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# **2023 SFMU/GICC-SFC/SFGG expert recommendations for the emergency management of older patients with acute heart failure. Part 2: Therapeutics, pathway of care and ethics**

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## **.1 Abbreviations**

ACE angiotensin-converting enzyme; AHF acute heart failure; ARB angiotensin II receptor blocker; ARNI angiotensin receptor-neprilysin inhibitor; CI confidence interval; ED emergency department; ESC European Society of Cardiology; GRADE Grading of Recommendations Assessment, Development and Evaluation; HFrEF heart failure with reduced ejection fraction; HR hazard ratio; MRA mineralocorticoid receptor antagonist; NIV non-invasive ventilation; NSTACS non-ST-segment elevation acute coronary syndrome; eOR odds ratio; RR risk ratio; SBP systolic blood pressure SGLT2 sodium-glucose cotransporter-2 ; SpO<sub>2</sub> oxygen saturation

## **2. Background**

Acute heart failure (AHF) is a complex, multifactorial, syndromic condition with various therapeutic options in the emergency setting and during the hospital stay [1,2]. Managing older patients with AHF involves several critical steps, including therapeutic interventions, pathway of care and ethical considerations [3]. Rapid diagnosis through symptoms such as dyspnoea, orthopnoea and oedema, initial assessment of symptoms and stabilization of major vital functions are the keys to therapeutic management [1–3]. Medical interventions include diuretics to relieve congestion and achieve optimal fluid status to manage fluid overload [4], vaso-dilators for patients with hypertension-induced AHF to reduce cardiac workload and non-invasive ventilation in patients with respiratory failure [5]. In addition, pharmacological treatments may include inotropic agents for patients with low cardiac output [1,2]. In older patients with AHF, the pathway of care often starts in the emergency department (ED) [6]. AHF management includes risk stratification to assess severity and co-morbidities, to determine the appropriate level of care, and early therapeutic intervention to initiate guideline-directed medical therapies before discharge from the ED [3,6]. After hospital admission, there is monitoring of vital signs, fluid balance and response to treatment. A multidisciplinary approach, involving cardiologists, geriatricians and other specialists, ensures close follow-up to prepare post discharge care and prevent rehospitalization [6,7]. Managing older patients with AHF requires a comprehensive approach that integrates rapid therapeutic interventions, a structured pathway of care and ethical considerations to ensure the best possible outcomes. Furthermore, it requires balancing of aggressive treatment with the patient's quality of life, and consideration of palliative care options when appropriate [1, 2, 6,7]. Indeed, resource allocation involves making ethical decisions regarding the use of limited resources, especially in emergency settings. Physicians and caregivers involved in the pathway of care should educate patients and caregivers on medication adherence and lifestyle modifications [7]. Ethical considerations should ensure that patients understand their condition and treatment options by informed consent, to respect patient autonomy in decision-making.

## **3. Methods**

A group of 29 experts from the Société française de médecine d'urgence (SFMU; French Society of Emergency Medicine), the Groupe insuffisance cardiaque et cardiomyopathies de la

Société française de cardiologie (GICC-SFC; Group of Heart Failure and Cardiomyopathy of the French Society of Cardiology) and the Société française de gériatrie et gérontologie (SFGG; French Society of Geriatrics and Gerontology) was convened (Appendix 1). The main objective of the expert panel was to provide recommendations on the emergency management of AHF in older patients (aged > 75 years). The authors used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method to assess the level of evidence in the literature, with grading from “No recommendation” to “Expert opinion” to “Moderate recommendation (G1)” and “Strong recommendation (G2)”, and with level of evidence scaling from “Low (-)” to “High (+)” [8]. The potential drawbacks of making strong recommendations in the presence of only low-level evidence were highlighted, and some recommendations with insufficient evidence were not graded. Five areas were discussed: prehospital management, diagnosis of AHF, therapeutics, pathway of care, and ethics, of which the last three are included herein. For each area, the expert panel formulated questions according to the population, intervention, comparison, outcomes (PICO) model, and an extensive literature search was performed [9]. The analysis of the literature and the formulation of recommendations were conducted according to the GRADE method [8].

## **4. Therapeutics in older patients with AHF**

### **4.1. Question 1**

In older patients with AHF, does a low-dose bolus of diuretic reduce the length of hospital stay or symptomatology on discharge from the ED?

#### **4.1.1. Rationale**

For 40 years, loop diuretics have been one of the key treatments for AHF. However, the effectiveness and benefit of diuretics are not clearly established in the older population, as no substantial study has been performed exclusively in this patient subgroup with AHF [1]. Nevertheless, the DOSE study compared high-dose diuretic therapy (2.5 times the daily dose) with low-dose therapy (daily dose equivalent) in hospitalized patients with AHF with a mean age of 66 years, and showed no difference between the two modalities in terms of the primary endpoint [10]. Recommendations published in 2019 by the Heart Failure Association of the European Society of Cardiology (ESC) propose a pragmatic approach, by giving an intravenous dose similar to the usual daily dose taken orally if the patients with AHF is already being treated with furosemide, or 20–40 mg intravenously if the patient is furosemide naïve. The diuretic dose is adjusted every 6 h according to diuresis, until decongestion is achieved. Diuresis > 100–150 mL/hour is considered satisfactory. For patients on long-term diuretic therapy, the initial dose is the equivalent of their daily dosage [11]. The maximum dose of furosemide not to be exceeded in 24 h is generally 400–600 mg, i.e. 100–150 mg every 6 h. However, in cases of renal insufficiency or diuretic resistance, up to 1000 mg may be administered intravenously over 24 h, and other diuretics (hydrochlorothiazide, spironolactone, acetazolamide, sodium-glucose cotransporter-2 [SGLT2] inhibitors or bumetanide) may be combined [1,12,13].

#### **4.1.2. Experts' answer**

Furosemide should be administered as an intravenous bolus in the event of congestion in older patients with AHF in the emergency setting, with the dosage adapted to the presence or absence of long-term diuretic treatment.

#### **4.1.3. Grade**

G1+.

### **4.2. Question 2**

In older patients with AHF, does continuous intravenous infusion of diuretics during the first 48 h reduce the length of hospital stay or improve symptoms on discharge from the ED?

#### **4.2.1. Rationale**

There are no specific data about the effectiveness and benefit of diuretic administration in the first 48 h in the older population, as no specific evaluation has been done in this subgroup of patients with AHF. However, the DOSE study compared continuous infusion and repeated boluses of furosemide every 12 h in patients hospitalized for AHF (mean age 66 years). In this trial, continuous infusion offered no benefit compared with repeated boluses (area under the curve for global visual analogue scale [VAS] score  $4236 \pm 1440$  vs  $4373 \pm 1404$ , respectively;  $P = 0.47$ ) [10].

#### **4.2.2. Experts' answer**

It is probably advisable to use an intravenous bolus rather than continuous infusion of furosemide in the older patient with AHF, with repeated doses every 6 h.

#### **4.2.3. Grade**

G2+

### **4.3. Question 3**

Does bolus administration of nitrates in the ED improve morbidity in older patients with AHF?

### 4.3.1. Rationale

Studies are discordant on the usefulness of nitrates in the medium-to-long term, and there are very few studies in AHF comparing bolus administration of nitrates with continuous intravenous administration in the emergency setting [14–16]. Still, according to the ESC recommendations, the use of nitrates can be considered in patients with AHF with a systolic blood pressure (SBP)  $\geq 110$  mmHg (Grade IIb) [1, 2]. Moreover, compared with the actual guidelines' recommendations, nitrates are underused in the ED in AHF (around 30%) [17, 18]. However, in compliance with the ESC guidelines' recommended therapies, a French multicentre study by Freund et al., carried out in older patients with AHF in the ED found no significant difference compared with standard management in terms of overall mortality, cardiovascular mortality, readmission, median length of stay or renal dysfunction [19]. A 2013 Cochrane meta-analysis found no effect on speed of symptom improvement (mean fixed-effect difference at 1 hour  $-0.20$ , 95% confidence interval [CI]  $-0.65$  to  $0.25$ ). However, the studies analysed included different populations, which may have included patients with ischaemic heart disease [20]. A multicentre registry of 8863 patients in cardiac intensive care by Shiraishi et al. found no significant difference in in-hospital mortality (7.5% with nitrates vs 8.8% without nitrates;  $P = 0.098$ ), intensive care unit length of stay or length of hospital stay [21]. Nevertheless, more recently, a post-hoc analysis of a prospective multicentre registry showed that the use of nitrates with a target SBP reduction of  $< 25\%$  was associated with a better diuretic response and lower mortality (adjusted hazard ratio [HR]  $0.74$ , 95% CI  $0.57$ – $0.96$ ) compared with the absence of vasodilators or the use of nitrates with a target SBP reduction  $> 25\%$  [16]. Nitrates also appeared to be more effective in patients with elevated SBP ( $> 180$  mmHg; odds ratio [OR]  $0.25$ , 95% CI  $0.10$ – $0.75$ ) and in patients without atrial fibrillation on the admission electrocardiogram (OR  $0.70$ , 95% CI  $0.60$ – $0.90$ ) [21].

