

## Noninvasive positive pressure ventilation for acute respiratory failure in emergency department: a qualitative review

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The roles of noninvasive positive pressure ventilation (NIPPV) as a treatment modality for patients presenting with acute respiratory failure (ARF) to the emergency department (ED) have not been clearly identified. The major advantages of NIPPV are avoiding patient's discomforts and complications relating to endotracheal intubation and mechanical ventilation. This review is to explore the current evidence on the effectiveness of NIPPV in various subgroups of patients with ARF. The rationales, advantages, complications and contraindications in the usage of NIPPV will also be discussed. There is robust evidence to support the use of NIPPV in severe acute exacerbation of chronic obstructive airway disease (COAD). A modest amount of favourable evidence supports the use of Continuous Positive Airway Pressure (CPAP) in cardiogenic pulmonary oedema, although the potential for harm has not been excluded. There exists no solid evidence supporting the use of NIPPV in asthma and pneumonia. Early institution of NIPPV in the ED is appropriate, feasible, likely to be beneficial and without major complications. Further good quality studies to evaluate the roles of NIPPV for ARF in the ED setting are needed to define which groups of patients can gain most benefit from this type of treatment. (*Hong Kong j.emerg.med.* 2003;10:173-180)

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### Introduction

Acute respiratory failure (ARF) is a common problem encountered by emergency physicians. Patients may require ventilatory support when pharmacological interventions fail to correct the underlying condition. Traditionally, endotracheal intubation is used to deliver the tidal volume to the lungs and offers protection of the airway. However, endotracheal intubation is invasive and complications arise both from the procedure itself and from the ventilatory assistance e.g. ventilator-associated pneumonia.<sup>1,2</sup>

Noninvasive positive pressure ventilation (NIPPV) is the provision of positive pressure ventilatory support to a spontaneously breathing patient without the use of endotracheal intubation. It avoids the discomforts and risks associated with endotracheal intubation. Over the past decades the application of this technique in emergency and critical care settings has been the subject of much debate.

I would like to review the pathophysiology of ARF, rationales, potential indications, advantages and complications of NIPPV in the emergency department (ED) setting. The discussion focuses on the use of NIPPV in subgroups of patients with ARF – chronic obstructive airway disease (COAD), asthma, acute cardiogenic pulmonary oedema and pneumonia – which are commonly encountered in the emergency department.

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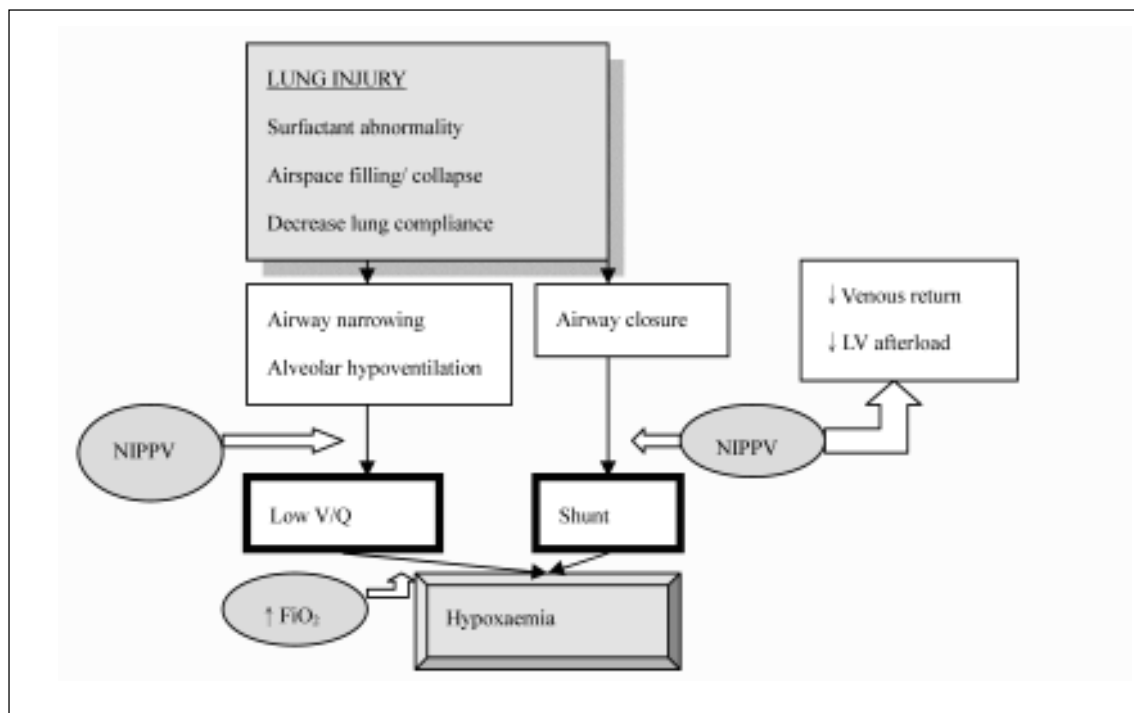
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## Historical perspective of noninvasive ventilation

