COMPREHENSIVE REVIEW

When Pressure is Positive: A Literature Review of the Prehospital Use of Continuous Positive Airway Pressure

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Conflicts of interest: The authors have no conflicts of interest to declare.

Keywords: acute pulmonary edema; CPAP; emergency care; paramedic; prehospital

Abbreviations:
APO: acute pulmonary edema [oedema]
CPAP: continuous positive airway pressure
COPD: chronic obstructive pulmonary disease
ETI: endotracheal intubation

Received: August 30, 2011
Revised: June 18, 2012
Accepted: September 22, 2012

Online publication: November 9, 2012

doi:10.1017/S1049023X12001562

Abstract

Background: Heart failure poses a significant burden of disease, resulting in 2,658 Australian deaths in 2008, and listed as an associated cause of death in a further 14,466 cases. Common in the hospital setting, continuous positive airway pressure (CPAP) therapy is a non-invasive ventilation technique used to prevent airway collapse and manage acute pulmonary edema (APO). In the hospital setting, CPAP has been known to decrease the need for endotracheal intubation in patients with APO. Therefore the objective of this literature review was to identify the effectiveness of CPAP therapy in the prehospital environment.

Methods: A review of selected electronic medical databases (Cochrane, Medline, EMBASE, and CINAHL) was conducted from their commencement date through the end of May 2012. Inclusion criterion was any study type reporting the use of CPAP therapy in the prehospital environment, specifically in the treatment of heart failure and acute pulmonary edema. References of relevant articles were also reviewed.

Results: The literature search located 1,253 articles, 12 of which met the inclusion criteria. The majority of studies found that the use of CPAP therapy in the prehospital environment is associated with reduced short-term mortality as well as reduced rates of endotracheal intubation. Continuous positive airway pressure therapy was also shown to improve patient vital signs during prehospital transport and reduce myocardial damage.

Discussion: The studies conducted of prehospital use of CPAP to manage APO have all demonstrated improvement in patient outcomes in the short term.

Conclusion: Available evidence suggests that the use of CPAP therapy in the prehospital environment may be beneficial to patients with acute pulmonary edema as it can potentially decrease the need for endotracheal intubation, improve vital signs during transport to hospital, and improve short-term mortality.

Williams B, Boyle M, Robertson N, Giddings C. When pressure is positive: a literature review of the prehospital use of continuous positive airway pressure. ***Prehosp Disaster Med.*** **2013;28(1):52-60.**

Introduction

In 2007, heart failure was the fifth leading cause of death for older females and the tenth for older males in Australia.[1] There were 45,000 patients discharged from hospital with a diagnosis of heart failure, and 5.8% of Australians over the age of 65 were reported to have died as a result of heart failure in 2007.[1] Data from Ambulance Victoria revealed that in 2009 paramedics attended 1,700 cases of acute pulmonary edema (APO) and 377 cases of cardiac failure.[2]

Non-invasive CPAP is a treatment procedure used to improve oxygenation and ventilation in conscious patients experiencing respiratory distress or respiratory failure.[3] During normal ventilation, air is drawn into the lungs along a negative pressure gradient created when the diaphragm contracts. Continuous positive airway pressure therapy provides a continuous positive pressure regardless of the phase of respiration. This acts to reduce atelectasis and pulmonary shunting, thus improving gas exchange and vital signs such as blood oxygen saturation.[3]

In hospital wards and emergency departments, CPAP therapy is currently indicated for conscious patients in acute respiratory distress as a result of congestive cardiac failure, or for acute exacerbations of chronic conditions such as chronic obstructive pulmonary

disease (COPD) and asthma.[4–6] A further benefit of CPAP therapy is its potential to reduce the incidence of prehospital endotracheal intubation (ETI), when combined with other appropriate treatment.[7,8] Given the unpredictable nature of the prehospital environment, ETI attempted in the field has been shown to be less successful than when attempted in the hospital, and is associated with higher rates of aspiration of gastric contents and other complications.[9,10] Endotracheal intubation is also known to cause traumatic injury to the upper airway, and results in increased risk of ventilator-associated pneumonia.[11] Studies have shown that patients arriving in hospital emergency departments already intubated are more likely to remain so, exposing them to the aforementioned risks.[12,13]

Despite the significant morbidity and mortality from heart failure, to the authors' knowledge, there are no published Australian prehospital studies examining paramedic-initiated CPAP for APO. Considering the success and benefits of in-hospital CPAP therapy in the treatment of patients with respiratory distress and APO, this raises the question of whether there is a place for CPAP therapy in the prehospital setting in Australia. Therefore, the objective of this literature review was to identify the effectiveness of CPAP therapy in the prehospital environment.

