Very early management of acute heart failure syndromes

Akut kalp yetersizliği sendromlarının en erken tedavisi

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Summary – Diagnosis and management of acute heart failure syndromes are described in the most recent ESC/ESICM guidelines. However, physicians dealing with these patients in their daily practice may need guidance in choosing therapeutic alternatives as soon as the dyspneic patient arrives to the emergency department. Herein, practical recommendations for the very early management of patients with acute heart failure syndromes are presented. Blood pressure- and symptom-driven strategy along with early initiation of goal-directed therapies are key take-home messages. Furthermore, early and frequent reassessment is also an imperative part of management so that adjustments in the initial therapeutic plan can be achieved in a timely fashion.

Özet – Akut kalp yetersizliği sendromlarının tanı ve tedavisi en güncel şekilde ESC/ESICM kılavuzlarında yer almıştır. Bununla birlikte, günlük pratikte bu hastalarla ilgilenen hekimler, dispneli bir hasta acil bölümüne ulaşır ulaşmaz tedavi seçeneklerini seçmede bir yol göstericiye gereksinim duyarlar. Bu yazıda, akut kalp yetersizliği sendromlarıyla başvuran hastaların en erken tedavisi konusunda pratik önerilerde bulunulmuştur. Kan basıncı ve semptomların yönlendirdiği strateji ve hedefe yönelik tedavilerin erken başlatılması özel olarak dikkate alınacak noktalardır. Başlangıç tedavisindeki düzenlemelerin zamanında yapılabilmesi için, erken ve sık aralıklarla değerlendirme yapmak da tedavinin ayrılmaz bir parçasıdır.

Acute heart failure is defined as a gradual or rapid change in heart failure signs and symptoms resulting in the need for urgent therapy.[1,2] It is a complex syndrome that involves various diagnoses and etiologies, requiring a lot of time and energy along with collaboration between many subspecialties of medicine.[1] However, very early management is usually performed arbitrarily in clinical practice, based mainly on symptoms and vital signs until the definitive diagnosis is made.[3,4] Recently, new studies have appeared in the literature providing clues to direct the management of AHF syndromes.[5] First of all, it is now relatively well established that AHF is not a single entity, but rather a fan of discrete clinical scenarios, each of which is related to the primary pathophysiological entity.[6] Although it is difficult to classify the patients into distinct diagnostic categories of the European Society of Cardiology within minutes following admission to emergency department, urgent therapy is usually needed.[7] Plus, even though physicians dealing with these patients rightfully estimate the early therapeutic needs, they are mostly left alone with experience-based recommendations.[2,4]

Abbreviation:
AHF Acute heart failure

Herein, an early therapeutic plan regarding patients with AHF syndromes is presented.

Very early treatment means prehospital phase and the first 6-12 hours after presentation.[4] This phase is critical for survival and early discharge of many patients. It was shown in a retrospective analysis of ADHERE that early administration of AHF-specific vasoactive therapy in the emergency department was associated with a shorter hospital stay (5.4 *vs*. 6.9 days, p<0.0001) and more chance to be discharged home (OR 1.154; 95% CI 1.005-1.325).[8]

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Diagnostic pathway (Fig. 1)

