POINT OF VIEW

# Implications of the new European Society of Cardiology guidelines for the treatment of acute heart failure: must we change our approach in the emergency department?

**PERE LLORENS**

Servicio de Urgencias-UCE-UHD, Hospital General Universitario de Alicante, Alicante, Spain.

## Introduction

Acute heart failure (AHF) is defined as the rapid onset of signs and symptoms secondary to abnormal heart function, generally characterized by increased pulmonary capillary pressure with pulmonary congestion, although some patients predominantly present reduced cardiac output and tissue hypoperfusion. The underlying mechanism may be cardiac or extra-cardiac; cardiac involvement is related with ischemia, alteration of cardiac rhythm, valve dysfunction, pericardial disease or preload and/or afterload alterations[1]. As is known, AHF patients require accurate diagnosis as well as immediate and long-term treatment, for symptom relief and to stabilize haemodynamic status in the acute phase in addition to preventing future episodes of acute decompensation and thus improve prognosis[2]. In recent years, AHF has become one of the most pressing problems faced by public health systems in developed countries, with an estimated prevalence in people aged > 70 years of 7-18%[3]. It is therefore no surprise to find that AHF is one of the most frequent reasons for visits to the Emergency Department (ED) and the main cause of hospitalization in elderly patients[4]. Moreover, of these admissions, 96% are ED referrals and only 4% programmed[5], which highlights the special importance of AHF for these services[6]. In recent years, the evidence shows that correct classification and risk stratification of these patients facilitates optimal long-term treatment involving drug prescription of proven efficacy on discharge and referral to multidisciplinary specialist units. The European Society of Cardiology has published, in 2005[1] and 2008[7], consensus guidelines which provide greater uniformity and scientific rigor for the management of patients with this syndrome. The objective of this article is to present relevant evidence on these guidelines to aid ED physicians in the initial evaluation of AHF and facilitate selection of the best therapeutic options.

## Initial evaluation

A clinical history and thorough physical examination are essential, with special emphasis on peripheral perfusion (skin temperature) and filling pressure (lung rales, oedemas and jugular ingurgitation) since they define the haemodynamic status and will guide us in the choice of a particular therapy. It is necessary to be methodical about requesting complementary studies and risk stratification; hyponatremia, impaired renal function, elevated tropinine, ischemic changes in the ECG, substantial elevation of BNP or NT-proBNP, hypotension, acidosis or hypercapnea, or poor diuresis identified in hypovolemic patients, are high risk predictors of morbidity and mortality[8,9].

There is no current consensus on determining acute phase natriuretic peptide levels. In my opinion, BNP or NT-proBNP should be included in the clinical evaluation of all patients with suspected or confirmed AHF in the ED, because: 1) of their diagnostic value (elevated negative values allow ruling out AHF with high reliability for the recommended cut off points) especially in patients with equivocal signs and symptoms or manifestations that may be confused with those of

**CORRESPONDENCE:** Dr. Pere Llorens. Servicio de Urgencias. Hospital General Universitario de Alicante. Pintor Baeza 12. 03010 Alicante, Spain. Email: llorens_ped@gva.es
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other diseases; 2) they aid risk stratification (facilitating decisions on admission or discharge, reducing ED stay time and confirms the need for closer ambulatory follow up); 3) they provide useful prognostic information (worsening, re-admission and death); and 4) they are useful as a therapeutic guide[10], although only complementary and never instead of clinical evaluation. The scientific evidence available on these biomarkers and their proven clinical utility make it unthinkable, in my opinion, to offer quality management of AHF in ED practice without them.

Echocardiography is also an essential tool, to evaluate structural, functional or other changes associated with AHF. The guidelines recommend using this technique as soon as possible in all cases, since these findings are generally directly influential in planning the therapeutic strategy. Like other ED physicians, I believe we should strive to acquire the necessary skills (by adapted, theoretical, practical and continuous training courses) to be able to perform guiding echographs in the ED, without invading or opposing the indications from classical echography which requires a high degree of professional qualification, with expert echographists and top of the range equipment[11].