Methods

A literature review was undertaken using specific medical electronic databases, from their commencement date through the end of May 2012; these included Cochrane, Medline, EMBASE, and CINAHL.

The following MeSH headings and keywords were used: emergency medical services; emergency medical technicians; ambulances; air ambulances; military medicine; emergency treatment; emergency medicine; first aid; emergency care; emergency patients; prehospital care; transportation of patients; pre-hospital; prehospital; out of hospital; out-of-hospital; ambulances; air ambulances; paramedic; right ventricular failure; left ventricular failure; congestive heart failure; pulmonary edema; continuous positive airway pressure; CPAP; pulmonary ventilation; and non-invasive ventilation.

Articles of any study type were included if they reported the use of CPAP therapy in patients with pulmonary edema in the prehospital setting. Articles were excluded if they were not written in English, involved a secondary transport from one hospital to another, featured animals in the study, or were letters to the editor or editorials. The reference list of retrieved articles was reviewed to ascertain if articles were missed during the initial search process.

The quality of the included articles was assessed according to the Australian National Health and Medical Research Council (NH&MRC) levels of evidence[14] (Table 1).

Level	Intervention
1	A systematic review of level II studies
2	A randomized controlled trial
3 (I)	A pseudo-randomized controlled trial (ie, alternative allocation or some other method)
3 (II)	A comparative study with concurrent controls: nonrandomized, experimental trial, cohort study, case–control study, interrupted time series with a control group
3 (III)	A comparative study without concurrent controls: historical control study, two or more single-arm studies, interrupted time series without a parallel control group
4	Case series with either post-test or pre-test and post-test outcomes

Table 1. Australian National Health and Medical Research Council Levels of Evidence[14]

Results

The search located 1,253 articles; initially, 38 publications met the inclusion criteria and further analysis of these articles showed 12 articles were suitable for further review.[4–8,11,15–20] A brief summary of each study is shown in Table 2; reasons for studies being excluded are summarized in Table 3.

Reduced Rate of Prehospital Endotracheal Intubation

In a non-randomized control group study comparing CPAP therapy and pre-existing treatment algorithms in the management of prehospital acute pulmonary edema (APO), it was found that the use of CPAP therapy was associated with a significantly lower rate of ETI.[11] Patients were enrolled in this study based on the treating paramedic's field impression of APO, and 24% of these patients ultimately received a hospital discharge diagnosis other than APO. To control for the potential confounding effects of misdiagnosis, data were analyzed for all patients on an intention-to-treat basis, and then repeated on the subset of patients with confirmed APO. When considering all patients in the study, ETI was performed on 25.26% of control patients compared with 8.92% of patients who received CPAP therapy ($P = .003$). Within the subset of patients with confirmed APO, the difference in intubation rates was slightly higher; 28.12% of control patients were intubated compared with 6.66% of CPAP therapy patients ($P = .001$).

These findings are important in the context of paramedic diagnosis and patient assessment, and provide some evidence that diagnosing respiratory pathology in the prehospital setting is often difficult due to limited diagnostic tools. Another study reported that no patients required intubation after being on CPAP; however, two of these patients required intubation prior to intensive care unit (ICU) admission.[4] A study by Warner also reported that no patients required prehospital intubation after CPAP treatment had commenced.[20] In addition, a recent retrospective review of a large ambulance provider in New Jersey (USA), revealed that ETI was reduced in the CPAP-treated group versus the non-CPAP treated group (4 vs 11, $P < .01$).[7] These findings provide further clinical evidence on the potential of prehospital CPAP.