Acute dyspnea is the most frequent symptom of AHF syndromes. However, it is neither sensitive nor specific for AHF syndromes as it is a frequent symptom of almost all emergency admissions. Recently, some scales regarding severity of dyspnea (Likert, VAS, etc.) were verified in the literature.[5,9] It is important to keep in mind that dyspnea simply means urgent need for treatment, which may not be easy to ascertain in a short time. Interestingly, when treated, those with worst dyspnea improve more according to a recent trial.[5] On the other hand, the importance of timely intervention is already established; when it is properly treated, many of patients with dyspnea improve, whereas some patients still remain dyspneic despite treatment. Hence, physicians may need tools to help differentiate cardiac dyspnea from other forms of dyspnea (either noncardiac or combined) in order to tailor therapy or to avoid wrong therapy. Herein, optimal use of some biomarkers can help such assessment.[10] Natriuretic peptides are now considered quantitative markers of cardiac stress that designates the extent of ventricular loading, though they are not perfect.[10] They are particularly useful in excluding heart failure with a reasonable negative predictive value.[2] However, it was shown that delays in utilizing natriuretic peptides were associated with delays in the initiation of therapy and increased mortality.[11] Hence, rational use of natriuretic peptides not only improves medical and economic outcomes, but also helps avoidance of serious adverse events in patients presenting with dyspnea.[11,12] The accepted thresholds to rule in or out AHF were described in the most recent guidelines (Fig. 2).[2] However, there are still areas of uncertainty in the use of natriuretic peptides in the emergency room particularly in obese patients and in patients with chronic renal failure.[13]

Perfusion- and congestion-based practical classifications of AHF syndromes are suggested in many guidelines.[2,14,15] There are four distinct categories: dry & warm, dry & cold, wet & warm, wet & cold. In order to achieve this, well-oriented clinical examination along with chest X-ray and electrocardiography could provide adequate information to move on. Extremities should be checked for signs of hypoperfusion (cold & clammy with vasoconstriction). Bilateral lung areas should be auscultated for any abnormality. Jugular veins should be evaluated for congestion and