## Organizing the treatment of AHF

The main immediate objectives in ED management of AHF are to improve symptoms, restore oxygenation, improve organ perfusion and haemodynamic parameters, and limit cardiac and renal damage. Recommended strategies for pre-hospital and early ED management have appeared[2,8], not to replace the guidelines but rather to facilitate their implementation, classifying patients in 5 scenarios according to initial systolic blood pressure (SBP) initial and congestive signs and symptoms: 1) dyspnoea and/or congestion with SBP > 140 mmHg, where non-invasive ventilation (NIV) is more efficient, increasing doses of nitrates and low diuretic doses; 2) dyspnoea and/or congestion with SBP 100-140 mmHg, where diuretics are the mainstay of treatment in the presence of chronic fluid retention, associated with nitrates; 3) dyspnoea and/or congestion with SBP < 100 mmHg, where we should consider volume administration (in the absence of initial congestion) and inotropics if the hypoperfusion persists, and vasoconstrictors; 4) dyspnoea and/or congestion with acute coronary syndrome, a specific protocol must be applied; 5) isolated right heart failure, when volume overload is recommended, using diuretics with SBP > 90 mmHg and inotropics with SBP < 90 mmHg.

Although AHF is a continuum, this immediate classification together with clinical judgement allows us to structure and organize the initial appropriate treatment in ED.

## Treatment

Use of the great majority of drugs in AHF management is based on recommendations – basically empirical – with few randomized clinical trials performed, and single-centre studies with small sample sizes. In general, these drugs improve haemodynamic parameters but do not reduce mortality or improve medium to long-term clinical evolution, probably because of the heterogeneity of the patient samples studied or late initiation of treatment.

The major changes in therapeutic recommendations introduced by the new guidelines[7] are shown below. They represent the result of expert opinion consensus but without much evidence from clinical trials, with a few exceptions.

### *Non-invasive Ventilation*

This should be administered early in patients with acute oedema of the lung and/or hypertensive cardiac failure, since it improves clinical parameters and respiratory distress. It must be used with precaution –not a counter indication– in cardiogenic shock and in right heart failure. Positive pressure applied at the end of expiration improves left ventricular function as it reduces the afterload. Three meta-analyses[12] have shown that its early application reduces the need for intubation

and improves short-term mortality. A recent multi-centre study[13] showed that it improved clinical parameters but had no effect on mortality. From my experience, NIV should be extended to other AHF scenarios in the ED, such as normotensive or hypotensive patients where there is associated respiratory load and/or hypoxemia which are difficult to correct with traditional methods of oxygenation.

### *Morphine*

Although the evidence in favour of morphine use is limited and recent work has reported an association with increased adverse events[14], current recommendations include its administration in se-

vere AHF; its most important effects include improvement of dyspnoea, anxiety, chest pain and patient collaboration with NIV.

*Loop diuretics*

These are recommended in the presence of congestive symptoms, and to be considered in patients with hypotension, hyponatremia and acidosis with low diuretic response. The guidelines emphasize the combined use of diuretics and nitrates to reduce the need for high doses of diuretics, and with moderate-severe congestion (especially in patients with chronic ingestion of oral diuretics), the physician should consider bolus administration followed by continuous infusion for greater effectiveness[15].

Controversy exists regarding the dose of diuretic to be administered initially in patients with AHF. In a recent study with 82.540 AHF patients, those receiving low-dose diuretics showed less risk of hospital mortality (2.1 % vs 2.4 %, $p < 0.05$), reduced hospital and ICU stay, and fewer adverse effects (changes in serum creatinine > 0.5 mg/dl: 5.1 % vs 8.2%, $p < 0.0001$)[16]. High doses activate the neuro-hormonal system and increase the excretion of sodium, potassium and magnesium, provoking myocardial damage and increasing the risk of arrhythmia[17]. Worsening of renal function in AHF patients is associated with poor prognosis and is an independent risk factor for re-admission and for death[18]. Continuous infusion of loop diuretic has been shown to be more efficient and safer than conventional bolus treatment, mainly in initial phases of hospital treatment, since it avoids the peak effects (vasoconstriction, post-diuretic rebound, reduced glomerular filtration rate, increased serum creatinine and ototoxicity) and is also an alternative therapy for diuretic-resistent patients[19,20].