The ESC guidelines propose continuing intravenous titration until clinical improvement and blood pressure control are achieved [1, 2]. Indeed, regarding the method of administration, in small cohort studies, the use of a bolus appears safer than continuous infusion, with no significant difference in mortality, but a difference in the occurrence of myocardial infarction in the first 24 h after admission and in the use of mechanical ventilation [14,15]. A larger registry study comparing bolus, continuous infusion and a combination of the two found a reduction in length of hospital stay and intensive care unit admission in the bolus group [16]. These treatments administered in intravenous boluses are well tolerated, even at high doses [22]. In a retrospective study of 136 older patients in the emergency setting, there was no more hypotension in the group treated with bolus nitrates than in the group not treated with nitrates [23]. Nitrates are also well tolerated in patients with severe aortic stenosis [24].

### 4.3.2. Experts' answer

It is probably advisable to give preference to bolus administration of nitrates in older patients with AHF with SBP  $> 110$  mmHg in the ED.

### **4.3.3. Grade**

G2+.

## **4.4. Question 4**

Does the use of opiates reduce morbidity and mortality in the older patient with AHF?

### **4.4.1. Rationale**

Morphine has been proposed for the symptomatic treatment of pain and dyspnoea in AHF, and was still listed as Class II Grade B in the 2016 ESC guidelines [2], but was no longer recommended in the 2021 guidelines [1]. Cohort studies show conflicting results in terms of mortality, improvement in dyspnoea and use of mechanical ventilation. In an ancillary study of 1052 patients with AHF, Gray et al. found no difference in mortality or improvement in respiratory distress in the 541 patients treated with morphine [25]. The same was true of a multivariable propensity score analysis in a cohort of 2336 patients [26]. By contrast, Caspi et al. demonstrated an increased risk of mortality (OR 1.43, 95% CI 1.05–1.98), use of non-invasive positive pressure ventilation (OR 2.78, 95% CI 1.95–3.96) and acute renal failure (OR 1.81, 95% CI 1.39–2.36) [27]. This morphine-related excess mortality risk was also found in a retrospective analysis of 147,000 patients (13% vs 2.4%) [28], and in another cohort of 6516 patients for 30-day mortality [29]. Recent literature reviews and meta-analyses have also found conflicting results on short- and long-term mortality, as well as on the use of mechanical ventilation. However, these meta-analyses are based on studies with low levels of evidence, or even unpublished studies [30–32]. Taken together, these data underline the absence of randomized controlled trials to answer the question posed. The results, although sometimes discordant, tend to show an unfavourable association between morphine use and prognosis [33].

### **4.4.2. Experts' answer**

Morphine should probably not be used for the specific therapeutic management of AHF in older patients.

### **4.4.3. Grade**

G2–.

## 4.5. Question 5

In older patients with AHF, does stopping beta-blockers at the initial management stage reduce morbidity and mortality?

### 4.5.1. Rationale

A meta-analysis published in 2015 by Prins et al. (n = 3143), incorporating five observational studies and one randomized trial, favours the continuation of beta-blocker therapy in patients hospitalized for AHF; two of these studies showed a significant increase in the risk of in-hospital mortality (OR 3.72, 95% CI 1.51–9.14), whereas four showed a reduction in a composite criterion combining early mortality and readmission (OR 1.59, 95% CI 1.03–2.45) [34]. More recently, Mirò et al. published a prospective observational study from a Spanish multicentre registry (1990 patients with a mean age of 78.1 years), showing a significant rise in in-hospital and 30-day mortality in the group of patients with discontinuation of beta-blocker therapy (OR 1.89, 95% CI 1.09–3.26 and OR 2.01, 95% CI 1.28–3.15, respectively) [35]. In addition, a Japanese registry study published in 2021 confirmed these findings in a population of the elderly with a mean age of 81 (interquartile range 72–86) years, specifying that patients receiving beta-blocker treatment on admission to hospital for AHF, compared with those not receiving treatment on admission, had a lower incidence of early cardiac or all-cause mortality [36]. Finally, using a prospective multicentre registry (n = 5005), Abi Khalil et al. confirmed the beneficial effect on early mortality of continuing beta-blocker treatment during hospitalization. However, the effects on medium-term mortality (at 3 and 12 months) and on the risk of in-hospital readmission were not demonstrated [37].

### 4.5.2. Experts' answer

Beta-blockers should probably not be discontinued in older patients admitted to the ED for AHF with heart failure with reduced ejection fraction (HFrEF). If this treatment needs to be suspended (i.e. bradycardia, low output, etc.), it should be resumed before the patient is discharged.

### 4.5.3. Grade

G2–.

## 4.6. Question 6

In older patients with AHF, does discontinuing angiotensin-converting enzyme (ACE) inhibitors/angiotensin II receptor blockers (ARBs) during initial management in the ED reduce morbidity and mortality?

### 4.6.1. Rationale

In the aftermath of an AHF episode, the question arises as to the effectiveness on morbidity and mortality of the early introduction of heart failure disease-modifying therapies, particularly in the older patient, where management is often suboptimal [38].

ACE inhibitors or ARBs are well established as beneficial long-term treatments in older patients with HFrEF, improving survival and reducing the risk of hospitalization for AHF [39]. In addition, numerous studies have shown that initiation or resumption of ACE inhibitor/ARB therapy before hospital discharge is associated with better short- and long-term survival, and with a lower risk of rehospitalization [40]. However, no high-level studies have evaluated the effect of interrupting ACE inhibitors/ARBs in AHF on short- or long-term morbidity and mortality. In an observational study, based on the GWTG-HF multicentre registry (n = 16,052; mean age  $78.3 \pm 7$  years), Gilstrap et al. showed a lower 30-day mortality in patients with HFrEF hospitalized for AHF if ACE inhibitor/ARB treatment was continued at discharge (3.5%) compared with discontinuation of treatment (8.8%) [40]. In addition, adjusted survival analysis showed a significantly raised risk of mortality in patients whose ACE inhibitor/ARB therapy was discontinued (HR 1.92, 95% CI 1.32–2.81;  $P < 0.001$ ). Moreover, the hospital readmission rate at 30 days and the 1-year mortality rate were raised significantly in patients whose ACE inhibitor/ARB therapy had been discontinued. Similarly, a study by Sanam et al. (477 propensity-matched patient pairs; mean age  $76 \pm 10$  years) found a lower readmission rate and lower 30-day and 1-year mortality rates for patients who received an introduction of an ACE inhibitor/ARB during hospitalization, compared with those who did not (HR 0.74, 95% CI 0.56–0.97; HR 0.56, 95% CI 0.33–0.98; and HR 0.77, 95% CI 0.62–0.96, respectively) [41]. In-hospital mortality was also lower in patients receiving ACE inhibitor/ARB therapy in a retrospective study by Iglesias et al. [42]. In a retrospective study of 174 relatively young patients, Kane et al. showed that the length of hospital stay for patients who received a continuation/increase of ACE inhibitor/ARB treatment (mean age  $66 \pm 13$  years) was shorter than that for patients for whom a suspension/decrease was proposed (mean age  $62 \pm 13$  years) ( $P = 0.009$ ). Still, the 30-day readmission rate did not differ between groups. In this study, the main reasons for suspension/diminution of ACE inhibitor/ARB therapy were acute renal failure (56.7%), hypotension (23.3%) or hyperkalaemia (10%) [43]. In a post-hoc analysis of a prospective

cohort (n = 900; mean age  $74 \pm 14$  years), Yoshioka et al. showed that the introduction of ACE inhibitors/ARBs within the first 48 h of hospitalization for AHF was associated with lower 1-year mortality (HR 1.99, 95% CI 1.11–3.56), without raising in-hospital mortality or length of hospital stay, and without worsening renal function [44]. Finally, in a retrospective study of the subpopulation of patients with AHF and type 1 cardio-renal syndrome (with a mean age of  $66.3 \pm 12.6$  years), Ilges et al. found no difference in in-hospital mortality, length of hospital stay or change in creatinine concentrations between patients who continued or stopped ACE inhibitors/ARBs [45]. Despite this, another study showed that patients with AHF associated with renal failure (with a mean age of  $68.9 \pm 11.2$  and  $69.7 \pm 10.8$  years in patients who continued or stopped ACE inhibitors/ARBs, respectively) were less likely to receive ACE inhibitor/ARB therapy, whereas the 30-day readmission rate and 1-year mortality were significantly improved when these therapies were continued in the event of hospitalization [46].

#### **4.6.2. Experts' answer 1**

It is probably advisable not to discontinue ACE inhibitors or ARBs in older patients admitted to the ED with AHF.

#### **4.6.3. Grade**

G2–.

#### **4.6.4. Experts' answer 2**

The experts suggest early resumption of ACE inhibitor/ARB therapy (ideally within the first 48 h, and at the latest before discharge from hospital) at the maximum tolerated dose if it has been suspended.