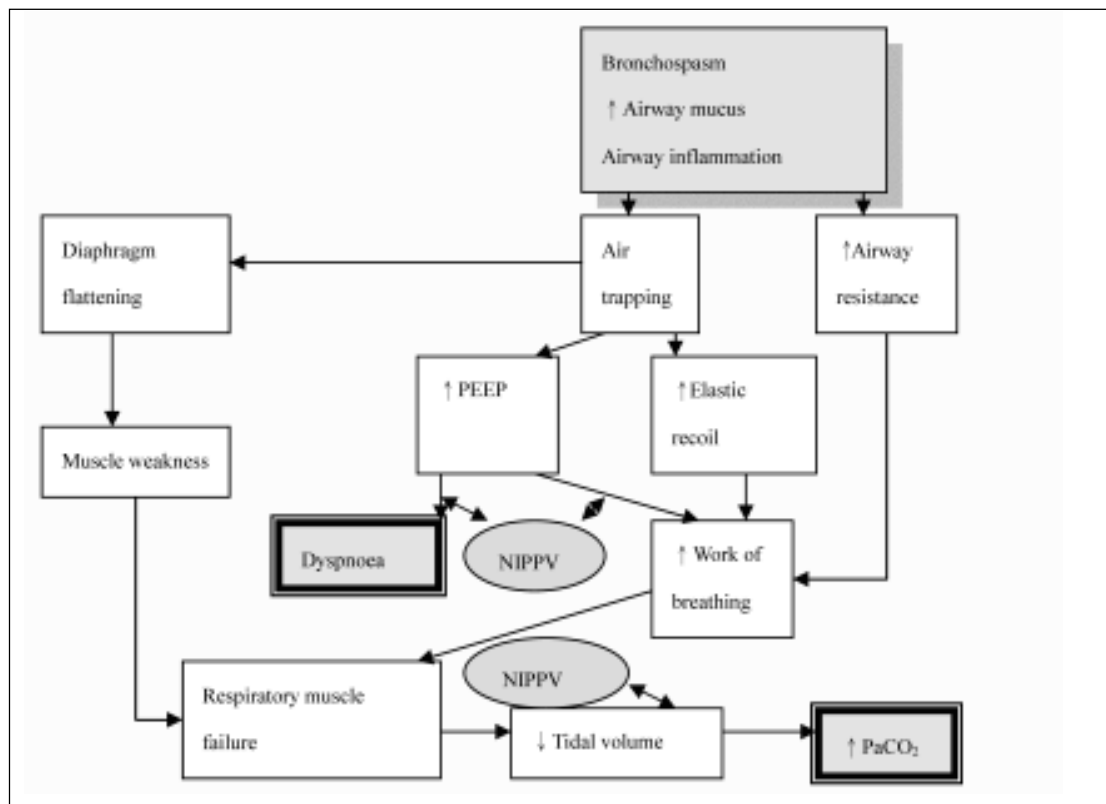
The poliomyelitis epidemic from the 1920s to the 1950s popularized the use of ventilatory support. Iron lungs (Drinker's ventilators)<sup>3</sup> were widely used to treat ARF at that time. During the early 1960s, however, control of the poliomyelitis epidemics with vaccines and the concomitant proliferation of positive pressure ventilation through endotracheal intubation caused a marked decrease in the usage of noninvasive ventilators.<sup>4,5</sup> Interest in noninvasive ventilation rekindled during the mid-1980s when nocturnal use of positive pressure ventilators were reported to reverse daytime gas exchange abnormalities and symptoms of chronic hypoventilation in patients with neuromuscular disease and COAD.<sup>6-8</sup> Over the past decades, there has been resurgence in the use of noninvasive ventilation, fueled by advances in technology (ventilators becoming more compact, affordable and portable) and supporting clinical trials.