In my opinion, we should use low-dose intravenous bolus and intermittent furosimide in patients with mild congestive symptoms, while in patients with moderate-severe congestive symptoms we should use continuous intravenous perfusion of higher dose diuretics.

Currently it is accepted that fluid overload in AHF patients is often due to fluid re-distribution rather than accumulation. Most patients with acute lung oedema or hypertensive AHF present euvolemia –or slight hypervolemia– so that increased diuresis may cause depletion of intravascular volume resulting in hypotension, reduced cardiac output and kidney failure[17], which is why they may benefit from the use of vasodilators –nitrates– with low-dose or no diuretics.

*Vasodilators*

The effect of nitrates is to reduce left and right ventricular filling pressure – the final cause of AHF – and improve lung congestion without compromising ejection volume, nor increasing oxygen consumption. It is therefore considered the most rational therapeutic agent for the management of AHF[21]. Early administration in the ED is associated with reduced mortality, invasive procedures and hospital stay[22]. The guidelines recommend the use of nitrates for AHF with SBP > 110 mmHg, and with precaution in patients with SBP of 90-110 mmHg. In my opinion, their use should be extended to other scenarios. In daily practice nitrates are only used in hypertensive AHF or acute lung oedema, and we are reluctant to use them in patients with chronic decompensated heart failure; normotensive or slightly hypertensive AHF patients are not often prescribed nitrates in combination with low-dose diuretics. The study EAHFE6 showed that only 26% of AHF patients received intravenous nitrates, although 93% had a NYHA functional status of III-IV and 85% received intravenous diuretics. However, as with any vasodilator, precaution must be exercised to avoid hypotension, especially in patients with kidney failure, a difficult task considering ED attendance overload[23].

*Inotropic drugs*

These agents are recommended in patients with low cardiac output and signs of hypoperfusion or persistent congestion despite the use of vasodilators and/or diuretics. The guidelines indicate that, when necessary, inotropics should be administered early and withdrawn as soon as congestion improves or systemic perfusion is restored, since they may promote and accelerate pathophysiological mechanisms associated with myocardial damage and increased incidence of arrhythmia. Thus in patients with atrial fibrillation, dobutamine and dopamine facilitate conduction via the AV node and may precipitate tachycardia.

The recent guidelines include two important changes regarding the use of inotropics. First, the recommendation IIa previously considered to be supported by level C evidence becomes level B. Secondly, therapeutic strategy in AHF requiring inotropics (Figure 1) has changed, with different recommendations according to SBP: now, patients with SBP > 100 mmHg should receive a vasodilator (or increase the dose of the existing agent) or levosimendan (as the only inotropic indicated for