#### **4.6.5. Experts' opinion**

Strong agreement.

#### **4.7. Question 7**

In older patients who have responded to treatment for AHF, does the early introduction of ACE inhibitors/ARBs and/or beta-blocker and/or mineralocorticoid receptor antagonists (MRAs) reduce morbidity and mortality?

#### **4.7.1. Rationale**

ACE inhibitors/ARBs are the cornerstone of heart failure treatment, particularly in patients with HFrEF. However, no matter how early the initiation of these therapeutic classes in AHF, the level of evidence is low, particularly in the older population [38, 44, 47]. Although ACE inhibitors/ARBs are well established as beneficial long-term treatments in older patients with HFrEF, the lack of evidence concerning acute phase management to improve survival and reduce the risk of hospitalization for AHF is still challenging [38, 39].

MRAs are used in HFrEF. In an AHF episode, high doses of spironolactone (100 mg) offer no benefit compared with more modest doses (25 mg) [48]. Several studies have shown that the administration of an MRA is associated with a reduction in events (death, hospitalization for all causes or for congestive heart failure) in the months following hospitalization, irrespective of left ventricular ejection fraction. The only randomized study evaluating early initiation of eplerenone was inconclusive, because of a lack of statistical power [49]. Two other studies have shown that the use of an MRA is associated with a reduction in mortality in the months following hospitalization in patients with HFrEF [50,51].

The use of beta-blockers as standard therapy for congestive heart failure before hospital admission confirms a lower mortality rate in older patients with AHF [36,38]. Furthermore, beta-blockers should not be discontinued in the event of AHF (except in cases of cardiogenic shock or severe bradycardia) [52]. Despite a beneficial effect on early mortality of continuing the treatment [34–38], beta-blockers are often not introduced during hospitalization because of fear of their negative inotropic effect and of haemodynamic failure, especially in the older population [6, 7, 17, 19]. According to the current guidelines' recommendations, beta-blockers should be initiated during hospitalization in naïve patients with AHF [1, 5].

Angiotensin receptor-neprilysin inhibitors (ARNIs; e.g. sacubitril valsartan) are frequently used in symptomatic HFrEF. The only two randomized studies evaluating the use of ARNIs in patients with AHF have non-clinical endpoints. However, several observational studies have shown an association between the initiation of ARNIs and a reduction in clinical events [53,54].

Selective inhibitors of SGLT2 (e.g. gliflozins) are recent molecules that have been widely used in congestive heart failure, as they reduce cardiovascular mortality and hospitalization for AHF [55]. A very recent study confirmed the benefit of early gliflozin introduction in AHF, irrespective of left ventricular ejection fraction, the age of patients included and the level of underlying frailty, and without the occurrence of notable adverse effects [56].

#### **4.7.2. Experts' answer 1**

In HFrEF, it is recommended to introduce early during hospitalization:

- an ACE inhibitor (preferentially to an ARB);
- a beta-blocker as soon as haemodynamic stability is achieved.

#### **4.7.3. Grade**

G1+.

#### **4.7.4. Experts' answer 2**

In HFrEF, in a patient already on an ACE inhibitor/ARB, the experts suggest that in post AHF care an ARNI could be initiated early as a replacement for an ACE inhibitor or an ARB, at a minimal initial dose, with monitoring of clinical (blood pressure) and biological (renal function) tolerance.

#### **4.7.5. Experts' opinion**

Strong agreement.

#### **4.7.6. Experts' answer 3**

In heart failure with preserved ejection fraction (left ventricular ejection fraction > 40%) there is currently insufficient evidence to recommend initiation of treatment with an ACE inhibitor/ARB or a beta-blocker.

#### **4.7.7. Experts' recommendation**

None.

#### **4.7.8. Experts' answer 4**

Regardless of left ventricular ejection fraction, the experts suggest considering the early introduction of

•an MRA, at a minimal initial dose, with monitoring of clinical (blood pressure) and biological (renal function and kalaemia)tolerance;

•a selective inhibitor of SGLT2 (e.g. a gliflozin).

#### **4.7.9. Experts' opinion**

Strong agreement.

### **4.8. Question 8**

In older patients hospitalized for AHF, can the use of a urinary catheter limit urinary incontinence?

#### **4.8.1. Rationale**

There are no studies on the real benefit of precise diuresis monitoring in older patients with AHF. On the other hand, numerous studies have identified potential side effects of urinary catheterization in the general population, as urinary tract infections account for 40% of healthcare-associated infections, up to 80% of which are related to the use of urinary catheters [57]. Nevertheless, this risk is reduced in patients with AHF (HR 0.75, 95% CI 0.64–0.89;  $P < 0.001$ ) [58]. More specifically, in older patients, a 2018 retrospective study of two groups of 100 patients (aged  $73 \pm 13$  years) hospitalized in cardiac intensive care for AHF, found in the urinary catheter group a longer length of hospital stay (9 vs 7 days), more frequent intra-hospital urinary complications (haematuria, urinary symptoms, intra-hospital urinary infections) (24 vs 5%), with a risk depending on the duration of urinary catheterization (the risk increased 5-fold when catheterization lasted  $> 6$  days), and a more frequent rate of urinary infection at 1 year (17 vs 6%; HR 3.145, 95% CI 1.240–7.978;  $P < 0.05$  for all). Furthermore, there was no difference in the rate of rehospitalization at 1 month or in cardiac co-morbidity at 1 year between the two groups [59]. Another prospective observational study from 2020 ( $n = 497$ ; mean age  $79 \pm 7$  years) found that invasive procedures, such as urinary catheterization, were predictive of the onset of delirium (OR 3.965, 95% CI 1.757–8.947) [60]. The indication for urinary catheterization is based on diuresis monitoring, but other collection techniques are possible, with fewer side effects. A randomized controlled trial, involving a total of 75 older patients, looked at the side effects of urinary catheters versus penile sheaths. This study found a non-significant trend towards fewer urinary tract infections in the penile sheath group, with patients describing less pain ( $P = 0.02$ ) and greater comfort in the same group ( $P = 0.02$ ) [61].

Furthermore, in the same study, patients without cognitive disorders were almost 5 times more likely to suffer complications (asymptomatic bacteriuria, urinary tract infection or death) in the urinary catheter group than in the penile sleeve group (HR 4.84, 95%CI 1.46–16.02;  $P = 0.01$ ) [61]. Other alternatives for monitoring the efficacy of diuretic treatment may be proposed (weighing of pads, etc.), but no matter how they are assessed, we have not found any articles. Similarly, no articles were found on the risk of de novo incontinence as a consequence of inadequate catheterization. If a urinary catheter has been placed on admission, it is advisable to remove it as soon as possible to prevent the risk of infection and dysuria. A recent Cochrane review suggests that removal, preferably late in the evening, limits the risk of re-catheterization [62].

#### **4.8.2. Experts' answer**

Urinary catheters for diuresis monitoring should probably not be used in the management of older patients with AHF.

#### **4.8.3. Grade**

G2–.

### **4.9. Question 9**

In older patients hospitalized for AHF, does placing them in a wheelchair and raising them to a standing position within 48 h reduce morbidity and mortality (loss of autonomy, length of hospital stay, serious adverse events or rehospitalization)?

#### **4.9.1. Rationale**

There is no randomized trial evaluating the effectiveness of an early mobilization strategy for older people admitted to the ED with AHF. However, some data exist in post ED care in haemodynamically stabilized patients. In a before-and-after study, early mobilization (< day 3) of patients hospitalized in cardiac intensive care ( $n = 1489$ ; 13% with AHF) raised the rate of patients returning home (83.9% vs 78.3%;  $P < 0.007$ ), and lowered the rate of in-hospital death (4.2% vs 6.8%;  $P = 0.04$ ) and the rate of return to the ED within 30 days (13.5% vs 19.2%;  $P = 0.003$ ) [63]. A randomized controlled trial in an acute post emergency geriatric ward found that an early (< 48 h) physical activity programme in 370 patients (30% hospitalized for heart failure) significantly improved functional capacity: mean difference between intervention group and standard care for Barthel score +6.9 95% CI 4.4–9.5; and for SPPB score +2.2, 95% CI 1.7–2.6 [64]. These results were confirmed in a multicentre study of 200 patients [65]. In all of these studies, implementation of an early mobilization programme

was not associated with an increase in length of hospital stay or adverse events. The time between admission and mobilization could be one of the potential predictors of rehospitalization in older patients with heart failure. In a study including 190 patients, early mobilization within 3 days of admission was associated with a lower risk of rehospitalization for AHF [66]. Furthermore, a Japanese retrospective study, analysing data from over 400,000 patients, suggested a lower loss of autonomy in patients aged > 80 years benefiting from early cardiac rehabilitation within the first 48 h [67]. In this study, 306,826 patients were finally analysed, of who 142,590 benefited from rehabilitation; of these, 45,428 received rehabilitation within the first 48 h. The literature also evaluated the factors limiting early access to this early rehabilitation. Thus, the factor most associated with early access is the existence of a pre-existing gait disorder before the AHF episode [68].

