



HAL
open science

Can we prevent intubation in patients with ARDS?

Alexandre Demoule, Nicholas Hill, Paolo Navalesi

► **To cite this version:**

Alexandre Demoule, Nicholas Hill, Paolo Navalesi. Can we prevent intubation in patients with ARDS?. Intensive Care Medicine, 2016, 42, pp.768 - 771. 10.1007/s00134-016-4323-6 . hal-01458149

HAL Id: hal-01458149

<https://hal.sorbonne-universite.fr/hal-01458149v1>

Submitted on 6 Feb 2017

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Can we prevent intubation in patients with ARDS?

Alexandre Demoule^{1,2}, Nicholas Hill³, Paolo Navalesi^{4,5,6}

(1) AP-HP, Groupe Hospitalier Pitié-Salpêtrière Charles Foix, Service de Pneumologie et Réanimation Médicale (*Département "R3S"*), F-75013, Paris, France.

(2) Sorbonne Universités, UPMC Univ Paris 06, INSERM, UMRS1158 Neurophysiologie respiratoire expérimentale et clinique, Paris, France.

(3) Division of Pulmonary, Critical Care and Sleep Medicine, Tufts Medical Center, Boston, MA, USA

(4) Dipartimento di Medicina Traslazionale, Università del Piemonte Orientale "Amedeo Avogadro", Novara.

(5) Anesthesia and Intensive Care Medicine, Sant'Andrea Hospital, Vercelli, Italy.

(6) CRRF Mons. L. Novarese, Moncrivello (VC), Italy.

Correspondence

Pr Alexandre Demoule

Service de Pneumologie et Réanimation médicale

Groupe hospitalier Pitié-Salpêtrière

47-83 boulevard de l'Hôpital

75651 Paris cedex 13

Paris

France

Tel : +33 142 16 67 61

alexandre.demoule@aphp.fr

Word count: 1231

Authors' contributions: Alexandre Demoule, Nicholas Hill and Paolo Navalesi wrote the manuscript.

Conflicts of interest: Alexandre Demoule has signed research contracts with Covidien, Maquet and Philips; he has also received personal fees from Covidien as well as equipment provided by Maquet and by Philips for research protocols. Nicholas Hill has received research support from Fisher Paykel and serves as a consultant for Fisher Paykel, Philips Respironics and ResMed. Paolo Navalesi contributed to the development of the helmet, the patent for which belongs to Intersurgical S.P.A., and receives royalties for that invention. PN research laboratory has received equipment and grants from Maquet Critical Care and Intersurgical S.P.A. PN also received honoraria/speaking fees from Maquet Critical Care, Draeger, Philips, Breas, Resmed, Hillrom and Linde AG.

Invasive mechanical ventilation is the cornerstone therapy for the acute respiratory distress syndrome (ARDS). However, because invasive mechanical ventilation is also associated with side effects and complications leading to substantial morbidity or even mortality, physicians have developed strategies to prevent endotracheal intubation. One of these strategies is non-invasive ventilation (NIV), which is the application of positive airway pressure via an external (noninvasive) interface.

Recently, a newer noninvasive device has seen increasing use that allows delivery of heated and humidified high-flow gas at body temperature and saturation and flows up to 60 l/min with FIO₂ adjustable up to 100 % through a soft wide-bore nasal cannula (HFNC).

Physiologic rationale for NIV and HFNC in ARDS

From a theoretical and physiological point of view, NIV and HFNC may both be beneficial in patients with mild ARDS. Fine-tuning of the fraction of inspired oxygen (FIO₂) apart, these two techniques work via different mechanisms. On one hand, NIV applies end-expiratory positive airway pressure and pressure support, the former increasing functional residual capacity and opening collapsed alveoli, thereby improving ventilation-perfusion matching and reducing intrapulmonary shunt as well as improving lung compliance, thus reducing respiratory load. The latter assists respiratory muscles during inspiration, reducing work of breathing and dyspnea.

On the other hand, HFNC generates a small positive pressure spike at end-expiration that depends on the nasal air flow and on the extent of mouth opening and appears to work mainly by flushing the nasal airspaces, reducing anatomical dead space [1]. In addition, by delivering warm and well-humidified gas through the nostrils and by avoiding the discomfort generated by the pressure that NIV masks exert on the face skin, HFNC is extremely well tolerated, much better than NIV, and can be applied continuously for long periods of time.

It is important to keep in mind that the major goal of NIV and HFNC in treating ARDS is to achieve a sufficient level of oxygenation. In this regard, NIV and HFNC may be viewed as “bandaid” therapies – if they aren’t addressing the underlying pathology sufficiently (eg septic shock or multiorgan system failure), alternative therapy such as endotracheal intubation with invasive mechanical ventilation should be initiated without delay.