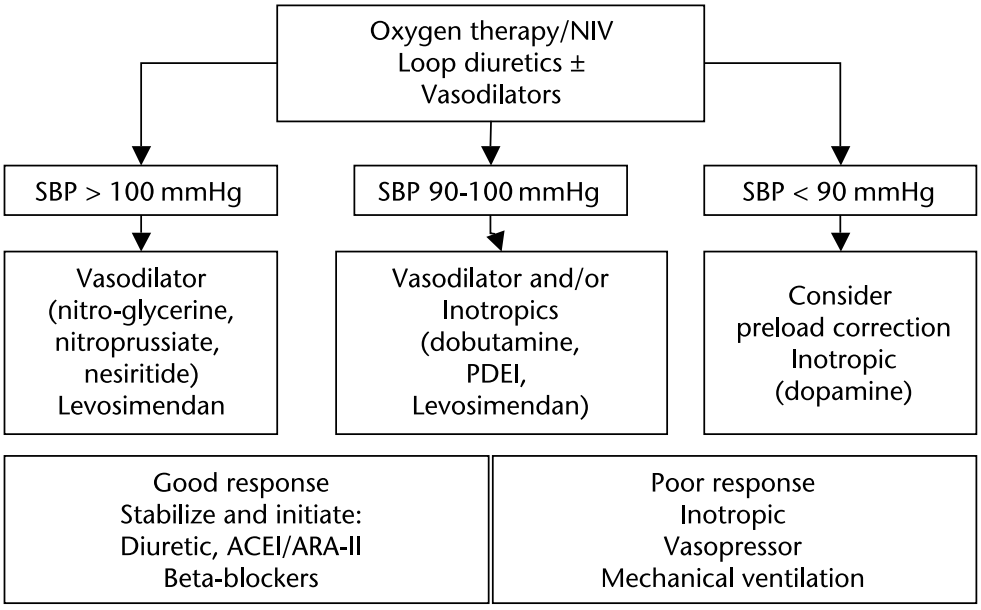


**Figure 1.** Strategy for the treatment of ED patients with acute heart failure, according to systolic blood pressure. NIV: non-invasive ventilation. PDEI: Phosphodiesterase III inhibitor. ACEI: angiotensin converting enzyme inhibitors. ARA-II: angiotensin receptor antagonists. SBP: systolic blood pressure.

these values of BP); patients with SBP of 90-100 mmHg should receive a vasodilator and/or inotropic (levosimendan, dobutamine or phosphodiesterase inhibitor are named). In my opinion, in this scenario, an inotropic is advisable, since a vasodilator should really be introduced under strict haemodynamic control in a critical care unit. In patients with SBP < 90 mmHg, evaluate the preload, administer volume if necessary and initiate dopamine. If the BP does not increase and there is inadequate systemic perfusion, add noradrenalin (this vasodilator is relegated to situations refractory to the administration of volume and dopamine).

Dopamine and dobutamine are recommended only in patients with hypotension or reduced cardiac indexes in the presence of signs indicating hypoperfusion or congestion, and must be administered with precaution in patients with cardiac frequency > 100 bpm[24,25].

The guidelines indicate that levosimendan may also be effective in patients with decompensated chronic heart failure, especially if they are on beta-blockers. Levosimendan has vasodilator properties, and the guidelines maintain the previous recommendation on avoiding loading doses when SBP is < 100 mmHg; if an initial loading dose is used, they advise using between 3 and 12 µg/Kg. In my opinion, coinciding with that of other authors, in patients with de novo AHF and SBP < 100 mmHg and/or excessive volume depletion, loading doses should not be used. The greatest clinical effect has been observed mainly in patients with decompensated chronic heart failure III-IV and SBP > 100 mmHg and/or chronic beta-blocker treatment[26,27].

*Digoxin*

This antiarrhythmic agent may be useful in AHF to control cardiac frequency in the context of atrial fibrillation with rapid ventricular rhythm.

*Angiotensin converting enzyme inhibitors (ACEI) and beta-blockers*

The guidelines maintain the previous recommendations to continue with these agents in AHF patients who were previously taking them, whenever possible, and only interrupt or reduce doses in the context of complications (for example, beta-blockers in the presence of bradycardia, complete ventricular atrial block, haemodynamic instability with signs of low output or in severe AHF with poor response to initial treatment).

Introduction of these agents, preferably before hospital discharge of in-patients with AHF, is recommended but there is no consensus on the optimal moment; generally, after stabilization, ACEI are recommended as from the second day and beta-blockers as from the fourth day of hospitali-

zation[1]. Before introducing beta-blockers, stabilization is absolutely necessary using treatment with ACEI/ARA-II. In my opinion, early ED administration of ACEI/ARA-II is possible in haemodynamically stable, mild or moderate AHF patients without excessive volume depletion, but always administered with precaution.

We must strive to adapt our ED protocols to meet the therapeutic guidelines and consensus recommendations for treating AHF patients; this will allow more integral management of these people and hopefully result in improvement in their quality of life.

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