

14 ± 5, expiratory 7 ± 3) [3]. Hence, the optimal settings which permit maintenance of SpO<sub>2</sub> greater than 88% need to be determined. Additionally, use of CPAP, which has been found to achieve similar improvements in respiratory distress and blood gases, is not considered in this study.

Finally, the outcome of this study was a composite of need for intubation and crossover to the alternative therapy at 72 h. This concerns us as crossover to alternative therapy is a subjective outcome in an unblinded study, which is subject to bias in favour of a newer therapy. More importantly, lack of therapy failure at 72 h might not be the most important goal in such patients. Any larger randomized trial addressing this key clinical question must address not only improvement in symptoms and restoration of oxygenation, but also improvement in short and long-term clinical outcomes including mortality.

Tejas Menon Suri, MD  
Anant Mohan, PhD

Department of Pulmonary, Critical Care and Sleep Medicine, All India Institute of Medical Sciences, New Delhi, India

Antonio Esquinas, PhD  
Intensive Care Unit, Hospital Morales Meseguer, Murcia, Spain

Vijay Hadda, MD  
Department of Pulmonary, Critical Care and Sleep Medicine, All India Institute of Medical Sciences, New Delhi, India

Corresponding author at: Department of Pulmonary, Critical Care and Sleep Medicine, All India Institute of Medical Sciences, Ansari Nagar, New Delhi 110029, India.

E-mail address: vijayhadda@yahoo.com.

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## Beyond NIPPV: HVNI Expands Potential Treatment Options For Acute Decompensated Heart Failure



Thank you for this observation. Patients were chosen for the inclusion of this trial because the treating physician felt that escalation to NIPPV would be the clinically appropriate next step in the patient's care. As to the safety and efficacy in heart failure, an important exclusion criterion in the study was known or suspected myocardial infarction, to help specifically address overwhelming cardiovascular compromise. This exclusion criterion also encompassed cardiogenic shock, or other forms of shock, which were excluded as hemodynamic instability. As with any study, there was also the ability for a clinician to exclude the patient from the study based on their best clinical judgement. NIPPV is currently the standard of care in patients with ADHF when conventional oxygen delivery is not sufficient [1]. Your point that NIPPV may be harmful in certain subsets of this patient population underscores the importance of identifying alternatives to NIPPV, such as HVNI, in

patients with ADHF. Patients were selected from an undifferentiated population presenting in the ED and represent a heterogeneous patient population [2]. These patients often had multiple pathologies, representative of a large proportion of patients seen in the ED. The authors recognize that this is a subgroup analysis resulting in interesting findings that suggest further study. We agree differentiation is an important goal - unfortunately this was a real-world study similar to what presents to the ED daily - undifferentiated patients. In subsequent trials in this population, further differentiating characterization will permit better 'success-phenotyping'.

The selection of pressure was initiated at 10 IPAP and 5 EPAP cmH<sub>2</sub>O. However, the clinical instructions in the protocol were to titrate pressures to achieve the clinical effect (specifically, to reduce the respiratory rate to 'low 20's' and achieve tidal volumes of 6–8 ml/kg ideal body weight). Therefore, mean peak pressures applied to the patients during therapy in the NIPPV assigned arm of the trial was IPAP of 13 ± 3 cmH<sub>2</sub>O and EPAP of 6 ± 1 cmH<sub>2</sub>O. These pressures are consistent with the Gray trial [3]. It is important to also point out that the failure rate to intubation among the ADHF patients randomized to the NIPPV arm of the study (0%), especially when viewed through the prism of the APACHE II score (>30), may suggest adequate management of respiratory distress with the applied pressures.

We agree that the crossover endpoint was necessarily subjective for many patients. The authors point out the subjective character of these in the original study and ascribe this to less clinical familiarity with high-velocity nasal insufflation among this diverse population. As crossover was a requirement of the IRB primarily to minimize patient risk, we agree that given both these data, and the primary study outcomes, a future trial could plausibly be designed which would eliminate the requirement for a subjective 'crossover' of therapy - leaving a definitive intubation as the endpoint. The study truncated the duration for the primary outcome measurement (particularly intubation) at 72 h, reasoning that beyond 72 h such an outcome became more difficult to ascribe wholly to the acute therapy applied on admission - particularly in these complex patients. Further, neither the original study nor the subgroup analysis was powered to evaluate long-term mortality endpoints. These data could help inform the design of such a subsequent study in the adult ADHF patient population presenting in the ED.

Steven T. Haywood, MD\*

Northeast Ohio Medical University, Rootstown, OH, USA

Summa Health System, Akron, OH, USA

Corresponding author at: 525 E Market St, 44304 Akron, USA.

E-mail address: steventhaywood@Gmail.com.

Leonithas I. Volakis, PhD  
Vapotherm, Inc, Exeter, NH, USA

Jessica S. Whittle, MD PhD  
University of Tennessee, Chattanooga, TN, USA  
The Erlanger Health System, Chattanooga, TN, USA

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