Results of clinical trials and meta-analyses

Relatively few studies have focused on the role of NIV in avoiding intubation in ARDS *per se*. In a prospective cohort study, Antonelli et al applied NIV to 147 ARDS patients admitted to the ICU not yet intubated [2]. Fifty-four per cent of these patients avoided intubation and had fewer ventilator associated pneumonias (2% vs. 20%; $P < 0.001$), and a lower ICU mortality (6% vs. 53%; $P < 0.001$).

To date, **only ten randomized** controlled studies have been conducted on use of NIV in patients with *de novo* hypoxemic acute respiratory failure [3-10] (Table 1), most at centres that are expert at delivery of NIV. Among these studies, three were performed on immunocompromised patients [5, 8, 9] **and two in patients who had recently undergone surgery [11, 12]**. Only two randomized controlled studies have thus far evaluated NIV in non-hypercapnic and immunocompetent patients with *de novo* hypoxemic acute respiratory failure. One suggested that NIV may reduce intubation rate and even mortality in a very selected population of patients [7] and the other reported no beneficial effects and a higher number of adverse events in patients receiving NIV consisting of continuous positive-end expiratory pressure (CPAP) [6]. A meta-analysis focusing on these two randomised controlled studies and another conducted in recipients of solid organ transplant [5-7] concluded that the addition of NIV to standard care in patients with ARDS did not reduce the intubation rate or ICU mortality [13].

Regarding HFNC, the only large randomized controlled trial in adults admitted to the ICU with acute hypoxemic respiratory failure ($\text{PaO}_2/\text{FiO}_2 < 300$ mmHg) has shown that HFNC did not reduce the overall intubation rate compared to standard oxygen or NIV (38, 47 and 50%, respectively, $p = 0.18$) although intubation rate was significantly less with HFNC in the subgroup of patients with a $\text{PaO}_2/\text{FiO}_2 < 200$ mmHg (35, 53 and 58%, respectively, $p = 0.009$, post hoc analysis) [14]. In addition, HFNC reduced ICU and 90 day mortality as compared to standard oxygen and NIV. The authors speculated that the greater mortality with NIV might have been related to the use of tidal volumes of > 9 ml/kg, predisposing to ventilator induced lung injury. However, it is worth noting that refractory shock was encountered more frequently in the NIV group, possibly suggesting a sicker cohort.

Potential risks of NIV and HFNC in ARDS patients

In ARDS patients, the reported rate of NIV failure averages 52% (from 14% to 70%) [15]. However, this failure rate is much lower in mild ARDS (34%) than in moderate or severe ARDS (68%) [16]. Moreover, crucial predisposing factors for NIV failure include altered level of consciousness and shock [16].

Although NIV failure in patients with *de novo* acute respiratory failure has been associated with a high mortality regardless of the severity of acute respiratory failure [17], a more recent study from francophone ICUs suggests that not only does the use of NIV in *de novo* acute respiratory failure seem to be decreasing, but also NIV failure is no longer associated with higher mortality. These recent data suggest improved patient selection and NIV application [18].

Reasons why NIV failure raises the risk of death in *de novo* hypoxemic acute respiratory failure include delay of needed intubation as the underlying condition progresses until the situation becomes catastrophic [6] and a high level of pressure support in

combination with deep inspiratory efforts that could generate high tidal volumes and excessive transpulmonary pressures, increasing lung stress and contributing to ventilator induced lung injury (VILI) [14]. Emerging studies suggest that HFNC has fewer adverse effects than NIV and may be less apt to contribute to VILI, perhaps because lung stretch is less [13]. On the other hand, a recent retrospective study [16] suggests that, just as with NIV, delayed intubation should be avoided with HFNC.

So can we avoid intubation in ARDS using noninvasive approaches?

For reasons stated above, NIV has been plagued by poor tolerance and high failure rates when used to treat ARDS. Although studies like that by Antonelli et al [2] demonstrate that NIV success in ARDS is associated with many fewer complications and a higher survival rate than NIV failure, randomized controlled trials have been unable to demonstrate convincingly that NIV improves outcomes, even intubation rate, in comparison to standard oxygen and intubation if necessary. HFNC might offer a suitable alternative to NIV, especially in patients with moderate or severe ARDS ($\text{PaO}_2/\text{FIO}_2 < 200$), amongst whom intubation rate was lower than in standard oxygen and NIV groups in the Frat study [14]. It is important to emphasize, however, that this was a post-hoc analysis and needs to be confirmed in future studies. In the meantime, what do we do? When ARDS patients become difficult to oxygenate using standard oxygen approaches, HFNC, by virtue of its better tolerance and ability to reduce room air entrainment and wash out dead space, is a logical next choice (Figure 1). Whether some patients failing HFNC could be salvaged by escalating to NIV is currently unclear. In either case, patients must be monitored very closely in an ICU with particular attention paid to the course during the first hour or two. Patients manifesting further deterioration or even failure to improve should be intubated without undue delay.