#### **4.9.2. Experts' answer**

Older patients managed in the ED for AHF should probably be offered early mobilization, or even an adapted exercise programme, in order to limit loss of functional autonomy.

#### **4.9.3. Grade**

G2+.

### **4.10. Question 10**

In older patients presenting with AHF with respiratory distress, in prehospital or emergency care, does oxygenation with non-invasive ventilatory support reduce morbimortality?

#### **4.10.1. Rationale**

Pulmonary congestion is generally associated with raised after load and/or left ventricular dysfunction, and can lead to hypoxaemia, which justifies oxygen therapy only if oxygen saturation (SpO<sub>2</sub>) is < 90% or arterial oxygen pressure (PaO<sub>2</sub>) is < 60 mm Hg (Grade IC) [1]. Oxygen administration must avoid hyperoxia, which is also deleterious and increases acid-base imbalances [69]. In respiratory distress, i.e. hypoxia with SpO<sub>2</sub> < 90% associated with respiratory rate > 25 breaths/min, non-invasive ventilation (NIV), involving the delivery of oxygen into the lungs via positive pressure without the need for endotracheal intubation, should be introduced as soon as possible [70–72]. Indeed, the effect of NIV is an increase in oxygenation and a decrease in the work of breathing and, in the case of ventilatory support, an additional improvement in alveolar ventilation, with further decreases in carbon dioxide levels [70]. The literature shows that the introduction of NIV significantly reduces the rate of

intubation in both inpatient and outpatient settings [70, 71, 73,74]. Therefore, NIV is proposed in case of respiratory distress associated with acute pulmonary oedema, especially in hypertensive AHF [70, 71]. Nevertheless, NIV should be started only with initiation of urgent pharmacological therapies according to the recommendations, although the literature does not specify which sequence to initiate [1, 2, 71,72, 74]. The effect on mortality remains more controversial, as the use of NIV does not reduce mortality in these patients [75, 76]. Continuous positive air-ways pressure may be preferred for acute pulmonary oedema in the prehospital setting because of its ease of use and set-up. NIV with spontaneous ventilation with inspiratory support and positive expiratory pressure, sometimes mistakenly referred to as “bilevel positive airways pressure”, should be preferred in intra-hospital care for patients with persistent signs of respiratory exhaustion, but also for those with acidosis with hypercapnoea or a history of chronic obstructive pulmonary disease [70, 72]. During NIV treatment, blood pressure should be monitored as it raises intrathoracic pressure, which in turn reduces venous return and thus right and left ventricular preload. In fact, it can also lead to a reduction in cardiac output and blood pressure, and should therefore be used with caution in patients with reduced preload and hypotension. In addition, raised pulmonary vascular resistance and right ventricular afterload may also be deleterious in cases of right ventricular dysfunction. Under no circumstances should it prevent or delay recourse to intubation and mechanical ventilation in the event of failure or signs of exhaustion threatening the patient’s vital prognosis [70]. Furthermore, at present, high-flow nasal oxygenation therapy has no indication in this clinical situation [77].

#### **4.10.2. Experts’ answer**

Oxygenation by NIV should probably be initiated in older patients managed in the ED for AHF with respiratory distress in order to limit morbidity and mortality.

#### **4.10.3. Grade**

G2+.

### **5. Pathway of care for the older patient with AHF**

#### **5.1. Question 1**

In older patients hospitalized for AHF, does cardiology ward management reduce morbidity and mortality?

### **5.1.1. Rationale**

Regardless of age, hospitalization in a cardiac unit is associated with a better prognosis in the event of AHF [1, 2, 78–81]. In registry studies, older patients are statistically less likely to be admitted to cardiology units, and their management is less likely to follow recommendations [80, 82, 83]. As a result of lack of resources and the rising prevalence of heart failure, not all patients can be admitted to cardiology units [6, 82, 83]. In addition, the older patient often has associated acute or chronic pathologies, for which multidisciplinary management in the medical or geriatric sector is sometimes necessary [83–85]. For patients managed by a medical team, the punctual intervention of a cardiologist or a mobile team dedicated to the management of AHF is associated with a better prognosis [78, 86, 87]. In an American retrospective study of older people admitted with a primary diagnosis of AHF, collaboration between non-cardiologists and cardiologists was associated with a better prognosis than exclusive management by a cardiologist or non-cardiologist [88]. Compared with patients managed exclusively by a cardiologist or non-cardiologist, patients managed in the medical sector by a non-cardiologist with a cardiology consultation had significantly more assessments of left ventricular function, more discharge prescriptions, including an ACE inhibitor, and fewer 90-day rehospitalizations (adjusted OR 0.54, 95% CI 0.34–0.86) [88]. In a study from a Spanish registry, patients included in an AHF management and follow-up programme from the time of admission had a better prognosis than those not included [89]. In a systematic review, Kul et al. compiled the results of five studies investigating the effect of an AHF management programme from hospital admission; they noted a significant reduction in mortality, rehospitalization and length of hospital stay, without any additional cost [90]. Patient frailty, assessed using a validated geriatric scale (Clinical Frailty Scale), is associated with the prognosis of older patients with AHF [78, 91–94]. Whereas the goals of care for non-frail older patients should be the same as for non-older patients, for frail patients, the goals of care should be tailored to each situation, considering the patient's co-morbidities, in addition to personalized AHF management [91]. Studies are awaited to assess the impact of this assessment on the patient's return home, quality of life, consumption of care and prognosis.

### **5.1.2. Experts' answer**

Older patients with AHF should probably be hospitalized in a cardiology unit to improve their prognosis. Failing that, in case of co-morbidities or associated pathologies, multidisciplinary management, including a cardiologist and a geriatrician, is probably required, followed by referral to a care network to improve prognosis.

### **5.1.3. Grade**

G2+.

## 5.2. Question 2

Does coronary angiography reduce morbidity and mortality in older patients hospitalized for AHF with non-ST-segment elevation acute coronary syndrome (NSTACS)?

### 5.2.1. Rationale

In the 2020 guidelines, the ESC specified that older patients with NSTACS should benefit from the same diagnostic and therapeutic strategies as younger patients [95]. A recent meta-analysis of 2323 older patients treated for NSTACS found no benefit in terms of mortality between 6 months and 5 years (risk ratio [RR] 0.85, 95% CI 0.7–1.04) after coronary angiography. On the other hand, there was a significant reduction in myocardial infarction recurrence (RR 0.59, 95% CI 0.49–0.71) and the need for emergency revascularization (RR 0.3, 95% CI 0.17–0.53), but an increased risk of bleeding (RR 2.12, 95% CI 1.21–3.74). There was no significant difference in the risk of stroke (RR 0.75, 95% CI 0.38–1.46) [96]. A 2012 randomized control-led trial of 313 patients aged > 75 years showed a benefit of invasive management only in patients with elevated troponin at initial management (HR 0.43, 95% CI 0.23–0.80), but not in those with normal troponin at admission (HR 1.67, 95% CI 0.75–3.70;  $P = 0.03$ ) [97]. Another randomized study, involving 457 patients, showed a benefit for invasive management on a composite endpoint (acute coronary syndrome, need for emergency revascularization, stroke and mortality) after a median follow-up of 1.5 years (HR 0.53, 95% CI 0.41–0.69;  $P = 0.0001$ ) [98]. However, in an ancillary study of the After Eighty trial, there was no evidence of an impact on quality of life at 1 year according to the 36-item Short-Form Survey (SF-36) [99]. An ancillary study of the TACTICS-TIMI 18 trial, involving 2220 older patients, showed a benefit for invasive management within 48 h on a 30-day composite criterion (mortality, acute coronary syndrome, rehospitalization, stroke and haemorrhage) (10.8% vs 21.6%;  $P = 0.016$ ) and a relative 56% reduction in mortality and/or the occurrence of acute coronary syndrome at 6 months [100]. Furthermore, other methodologically weaker studies showed a benefit for early invasive management [101–104]. Medical intuition alone does not appear to be sufficient, as it raises the risk of mortality by a factor of 6 by reducing the use of appropriate management (OR 6.0, 95% CI 2.3–15.5;  $P < 0.001$ ) [105]. Risk stratification therefore requires the use of validated scores. Among them, the GRACE score appears to be better than the TIMI risk score for stratifying 1-year mortality risk [106,107]. A study of 114 patients showed better risk assessment when several scores (GRACE, EuroSCORE, AMIS and SYNTAX) were used [108]. In addition, patient frailty should be assessed using the validated Clinical Frailty Scale [92]. The therapeutic decision will be weighed up against the ischaemic and haemorrhagic risk, co-morbidities and the existence of agitation, which could complicate the procedure.

### **5.2.2. Experts' answer**

The experts suggest that older patients with AHF possibly linked to coronary pathology should be eligible for semi-emergency coronary angiography. This decision will be weighed according to the patient's level of frailty and bleeding risk, as assessed by validated scores.

### **5.2.3. Experts' opinion**

Strong agreement.