Reduced Short-Term Mortality

In a randomized, controlled trial published in 2007, 63 patients who received early treatment with CPAP therapy were shown to have reduced in-hospital mortality rates when compared to those patients who received delayed CPAP therapy.[8] In the study, patients were randomly allocated into early and late CPAP therapy groups, with the early CPAP group receiving CPAP therapy immediately, and the late CPAP group receiving CPAP therapy 15 minutes after standard medical treatment had been initiated. The in-hospital

https://doi.org/10.1017/S1049023X12001562 Published online by Cambridge University Press

Author, Year	Study Type & Level of Evidence (National Health & Medical Research Council)	Study Size (n)	Age Mean (SD)	Patient Group	Key Findings	Limitations
Warner, 2010[20]	Observational study Level: 3	89	Not stated	Patients > 12 years of age with acute respiratory distress, respiratory rate > 25 per minute, pulse oximetry <95% on supplementary oxygen, GCS > 10, systolic BP > 90 mmHg.	Patient who received CPAP were not intubated in the prehospital setting or in the ED, there were less hospital and ICU admissions with hospital and ICU length of stay less.	Small participant numbers, non-randomized study Subjective use of CPAP device Patients not analyzed according to cause of respiratory distress
Garuti et al, 2010[18]	Prospective non-randomized observational study	35	80.1 (7.9)	Patients with acute respiratory failure from any cause.	CPAP reduced mortality by 94%; hospital length of stay was decreased by 66%.	Small prehospital sample Part of a three-way study Nurses undertook the intervention.
Foti et al, 2009[16]	Controlled clinical trial Level: 3	121	ALS (Physician) 78.5 (7.8) ALS (Nurse) 77.6 (10.1)	Patients with suspected acute cardiogenic pulmonary edema (ACPE) rescued by ALS (Physician) between 1/12/1998 and 31/12/199 and rescued by ALS (Nurse) between 1/2/2001 and 1/12/2002	No patients required prehospital intubation There were no adverse events from the device. Patients physiological status improved in both groups	The study was not randomized Generalizability is limited as the study was conducted by non-paramedic staff
Dieperink et al, 2009[15]	Prospective case series Level: 3	32	82 years	Patients presenting severe with acute respiratory distress during the period March to December 2006 were eligible for the study	Patients who received CPAP therapy and nitroglycerin and frusemide had improved oxygen saturation (79% to 96%). While nursing staff correctly diagnosed APO in 81% of patients, no clear survival benefit was found using CPAP.	Unblinded study Variation in patient etiology between study groups Generalizability is limited as the study was conducted by non-paramedic staff
Thompson et al, 2008[5]	Randomized controlled trial Level: 1	71	Control group: 70.5 years Experimental group: 69 years	Patients presenting to advanced life support paramedics with acute respiratory distress during the period January, 2002 and March, 2006 were eligible for the study Patients in the severest subset of the shortness of breath cohort were selected	Patients who received CPAP therapy in combination with usual care interventions (nitroglycerine, frusemide, morphine, salbutamol and ipratropium bromide) were significantly less likely to be intubated than patients receiving usual care interventions only	Patients who failed to give consent were not recorded No valid severity of respiratory distress score was used to determine eligibility No absolute objective criteria for endotracheal intubation was used

Table 2. Included Studies *(continued)*

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Author, Year	Study Type & Level of Evidence (National Health & Medical Research Council)	Study Size (n)	Age Mean (SD)	Patient Group	Key Findings	Limitations
					There was an absolute reduction in mortality of 21% in patients who received CPAP therapy compared to those patients who did not	Generalizability is limited as the study was conducted in an urban environment with short transport to hospital times
Plaisance et al, 2007[8]	Randomized controlled trial Level: 1	124	69.7 (9)	Adult patients with clinical symptoms of acute pulmonary oedema treated by ALS responders between January, 1998 and December, 1999	Patients who received early CPAP therapy had greater improvement in physiological variables, and a reduced rate of ETI and in-hospital mortality than those for whom CPAP therapy was delayed. CPAP therapy can improve patient condition even when used in isolation (without pharmacological treatment)	Unblinded study Variation in patient aetiology between study groups
Hubble et al, 2006[11]	Nonrandomized control group design Level: 2	215	Control group: 70.1 years Experimental group: 73.9 years ($P = .03$)	All consecutive adult patients (18 years or older) transported by the two participating EMS systems between July 1, 2004, and June 30, 2005, with a field diagnosis of acute cardiogenic pulmonary edema	Group receiving CPAP therapy had a significantly lower rate of ETI, a significantly lower mortality rate, and significantly more improvement in respiratory rate, heart rate and dyspnoea score, when compared to the control group	Nonrandomized study Control and experimental groups were transported to different hospitals by different EMS services Variation in treatment between control and experimental groups other than use of CPAP therapy e.g. average dosage of frusemide, morphine and nitroglycerine; flow rate and concentration of oxygen delivered Potential sampling bias; inclusion in study based on field diagnosis of acute pulmonary edema

