

PREHOSPITAL THERAPY FOR ACUTE CONGESTIVE HEART FAILURE: STATE OF THE ART

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ABSTRACT

Acute congestive heart failure (CHF) is one of the most common syndromes encountered in emergency care settings. Correct diagnosis and treatment for pulmonary edema, the most common acute manifestation of CHF, are of primary importance as misdiagnosis can result in deleterious consequences to patients. The pathogenesis of acute pulmonary edema (APE) is currently believed to arise primarily from the redistribution of intravascular fluid to the lungs secondary to acutely elevated left ventricular (LV) filling pressures. This understanding has provided a basis for the management of acute APE, which entails reduction of LV preload, reduction of LV afterload, ventilatory support, inotropic support as needed, and identification and treatment of other underlying factors contributing to elevated LV filling pressures. The agent most applicable and effective for field treatment is nitroglycerin. Diuretics and morphine should be used with caution, as they carry higher risks, especially in misdiagnosed patients. The role of angiotensin-converting enzyme (ACE)

inhibitors has yet to be demonstrated in a prehospital setting. Noninvasive positive pressure ventilation methods are effective adjuncts to current treatment, but their mode of delivery presents technical challenges. The development of novel rapid diagnostic tools, currently in progress, might prove valuable for emergency medical services (EMS) personnel in the future. But for now, EMS personnel must rely on their fundamental skills of history taking and physical examination for accurate diagnosis of CHF. **Key words:** congestive heart failure; CHF; acute management; prehospital care; pathogenesis; diagnosis; acute pulmonary edema.

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Congestive heart failure (CHF) is the only cardiovascular disease with increasing prevalence. There are as many as 5 million Americans who have the disease, and more than 500,000 cases are newly diagnosed each year. It is a major disease of the elderly and most patients hospitalized for CHF are older than 65 years of age.¹ Heart failure results in more than 2 million hospitalizations annually in the United States and accounts for 2–3% of the national health care budget.² Approximately 300,000 patients die of this disease every year.³

Congestive heart failure is a complex disease, which includes at least four clinical syndromes—acute pulmonary edema (APE), cardiogenic shock, hypertensive crisis, and chronic heart failure.⁴ Of these, APE and cardiogenic shock are the two most critical syndromes. Although the major clinical manifestations in both are a combination of decreased periph-

eral perfusion and pulmonary congestion, they differ in pathophysiology and hemodynamic changes. Accordingly, these syndromes require different therapeutic modalities.

Acute pulmonary edema, the most common clinical manifestation of CHF,⁵ is a life-threatening respiratory emergency usually occurring outside the hospital. The overall prehospital mortality rate for APE has been assessed to be about 8% in a retrospective Italian study.⁶ A favorable outcome for CHF patients is thus dependent on rapid assessment and treatment initiated in the field.

Here we review the pathogenesis and treatment of APE and consider the effectiveness and relevance of various options in a prehospital setting.

PATHOGENESIS OF APE

Acute pulmonary edema can have a cardiogenic or noncardiogenic etiology. In the former, pulmonary edema results from increased microvascular hydrostatic pressure, while in the latter, edema arises from increased pulmonary capillary permeability. The end result, however, is the same in both cases—an excessive accumulation of extravascular lung fluid.⁷ The primary cause of cardiogenic APE is cardiac dysfunction (Table 1). Noncardiogenic APE may be caused by several diverse inciting events or diseases such as systemic or pulmonary infection, severe trauma, septic shock, toxic inhalation, or aspiration of gastric contents.⁹ Since the two types of APE have the same clinical manifestations—dyspnea, diaphoresis, decreased lung compliance, anxiety,

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TABLE 1. Precipitating Causes of Acute Cardiogenic Pulmonary Edema (APE)*

Cause	Incidence
Worsening heart failure	26%
Coronary insufficiency	21%
Subendocardial infarction	16%
Transmural infarction	10%
Acute dysrhythmia	9%
Medication noncompliance	7%
Dietary indiscretion	3%
Valvular insufficiency	3%
Other	5%

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and increased shunt fraction—it can be extremely difficult to distinguish between the two.⁷

Acute pulmonary edema is often difficult to distinguish clinically from chronic obstructive pulmonary disease (COPD) exacerbations and other acute pulmonary disorders. The rate of misdiagnosis of CHF in the prehospital setting has been documented to be as high as 23% in one study¹⁰ and 32% in another.¹¹ The correct identification of the precipitating events and the immediate administration of appropriate treatment are critical for a positive outcome in CHF patients, because inappropriate therapy initiated as a result of misdiagnosis may result in deleterious effects. Hoffman and Reynolds¹⁰ reported that adverse effects were more common in misdiagnosed patients. Untoward effects included 1) respiratory depression (with or without lethargy) in patients who received morphine; 2) hypotension and bradycardia in patients who received both morphine and nitroglycerin; and 3) arrhythmia associated with hypokalemia and hypotension in patients who received furosemide.