## **5.3. Question 3**

In older patients initially treated for AHF, but not hospitalized, does cardiologist follow-up reduce morbidity and mortality?

### **5.3.1. Rationale**

With regard to prevalence, prospective multicentre studies have found a non-hospitalization rate of between 20% and 35% for patients with AHF at the end of emergency care [109–112]. In addition, non-hospitalized patients appear to be at greater risk of return to the ED, and have a higher 7-day mortality rate [110]. The 2021 ESC recommendations suggest at least one visit between 1 and 2 weeks after discharge, without specifying whether it should be carried out by general practitioners or cardiologists; this would reduce the rate of 30-day rehospitalization. However, these recommendations are not based on prospective randomized controlled trials [1]. The majority of articles found studied follow-up after hospitalization for AHF. The first is a French single-centre randomized controlled trial of patients aged > 80 years, which studied the impact of scheduled follow-up at 3, 6 and 9 weeks and 3, 6, 9 and 12 months after hospital discharge. This study was stopped prematurely because quality of life was significantly improved at 6 months (primary endpoint on the Minnesota Living with Heart Failure Questionnaire), as was mortality [113]. A Canadian cohort study of over 10,000 patients, with a mean age > 75 years, investigated the benefit of post-emergency follow-up for AHF by a general practitioner alone, a cardiologist alone, collaborative management or no management at all. Regardless of the type of follow-up, there was a benefit in terms of mortality. This benefit was even greater in the case of consultation by a cardiologist, and improved in case of multidisciplinary management. These results were confirmed on a composite criterion including mortality, re-consultations in the ED and heart failure rehospitalization [114].

### **5.3.2. Experts' answer**

Patients with AHF who are not hospitalized at the end of their stay in the ED must be able to benefit from a short-term follow-up programme (within 7 days). This decision will be weighted according to the patient's level of frailty and autonomy.

### **5.3.3. Grade**

G1+.

## **6. Ethics for the older patient with AHF**

### **6.1. Question 1**

Does palliative care improve the quality of life of a terminally ill older patient with AHF in the ED?

#### **6.1.1. Rationale**

End-stage heart failure is characterized by symptomatic patients remaining in stage IV of the New York Heart Association classification, despite full diagnostic investigation and optimal medical treatment. The integration of palliative care into the management of patients with end-stage heart failure is recommended by the ESC [1, 2, 115]. Indeed, a systematic review showed a modest improvement in quality of life and a reduction in hospitalization rates, with no influence on survival time [116]. Patients likely to benefit from palliative care can be identified by advanced age, coexistence with chronic obstructive pulmonary disease, persistent hypotension, worsening renal failure and ongoing symptoms [117]. The most common symptoms of end-stage heart failure are dyspnoea, oedema, thirst, pain, anxiety and depression. Therapeutic solutions can be tried in these patients. In this context, whereas oxygen has relatively no effect in long-term dyspnoea, morphine has an interesting effect [118]. Similarly, although non-invasive ventilation has not been specifically tested in this population, it probably has no place. Finally, for dependent patients living in care facilities, such as nursing homes, the relevance of transport to hospital may be questioned, particularly if palliative nursing care is available on site.

#### **6.1.2. Experts' answer**

Palliative care is recommended for patients with advanced heart failure presenting to the ED with AHF, as it improves quality of life without reducing survival time.

### 6.1.3. Grade

G1+.

#### Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.acvd.2024.09.004>. Disclosure of interest N.P. has received consulting fees from VYGON SA (CPAP-Boussignac), symposia lecture fees and congress invitations from Fisher & Paykel Healthcare SAS (Optiflow), and is involved in an independent clinical research programme for Roche Diagnostics (no fee or grant) and a fundamental research programme for Boehringer Ingelheim GMBH (no fee or grant). C.D. has received congress invitations from Boehringer, consulting, lecture fee and research grants from Abott, consulting and lecture fees from Abiomed and Satelia, and consulting fees from AstraZeneca. A.B. has received consultancy fees from Pfizer, Vifor Pharma, Boehringer and AstraZeneca and has been involved in symposia for Novartis and Vifor Pharma. M.P. has received lecture fees from Bristol Myers Squibb, consultancy fees from AstraZeneca and a congress invitation from Novartis. N.G. has received honoraria from AstraZeneca, Bayer, Boehringer Ingelheim, Lilly, Novo Nordisk, Novartis, NP Medical, Roche Diagnostics and Echoscens. F. Roca has been involved in oral communications for Pfizer, Bayer and Sanofi and consulting for Novartis, and has received a congress invitation from Novartis. P.J. has received honoraria from AstraZeneca, Bayer, Novo Nordisk, Novartis, NP Medical, Boehringer Ingelheim and Pfizer. F.M. has received honoraria from Novartis, Pfizer, Vifor, Boehringer and Bristol Myers Squibb. T.C. has been involved in consulting for Novartis. The other authors declare that they have no competing interest.

## Références

- [1] McDonagh TA, Metra M, Adamo M, Gardner RS, Baumach A, Bohm M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J* 2021;42:3599–726.
- [2] Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J* 2016;37:2129–200.

- [3] Flaherty JD, Bax JJ, De Luca L, Rossi JS, Davidson CJ, Filippatos G, et al. Acute heart failure syndromes in patients with coronary artery disease early assessment and treatment. *J Am Coll Cardiol* 2009;53:254–63.
- [4] Lala A, McNulty SE, Mentz RJ, Dunlay SM, Vader JM, Abou Ezzeddine OF, et al. Relief and recurrence of congestion during and after hospitalization for acute heart failure: insights from Diuretic Optimization Strategy Evaluation in Acute Decompensated Heart Failure (DOSE-AHF) and Cardiorenal Rescue Study in Acute Decompensated Heart Failure (CARESS-HF). *Circ Heart Fail* 2015;8:741–8
- [5] Deniau B, Costanzo MR, Sliwa K, Asakage A, Mullens W, Mebazaa A. Acute heart failure: current pharmacological treatment and perspectives. *Eur Heart J* 2023;44:4634–49.
- [6] Boureau AS, Annweiler C, Belmin J, Bouleti C, Chacornac M, Chuzeville M, et al. Practical management of frailty in older patients with heart failure: Statement from a panel of multidisciplinary experts on behalf the Heart Failure Working Group of the French Society of Cardiology and on behalf French Society of Geriatrics and Gerontology. *ESC Heart Fail* 2022;9:4053–63.
- [7] Cyrille NB, Patel SR. Late in-hospital management of patients hospitalized with acute heart failure. *Prog Cardiovasc Dis* 2017;60:198–204.
- [8] Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;336:924–6.
- [9] Schardt C, Adams MB, Owens T, Keitz S, Fontelo P. Utilization of the PICO framework to improve searching PubMed for clinical questions. *BMC Med Inform Decis Mak* 2007;7:16.
- [10] Felker GM, Lee KL, Bull DA, Redfield MM, Stevenson LW, Goldsmith SR, et al. Diuretic strategies in patients with acute decompensated heart failure. *N Engl J Med* 2011;364:797–805.
- [11] Mullens W, Damman K, Harjola VP, Mebazaa A, Brunner-La Rocca HP, Martens P, et al. The use of diuretics in heart failure with congestion - a position statement from the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail* 2019;21:137–55.
- [12] Ellison DH, Felker GM. Diuretic treatment in heart failure. *N Engl J Med* 2017;377:1964–75.
- [13] Felker GM, Ellison DH, Mullens W, Cox ZL, Testani JM. Diuretic therapy for patients with heart failure: JACC state-of-the-art review. *J Am Coll Cardiol* 2020;75:1178–95.
- [14] Cotter G, Metzko E, Kaluski E, Faigenberg Z, Miller R, Simovitz A, et al. Randomised trial of high-dose isosorbide dinitrate plus low-dose furosemide versus high-dose furosemide plus low-dose isosorbide dinitrate in severe pulmonary oedema. *Lancet* 1998;351:389–93.

