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Non-invasive Ventilation: A Gimmick or Does It Really Affect Outcomes?

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Abstract Heart failure affects 5.1 million Americans every year and leads to over 900,000 annual emergency department (ED) visits. Of those patients, over 80 % will be admitted to the hospital. In the ED, treatment focuses on preload and afterload reduction through the use of diuretics and vasodilators. For those patients requiring oxygen, particularly those in respiratory distress, non-invasive ventilation improves symptoms by increasing ventilation, decreasing preload and afterload, decreasing work of breathing, and increasing gas exchange. Non-invasive ventilation is an effective intervention and is considered an important component of therapy in ED patients with acute heart failure.

Keywords Non-invasive ventilation · Emergency department · Acute heart failure

Introduction

Heart failure is one of the most common diseases in the United States with an estimated 5.1 million Americans being affected. As our population ages, this burden of disease is expected to increase by 46 % between 2012 and 2030. Patients with heart failure regularly present to the emergency department (ED) with symptoms of volume overload and sometimes respiratory distress, with over 900,000 annual visits. Of these, over 80 % are admitted to the hospital [1]. This resulted in hospitalizations, including ICU stays, with a median length of stay >3 days and costs of over $30 billion in 2012. In addition, the burden of morbidity and mortality with acute heart failure (AHF) is significant, with 4 % of heart failure patients dying in the hospital once admitted. And this rate increases significantly to 36 % in those patients requiring mechanical ventilation.

AHF treatment in the ED focuses on decongestion through preload and afterload reduction. The initial approach includes assessing the patient's level of stability by measuring vital signs and work of breathing. Following this, interventions may be initiated including diuretics, vasodilators, and supplemental oxygenation if the patient is hypoxic.

Intravenous diuretics are considered a mainstay of treatment at a dose greater than or equal to the patient's usual daily dose (Class IB recommendation). The 2011 DOSE trial, which compared intermittent furosemide therapy to continuous infusion found that higher dose furosemide (equal to 2.5 times patient's maintenance dose) produced greater net fluid loss, improved weight loss, and decreased dyspnea [2]. However, this treatment arm also had a slightly higher incidence of worsening renal function. Intravenous vasodilators including nitroglycerin, nitroprusside, and nesiritide may also be used in the non-hypotensive patient.

However, there are also nonpharmacologic methods of managing AHF, particularly for those patients in respiratory distress from acute pulmonary edema. In these instances, non-invasive ventilation may be used. AHF is the second most common indication for non-invasive ventilation. Its therapeutic effect is almost instantaneous, and it

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provides the treating physician with a window of time for diuretics or vasodilators to be delivered.

The purpose of this article is to review the literature and determine how effective non-invasive ventilation is in treating AHF. Specific outcomes discussed include mortality, need for intubation, and improvements in work of breathing. We will first set the stage by reviewing the pertinent pathophysiology of AHF and the mechanism by which non-invasive ventilation impacts these outcomes. The answers to these questions have profound effects on patient care including length of stay, hospital costs, and morbidity and mortality outcomes.

Pathophysiology

Acute cardiogenic pulmonary edema may occur gradually or be rapid in onset. It is often associated with dyspnea caused by fluid filling the interstitial and alveolar spaces in the lungs. It can occur due to total body volume overload as in the case of dietary or medication indiscretion or missed dialysis sessions, and as the result of fluid redistribution, as in the case of severe hypertension resulting in profoundly elevated afterload [3, 4].

Non-invasive ventilation works by increasing ventilation, decreasing preload and afterload, decreasing work of breathing, and increasing gas exchange. Increased thoracic pressure works to decrease preload by decreasing venous return to the heart. This can lead to increased contractility by a change in the frank starling curve. In addition, it decreases afterload, which decreases the amount of work required by the left ventricle to perfuse tissues. Within 1 h of Continuous positive airway pressure (CPAP) application it has been shown to reduce patient's feelings of breathlessness, improve their respiratory rate and heart rate, and improve their acidosis when compared to inhaled oxygen alone.