## Pathophysiology of respiratory failure and mechanism of NIPPV

The respiratory system consists of a gas exchanging organ (the lung) and a ventilatory pump (respiratory muscles/thorax), either or both of which can fail and precipitate respiratory failure. Respiratory failure occurs when gaseous exchange is insufficient, resulting in hypoxaemia with or without hypercapnia. Practically, respiratory failure occurs when the Partial Arterial Oxygen Pressure ( $\text{PaO}_2$ ) is  $<8$  kPa (60 mmHg) or the Partial Arterial Carbon Dioxide Pressure ( $\text{PaCO}_2$ ) is  $>7$  kPa (55 mmHg),<sup>9</sup> in arterial blood gas analysis (ABG). Respiratory failure can be divided into two broad categories – Type I or primary hypoxaemic respiratory failure and Type II or primary ventilatory failure. Figures 1 and 2 illustrate the pathophysiology of ARF and how NIPPV works in improving oxygenation and correcting hypercapnia.



**Figure 1.** Pathophysiology of hypoxaemic respiratory failure.<sup>10</sup> V/Q= Ventilation/Perfusion,  $\text{FiO}_2$ = Fraction of Inspiratory Oxygen, LV=Left Ventricle.



**Figure 2.** Pathophysiology of primary ventilatory failure.<sup>10</sup> PEEP=Positive End Expiratory Pressure, PaCO<sub>2</sub>= Partial Arterial Carbon Dioxide Pressure.

## What are the rationales and benefits of NIPPV in acute respiratory failure?

Endotracheal intubation (ETI) and mechanical ventilation (MV) have been regarded as the gold standard for ventilatory support in ARF patients. However, ETI and MV are associated with well known hazards and complications.<sup>11</sup>

Key problems relating to intubation include:

1. *Risk related to the intubation procedure*
  - a. Appropriate placement of ETI into the trachea is not always easy. Tube misplacement, if left undiagnosed, can result in fatal outcome.<sup>12</sup>
  - b. ETI is an invasive procedure. The increased sympathetic tone may worsen ischaemia in the setting of coronary artery disease.<sup>13</sup> Furthermore, ETI without a neuroprotective induction agent can increase the intracranial pressure.<sup>14</sup>

- c. Trauma related to tube insertion e.g. fractured teeth, laryngeal injury.

### 2. *Potential sources of pulmonary infection*

The presence of an endotracheal tube disturbs the natural defense mechanism of the airway. From 4% to 8% of patients experience pulmonary aspiration during intubation.<sup>12</sup> Moreover, the portion of the airway immediately above the endotracheal tube cuff accumulates oropharyngeal secretions which may become a reservoir for bacteria growth. Endotracheal tube related pneumonia is accompanied by a high mortality.<sup>15</sup>

### 3. *Inherent discomfort*

ETI precludes expectoration, eating, and speech communication. Sedation is needed in most patients to reduce the pain and discomfort. This requirement may render the patient more dependent on the ventilator and prolong the

weaning process.<sup>11</sup> It sometimes makes physical examination for inter-current problems difficult.

#### 4. *Delays in initiation of ventilatory support*

The invasive nature of ETI may make the physician hesitant in initiating mechanical ventilation until the late stage of respiratory failure. Delay in ventilatory support may induce muscle fatigue, requiring a longer period for respiratory muscle recovery if ventilatory assistance is eventually required.

NIPPV spares patients of the risks and complications relating to ETI. (Table 1) Although NIPPV sounds like a good alternative to ETI and MV in patients with ARF, the potential benefits must be weighed against the complications of NIPPV. (Table 2) Not every ARF patient is suitable for NIPPV. In patients requiring airway protection or airway access to remove retained secretions, and in most patients with altered mental status or significant airway oedema, the airway control offered by ETI outweighs its invasive drawback. Table 3 shows the contraindications of NIPPV.