Several initiating events or conditions, including myocardial ischemia, hypertensive crisis, fluid excess, medication noncompliance, diet, and overexertion, may trigger CHF exacerbation. Each may set in motion a vicious cycle of events

that result in cardiogenic APE. The key components of this cycle, outlined in Figure 1, all involve left ventricular (LV) dysfunction.¹² A marked increase in systemic vascular resistance in conjunction with impaired myocardial contractility caused by either systolic or diastolic dysfunction results in pulmonary edema. The increase in vascular resistance leads to an increase in LV diastolic pressure, resulting in increased pulmonary venous pressure. This increases hydrostatic pressure, which then forces fluid to leak out of the pulmonary capillaries into the pulmonary interstitial space and alveoli, producing edema. As edema worsens, so does oxygen diffusion, such that the oxygen saturation drops and compromises cardiac contractility, further inducing the edema.¹³

Field Assessment

A comprehensive primary and secondary physical examination of patients, including prior patient his-

tory, recent illness, prescribed medications, medication compliance, and diet, constitutes an important first step in the diagnosis of CHF in the field (Table 2). Critical elements of the physical exam include accurate interpretation of vital signs. Because APE is often associated with marked elevation in systolic blood pressure, medics should strongly consider APE in the context of acute respiratory distress, hypoxemia, tachypnea, rales or wheezing, and marked hypertension even in the absence of peripheral edema. Such patients often have histories of poorly controlled hypertension and/or prior cardiac disease. Blood pressures >180/120 mm Hg are common in this setting, and in fact are a good sign of reversibility—rapid reduction in blood pressure typically produces prompt relief of respiratory distress. Marked hypertension associated with acute respiratory distress and wheezing, particularly in elderly patients without histories of asthma or intercurrent infection, is strongly

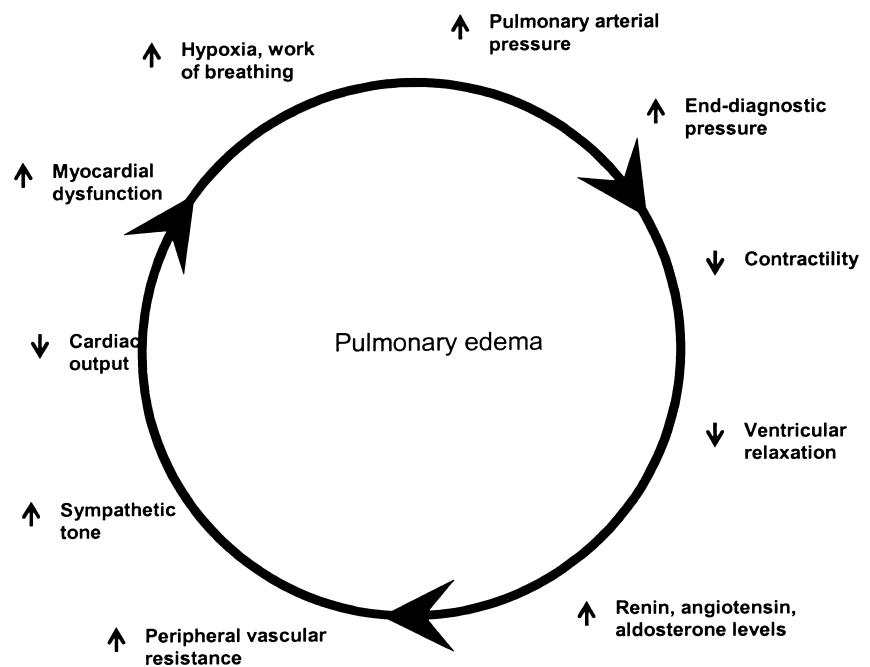


FIGURE 1. Processes involved in pulmonary edema. Cycle may begin at any point but once begun is self-perpetuating. Reprinted with permission from: Sacchetti AD, Harris RH. Acute cardiogenic pulmonary edema. What's the latest in emergency treatment? Postgrad Med. 1998;103:145-66. © The McGraw-Hill Companies.

suggestive of APE. Such a presumptive diagnosis may be supported by evidence of prescription cardiovascular medications and the absence of respiratory medications such as metered-dose inhalers. Emergency medical services (EMS) personnel should always consider alternate conditions, such as pulmonary embolism, pneumonia, asthma, and even drug overdose, before diagnosing patients as having APE. While rhythm strips and 12-lead electrocardiograms (ECGs) are useful in identifying arrhythmia or acute coronary syndrome, they are nonsensitive and nonspecific.^{14,15} Furthermore, ECG and rhythm strip tracings are prone to misinterpretation.¹⁶

In addition to these diagnostic tests, a number of diagnostic aids have been recently proposed for fast and accurate help in the evaluation of CHF. A rapid assay of blood levels of B-type natriuretic peptide (BNP), a neurohormone secreted mainly in the cardiac ventricles as a response to volume expansion and pressure overload, has been reported to be useful in establishing or excluding the diagnosis of CHF in patients with acute dyspnea in the emergency department (ED).¹⁷⁻²² Noninvasive cardiac output (NICO) devices, such as impedance cardiography,²³ have also been suggested as diagnostic tools, but their complexities make such tools currently irrelevant to EMS use.

