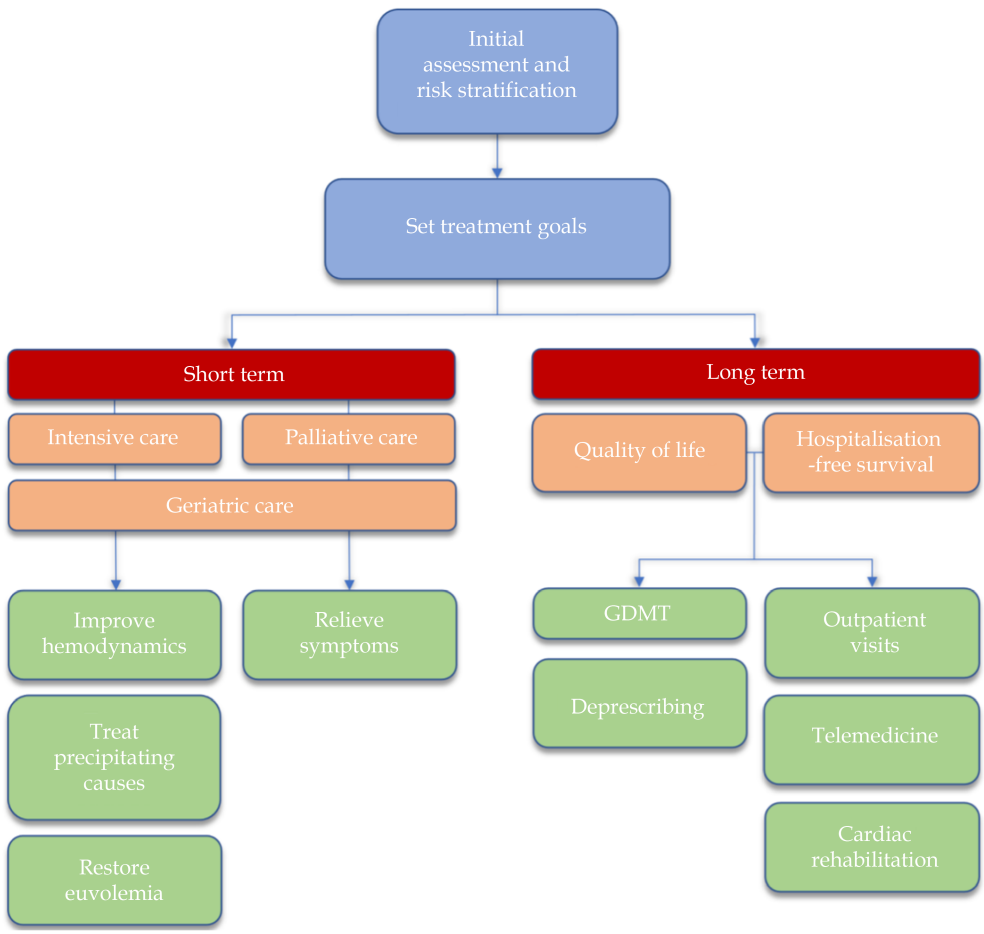

Figure 2 Decision making in the management of elderly patients with AHF. AHF: acute heart failure; GDMT: guideline-based medical therapy.

presentation in the emergency department, through a specific risk assessment and the setting of treatment goals. Thereafter, invasive and non-invasive management should be provided accordingly. In selected patients with poor prognosis, the early discussion of a palliative care path is recommended, always involving the patient and their environment in treatment decisions. An accurate planning on follow-up visits and/or the referral to a CR should be provided at discharge. The final goal is to reduce as much as possible the disease burden and to increase the patients' quality of life.

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