**Table 1.** Advantages of NIPPV

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1. Decrease the frequency of nosocomial infection.<sup>15</sup>
  2. Decrease patient's discomforts relating to ETI. Patient can talk which facilitates better communication with medical staffs. Patient can drink small amount of liquid, expectorate or receive nebulized bronchodilator therapy.
  3. Less use of sedative drug and muscle relaxant.
  4. Noninvasive ventilation is simple and easy to institute because it obviates the need for ETI, facilitates earlier intervention and potentially eliminates life-threatening delays in ventilatory support.<sup>11</sup>
  5. Potential cost saving in the setting of severe acute exacerbation of chronic obstructive airway disease.<sup>16</sup>
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**Table 2.** Complications of NIPPV

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1. Facial skin necrosis at site of mask contact is seen in approximate 10% of patients in published reports.<sup>17</sup> It usually clears up with an interface change or cessation of NIPPV.
  2. Pulmonary aspiration. The unprotected airway is more prone to pulmonary aspiration. Furthermore, the high gas flow that occurs at the airway during NIPPV causes gastric insufflation. However, clinically significant aspiration is rare, perhaps a result of the resting tone of the patent oesophageal sphincter normally retaining its seal against the pressure used in NIPPV, which is generally less than 30 cm H<sub>2</sub>O.<sup>11</sup>
  3. Transient hypoxaemia secondary to inadvertent removal of the mask is a significant hazard in patients who are oxygen dependent. However, proper monitoring in the ED and appropriate ventilator alarm setting can prevent this problem.
  4. Other minor complications – nasal congestion, eye irritation, and sinus complaints.
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**Table 3.** Contraindications of NIPPV<sup>11,18</sup>

#### *Absolute contraindications*

1. The need for a secure airway. NIPPV does not offer airway protection. Preferably patients should be awake, cooperative and have spontaneous breathing.
2. Patients with compromised cough and secretion clearance should be intubated because of the ongoing need to clear central airway secretions.
3. Patients without an intact respiratory drive e.g. patients in cardiac or respiratory arrest.
4. Upper airway obstruction.
5. Altered mental status not due to CO<sub>2</sub> retention.

#### *Relative contraindications*

1. Inability to adequately fit and seal the mask secondary to facial deformity, surgery or maxillofacial fracture.
  2. Uncooperative patients, or one who will not leave the mask in place, cough when prompted or unable to remove the mask in the event of emesis.
  3. Haemodynamic instability.
  4. Claustrophobia.
  5. Morbid obesity.
  6. Recent gastric surgery (within one week).
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## Literature review on the indications of NIPPV for acute respiratory failure

Acute respiratory failure is a common problem encountered by emergency physicians. The following discussion explores the current evidence on the effectiveness of NIPPV in various subgroups of patients with acute respiratory failure. Searching strategies included: 1) Computerized literature search using two search engines: (a) OVID MEDLINE (1966 to December Week 3 2002); (b) OVID EMBASE (1980 to 2002 Week 51) with search keywords 'acute respiratory failure' (explode) AND 'NIPPV' (explode) AND 'emergency department' (limited to human and English language). 2) Published abstracts from scientific meetings. 3) Bibliographies of relevant articles. Patients with ARF are categorized into three broad groups: 1) Primary ventilatory failure including COAD and asthma. 2) Primary hypoxaemic failure including pneumonia and cardiogenic pulmonary oedema. 3) Patients with advance directive of "not to be intubated".