References

1. Spoletini G, Alotaibi M, Blasi F, Hill NS (2015) Heated Humidified High-Flow Nasal Oxygen in Adults: Mechanisms of Action and Clinical Implications. *Chest*
2. Antonelli M, Conti G, Esquinas A, Montini L, Maggiore SM, Bello G, Rocco M, Maviglia R, Pennisi MA, Gonzalez-Diaz G, Meduri GU (2007) A multiple-center survey on the use in clinical practice of noninvasive ventilation as a first-line intervention for acute respiratory distress syndrome. *Crit Care Med* 35: 18-25
3. Confalonieri M, Potena A, Carbone G, Porta RD, Tolley EA, Umberto Meduri G (1999) Acute respiratory failure in patients with severe community-acquired pneumonia. A prospective randomized evaluation of noninvasive ventilation. *Am J Respir Crit Care Med* 160: 1585-1591
4. Martin TJ, Hovis JD, Costantino JP, Bierman MI, Donahoe MP, Rogers RM, Kreit JW, Scirba FC, Stiller RA, Sanders MH (2000) A randomized, prospective evaluation of noninvasive ventilation for acute respiratory failure. *Am J Respir Crit Care Med* 161: 807-813
5. Antonelli M, Conti G, Bufi M, Costa MG, Lappa A, Rocco M, Gasparetto A, Meduri GU (2000) Noninvasive ventilation for treatment of acute respiratory failure in patients undergoing solid organ transplantation: a randomized trial. *Jama* 283: 235-241
6. Delclaux C, L'Her E, Alberti C, Mancebo J, Abroug F, Conti G, Guerin C, Schortgen F, Lefort Y, Antonelli M, Lepage E, Lemaire F, Brochard L (2000) Treatment of acute hypoxemic nonhypercapnic respiratory insufficiency with continuous positive airway pressure delivered by a face mask: A randomized controlled trial. *Jama* 284: 2352-2360

7. Ferrer M, Esquinas A, Leon M, Gonzalez G, Alarcon A, Torres A (2003) Noninvasive ventilation in severe hypoxemic respiratory failure: a randomized clinical trial. *Am J Respir Crit Care Med* 168: 1438-1444
8. Hilbert G, Gruson D, Vargas F, Valentino R, Gbikpi-Benissan G, Dupon M, Reiffers J, Cardinaud JP (2001) Noninvasive ventilation in immunosuppressed patients with pulmonary infiltrates, fever, and acute respiratory failure. *N Engl J Med* 344: 481-487
9. Lemiale V, Mokart D, Resche-Rigon M, Pene F, Mayaux J, Faucher E, Nyunga M, Girault C, Perez P, Guitton C, Ekpe K, Kouatchet A, Theodose I, Benoit D, Canet E, Barbier F, Rabbat A, Bruneel F, Vincent F, Klouche K, Loay K, Mariotte E, Bouadma L, Moreau AS, Seguin A, Meert AP, Reignier J, Papazian L, Mehzari I, Cohen Y, Schenck M, Hamidfar R, Darmon M, Demoule A, Chevret S, Azoulay E (2015) Effect of Noninvasive Ventilation vs Oxygen Therapy on Mortality Among Immunocompromised Patients With Acute Respiratory Failure: A Randomized Clinical Trial. *JAMA* 314: 1711-1719
10. Antonelli M, Conti G, Rocco M, Bufi M, De Blasi RA, Vivino G, Gasparetto A, Meduri GU (1998) A comparison of noninvasive positive-pressure ventilation and conventional mechanical ventilation in patients with acute respiratory failure. *N Engl J Med* 339: 429-435
11. Auriant I, Jallot A, Herve P, Cerrina J, Le Roy Ladurie F, Fournier JL, Lescot B, Parquin F (2001) Noninvasive ventilation reduces mortality in acute respiratory failure following lung resection. *Am J Respir Crit Care Med* 164: 1231-1235
12. Jaber S, Lescot T, Futier E, Paugam-Burtz C, Seguin P, Ferrandiere M, Lasocki S, Mimoz O, Hengy B, Sannini A, Pottecher J, Abback P, Riu B, Belafia F, Constantin J, Masseret E, Beaussier M, Verzilli D, De Jong A, Chanques G, Brochard L, Molinari N, for the NIVAS Study Group (2016) Effect of noninvasive ventilation on tracheal

reintubation among patients with hypoxemic respiratory failure following abdominal surgery. A randomized clinical trial. JAMA