There are two primary modes of non-invasive ventilation. continuous positive airway pressure continuously provides a set positive pressure to reduce the risk of alveolar collapse during expiration. However, the patient has to be able to tolerate increased pressure during expiration. Bilevel positive airway pressure (BiPAP), on the other hand, provides increased pressure during inspiration and senses a patient's inspiratory effort. It also provides pressure support in expiration. This results in decreased work of breathing. BiPAP allows for larger tidal volumes than CPAP.

We have broken down CPAP and BiPAP to explore the differences in the table below (Table 1).

For both CPAP and BiPAP, certain contraindications exist that must be taken into consideration. For one, given the tight fitting nature of the mask and the possibility of aspiration, altered mental status is considered a contraindication unless the patient is being directly monitored and non-invasive ventilation is being utilized for preoxygenation as a bridge to intubation. In addition, non-invasive ventilation can affect preload and therefore hemodynamic instability, including cardiac arrhythmias, is also a relative contraindication. A final contraindication is anything that risks airway obstruction or aspiration such as the inability to handle secretions or suspected upper airway obstruction.

NIV in the Prehospital Setting

Meta-analyses of positive pressure ventilation in the prehospital setting by EMS demonstrate a clear improvement in outcomes. In a meta-analysis of seven randomized control trials of NIV, Mal et al. found that initially NIV in the field for patient's in severe respiratory distress decreased in-hospital mortality (RR 0.58; 95 % CI 0.35–0.95; NNT = 18) and need for invasive ventilation (RR 0.37; 95 % CI 0.24–0.58; NNT = 8) [5]. It did not, however, decrease length of stay or need for ICU admission. This suggests NIV may impact patient outcomes when applied in the prehospital setting, prior to initiation of in-hospital care.

NIV in ED Patients with Acute Heart Failure

The approach to using non-invasive ventilation in ED patients is similar to the prehospital setting. NIV provides ventilatory support while the practitioner begins other therapies. Importantly, it has been shown to be effective in other acute respiratory processes such as asthma and COPD exacerbations. Thus, its use prior to definitive testing such as chest radiograph or b-type natriuretic peptide results, even in the resource-rich hospital setting, is generally considered safe and effective.

NIV also has profound early effects of patient's perceptions of breathlessness, respiratory rate, and hypoxia. In a randomized control trial, Masip, et al. compared NIV to conventional oxygen therapy with a Venturi mask [6•]. They found that even within 15 min, patients on NIV showed improved oxygen saturation and that this improvement persisted for several hours. In addition, they also reported that patient's saw a dramatic decrease in their respiratory rate and improvement in their comfort of breathing compared to the control group.

A retrospective study, which used the Acute Decompensated Heart Failure National Registry, looked at mortality in association with non-invasive ventilation [7]. They also looked at outcomes of non-invasive ventilation as a bridge to endotracheal intubation versus immediate

Table 1 Breakdown of CPAP and BiPAP

	CPAP	BiPAP
Delivery method	Full facemask	May be full face mask or nasal only
Mode of support	Expiratory only	Expiratory and inspiratory
Patient requirements	May be passive	Ability to coordinate breathing cycle
Typical starting settings (cmH_20)	5	10/5

endotracheal intubation. This study included 2430 patients who received ventilatory assistance out of 37,372 hospitalized patients with AHF admitted from the ED. They compared patients who: (1) did not receive ventilatory support; (2) received non-invasive ventilation alone; (3) non-invasive ventilation that failed to stabilize the patient who subsequently required mechanical ventilation; and (4) patients who only underwent endotracheal intubation. Of the 2430 patients they included in their analysis, 1760 (72.4 %) received non-invasive ventilation. Of those, 72 (4.1 %) failed non-invasive ventilation and subsequently required endotracheal intubation. The authors found that patients who received non-invasive ventilation over endotracheal intubation were no worse off. They concluded that non-invasive ventilation is an effective treatment strategy and that it may prevent endotracheal intubation and the morbidity and mortality associated with it. They also concluded that a therapeutic trial of non-invasive ventilation versus immediate endotracheal intubation was no worse in terms of mortality, ICU length of stay, overall hospital LOS, or progression to discharge.