Table 2. *(continued).* Included Studies

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Author, Year	Study Type & Level of Evidence (National Health & Medical Research Council)	Study Size (n)	Age Mean (SD)	Patient Group	Key Findings	Limitations
Kallio et al, 2003[4]	Retrospective cohort study Level: 2	121	Not indicated	All consecutive patients with a clinical impression of acute pulmonary oedema treated by a mobile intensive care unit, January 1, 1998- December 31, 1999	Patients who received CPAP therapy had a significant elevation in blood oxygen saturation, and significant reductions in respiratory rate, heart rate and systolic blood pressure Prehospital and in-hospital rates of ETI among patients who received CPAP therapy were low	Retrospective study; cannot control for hemodynamic effects of nitroglycerine and morphine Limited access to necessary data Results possibly confounded by administration of oxygen therapy for an unspecified period of time before paramedics arrived and commenced CPAP therapy
Templier, 2003[19]	Prospective open study Level: 3	57	Not stated	Patients with suspected acute cardiogenic pulmonary edema (ACPE) over a 12-month period, June 1, 1999 through May 31, 2000	CPAP in place for 88% of patients on arrival at hospital, 4% required prehospital intubation, the majority of patients had concomitant drug therapy. All patients showed a decrease in pulse rate, respiratory rate, and BP. All patients showed an increase in oxygen saturation.	Medical directed, not paramedic
Kosowsky et al, 2001[6]	Prospective case series analysis Level: 3	19	68.9 years	Any patient in respiratory distress transported by a paramedic unit to one of three emergency departments from January through April, 2000, was eligible for the study. CPAP therapy was administered to patients with suspected acute cardiogenic pulmonary oedema in imminent need of ETI.	Patients had a noticeable improvement in oxygen saturation within minutes of commencing CPAP therapy. None of the patients were intubated in the field, and 63% avoided ETI completely. The success of CPAP therapy is dependent on appropriate patient selection.	Small sample size Unblinded study Large variation in age and severity of presenting condition within the study population
Gardtman et al, 2000[17]	Retrospective case series analysis	300	Period 1: 77 years	Consecutive patients with acute severe heart failure transported by a Mobile Coronary Care	More aggressive prehospital intervention reduced the severity	Small sample size

Table 2. *(continued).* Included Studies

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Author, Year	Study Type & Level of Evidence (National Health & Medical Research Council)	Study Size (n)	Age Mean (SD)	Patient Group	Key Findings	Limitations
	Level: 3		Period 2: 76.5 years	Unit before and after the introduction of an intensified treatment regime (CPAP therapy, frusemide and nitroglycerine)	of symptoms during transport and limited the extent of myocardial damage. No significant improvement in long-term outcomes (mortality and rates of rehospitalisation) was observed.	Observational, unblinded study Inability to delineate positive effects of various interventions (CPAP therapy, frusemide, nitroglycerine) Number of patients with missing information was high
Dib, Matin & Luckert, 2012[7]	Retrospective case series analysis Level: 3	387	2 years	Respiratory rate > 25 breaths/min, labored and shallow breathing, bilateral rales, history of CHF, intact mental status, and prehospital clinical diagnosis of CHF.	The increase in SaO2 for the CPAP group (9%) vs. the non-CPAP group (5%) was statistically significant ($P < .01$). Systolic blood pressure (BP) reduction (CPAP [27.1 mm Hg], non-CPAP [19.9 mm Hg], $P < .01$), diastolic BP reduction (CPAP [14.1 mm Hg], non-CPAP [7.4 mm Hg], $P < .01$), heart rate reduction (CPAP [17.2 beats/min], non-CPAP [9.6 beats/min], $P < .01$), respiratory rate reduction (CPAP [5.63], non-CPAP [4.09], $P < .01$), [and ETI reduction (CPAP [2.6%], non-CPAP [5.46%], $P < .01$), all were statistically significant.	Small sample size Observational, unblinded study non-randomization of study subjects, and no hospital follow-ups