MANAGEMENT OF APE

Fluid accumulation in the lungs associated with APE, until recently, was attributed to excess accumulation of total body fluid. Accordingly, treatment of APE was aimed at removing excess fluid from the lungs by promoting massive diuresis. However, this explanation for APE could not reconcile the fact that APE typically occurs during early morning hours when fluid intake is minimal. The current explanation is that APE results from fluid redistribution within the body whereby a

part of the intravascular volume is redistributed to the lungs as a consequence of increased intravascular pressure as outlined above.¹³ Primary objectives for the treatment of acute CHF are to reduce pulmonary capillary pressure, to redistribute pulmonary fluid, and to improve forward flow.^{12,13} These may be achieved by reducing LV preload and afterload, providing ventilatory and inotropic supports, and identifying and treating the underlying etiology of the syndrome (Table 3). It should be recognized that these treatment measures are intended for APE patients who are normotensive or hypertensive and not those who are hypotensive. The latter comprises cardiogenic shock secondary to severe LV systolic dysfunction; treatment of these critically ill patients is beyond the scope of this review.

Reduction of LV Preload

The initial effort to reduce the pulmonary congestion in patients presenting with APE should be to reduce the pressure and volume of blood flow to these capillaries. This may be accomplished by dilating the venous capacitance system. This will result in decreased blood return to the right ventricle (preload), thereby reducing blood flow to the pulmonary vascular bed. The net result is a reduction in LV preload, which then allows the LV output to more closely match inflow from the pulmonary system.¹² Pharmacologic therapy to reduce LV preload includes the use of nitrates, morphine, and loop diuretics such as furosemide.

Nitrates

Nitrates at lower dosages are primarily venodilators effective in decreasing pulmonary artery pressure. Intracellularly, they react with and convert sulfhydryl groups to S-nitrosothiols and nitric oxide. These reactive groups then activate guanylate cyclase, which catalyses the formation of cyclic guanosine

TABLE 2. Diagnosis of Congestive Heart Failure

Prior history and comorbid states
<ul style="list-style-type: none"> • Hypertension or cardiovascular disease • Fever or sputum • Presence of sepsis or ischemia • Ischemic heart disease • Valvular disease • Anemia • Dysrhythmias • Thyroid disease
Current situation
<ul style="list-style-type: none"> • Medications (prescribed regimen and current compliance; other drug use) • Diet or exercise indiscretions • Signs of pulmonary edema such as tachypnea, low oxygen saturation, rales, hypoxia • Signs of chronic obstructive pulmonary disease, asthma, or airway obstruction
Tools
<ul style="list-style-type: none"> • Pulse oximetry • End-tidal carbon dioxide trends • Electrocardiogram rhythm and 12-lead if does not delay transport
Potential future diagnostic aids
<ul style="list-style-type: none"> • B-type natriuretic peptide • Noninvasive cardiac output

TABLE 3. Management of Acute Congestive Heart Failure (CHF): Overview

<ul style="list-style-type: none"> • Identify CHF • Identify and treat specific etiology when possible • Reduce left ventricular (LV) preload • Reduce LV afterload • Provide inotropic support when needed • Provide oxygen and ventilatory support when needed • Match receiving facility with needed resources
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monophosphate (cGMP). This nucleotide induces the reentry of calcium back into the sarcoplasmic reticulum of vascular smooth muscle, thereby causing its relaxation.²⁴

Nitroglycerin is currently the vasodilator agent of choice for the reduction of LV preload in the field. It is fast acting, efficient, and easy to administer.^{12,13} Nitroglycerin's effectiveness in reducing mortality in patients with APE in the prehospital setting has been demonstrated by Bertini et al.⁶ In this study, even hypotensive patients (systolic

blood pressure <100 mm Hg), were found to respond positively to nitroglycerin. Likewise, Hoffman and Reynolds compared a number of prehospital management protocols for APE and concluded that nitroglycerin was beneficial, while morphine and furosemide had no additive effect when combined with nitroglycerin and were occasionally deleterious.¹⁰ The beneficial hypotensive effect of nitroglycerin must be closely monitored to ensure that the reduction in blood pressure does not significantly counteract LV preload. A potential disadvantage of nitroglycerin is that it can lead to hypotension,⁹ particularly in patients without adequate preload (e.g., hypovolemia and inferior wall myocardial infarction with significant right ventricular involvement).