A meta-analysis of 17 randomized controlled trials on CPAP and/or non-invasive ventilation in the treatment of AHF looked at the use of CPAP and medical therapy compared to standard medical therapy or the use of CPAP and medical therapy compared with non-positive pressure ventilation and medical therapy [8]. They evaluated the need for endotracheal intubation, all-cause mortality, and the risk of newly developed acute myocardial infarction following delivery of the study interventions. They found that CPAP led to a 22 % risk reduction in the need for endotracheal intubation and a 13 % risk reduction in mortality. Similarly, for non-invasive positive pressure ventilation, they found an 18 % risk reduction in the need for endotracheal intubation as well as a 7 % risk reduction of mortality, although this was not statistically significant. They concluded that both CPAP and BiPAP were effective at reducing the need for intubation and that both likely improve mortality rates, although they were underpowered to find a difference in mortality for BiPAP. Finally, while an earlier study found a higher incidence of myocardial infarction (MI) with NPPV, they found no significant difference in risk of MI between NPPV when compared to convenient medical therapy. The prior study that found a higher incidence of MI was probably confounded by the fact that more patients in the NPPV arm presented with chest pain, and were likely being enrolled as their ACS was evolving.

In another meta-analysis, Peter et al. looked at mortality with CPAP versus standard medical therapy, BiPAP versus standard therapy, and CPAP versus standard therapy from 23 different trials [9••]. They found that CPAP significantly lowered mortality versus standard therapy (relative risk 0.59, 95 % CI 0.38–0.90, p +0.015) and a trend toward the same with NIPPV. They did not find a significant difference between BiPAP and CPAP. They did, however, find weak evidence that perhaps BiPAP is associated with increased risk of MI compared to CPAP (1.49, CI 0.92–2.42, $p = 0.11$). They too conclude that non-invasive positive pressure ventilation is associated with decreased mortality.

The largest randomized control trial by Gray was powered to look at differences in mortality in patients with AHF who were initially treated in the ambulance by physicians [10••]. They compared CPAP to BiPAP and standard oxygen therapy in a 1:1:1 randomization schema. They enrolled a total of 1069 patients (CPAP = 346, BiPAP = 356, standard oxygen therapy = 367) and found non-invasive ventilation led to greater improvement at 1 h in patient's subjective breathlessness as well as their heart rate, acidosis as determined by ABG, and hypercapnia. However, they did not find a difference in rate of intubation (2.8 % overall) or 7 day mortality for non-invasive ventilation versus standard oxygen therapy alone. Further, there was no significant difference in MI between NIV and standard therapy, or between BiPAP and CPAP. This study is the largest to date, and suggests NIV is an excellent therapy to improve oxygenation, ventilation and work of breathing, but may have no impact on rates of intubation or mortality. Importantly, it provides therapeutic respiratory support for the patient while other AHF therapies are delivered.

Conclusions

In conclusion, although a large randomized trial suggests there is no impact on mortality, the preponderance of the available evidence suggests NIV results in improvement in breathlessness, ventilation and oxygenation, with perhaps a decreased need for endotracheal intubation. This has the potential to decrease cost, complications such as ventilator-associated pneumonia, and the symptoms of ED patients presenting with acute pulmonary edema due to AHF.

Compliance with Ethics Guidelines

Conflicts of Interest Dr. Collins has received the following research support: NIH/NHLBI, Medtronic, Cardiorentis, Abbott Point-of-Care, Novartis, The Medicines Company, Astellas, Intersection Medical, Radiometer, Trinity, Cardioxyl. He has also completed consulting for the following groups: Trevena, Novartis, Otsuka, Radiometer, The Medicines Company, Medtronic, Intersection Medical, Cardioxyl, Abbott Point-of-Care. Dr. Behringer has nothing to disclose.

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