Table 2. *(continued).* Included Studies
Abbreviations: ALS, advanced life support; CHF, congestive heart failure; ETI, endotracheal intubation.

mortality rate of patients in the early CPAP group was 3.23%, while in the late CPAP group, it was 15% ($P = .05$). In a retrospective review (Dib et al) involving 387 patients, no prehospital mortalities were reported in either CPAP-treated groups or non-CPAP-treated groups.[7] A study by Garuti et al reported a reduction in mortality of 94% in the prehospital component of the study compared to standard prehospital management, $P = .011$.[18] Whether these outcomes could be improved in other prehospital settings is an area for further research, and would be an important addition to the limited body of knowledge.

Improvement in Physiological Variables (Vital Signs)

A retrospective cohort study published in 2003 found that patients with suspected APO treated with CPAP therapy had a

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Author, Year	Reason for Exclusion
Baird et al, 2009[21]	This paper reported on CPAP for neonatal patients during interhospital transfer by a medical team.
Bledsoe, 2009[22]	This is a descriptive paper that mentions the use of CPAP in managing congestive heart failure.
Bledsoe and Bojan, 2004[23]	This is a descriptive paper that mentions the use of CPAP in managing flash pulmonary edema.
Bomont and Cheema, 2006[24]	This paper reported on CPAP for neonatal patients during interhospital vehicle transfer.
Bruge et al, 2008[25]	This paper described the use of bilevel positive airway pressure (BiPAP) for acute respiratory distress management.
Brywcznski et al, 2009[3]	The paper was written for a journal club and commented on the included study by Thompson et al.[5]
Corey, 2007[26]	This is a descriptive paper that mentions the use of CPAP in managing congestive heart failure.
Dominguez, 2002[27]	This is a case study that mentions CPAP as a possibility for prehospital management of congestive heart failure.
Goss and Zygowiec, 2006[28]	This is a descriptive paper that mentions the use of CPAP in managing pulmonary edema and chronic obstructive pulmonary disease.
Hastings et al, 1998[29]	This is a descriptive paper that mentions the use of CPAP in managing congestive heart failure.
Hatlestad, 2002[30]	This is a descriptive paper that mentions the use of CPAP as one strategy in managing acute respiratory failure.
Hewitt and Persse, 2007[31]	This is a descriptive paper that mentions the use of CPAP in managing acute respiratory failure that commences in the prehospital setting and continues in the hospital.
Hildwine, 2006[32]	This is a descriptive paper that mentions the use of compact 10 cm of CPAP device for the prehospital setting.
Hubble et al, 2008[33]	This was an economic analysis of prehospital CPAP that did not report patient outcomes.
Mattu and Lawner, 2009[34]	This is a descriptive paper that mentions the use of CPAP as one of several management options for treating congestive heart failure.
Oherrick, 2009[35]	This is a descriptive paper that outlines the pathophysiology behind congestive heart failure and the prehospital management, including CPAP, relevant to the emergency department.
Schrank, 2007[36]	This is a descriptive paper highlighting the pathophysiology behind the use of CPAP in managing congestive heart failure.
Simpson and Bendall, 2011[37]	This was a literature review of non-invasive management, including CPAP, in managing acute cardiogenic pulmonary oedema.
Sullivan, 2005[38]	This is a descriptive paper that mentions the use of CPAP in managing congestive heart failure, chronic obstructive pulmonary disease, and asthma.
Wesley, 2007[39]	This is a descriptive paper about adding the use of CPAP to the basic EMT scope of practice.
Younger, 2007[40]	This is a descriptive paper that mentions the use of a nitroglycerine infusion in conjunction with CPAP.