Morphine

While morphine has been used for decades to treat acute myocardial infarction (MI), unstable angina, and acute heart failure, few clinical trials have demonstrated its effectiveness in acute CHF. Its popularity in treating pulmonary edema is due to its vasodilatory and anti-anxiety effects, although morphine's vasodilatory effects are transient and the result of histamine release.¹² Recently, concerns have been raised over the use of morphine in treating acute CHF in the ED. A retrospective study of the ED management of APE and intensive care unit (ICU) admissions showed that morphine administered in the ED was associated with significant increases in ICU admissions and the need for endotracheal intubations (ETIs) when compared with sublingual captopril.²⁵ Additionally, a prospective study of morphine treatment in prehospital APE showed that the drug was minimally effective as single therapy or in combination with nitrates.¹⁰ Furthermore, the effects of morphine in depressing respiration and the central nervous system may lead

to deleterious effects in misdiagnosed patients.¹⁰

Furosemide

Furosemide has been a mainstay of treatment for APE since the 1960s, although its effectiveness has been examined in only a few studies. Its primary mechanism of action involves the inhibition of sodium reabsorption in the ascending limb of Henle's loop in the renal medulla. This results in elevated levels of renal salt, with water being excreted. The net effects of this action are a lowering of plasma volume, a decrease in LV preload, and a decrease in pulmonary congestion. These effects are beneficial in patients presenting with pulmonary volume overload.⁸ Besides its diuretic effects, furosemide also influences neurohumoral changes, probably induced through its diuretic effect. Its neurohumoral effects include both vasodilating (by promoting renal prostaglandin E₂ and atrial natriuretic peptide secretion) and vasoconstricting effects.²⁶ The latter can result in peripheral elevation of mean arterial pressure, LV pressure, heart rate, and systemic vascular resistance through enhancement of the renin-angiotensin system (RAS). Stroke volume index and pulmonary capillary wedge pressure initially decrease but subsequently increase after the RAS is enhanced (usually within 15 minutes). The latter effects are obviously not beneficial in the treatment of acute CHF, particularly in the absence of volume overload.^{12,13} Furthermore, misdiagnosis of CHF and subsequent inducement of inappropriate diuresis can lead to increased morbidity and mortality in patients with conditions such as pneumonia, sepsis, or COPD.^{8,10}

Combined Drug Therapies with Nitroglycerin, Furosemide, and Morphine

Nitrates are frequently combined with loop diuretics in treating pul-

monary edema. A complex, randomized, prospective clinical study from Israel investigated the efficacy and safety of these drugs in treating patients presenting with severe pulmonary edema in the prehospital setting.²⁷ This study concluded that intravenous (IV) nitrates, administered as repeated high-dose boluses (3 mg every 5 minutes) after a low dose (40 mg) of furosemide, were associated with lower ETI and MI rates than the administration of low-dose nitrates (1 mg/hour, increased by 1 mg/hour every 10 minutes) and high-dose furosemide (80 mg every 15 minutes). A prospective, observational study on the use of sublingual nitroglycerin in the prehospital setting in cases of presumed MI or CHF analyzed treatment-related adverse events in 300 patients. Only four patients experienced adverse events, most of which were bradycardic-hypotensive reactions, and all recovered subsequently.²⁸

A retrospective case review evaluated the outcomes of 57 patients—presumed to have prehospital APE—who were treated in the field with combinations of nitroglycerin, furosemide, and/or morphine.¹⁰ Although this was only a small study, any combination treatment comprising of nitroglycerin was associated with both subjective and objective (respiratory and heart rates, blood pressure, respiratory distress, mental status) improvement. Combination treatment with furosemide and morphine without nitroglycerin, on the other hand, resulted in a substantial number of patients not responding to treatment, with some actually deteriorating. Ultimately, 23 of 57 (47%) patients in this study were found not to have pulmonary edema.

A larger retrospective case series evaluated outcomes in 493 patients receiving prehospital nitroglycerin, furosemide, and/or morphine versus no treatment for CHF. Mortality was significantly reduced in the

more critical patients receiving any prehospital drug than among those given no treatment (5% versus 33%, $p < 0.01$). When the entire study population—critical and uncritical patients—were considered, the mortality was still significantly lower in the group that received any prehospital treatment (6.7% versus 15.4%, $p < 0.01$).²⁹

Reduction of LV Afterload

A variety of pharmacological agents, including nitroglycerin at higher doses, angiotensin-converting enzyme (ACE) inhibitors, nitroprusside, dobutamine, and dopamine, may be useful in the reduction of LV afterload.