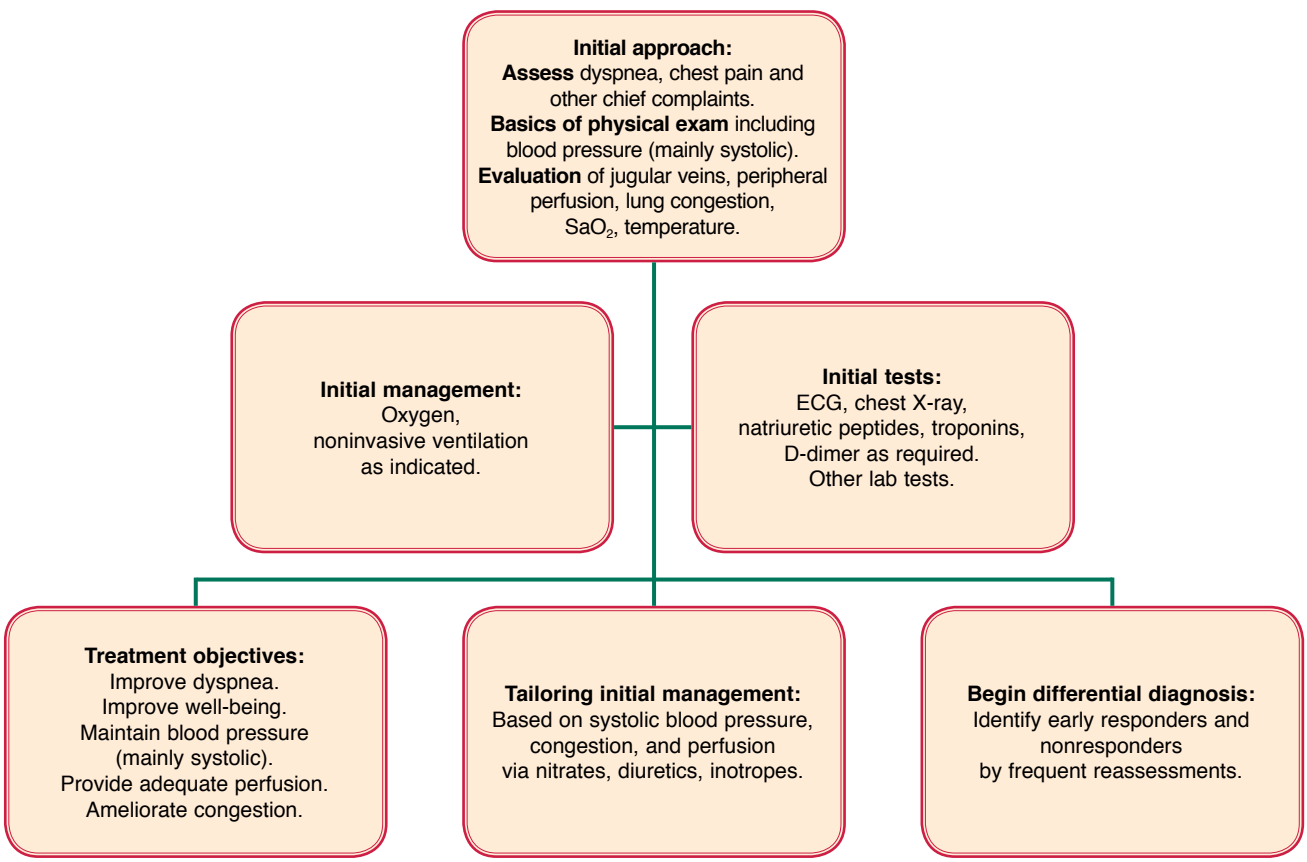

Figure 1. Very early management of acute heart failure syndromes.

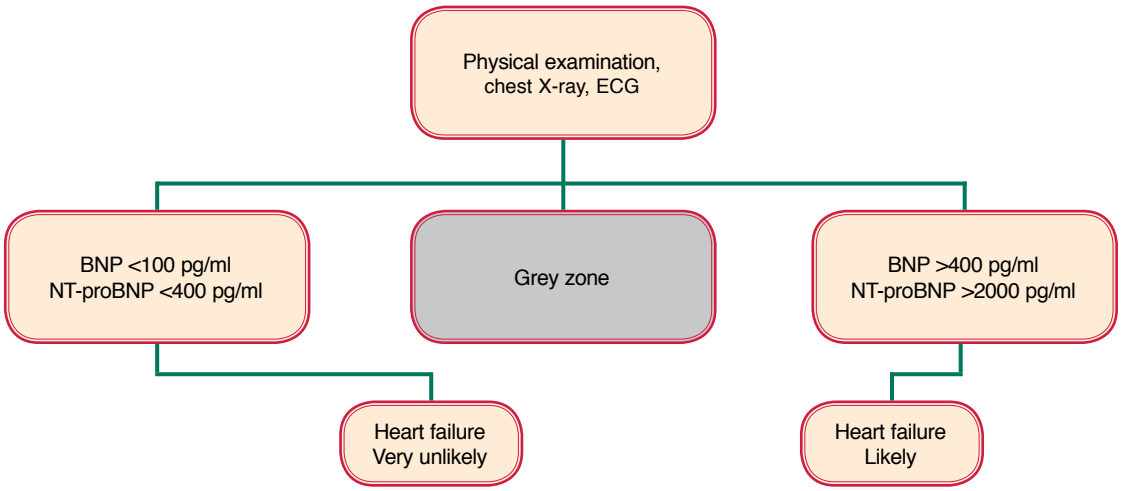

Figure 2. Thresholds for natriuretic peptides in acute heart failure syndromes.