Table 3. Excluded Studies
Abbreviations: CPAP, continuous positive airway pressure; EMT, emergency medical technician.

significant improvement in blood oxygen saturation (from 77% before CPAP therapy to 90% during CPAP therapy; $P < .0001$).[4] There were also statistically significant reductions in patient respiratory rate (from 34 before CPAP therapy to 28 during CPAP therapy; $P < .0001$), heart rate (from 108 before CPAP therapy to 100 during CPAP therapy; $P = .001$), and systolic blood pressure (from 173 before CPAP therapy to 166 during CPAP therapy; $P = .0002$). Similar results were reported by Dib et al, who found an improvement in the CPAP-treated versus non-CPAP treated groups across a number of vital signs: oxygen saturation, heart rate, and systolic and diastolic blood pressure. The retrospective study found an improvement in oxygen saturation by nine percent ($P < .01$); a reduction in heart rate (17.2 beats/min vs 9.6 beats/min; $P < .01$); reduction in respiratory rate (5.13/min vs 4.09/min; $P < .01$) and reductions in diastolic and systolic blood pressures (14.1 mmHg vs 7.4 mmHg; $P < .01$ and 27.1 mmHg vs 19.9 mmHg; $P < .01$, respectively).[7]

Similar findings were found in a prospective study published in 2009.[15] Due to the retrospective nature of this study, the hemodynamic effects of nitroglycerin and morphine cannot be

https://doi.org/10.1017/S1049023X12001562 Published online by Cambridge University Press

excluded. However, a randomized controlled trial conducted by Plaisance et al in 2007 found that CPAP therapy was more effective at improving physiological variables in suspected APO patients than pharmacological treatment.[8] In that study, patients received CPAP therapy with the addition of pharmacological treatment after 15 minutes, or pharmacological agents with the addition of CPAP therapy after fifteen minutes. The inclusion of pharmacological agents in the early CPAP group did not produce any observable benefit, whereas the addition of CPAP therapy to pharmacological agents in the late CPAP group was associated with a significant improvement in the patient's condition.

Reduced Myocardial Damage

The retrospective case series analysis published in 2000 indicated that more aggressive treatment in the prehospital management of acute severe heart failure may reduce the extent of myocardial damage.[17] In this study, participants who received more intensive treatment (nitroglycerine, frusemide and CPAP therapy) had significantly less myocardial damage as indicated by the activity of serum creatine kinase and serum aspartate aminotransferase than those who did not. These findings have some application to the Australian prehospital sector, since all paramedics have pharmacological agents and guidelines specifically tailored for CPAP. Thus, there is an opportunity to undertake a similar randomized controlled trial.

Discussion

It is difficult to draw solid conclusions from the findings, as the studies reviewed were predominately low-level studies. Though several of studies demonstrated good internal validity, they lacked sufficient participant numbers to produce conclusive results, and therefore lacked external validity.

The available literature suggests that the use of prehospital CPAP therapy as part of the management of pulmonary edema may be beneficial; namely, it can reduce the need for prehospital endotracheal intubation and reduce short-term mortality, and can improve physiological variables such as oxygen saturation, heart rate, respiratory rate, and systolic and diastolic blood pressure during prehospital transport. There is also evidence to suggest that it may reduce myocardial damage.

The studies conducted of prehospital use of CPAP to manage APO have all demonstrated improvement in patient outcomes, either in the short term (a decrease in heart rate, respiratory rate and an increase in conscious state and oxygen saturation) or long term (decreased mortality rates). Where they were compared, intubation rates were decreased when CPAP was used as part of the management, either individually or in conjunction with drug intervention. The actual and mean hospital and ICU lengths of stay for patients treated with CPAP in the prehospital setting were also decreased, in most cases significantly.

There is a significant deficit in high-quality research pertaining to non-invasive management of APO in the prehospital setting. A large amount of current literature lacks external validity. To date there have been only two randomized controlled trials in the prehospital setting investigating the use of CPAP in the management of APO. There is a need for additional randomized controlled trials to determine the effectiveness of prehospital CPAP in the early management of patients with APO. The prehospital studies also need to emphasize paramedic management using CPAP, and associated technological issues and interactions with paramedic medications, as there is a potentially different overall treatment regime available to physicians.

Limitations

This study is potentially limited by the possibility that journal articles published in languages other than English may have been missed. Omission of manual searching for journal articles not listed in the electronic databases also may have resulted in missing some relevant articles. The findings of this study should be interpreted with caution, as there was a lack of high-quality studies and most of the located studies had small sample sizes.

Conclusion

The evidence suggests that the use of CPAP therapy in the prehospital environment may be beneficial to patients with acute pulmonary edema as it can potentially decrease the need for endotracheal intubation, improve vital signs during transport to hospital, and improve short-term mortality. There is also a need for large, prehospital, multicenter, randomized, controlled trials to determine the outcomes of early CPAP therapy in patients with acute pulmonary edema.

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