Nitrates at Higher Doses

High-dose nitrates can reduce both preload and afterload and potentially increase cardiac output.³⁰ Because many CHF patients present with very elevated arterial and venous pressure, frequent doses of nitrates may be required to control blood pressure and afterload. Some patients develop tolerance to nitroglycerin, requiring continued administration of higher than usual doses. This tolerance is thought to be the result of depletion of intracellular sulfhydryl groups. Another concern with high doses of nitrates is that certain patients are very sensitive to even normal doses and may experience marked hypotension. These are typically patients with tenuous preload status (e.g., hypovolemia or significant right ventricular infarction in the setting of inferior wall MI). It is therefore critical to monitor blood pressure during high-dose nitrate therapy.

ACE Inhibitors

The ACE inhibitors play a primary role in chronic CHF therapy and have multiple therapeutic advantages for treating APE. These include: reducing both preload and afterload, increasing splanchnic flow, decreasing LV diastolic dys-

function, reducing sodium retention, and reducing sympathetic stimulation. Captopril is an ACE inhibitor that has been studied in the prehospital setting.¹² When a standard tablet is administered sublingually, it rapidly dissolves and has an onset of action of less than 10 minutes. Clinical effects are seen within 15 minutes, with peak effects occurring within 30 minutes.^{31–33} A retrospective study of 181 patients with APE treated in the ED examined the relationship between pharmacologic treatments and rates of ICU admissions.²⁵ Patients in this study were treated with captopril (26%), nitroglycerin (81%), morphine (49%), and/or loop diuretics (73%). Patients receiving captopril had decreased rates of ICU admissions and ETIs as well as shorter ICU stays. A prospective, placebo-controlled, randomized study evaluated the addition of sublingual captopril to the standard treatment regimen (oxygen, nitrates, morphine, and furosemide) in patients brought to the ED with APE.³³ Using a clinical APE distress score for assessment, compared with placebo, the addition of captopril was found to significantly reduce distress scores over the first 40 minutes after administration. This study indicated that certain features of ACE inhibitors are amenable to field use, including ease of sublingual administration, fast onset of action, and low cost.^{12,31,35} However, captopril use may be associated with potential concerns, which include occasional hypotension and a variable duration of effect in comparison with nitrates. In addition, there is some evidence to suggest that aspirin used in conjunction with ACE inhibitors may reduce the advantage of ACE inhibitors in CHF.³⁴ However, no double-blind studies have been conducted to confirm this.

Besides the sublingual route, ACE inhibitors may also be administered intravenously. Enalaprilat maleate is the only IV ACE inhibitor available in the United States. IV capto-

pril, on the other hand, is available in England.³⁵ The efficacy and safety of IV enalaprilat in the treatment of pulmonary edema and CHF have been demonstrated in two small, randomized trials.^{36,37}

Nitroprusside

Acute pulmonary edema patients presenting with severe hypertension and those refractory to nitrate and ACE inhibitor treatments may be candidates for administering nitroprusside sodium.⁸ Nitroprusside is a potent agent capable of directly causing vasodilation in vessels resistant to other vasodilators. The net effect is a reduction in blood pressure and a reduction in LV preload and afterload. Nitroprusside's main side effects include hypotension and cyanide and thiocyanate toxicity, with prolonged use.⁹ There is a need, therefore, to continuously monitor blood pressure in these patients. The need for a carefully titrated continuous infusion, the use of glass containers shielded from light, and the challenges in prehospital continuous blood pressure monitoring preclude the use of nitroprusside in the field environment.²⁵

Natriuretic Peptides

B-type natriuretic peptide (BNP) such as nesiritide are currently being developed as alternative treatment options for CHF, in addition to their potential diagnostic application. Nesiritide is a potent vasodilator.³⁸ It decreases systemic vascular resistance, systemic arterial pressure, pulmonary capillary wedge pressure, right atrial pressure, and mean pulmonary arterial pressure. In addition, it can increase stroke volume, cardiac output, and may also promote diuresis. The major adverse effect of nesiritide is its dose-related hypotension. Although nesiritide represents an alternative to high-dose nitrates in the management of CHF in the hospital, its use in a prehospital setting has yet to be tested.

Ventilatory Support

Patients with acute CHF may be treated with a spectrum of ventilatory support modalities based upon the patient's clinical condition and comorbid factors. Standard initial treatment includes oxygen (O₂) therapy to maintain O₂ saturation of at least 92–93% and the use of inhaled bronchodilators when bronchospasm is evident. In severe respiratory failure (e.g., altered mental status and ineffective respiratory effort), mechanical ventilation with ETI is recommended. However, ETI is associated with various adverse effects, including infectious (e.g., nosocomial pneumonia, sinusitis) and noninfectious (e.g., barotrauma, oral, nasal, or laryngeal trauma, respiratory muscle weakness, prolonged weaning) complications.^{39–42} In order to avoid these complications and lengthy ICU stays, noninvasive ventilatory support is being used increasingly.