- [15] Sharon A, Shpirer I, Kaluski E, Moshkovitz Y, Milovanov O, Polak R, et al. High-dose intravenous isosorbide-dinitrate is safer and better than Bi-PAP ventilation combined with conventional treatment for severe pulmonary edema. *J Am Coll Cardiol* 2000;36:832–7.
- [16] Wilson SS, Kwiatkowski GM, Millis SR, Purakal JD, Mahajan AP, Levy PD. Use of nitroglycerin by bolus prevents intensive care unit admission in patients with acute hypertensive heart failure. *Am J Emerg Med* 2017;35:126–31.
- [17] Gorlicki J, Minka FH, Chouihed T, Desmettre T, Feral-Pierssens AL, Laribi S, et al. Low compliance to guidelines in the management of acute heart failure in emergency elderly patients: a multicenter pilot prospective study. *Eur J Emerg Med* 2019;26:379–80.
- [18] Kitai T, Tang WHW, Xanthopoulos A, Murai R, Yamane T, Kim K, et al. Impact of early treatment with intravenous vasodilators and blood pressure reduction in acute heart failure. *Open Heart* 2018;5:e000845.[
- [19] Freund Y, Cachanado M, Delannoy Q, Laribi S, Yordanov Y, Gorlicki J, et al. Effect of an emergency department care bundle on 30-day hospital discharge and survival among elderly patients with acute heart failure: the ELISABETH Randomized Clinical Trial. *JAMA* 2020;324:1948–56.
- [20] Wakai A, McCabe A, Kidney R, Brooks SC, Seupaul RA, Diercks DB, et al. Nitrates for acute heart failure syndromes. *Cochrane Database Syst Rev* 2013;2013:CD005151.
- [21] Shiraishi Y, Kohsaka S, Katsuki T, Harada K, Miyazaki T, Miyamoto T, et al. Benefit and harm of intravenous vasodilators across the clinical profile spectrum in acute cardiogenic pulmonary oedema patients. *Eur Heart J Acute Cardiovasc Care* 2020;9:448–58.
- [22] Kozhuharov N, Goudev A, Flores D, Maeder MT, Walter J, Shrestha S, et al. Effect of a strategy of comprehensive vasodilation vs usual care on mortality and heart failure rehospitalization among patients with acute heart failure: the GALACTIC Randomized Clinical Trial. *JAMA* 2019;322:2292–302.
- [23] Freund Y, Delerme S, Boddaert J, Baker E, Riou B, Ray P. Isosorbide dinitrate bolus for heart failure in elderly emergency patients: a retrospective study. *Eur J Emerg Med* 2011;18:272–5.
- [24] Khot UN, Novaro GM, Popovic ZB, Mills RM, Thomas JD, Tuzcu EM, et al. Nitroprusside in critically ill patients with left ventricular dysfunction and aortic stenosis. *N Engl J Med* 2003;348:1756–63.
- [25] Gray A, Goodacre S, Seah M, Tilley S. Diuretic, opiate and nitrate use in severe acidotic acute cardiogenic pulmonary oedema: analysis from the 3CPO trial. *QJM* 2010;103:573–81
- [26] Iakobishvili Z, Cohen E, Garty M, Behar S, Shotan A, Sandach A, et al. Use of intravenous morphine for acute decompensated heart failure in patients with and without acute coronary syndromes. *Acute Card Care* 2011;13:76–80.

- [27] Caspi O, Naami R, Halfin E, Aronson D. Adverse dose-dependent effects of morphine therapy in acute heart failure. *Int J Cardiol* 2019;293:131–6.
- [28] Peacock WF, Hollander JE, Diercks DB, Lopatin M, Fonarow G, Emerman CL. Morphine and outcomes in acute decompensated heart failure: an ADHERE analysis. *Emerg Med J* 2008;25:205–9.
- [29] Miro O, Gil V, Martin-Sanchez FJ, Herrero-Puente P, Jacob J, Mebazaa A, et al. Morphine use in the ED and outcomes of patients with acute heart failure: a propensity score-matching analysis based on the EAHFE Registry. *Chest* 2017;152:821–32.
- [30] Gil V, Dominguez-Rodriguez A, Masip J, Peacock WF, Miro O. Morphine use in the treatment of acute cardiogenic pulmonary edema and its effects on patient outcome: a systematic review. *Curr Heart Fail Rep* 2019;16:81–8.
- [31] Lin Y, Chen Y, Yuan J, Pang X, Liu H, Dong S, et al. Intravenous morphine use in acute heart failure increases adverse outcomes: a meta-analysis. *Rev Cardiovasc Med* 2021;22:865–72.
- [32] Zhang D, Lai W, Liu X, Shen Y, Hong K. The safety of morphine in patients with acute heart failure: a systematic review and meta-analysis. *Clin Cardiol* 2021;44:1216–24.
- [33] Witharana TN, Baral R, Vassiliou VS. Impact of morphine use in acute cardio-genic pulmonary oedema on mortality outcomes: a systematic review and meta-analysis. *Ther Adv Cardiovasc Dis* 2022;16, 17539447221087587.
- [34] Prins KW, Neill JM, Tyler JO, Eckman PM, Duval S. Effects of beta-blocker withdrawal in acute decompensated heart failure: a systematic review and meta-analysis. *JACC Heart Fail* 2015;3:647–53.
- [35] Miro O, Muller C, Martin-Sanchez FJ, Bueno H, Mebazaa A, Herrero P, et al. BETAWIN-AHF study: effect of beta-blocker withdrawal during acute compensation in patients with chronic heart failure. *Clin Res Cardiol* 2016;105:1021–9.
- [36] Tamaki Y, Yaku H, Morimoto T, Inuzuka Y, Ozasa N, Yamamoto E, et al. Lower in hospital mortality with beta-blocker use at admission in patients with acute decompensated heart failure. *J Am Heart Assoc* 2021;10:e020012.
- [37] Abi Khalil C, Sulaiman K, Mahfoud Z, Singh R, Asaad N, AlHabib KF, et al. Non-withdrawal of beta blockers in acute decompensated chronic and denovo heart failure with reduced ejection fraction in a prospective multi-centre study of patients with acute heart failure in the Middle East. *BMJ Open* 2017;7:e014915.
- [38] Seo WW, Park JJ, Park HA, Cho HJ, Lee HY, Kim KH, et al. Guideline-directed medical therapy in elderly patients with heart failure with reduced ejection fraction: a cohort study. *BMJ Open* 2020;10:e030514.

- [39] Stolfo D, Savarese G. Use of renin-angiotensin-aldosterone system inhibitors in older patients with heart failure and reduced ejection fraction. *Card Fail Rev* 2019;5:70–3.
- [40] Gilstrap LG, Fonarow GC, Desai AS, Liang L, Matsouaka R, DeVore AD, et al. Initiation, continuation, or withdrawal of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers and outcomes in patients hospitalized with heart failure with reduced ejection fraction. *J Am Heart Assoc* 2017;6:e004675.
- [41] Sanam K, Bhatia V, Bajaj NS, Gaba S, Morgan CJ, Fonarow GC, et al. Renin-angiotensin system inhibition and lower 30-day all-cause readmission in medicare beneficiaries with heart failure. *Am J Med* 2016;129:1067–73.
- [42] Iglesias J, Ghetiya S, Ledesma KJ, Patel CS, Levine JS. Interactive and potentially independent roles of renin-angiotensin-aldosterone system blockade and the development of cardiorenal syndrome type 1 on in-hospital mortality among elderly patients admitted with acute decompensated congestive heart failure. *Int J Nephrol Renovasc Dis* 2019;12:33–48.
- [43] Kane JA, Kim JK, Haidry SA, Saliccioli L, Lazar J. Discontinuation/dose reduction of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers during acute decompensated heart failure in african-american patients with reduced left-ventricular ejection fraction. *Cardiology* 2017;137:121–5.
- [44] Yoshioka K, Matsue Y, Yamaguchi T, Kitai T, Kagiya N, Okumura T, et al. Safety and prognostic impact of early treatment with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers in patients with acute heart failure. *Am J Cardiovasc Drugs* 2019;19:597–605.
- [45] Ilges DT, Dermody ML, Blankenship C, Mansfield V, Van Tuyl JS. Impact of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers on renal function in type 1 cardiorenal syndrome. *J Cardiovasc Pharmacol Ther* 2021;26:611–8.
- [46] Berger AK, Duval S, Manske C, Vazquez G, Barber C, Miller L, et al. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers in patients with congestive heart failure and chronic kidney disease. *Am Heart J* 2007;153:1064–73.
- [47] Seko Y, Kato T, Morimoto T, Yaku H, Inuzuka Y, Tamaki Y, et al. Starting neurohormonal antagonists in patients with acute heart failure with mid-range and preserved ejection fraction. *Circ J* 2022;86:1547–58.
- [48] Butler J, Anstrom KJ, Felker GM, Givertz MM, Kalogeropoulos AP, Konstam MA, et al. Efficacy and safety of spironolactone in acute heart failure: the ATHENA-HF randomized clinical trial. *JAMA Cardiol* 2017;2:950–8.
- [49] Asakura M, Ito S, Yamada T, Saito Y, Kimura K, Yamashina A, et al. Efficacy and Safety of Early Initiation of Eplerenone Treatment in Patients with Acute Heart Failure (EARLIER trial): a multicentre, randomized, double-blind, placebo-controlled trial. *Eur Heart J Cardiovasc Pharmacother* 2022;8:108–17.[