estimation of right-sided filling pressures along with proper chest auscultation. Presence and grading of leg edema (or sacral edema in patients confined to bed), presence and grading of hepatomegaly should be engaged into clinical decision making. Evaluation of mentation should be an integral part of the initial exam. On the other hand, though echocardiography is not part of routine practice of emergency medicine, it should be performed at the earliest time to identify the etiology.[6] Systolic blood pressure (first measured at admission) is described as the most important predictive factor of morbidity and mortality in AHF syndromes. Classification by levels of admission systolic blood pressure can markedly facilitate early risk stratification of AHF patients.[6,16] Actually, in the landmark study that measured performance of perfusion- and congestion-based evaluation in heart failure, perfusion was mainly based on derivatives of blood pressure.[17] Compromised perfusion was evaluated based on the presence of a narrow proportional pulse pressure (systolic-diastolic blood pressure/systolic blood pressure <25%), pulsus alternans, symptomatic hypotension, plus cool extremities and/or impaired mentation. Systolic blood pressure can be classified into three levels as high (>140 mmHg), normal (100-140 mmHg), and low (<100 mmHg) blood pressure.[6] In AHF syndromes, left ventricular systolic function is likely to be preserved in patients presenting with high blood pressure, whereas those with low to normal systolic blood pressure at admission might have impaired systolic function.[18] The presence of low systolic blood pressure accompanied by impaired systolic function defines the patients at the highest risk for death.[18] Hence, clinical judgment along with systolic blood pressure and other practical information could be vital. On the other hand, frequent reassessment in order to accurately identify responders and nonresponders to very early management should be an integral part of management. In hemodynamically unstable patients who are either not responding in a predictable fashion or refractory to initial therapy, and in patients with congestion and hypoperfusion and/or organ hypoperfusion, early referral to intensive or coronary care unit along with direct monitoring of cardiac output and filling pressures must be made as early as possible.[4,6,14]

Comorbidities represent a frequent accompaniment of AHF syndromes. They may influence the prognosis of patients with AHF. Hence, they should be controlled and managed as soon as possible after presentation. There are some detrimental medications to consider. Non-steroidal anti-inflammatory drugs, COX-2 inhibitors, thiazolidinediones, sympathomimetics, tricyclic antidepressants, class I and III antiarrhythmics (except amiodarone), and non-dihydropyridine calcium channel blockers should be stopped in patients presenting with AHF syndromes.[2] Beta-blockers can be safely kept during acute decompensations unless decompensation is directly linked to beta-blockers or the patient is in cardiogenic shock.[19] Furthermore, a very recent analysis of the SURVIVE trial has shown that, in severe acutely decompensated patients with heart failure, who were admitted on beta-blockers, continuation of beta-blockers at discharge was associated with 1-month and 6-month mortality benefit.[20] Interesting enough, highest mortality was observed among patients who were admitted on beta-blockers, but were discharged without beta-blockers.

Biological tests are important to consider, including sodium, potassium, glucose, blood urea nitrogen

or urea, serum creatinine, CK-MB and/or troponin T or I, D-dimer, and complete blood count. It is important to remember that troponins confer little benefit in differential diagnosis in this setting, as heart failure itself might also be associated with *de novo* increase in troponins.[21] Hence, symptoms suggestive of acute coronary syndrome should be investigated thoroughly. Acute heart failure syndromes may also worsen organ function, particularly renal and liver functions. Impaired end-organ function was shown to influence outcomes in patients with heart failure.[2] Hence, evidence for poor organ perfusion along with low cardiac output and low systolic blood pressure may indicate the urgent need for inotropic therapy in these patients.[4]

Therapeutic pathway (Fig. 1)