Noninvasive Positive Pressure Ventilation

Noninvasive positive pressure ventilation (NIPPV), traditionally used for COPD and asthma,^{43–47} is now considered an effective adjunct treatment for APE.^{48–52} The therapeutic effect of noninvasive pressure support lies in its ability to increase intra-alveolar pressure. This shifts the flow of fluid back into the pulmonary capillaries and thereby reduces pulmonary congestion. Two different methods of providing NIPPV are used: continuous positive airway pressure (CPAP), which provides a constant level of positive pressure applied throughout inspiration and exhalation, and bilevel positive airway pressure (BiPAP), which allows provision of higher pressure during inspiration than expiration.⁵³

Several randomized, controlled trials outside the United States showed that CPAP administered through a face or nasal mask for ICU patients with APE was effec-

tive in improving oxygenation, respiration, and hemodynamics and may reduce the need for ETI or ventilator treatment.^{54–56} A meta-analysis by Pang et al. of three randomized clinical trials showed a 26% reduction in intubation rates and a 7% decrease in hospital mortality when CPAP was compared with standard therapy.⁵⁷ A retrospective chart review of 75 ED patients presenting with APE in Australia found that adjunctive treatment with CPAP delivered by a face mask was effective and well tolerated. Only three patients (4%) required subsequent ETI and mechanical ventilation. The in-hospital mortality rate was 15%, while 71% of patients were discharged from the ED to general wards. No adverse events were observed in 89% of the patients during CPAP therapy. Five percent of the patients were unable to tolerate the face mask.⁵⁸

Only a few prehospital studies involving CPAP have been conducted. A Swedish study compared outcomes after treatments for acute heart failure during two time periods: one period of standard treatment consisting of nitroglycerin, furosemide, or both (first period) and one period of intensified treatment with nitroglycerin, furosemide, and CPAP (second period).⁵ The use of drug therapy and CPAP in patients increased dramatically from the first period to the second period: nitroglycerin from 4% to 68%, furosemide from 13% to 84%, and CPAP from <1% to 91%. A greater percentage of patients in the second period had fulminant pulmonary edema (FPE) on ambulance admission (78% versus 60% for the first period, $p < 0.0001$), but on admission to the hospital, a lower percentage of patients had FPE during the second period (76% versus 93% for the first period, $p < 0.0001$). There was also a significantly lower mean level of serum creatine kinase (CK-MB) in patients in the second period, implying less myocardial dam-

age ($p = 0.007$). Although there was an improvement in symptoms during transport with less myocardial damage, mortality remained high, with no significant difference between treatment groups.

A small, prospective case-series analysis on the prehospital use of CPAP by trained paramedics in 19 patients with cardiogenic pulmonary edema showed that none of the patients required field intubation and that hemoglobin oxygen saturation increased from a mean of 83.3% to 95.4% after CPAP administration via a face mask.¹¹ Two patients intolerant of CPAP required ETI upon ED arrival, and an additional five patients required ETI within 24 hours. There were no adverse events related to CPAP therapy. These results demonstrate that field use of CPAP is feasible, but certain obstacles need to be overcome. In particular, the authors noted that the paramedic's lack of experience with this therapy led to problems with achieving good mask fit and titrating pressure levels.

Bilevel positive airway pressure (BiPAP) has been investigated as an alternative to CPAP in a number of conditions but has shown a significant advantage over CPAP only in patients whose respiratory failure is due to COPD exacerbation.⁵⁹ A number of individual studies reported some success with BiPAP and some problems associated with its use in treating acute CHF. A small, randomized, prospective trial of APE treatment with BiPAP or CPAP showed that there was a more rapid improvement in ventilation and vital signs with BiPAP than with CPAP. However, there was a significantly higher rate of MI associated with BiPAP treatment than with CPAP treatment (71% with BiPAP versus 31% with CPAP) if a previously excluded patient was used in the statistical analysis ($p = 0.02$).⁶⁰ Two additional studies with small patient numbers also supported the effectiveness of BiPAP. Results from a study in Italy of ICU patients in acute res-

piratory failure reinforced the effectiveness of gas exchange with less morbidity for BiPAP compared with conventional ventilation,⁶¹ while a study from Spain documented a significantly faster resolution of APE with BiPAP.⁶² However, more adverse events were again reported in a study from Israel comparing BiPAP (55% MIs) with high-dose nitrate therapy (10% MIs) ($p = 0.006$).⁶³ Very different results were reported from one of the few in-hospital studies conducted in the United States. This study found no significant differences in intubation rates, mortality, or incidences of acute MIs observed in patients with acute CHF treated with BiPAP compared with oxygen flow delivered by mask (MASK). For the patients (21 with BiPAP, 17 with MASK) included in the study, the intubation rate was 23.5% for BiPAP and 41.2% for MASK, and the acute MI rate was 19% for BiPAP and 29.4% for MASK.⁶⁴

In an out-of-hospital study of patients with presumed CHF, EMS personnel considered the use of BiPAP to be safe and judged this method to improve dyspnea and respiratory distress in their patients.⁶⁵ Although oxygen saturation was significantly greater for the BiPAP plus conventional treatment group compared with the conventional treatment group, treatment times, lengths of hospital stay, intubation rates, and death rates were not significantly different between the groups.