- [50] Na SJ, Youn JC, Lee HS, Jeon S, Lee HY, Cho HJ, et al. The prescription characteristics, efficacy and safety of spironolactone in real-world patients with acute heart failure syndrome: a prospective nationwide cohort study. *Front Cardiovasc Med* 2022;9:791446.
- [51] Rossi R, Crupi N, Coppi F, Monopoli D, Sgura F. Importance of the time of initiation of mineralocorticoid receptor antagonists on risk of mortality in patients with heart failure. *J Renin Angiotensin Aldosterone Syst* 2015;16:119–25.14
- [52] Jondeau G, Neuder Y, Eicher JC, Jourdain P, Fauveau E, Galinier M, et al. B-CONVINCED: Beta-blocker CONTinuation Vs. INTerruption in patients with Congestive heart failure hospitalizED for a decompensation episode. *Eur Heart J* 2009;30:2186–92.
- [53] Velazquez EJ, Morrow DA, DeVore AD, Duffy CI, Ambrosy AP, McCague K, et al. Angiotensin-neprilysin inhibition in acute decompensated heart failure. *N Engl J Med* 2019;380:539–48.
- [54] Wachter R, Senni M, Belohlavek J, Straburzynska-Migaj E, Witte KK, Kobalava Z, et al. Initiation of sacubitril/valsartan in haemodynamically stabilised heart failure patients in hospital or early after discharge: primary results of the randomised TRANSITION study. *Eur J Heart Fail* 2019;21:998–1007.
- [55] Butt JH, Dewan P, Merkely B, Belohlavek J, Drozd J, Kitakaze M, et al. Efficacy and safety of dapagliflozin according to frailty in heart failure with reduced ejection fraction: a post hoc analysis of the DAPA-HF Trial. *Ann Intern Med* 2022;175:820–30.
- [56] Voors AA, Angermann CE, Teerlink JR, Collins SP, Kosiborod M, Biegus J, et al. The SGLT2 inhibitor empagliflozin in patients hospitalized for acute heart failure: a multinational randomized trial. *Nat Med* 2022;28:568–74.
- [57] Dadi NCT, Radochova B, Vargova J, Bujdakova H. Impact of healthcare-associated infections connected to medical devices-an update. *Microorganisms* 2021;9:2332, <http://dx.doi.org/10.3390/microorganisms9112332>
- [58] Leticia-Kriegel AS, Salmasian H, Vawdrey DK, Youngerman BE, Green RA, Furuya EY, et al. Identifying the risk factors for catheter-associated urinary tract infections: a large cross-sectional study of six hospitals. *BMJ Open* 2019;9:e022137.
- [59] Jang AY, O'Brien C, Chung WJ, Oh PC, Yu J, Lee K, et al. Routine in dwelling urethral catheterization in acute heart failure patients is associated within creased urinary tract complications without improved heart failure out-comes. *Circ J* 2018;82:1632–9
- [60] Mossello E, Baroncini C, Pecorella L, Giulietti C, Chiti M, Caldi F, et al. Predictors and prognosis of delirium among older subjects in cardiac intensive care unit: focus on potentially preventable forms. *Eur Heart J Acute Cardiovasc Care* 2020;9:771–8.
- [61] Saint S, Kaufman SR, Rogers MA, Baker PD, Ossenkop K, Lipsky BA. Condom versus indwelling urinary catheters: a randomized trial. *J Am Geriatr Soc* 2006;54:1055–61.

- [62] Ellahi A, Stewart F, Kidd EA, Griffiths R, Fernandez R, Omar MI. Strategies for the removal of short-term indwelling urethral catheters in adults. *Cochrane Database Syst Rev* 2021;6:CD004011.
- [63] Semsar-Kazerooni K, Dima D, Valiquette J, Berube-Dufour J, Goldfarb M. Early mobilization in people with acute cardiovascular disease. *Can J Cardiol* 2021;37:232–40.
- [64] Martinez-Velilla N, Casas-Herrero A, Zambom-Ferraresi F, Saez de Asteasu ML, Lucia A, Galbete A, et al. Effect of exercise intervention on functional decline in very elderly patients during acute hospitalization: a randomized clinical trial. *JAMA Intern Med* 2019;179:28–36.
- [65] Martinez-Velilla N, Abizanda P, Gomez-Pavon J, Zambom-Ferraresi F, Saez de Asteasu ML, Fiatarone Singh M, et al. Effect of an exercise intervention on functional decline in very old patients during acute hospitalizations: results of a multicenter, randomized clinical trial. *JAMA Intern Med* 2022;182:345–7.
- [66] Kono Y, Izawa H, Aoyagi Y, Ishikawa A, Sugiura T, Mori E, et al. Predictive impact of early mobilization on rehospitalization for elderly Japanese heart failure patients. *Heart Vessels* 2020;35:531–6.
- [67] Ueno K, Kamiya K, Kaneko H, Okada A, Itoh H, Fujiu K, et al. Acute-phase initiation of cardiac rehabilitation for short-term improvement in activities of daily living in patients hospitalized for acute heart failure. *J Cardiovasc Dev Dis* 2022;9:97, <http://dx.doi.org/10.3390/jcdd9040097>.
- [68] Kubo I, Izawa KP, Kajisa N, Ogura A, Kanai M, Matsumoto D. Factors delaying the progress of early rehabilitation of elderly Japanese patients with heart failure. *Aging Clin Exp Res* 2020;32:399–406.
- [69] Branson RD, Johannigman JA. Pre-hospital oxygen therapy. *Respir Care* 2013;58:86–97.
- [70] Masip J, Peacock WF, Price S, Cullen L, Martin-Sanchez FJ, Seferovic P, et al. Indications and practical approach to non-invasive ventilation in acute heart failure. *Eur Heart J* 2018;39:17–25.
- [71] Masip J, Roque M, Sanchez B, Fernandez R, Subirana M, Exposito JA. Noninvasive ventilation in acute cardiogenic pulmonary edema: systematic review and meta-analysis. *JAMA* 2005;294:3124–30.
- [72] Mebazaa A, Gheorghide M, Pina IL, Harjola VP, Hollenberg SM, Follath F, et al. Practical recommendations for prehospital and early in-hospital management of patients presenting with acute heart failure syndromes. *Crit Care Med* 2008;36:S129–39.
- [73] Bersten AD, Holt AW, Vedig AE, Skowronski GA, Baggoley CJ. Treatment of severe cardiogenic pulmonary edema with continuous positive airway pressure delivered by face mask. *N Engl J Med* 1991;325:1825–30.

- [74] Weng CL, Zhao YT, Liu QH, Fu CJ, Sun F, Ma YL, et al. Meta-analysis: noninvasive ventilation in acute cardiogenic pulmonary edema. *Ann Intern Med* 2010;152:590–600.
- [75] Goodacre S, Stevens JW, Pandor A, Poku E, Ren S, Cantrell A, et al. Pre-hospital noninvasive ventilation for acute respiratory failure: systematic review, network meta-analysis, and individual patient data meta-analysis. *Acad Emerg Med* 2014;21:960–70.
- [76] Gray A, Goodacre S, Newby DE, Masson M, Sampson F, Nicholl J, et al. Noninvasive ventilation in acute cardiogenic pulmonary edema. *N Engl J Med* 2008;359:142–51
- [77] Makdee O, Monsomboon A, Surabenjawong U, Praphruetkit N, Chaisirin W, Chakorn T, et al. High-flow nasal cannula versus conventional oxygen therapy in emergency department patients with cardiogenic pulmonary edema: a randomized controlled trial. *Ann Emerg Med* 2017;70:465–72.e2.
- [78] Boom NK, Lee DS, Tu JV. Comparison of processes of care and clinical outcomes for patients newly hospitalized for heart failure attended by different physician specialists. *Am Heart J* 2012;163:252–9.
- [79] Cleland JG, McDonagh T, Rigby AS, Yassin A, Whittaker T, Dargie HJ, et al. The national heart failure audit for England and Wales 2008-2009. *Heart* 2011;97:876–86.
- [80] Gorlicki J, Boubaya M, Cottin Y, Angoulvant D, Soulat L, Guinemer S, et al. Patient care pathways in acute heart failure and their impact on in-hospital mortality, a French national prospective survey. *Int J Cardiol Heart Vasc* 2020;26:100448.
- [81] Jong P, Gong Y, Liu PP, Austin PC, Lee DS, Tu JV. Care and outcomes of patients newly hospitalized for heart failure in the community treated by cardiologists compared with other specialists. *Circulation* 2003;108:184–91.
- [82] Cluzol L, Cautela J, Michelet P, Roch A, Kerbaul F, Mancini J, et al. Pre-hospital and in-hospital course of care for patients with acute heart failure: features and impact on prognosis in “real life”. *Arch Cardiovasc Dis* 2017;110:72–81.
- [83] Komajda M, Hanon O, Hochadel M, Follath F, Swedberg K, Gitt A, et al. Management of octogenarians hospitalized for heart failure in Euro Heart Failure Survey I. *Eur Heart J* 2007;28:1310–8.
- [84] De Matteis G, Covino M, Burzo ML, Della Polla DA, Franceschi F, Mebazaa A, et al. Clinical characteristics and predictors of in-hospital mortality among older patients with acute heart failure. *J Clin Med* 2022;11:439, <http://dx.doi.org/10.3390/jcm11020439>.
- [85] Logeart D, Thabut G, Jourdain P, Chavelas C, Beyne P, Beauvais F, et al. Pre-discharge B-type natriuretic peptide assay for identifying patients at high risk of re-admission after decompensated heart failure. *J Am Coll Cardiol* 2004;43:635–41