Oxygen should be administered as early as possible with the aim to achieve an arterial oxygen saturation of ≥95% in patients with AHF syndromes.[2,4] In patients with chronic obstructive pulmonary disease, the target level is 90% in order to avoid hypercapnia. Noninvasive ventilation is recommended as early as possible in most AHF patients, especially in patients with acute cardiogenic pulmonary oedema and hypertensive AHF in order to reduce the need for intubation and short-term mortality,[2] though it was challenged by the 3CPO trial.[22] Criteria for noninvasive ventilation should be as follows (all should be met):[23] pH <7.35, $PaCO_2$ >50 mmHg, PaO_2 <60 mmHg (on FiO_2 0.21), patient should be able to protect airway and clear airway secretions, and exclusion of pneumothorax. Vital signs should be monitored every five minutes in these patients until clinical stability. Loop diuretics, especially furosemide, are the first-line agents for the treatment of patients with AHF syndromes. However, the need for diuretics should be defined by volemic status and congestion of the patient. Patients who do not have signs of systemic congestion, but have dyspnea with varying degrees of lung abnormalities (specific or not) have either pathologies associated with volume redistribution or noncardiac pathologies. High-dose diuretics may be detrimental in patients with normo- or hypovolemia in the absence of signs of systemic congestion, whereas they are life-saving in patients with hypervolemia and congestion. Initially, most patients with AHF syndromes and volume overload could be given an intravenous bolus of furosemide 20-40 mg (0.5-1 mg of bumetanide; 10-20 mg of torasemide) at admission.[2] Of note, AHF patients with high blood pressure at admission usually suffer from volume redistribution rather than volume overload; hence, diuretics are not needed at higher doses. Patients should be assessed frequently in the initial phase to follow urine output, which should be >0.5 ml/kg/hr. Dose of diuretics should be repeated once after 45-60 minutes in case of lack of urine. These agents are preferentially beneficial in AHF patients with normal to low blood pressure and varying degrees of congestion at admission. Of note, the most recent guidelines state that the total furosemide dose should remain <100 mg in the first 6 hours and 240 mg during the first 24 hours.[2] However, in a very recent study, it was shown that high-dose diuretics did not do harm to patients with congested heart failure.[24] Furthermore, continuous infusion, contrary to common belief, was not superior to bolus intravenous therapy with furosemide, the most frequently used loop diuretic.[24] On the other hand, diuretic resistance could possibly be overcome by sequential nephron blockade, which could be provided by administration of thiazides (oral hydrochlorothiazide 25 mg po) and aldosterone antagonists (spironolactone, eplerenone 25-50 mg po) prior to loop diuretics. Alternatively, ultrafiltration may be considered.[25] Intravenous vasodilators are recommended in early treatment of patients with AHF syndromes in the absence of overt symptomatic hypotension, and other absolute contraindications. Intravenous vasodilators decrease filling pressures and systemic vascular resistance and improve dyspnea while maintaining or increasing coronary blood flow at a cost of decreasing blood pressure. Hence, these agents are preferentially beneficial in AHF patients with high blood pressure at admission. Intravenous nitroglycerin can be administered initially at a dose of 10-20 μg/min, with increments of 5-10 μg/min every 3 to 5 minutes as needed.[2] Frequent noninvasive blood pressure measurements are suggested during therapy of patients with AHF syndromes. Inotropic agents should be reserved to a small group of patients, mainly those with signs of low cardiac output or cardiogenic shock,[6] and vasopressor agents should be used in the presence of low systolic blood pressure on top of low cardiac output. Inotropes are not recommended in patients with normal-high blood pressure and/or preserved ejection fraction. Thus, traditional inotropes (dobutamine, dopamine) or the new inodilator levosimendan should be used early in patients with evidence for poor organ perfusion and low blood pressure. Of note, inotropes mainly protect patients from the most catastrophic outcome for a short period of time at a cost of consuming myocardial sources until more definitive therapy is introduced. However, levosimendan

should be preferred in patients with a previous history of heart failure and/or receiving beta-blockers.[26] If blood pressure remains low (<100 mmHg), then a vasoconstrictor should be considered after optimizing preload preferably with a central line. Epinephrine is not recommended as first-line therapy. It is used as rescue therapy in cardiac arrest.[2]

Intra-aortic balloon pump could be the first-line device for patients with AHF syndromes, especially in the presence of acute coronary syndrome with low cardiac output.[4] It can be rapidly placed in the cardiac catheterization laboratory or in the intensive or coronary care unit. Early mechanical device therapy may be useful in patients who do not respond to other therapies during the first 6-12 hours after presentation.[4,27] Though technically challenging, early use of these devices may promote recovery in some patients.[27]

In conclusion, patients with AHF syndromes represent a heterogeneous population at high risk for short-term morbidity and mortality. Early initiation of diagnostic and goal-directed treatment strategies along with early and frequent reassessment are key factors in improving patient outcomes.

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