Of the two types of noninvasive ventilatory support, there is good supporting evidence for the effectiveness of CPAP. The technology is reasonable for field implementation, but there is room for further refinement, especially regarding the volume of oxygen consumption. Greater experience of field providers should also lead to better outcomes, as this therapy is not only patient-dependent, but operator-dependent as well. In the case of BiPAP, the risk-benefit ratio has not

been established definitively in the literature. In addition, the existing technology for BiPAP is suboptimal for out-of-hospital use. Further field trials investigating the implementation of these modalities and testing technological refinements are needed.

Inotropic Support

Intravenous positive inotropic support is reserved for CHF patients who are refractory to nitrates, diuretics, and ACE inhibitors and for patients presenting with decompensated heart failure. Inotropic agents such as dobutamine, dopamine, and phosphodiesterase inhibitors stimulate cardiac contractility as well as dilate peripheral blood vessels. The former increases cardiac output, while the latter decreases pulmonary wedge pressures.⁹ Dopamine at low dose and dobutamine at low to medium doses can also be used for afterload reduction. The beneficial effects of inotropic agents, however, are apparently short-lived. These agents are believed to accelerate the underlying problem, which may subsequently result in rapid deterioration of the condition and increased mortality.⁶⁶ Furthermore, inotropic agents can produce tachycardia, myocardial ischemia, and dysrhythmias, the latter due to its effects in increasing oxygen demand.⁹ Thus, inotropic agents are not recommended for the routine treatment of APE.

It should be noted, however, that inotropic support is often needed for severe hypoperfusion states when other treatment modalities are not available. In addition, in a small proportion of patients who are mildly hypotensive (systolic blood pressure 80–110 mm Hg) but who are not clinically in shock, dobutamine is the agent of choice. Nitroglycerin or other pure vasodilators cannot be administered to these patients due to the existing low blood pressure. The vasodilatory effect of dobutamine

will hopefully bring about improved blood flow with increased cardiac output but without changing blood pressure in these hypotensive patients.

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CONSENSUS PRESENTATION

The consensus of the group focused on the importance of understanding that the pathogenesis of APE is related to intravascular fluid redistribution rather than to primary volume overload (Fig. 1). Management of suspected APE begins with correct assessment and management of underlying causes of elevated ventricular filling pressures, and continues with improving oxygenation with the application of ventilatory support, reduction of LV preload and afterload with nitroglycerin, and inotropic support when necessary. Care must be taken with drugs such as furosemide and morphine, as patient outcomes can be adversely affected when administered for conditions mimicking APE. EMS personnel must assiduously seek hallmarks of acute CHF as opposed to other medical conditions associated with acute dyspnea. Sophisticated, rapid tools such as quantitative BNP assays and noninvasive hemodynamic devices may one day provide greater diagnostic accuracy in the field (Table 2).

A guide based on clinical evidence for treating prehospital patients suffering from acute CHF was suggested (Table 4). This strategy outlined a classification of treatment levels based on the severity of symptoms. A patient whose only complaint is dyspnea on exertion (class I) requires supplemental O₂ and routine monitoring of vital

TABLE 4. Classification for Treatment

Class	Characteristics	Treatment*	Comments
I Asymptomatic	Dyspnea on exertion but not currently at rest	Provide supplemental O ₂	Maintain SaO ₂ > 93%
		Consider intravenous access	Saline lock
II Mild Symptoms	Mild dyspnea even at rest and despite O ₂ treatment Able to speak full sentences If SBP > 110 mm Hg	Low-dose nitroglycerin (0.4 mg Q 4–5 minutes)	If no contraindication to nitrates (e.g., sildenafil within 24 hours) and if SBP > 110 mm Hg
		Definite IV access	—
		Monitor ECG	12-lead when available
		Chew aspirin	If suspect coronary ischemia
III Moderate Symptoms	Moderate dyspnea (SaO ₂ < 93% on O ₂) SBP > 110 mm Hg Unable to speak full sentences Normal mental status	Bronchodilator	If wheezing (use nebulizer if MDI cannot be used)
		High-dose SL nitroglycerin	If SBP > 110 mm Hg
		Consider furosemide	If peripheral edema
IV Severe Symptoms	Severe dyspnea—respiratory failure: hypoxia, altered sensorium, diaphoresis, and one-word sentences	High-dose SL nitroglycerin (0.8–2 mg Q 3–5 min)	Watch carefully for hypotension (use only if SBP > 110 mm Hg)
		Bronchodilators—nebulizers	Watch for respiratory depression
		Consider morphine (2–4 mg)	For agitation
		Furosemide	If peripheral edema
		Inotropic agents	For mild cardiogenic shock or hypotension
		Vasopressors	For severe shock/hypotension
Consider ETI or NIPPV	If time and patient tolerance permit		