### A. Primary ventilatory respiratory failure

#### 1. NIPPV in patients with COAD exacerbation

Two meta-analyses of randomized controlled clinical trials (RCT) in ARF comparing addition of NIPPV to standard therapy versus standard medical therapy alone were identified. Keenan et al<sup>19</sup> in 1997 included seven RCT. They showed that NIPPV was associated with decreased mortality (odds ratio=0.29, 95% confidence interval 0.15 to 0.59) and reduced need for endotracheal intubation (odds ratio=0.2, 95% confidence interval 0.11 to 0.36). Sensitivity analysis suggested a greater benefit in COAD patients. Keenan et al concluded that the addition of NIPPV to standard therapy in patients with acute exacerbation of COAD improved survival and decreased the need of endotracheal intubation. The benefits of NIPPV in non-COAD patients are still not clear. Peter et al<sup>20</sup> published another meta-analysis in March 2002 and included eight more RCT making a total of 15 RCT. The primary objective of this meta-analysis was to address the role of NIPPV in reducing mortality in patients with acute

respiratory failure secondary to COAD exacerbations and other non-COAD parenchymal processes. The secondary outcomes considered were the need for mechanical ventilation, hospital length of stay, and complication rates. It showed that NIPPV was associated with reduction in mortality (8%,  $p=0.03$ ), reduced need for mechanical ventilation (19%,  $p=0.001$ ) and shortened hospital length of stay (2.74 days,  $p=0.004$ ). Complication rates were not significantly different in the standard medical therapy group and the NIPPV treated patients. Subgroup analysis in the COAD cohort which consisted of 405 patients in the NIPPV group and 388 patients in the standard medical therapy group again showed significant reductions in mortality (13%,  $p=0.001$ ), need for mechanical ventilation (18%,  $p=0.02$ ), and hospital length of stay (5.56 days,  $p=0.01$ ) in the group treated with NIPPV. For the non-COAD subgroup, there was no demonstrated reduction in mortality (0%,  $p=0.98$ ). However, there was significant reduction in the need for mechanical ventilation (22%,  $p=0.001$ ). In summary, substantial reductions in mortality and the need for mechanical ventilation were associated with NIPPV in acute respiratory failure, especially in the COAD subgroup. *In conclusion, there is very strong evidence to support the use of NIPPV in severe acute exacerbation of COAD.*

#### 2. NIPPV in patients with asthmatic attack and status asthmaticus

In patients presenting with asthmatic attack, hospital deaths are so rare and cannot be used as outcome parameters. The outcomes of interest in this group are the need for intubation and length of hospital stay. Only one un-blinded RCT could be identified.<sup>21</sup> In this trial, patients with mild to moderate asthma were randomized to receive their treatment with beta-agonist with or without NIPPV. Two emergency physicians were responsible for enrolling all patients and no mention was made of randomization concealment. None of the patients required intubation, and two patients in each group were admitted to hospital with no data available on their length of hospital

stay. The peak expiratory flow rate improvement was greater in the NIPPV group ( $40\pm 14\%$  to  $69\pm 19\%$ ) versus control group ( $37\pm 13\%$  to  $57\pm 21\%$ ) with  $p=0.0013$ . The confidence interval was not mentioned. However, the clinical relevance of this difference was hard to judge. Three uncontrolled studies<sup>22-24</sup> of NIPPV in status asthmaticus demonstrated an improvement in gas exchange and a decrease in the need for intubation. However, without the use of control group, inferences about the effects of treatment are limited. *There is therefore insufficient evidence to support the use of NIPPV in patients with asthmatic attack. Further RCT that completely address the role of NIPPV in asthmatic attack are needed.*

## **B. Primary hypoxaemic respiratory failure**

### **1. NIPPV in patients with cardiogenic pulmonary oedema**

Three randomized controlled trials<sup>25-27</sup> on the use of Continuous Positive Airway Pressure (CPAP) versus oxygen in patients with cardiogenic pulmonary oedema suggested that CPAP improved oxygenation, decreased hypercapnia; decreased the need for endotracheal intubation and length of hospital stay in intensive care units. Pang et al<sup>28</sup> in a systematic review concluded that CPAP was associated with decrease in need for intubation (risk difference  $-26\%$ , 95% confidence interval  $-13$  to  $-38\%$ ) and a decreasing trend in hospital mortality (risk difference  $-6.6\%$ , 95% confidence interval  $3$  to  $-16\%$ ) compared with standard therapy alone. Another RCT by Mehta et al,<sup>29</sup> however, found a higher incidence of myocardial infarction in the groups treated with Bilevel Positive Airway Pressure (BiPAP) versus CPAP (71% versus 31%,  $p=0.02$ ). Patients in the BiPAP group had higher rates of chest pain as compared with patients in the CPAP group. *In summary, a modest amount of favourable evidence exists to support the use of CPAP in patients with cardiogenic pulmonary oedema. CPAP appears to decrease the intubation rate and mortality, although the potential for harm (acute myocardial infarction) has not been excluded. The role of NIPPV in this setting requires further studies before it can be widely recommended.*<sup>28</sup>