- [86] Fonseca C, Ceia F, Sarmiento PM, Marques F, Covas R, Aleixo A. Translating guidelines into clinical practice: benefits of an acute heart failure unit. *Rev Port Cardiol* 2007;26:1111–28.
- [87] Zuily S, Jourdain P, Decup D, Agrinier N, Loiret J, Groshens S, et al. Impact of heart failure management unit on heart failure-related readmission rate and mortality. *Arch Cardiovasc Dis* 2010;103:90–6.
- [88] Ahmed A, Allman RM, Kiefe CI, Person SD, Shaneyfelt TM, Sims RV, et al. Association of consultation between generalists and cardiologists with quality and outcomes of heart failure care. *Am Heart J* 2003;145:1086–93
- [89] Comin-Colet J, Verdu-Rotellar JM, Vela E, Cleries M, Bustins M, Mendoza L, et al. Efficacy of an integrated hospital-primary care program for heart failure: a population-based analysis of 56,742 patients. *Rev Esp Cardiol (Engl Ed)* 2014;67:283–93.
- [90] Kul S, Barbieri A, Milan E, Montag I, Vanhaecht K, Panella M. Effects of care pathways on the in-hospital treatment of heart failure: a systematic review. *BMC Cardiovasc Disord* 2012;12:81
- [91] Flores-Alvarez FJ, Sillero-Herrera A, Cuesta-Gavino J, Fernandez-Sanchez ML, Vega-Sanchez J, Lopez-Fe JL, et al. Frailty as a predictor of clinical problems and events that require elderly patients with heart failure to use health resources. *Arch Gerontol Geriatr* 2022;101:104698.
- [92] Rodriguez-Queralto O, Formiga F, Lopez-Palop R, Marin F, Vidan MT, Martinez-Selles M, et al. FRAIL Scale also predicts long-term outcomes in older patients with acute coronary syndromes. *J Am Med Dir Assoc* 2020;21:683–7.e1.
- [93] Vidan MT, Blaya-Novakova V, Sanchez E, Ortiz J, Serra-Rexach JA, Bueno H. Prevalence and prognostic impact of frailty and its components in non-dependent elderly patients with heart failure. *Eur J Heart Fail* 2016;18:869–75
- [94] Wang GG, Wang SJ, Qin J, Li CS, Yu XZ, Shen H, et al. Characteristics, management, and outcomes of acute heart failure in the emergency department: a Multicenter Registry Study with 1-year Follow-up in a Chinese Cohort in Beijing. *Chin Med J (Engl)* 2017;130:1894–901
- [95] Collet JP, Thiele H, Barbato E, Barthelémy O, Bauersachs J, Bhatt DL, et al. 2020 ESC Guidelines for the management of acute coronary syndromes inpatients presenting without persistent ST-segment elevation. *Eur Heart J* 2021;42:1289–367.
- [96] Abusnina W, Radaideh Q, Al-Abdouh A, Ismayl M, Algheriani H, Lee J, et al. Routine invasive strategy in elderly patients with non-ST elevation acute coronary syndrome: an updated systematic review and meta-analysis of randomized trials. *Curr Probl Cardiol* 2022;47:101304.

- [97] Savonitto S, Cavallini C, Petronio AS, Murena E, Antonicelli R, Sacco A, et al. Early aggressive versus initially conservative treatment in elderly patients with non-ST-segment elevation acute coronary syndrome: a randomized controlled trial. *JACC Cardiovasc Interv* 2012;5:906–16
- [98] Tegn N, Abdelnoor M, Aaberge L, Endresen K, Smith P, Aakhus S, et al. Invasive versus conservative strategy in patients aged 80 years or older with non-ST-elevation myocardial infarction or unstable angina pectoris (After Eighty study): an open-label randomised controlled trial. *Lancet* 2016;387:1057–65
- [99] Tegn N, Abdelnoor M, Aaberge L, Høyen Ranhoff A, Endresen K, Gjertsen E, et al. Health-related quality of life in older patients with acute coronary syndrome randomised to an invasive or conservative strategy. The After Eighty randomised controlled trial. *Age Ageing* 2018;47:42–7.
- [100] Bach RG, Cannon CP, Weintraub WS, Di Battiste PM, Demopoulos LA, Anderson HV, et al. The effect of routine, early invasive management on outcome for 15 elderly patients with non-ST-segment elevation acute coronary syndromes. *Ann Intern Med* 2004;141:186–95.
- [101] Goncalves FF, Guimaraes JP, Borges SC, Mateus PS, Moreira JJ. Impact of coronary angioplasty in elderly patients with non-ST-segment elevation myocardial infarction. *J Geriatr Cardiol* 2020;17:449–54.
- [102] Rana O, Moran R, O’Kane P, Boyd S, Swallow R, Talwar S, et al. Percutaneous coronary intervention in the very elderly ( $\geq 85$  years): trends and outcomes. *Br J Cardiol* 2013;20:27–30.
- [103] Rathod K, Knight C. Percutaneous coronary intervention in old age – effective or intrusive. *Br J Cardiol* 2013;20:6–7.
- [104] Siddiqui AJ, Omerovic E, Holzmann MJ, Bohm F. Association of coronary angiographic lesions and mortality in patients over 80 years with NSTEMI. *Open Heart* 2022;9:e001811, <http://dx.doi.org/10.1136/openhrt-2021-001811>.
- [105] Chew DP, Juergens C, French J, Parsonage W, Horsfall M, Brieger D, et al. An examination of clinical intuition in risk assessment among acute coronary syndromes patients: observations from a prospective multi-center international observational registry. *Int J Cardiol* 2014;171:209–16.
- [106] Lofmark H, Muhrbeck J, Eggers KM, Linder R, Ljung L, Martinsson A, et al. HEART-score can be simplified without loss of discriminatory power in patients with chest pain – introducing the HET-score. *Am J Emerg Med* 2023;74:104–11.
- [107] Steg PG, Goldberg RJ, Gore JM, Fox KA, Eagle KA, Flather MD, et al. Baseline characteristics, management practices, and in-hospital outcomes of patients hospitalized with acute coronary syndromes in the Global Registry of Acute Coronary Events (GRACE). *Am J Cardiol* 2002;90:358–63.

- [108] Vassalli G, d'Angeli I, Scherff F, Surder D, Mantovani A, Pasotti E, et al. Comparison of clinical and angiographic prognostic risk scores in elderly patients presenting with acute coronary syndrome and referred for percutaneous coronary intervention. *Swiss Med Wkly* 2015;145:w14049.
- [109] Ezekowitz JA, Bakal JA, Kaul P, Westerhout CM, Armstrong PW. Acute heart failure in the emergency department: short and long-term outcomes of elderly patients with heart failure. *Eur J Heart Fail* 2008;10:308–14.
- [110] Lee DS, Schull MJ, Austin PC, Laupacis A, Chong A, et al. Early deaths in patients with heart failure discharged from the emergency department: a population-based analysis. *Circ Heart Fail* 2010;3:228–35.
- [111] Miro O, Gil V, Herrero P, Martin-Sanchez FJ, Jacob J, Llorens P, et al. Multicentric investigation of survival after Spanish emergency department discharge for acute heart failure. *Eur J Emerg Med* 2012;19:153–60.
- [112] Storrow AB, Jenkins CA, Self WH, Alexander PT, Barrett TW, Han JH, et al. The burden of acute heart failure on U.S. emergency departments. *JACC Heart Fail* 2014; 2:269–77.
- [113] Vorilhon C, Jean F, Mulliez A, Clerfond G, Pereira B, Sapin V, et al. Optimized management of heart failure patients aged 80 years or more improves outcomes versus usual care: the HF80 randomized trial. *Arch Cardiovasc Dis* 2016;109:667–78.
- [114] Lee DS, Stukel TA, Austin PC, Alter DA, Schull MJ, You JJ, et al. Improved outcomes with early collaborative care of ambulatory heart failure patients discharged from the emergency department. *Circulation* 2010;122:1806–14.
- [115] Hill L, Prager Geller T, Baruah R, Beattie JM, Boyne J, de Stoutz N, et al. Integration of a palliative approach into heart failure care: a European Society of Cardiology Heart Failure Association position paper. *Eur J Heart Fail* 2020;22:2327–39.[
- [116] Sahlollbey N, Lee CKS, Shirin A, Joseph P. The impact of palliative care on clinical and patient-centred outcomes in patients with advanced heart failure: a systematic review of randomized controlled trials. *Eur J Heart Fail* 2020;22:2340–6.
- [117] Pocock SJ, Ariti CA, McMurray JJ, Maggioni A, Kober L, Squire IB, et al. Predicting survival in heart failure: a risk score based on 39,372 patients from 30 studies. *Eur Heart J* 2013;34:1404–13.
- [118] Johnson MJ, McDonagh TA, Harkness A, McKay SE, Dargie HJ. Morphine for the relief of breathlessness in patients with chronic heart failure—a pilot study. *Eur J Heart Fail* 2002;4:753–6.16