*Treatment at each level should consider the lowest dose applicable; SL = sublingual; MDI = metered-dose inhaler; SBP = systolic blood pressure; IV = intravenous; ECG = electrocardiogram; ETI = endotracheal intubation; NIPPV = noninvasive passive pressure ventilation.

signs and pulse oximetry. Consideration may be given for IV access, but this is optional. For patients with signs of increasing severity of heart failure, the treatment options range from: low-dose nitroglycerin (Class II), to high-dose nitroglycerin/furosemide (Class III), to high-dose nitroglycerin/morphine, inotropic support/vasopressors, and NIPPV (Class IV).

TREATMENT OPTIONS

Nitrates were recommended as first-line therapy for APE in the field with symptom resolution as

the primary treatment goal. Nitrates act as venodilators, providing both subjective and objective improvement, and might (with high-dose, repeated sublingual or spray administration) decrease ETI rates, incidences of MIs, and mortality. Blood pressure is an important gauge of effective nitrate dosing. Endpoints should be primarily guided by the patient's level of dyspnea and oxygen saturation, and avoiding hypotension. In patients with systolic blood pressures below 100–110 mm Hg, nitroglycerin should not be routinely administered. Intravenous nitrates

are an option; however, this is more cumbersome and requires close hemodynamic monitoring. Nitroglycerin paste has a slower onset of action than the preferred sublingual or spray formulations, but is an option for patients in extremis. Furthermore, participants believed that the sustained effect of the paste is an acceptable alternative to repeated sublingual administration in patients whose acute symptoms have resolved.

The use of loop diuretics such as furosemide requires careful consideration. While furosemide is beneficial in decreasing the pulmonary

capillary wedge pressure, it also increases the systemic vascular resistance. The group's primary concern involved the increased morbidity and mortality associated with prehospital administration of diuretics in conditions that mimic APE. The use of diuretics in combination with nitrates has also been proved to have no early clinical benefit. The group agreed that in the absence of peripheral edema or other evidence of excess total body water (such as documented acute weight gain), routine diuretic administration should be avoided.

Evidence for the use of ACE inhibitors is not currently sufficient to substantiate their use in the prehospital care of APE. Although they have an essential role in chronic heart failure, the lack of supporting data and potential disadvantages including hypotension, adverse interaction with aspirin, decrease in the glomerular filtration rate, and longer duration of action preclude endorsing their use in APE at this time. Inotropic agents, including dopamine and dobutamine, are more applicable for patients with incipient cardiogenic shock.

Bronchodilator use is appropriate when wheezing is the result of bronchospasm, but should not preclude delivery of other specific therapy for CHF, such as nitroglycerin or CPAP. Noninvasive ventilatory support with CPAP or BiPAP offers APE patients physiologic advantages, since they have been shown in non-EMS settings to increase lung volume, reduce the effort of breathing, and improve hemoglobin oxygen saturation and vital signs. However, it is not clear whether CPAP or BiPAP provides a consistent outcome advantage. Initial field studies have been promising, but issues such as the need for specialized training in mask adjustment and pressure titration, high-volume oxygen consumption requirement for operation, or suboptimal portability due to the need for an electrical power source present logistical obstacles.

The use of BNPs (e.g., nesiritide), both in the diagnosis and in the management of CHF, needs to be further evaluated, especially in the prehospital setting.

CONCLUSION

Decisions in the field for treatment of acute CHF should be coordinated with available facilities and resources in the ED. Acute pulmonary edema is a common and often life-threatening condition encountered by prehospital emergency medical personnel. Patients with this condition must receive rapid, accurate assessment and aggressive treatment. High-dose nitrates represent the out-of-hospital treatment of choice, while diuretics and morphine should be reserved for select patient groups. More data are needed on the efficacy and safety of ACE inhibitors to justify their use in the field. CPAP has been shown to be effective, but more experience and refinement of delivery systems for the prehospital environment are needed. Logistical delivery issues also exist for BiPAP, and there is currently less convincing evidence of its safety in this setting. Emerging diagnostic assays and tools offer promise of fast and accurate diagnosis of CHF. Finally, transport of APE patients should be matched with the cardiovascular care resources of receiving facilities to optimize chances of survival.

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