### **2. NIPPV in patients with pneumonia**

There was no RCT on the use of NIPPV for patients with pneumonia in ARF. Keenan et al<sup>19</sup> reviewed seven uncontrolled studies with a total of 36 pneumonia patients treated with NIPPV. Ten (28%) subsequently required intubation and another 10 (28%) died. However, without a control group, the inference about the effect of treatment is limited. *In summary, there is insufficient evidence to support the use of NIPPV in patients with acute respiratory failure primarily the result of pneumonia. Additional RCT are required.*

## **C. NIPPV in patients with advance directive of "not to be intubated"**

The use of NIPPV may be justified in selected patients with advance directive of "not to be intubated" who have reversible causes of ARF.<sup>10</sup> The theoretical advantages of NIPPV are providing patient comfort, dignity and facilitating physician-patient interaction in the assessment on the reversibility of ARF. Studies on this subject were retrospective or uncontrolled.<sup>23,30</sup> These studies showed that NIPPV might reduce dyspnoea and preserve autonomy in carefully selected patients. *In summary, little evidence exists to support the use of NIPPV in "not to be intubated" patients who have reversible elements of their acute respiratory failure. However, given the theoretical advantages and the noninvasive nature of NIPPV, it is justified in carefully selected groups of patients. Further well-controlled studies are needed to clarify this problem.*

## **Is early institution of NIPPV in the ED beneficial to ARF patients?**

Although the majority of studies involving NIPPV were conducted in the intensive care setting, one study reviewing the utilization of NIPPV in a teaching hospital showed that 62.1% of NIPPV was started primarily in the ED.<sup>31</sup> The potential benefits of NIPPV used in the ED include early intervention to prevent further respiratory deterioration, access to respiratory support for patients who are not candidates for intensive care and the provision of support in a less intimidating setting.<sup>10</sup> Retrospective analyses,

uncontrolled studies, and some RCT indicated that NIPPV could be successfully initiated in emergency departments.<sup>32-34</sup> In Hong Kong, NIPPV is available in most emergency departments. A prospective study involving 28 ED patients with ARF performed in a regional hospital in Hong Kong showed that NIPPV was feasible, likely to be beneficial and without major complications in local ED setting.<sup>35</sup> However, Wood et al<sup>36</sup> in his RCT of NIPPV in the emergency department showed an increase in hospital mortality rate, delay in tracheal intubation and the initiation of mechanical ventilation in some ARF patients. That study had numerous design limitations. A Cochrane systematic review and meta-analysis<sup>37</sup> published in 2003 involving eight high quality RCT concluded that NIPPV should be the first line intervention in addition to usual medical care to manage ARF secondary to COAD exacerbation in all suitable patients. NIPPV should be tried early in the course of ARF and before severe acidosis, to reduce mortality, avoid ETI and decrease treatment failure. *It may imply that early institution of NIPPV for ARF patients, especially COAD exacerbation in the ED setting, is appropriate and potentially beneficial in terms of avoiding ETI, reducing morbidity, mortality, length of hospital stay and hospital cost. However further larger good quality clinical studies are needed to answer this question.*

## Conclusion

NIPPV seems to be an attractive option of ventilatory support for patients with ARF as it avoids the discomforts and complications related to endotracheal intubation. Evidence from good quality RCT and meta-analysis showed that NIPPV is an effective treatment for acute exacerbation of COAD. The benefits of NIPPV in non-COAD patients with ARF are not so clear yet. Early institution of NIPPV in ED is appropriate, feasible, likely to be of benefit and without major complications. The overall condition of the patient, patient's tolerance to the mask, and reversibility of the underlying condition must be taken into account when a trial of NIPPV is being offered in the ED. Intensive monitoring and anticipation of therapeutic failure are important to the success of

NIPPV. Future good quality studies to evaluate the roles of NIPPV for ARF in the ED setting are needed to define which groups of patients will be benefited most from this type of treatment.

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