13. Agarwal R, Reddy C, Aggarwal AN, Gupta D (2006) Is there a role for noninvasive ventilation in acute respiratory distress syndrome? A meta-analysis. *Respir Med* 100: 2235-2238
14. Frat JP, Thille AW, Mercat A, Girault C, Ragot S, Perbet S, Prat G, Boulain T, Morawiec E, Cottureau A, Devaquet J, Nseir S, Razazi K, Mira JP, Argaud L, Chakarian JC, Ricard JD, Wittebole X, Chevalier S, Herbland A, Fartoukh M, Constantin JM, Tonnelier JM, Pierrot M, Mathonnet A, Beduneau G, Deletage-Metreau C, Richard JC, Brochard L, Robert R (2015) High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *N Engl J Med* 372: 2185-2196
15. Agarwal R, Aggarwal AN, Gupta D (2010) Role of noninvasive ventilation in acute lung injury/acute respiratory distress syndrome: a proportion meta-analysis. *Respir Care* 55: 1653-1660
16. Thille AW, Contou D, Fragnoli C, Cordoba-Izquierdo A, Boissier F, Brun-Buisson C (2013) Non-invasive ventilation for acute hypoxemic respiratory failure: intubation rate and risk factors. *Crit Care* 17: R269
17. Demoule A, Girou E, Richard JC, Taille S, Brochard L (2006) Benefits and risks of success or failure of noninvasive ventilation. *Intensive Care Med* 32: 1756-1765
18. Demoule A, Chevret S, Carlucci A, Kouatchet A, Jaber S, Meziani F, Schmidt M, Schnell D, Clergue C, Aboab J, Rabbat A, Eon B, Guerin C, Georges H, Zuber B, Dellamonica J, Das V, Cousson J, Perez D, Brochard L, Azoulay E (2015) Changing use of noninvasive ventilation in critically ill patients: trends over 15 years in francophone countries. *Intensive Care Med*

Figure Legend

Figure 1. Algorithm for a practical use of high flow nasal canulae (HFNC) and non-invasive mechanical ventilation (NIV) in acute respiratory distress syndrome (ARDS)

Table 1. Summary of the main studies on non-invasive ventilation in de novo hypoxemic respiratory failure

Study	Patients	PaO ₂ /FiO ₂ , mmHg	Patients included (n)		Intubation rate (%)		ICU Mortality rate (%)	
			NIV	CTL	NIV	CTL	NIV	CTL
Antonelli et al. 1998 [10]	Pneumonia, trauma, postoperative, ACPE	NIV 116±24 CTL 124±25	32	32	31	100	31	50
Confalonieri et al. 1999 [3]*	Pneumonia, COPD	NIV 165±30 CTL 164±52	16	17	6	8	38 ^a	24 ^a
Delclaux et al. 2000 [6]	Pneumonia, aspiration, near drowning, ACPE	CPAP 140 (59–288) CTL 148 (68–283)	56	60	38	40	21	25
Antonelli et al. 2000 [5]	Solid organ transplant recipients	NIV 129±30 CTL 129±30	20	20	20	70	20	50
Martin et al. 2000 [4]*	Hypoxemic and hypercapnic respiratory failure	NIV 103±35 CTL 110±43	14	18	36	67	29	56
Auriant et al. 2001 [11]	Postoperative, lung resection	NIV 127±42 CTL 127±43	24	24	21	50	13 ^a	38 ^a
Hilbert et al. 2001 [8]	Immunocompromized patients	NIV 141±24 CTL 136±23	26	26	46	77	38	69
Ferrer et al. 2003 [7]	Pneumonia, trauma, ACPE, ARDS	NIV 102±21 CTL 103±23	51	54	25	52	18	39
Lemiale et a. 2015 [9]	Immunocompromized patients	NIV 156 (95–248) CTL 130 (86–205)	191	183	38	45	24 ^b	27 ^b
Jaber et al. 2016 [12]	Postoperative, abdominal surgery	NIV 201±69 CTL 188±71	148	145	33	46	15 ^c	22 ^c

NIV, non-invasive ventilation; CTL, control; ACPE, acute cardiogenic pulmonary edema, COPD, chronic obstructive pulmonary disease; CPAP, continuous positive airway pressure.

Continuous variable are expressed as mean ± or median (interquartile range) and categorical variable as number (%).

*Data restricted to the “hypoxemic” acute respiratory failure group.

^a hospital mortality; ^b all cause 28-days mortality; ^c all cause 90-days mortality.

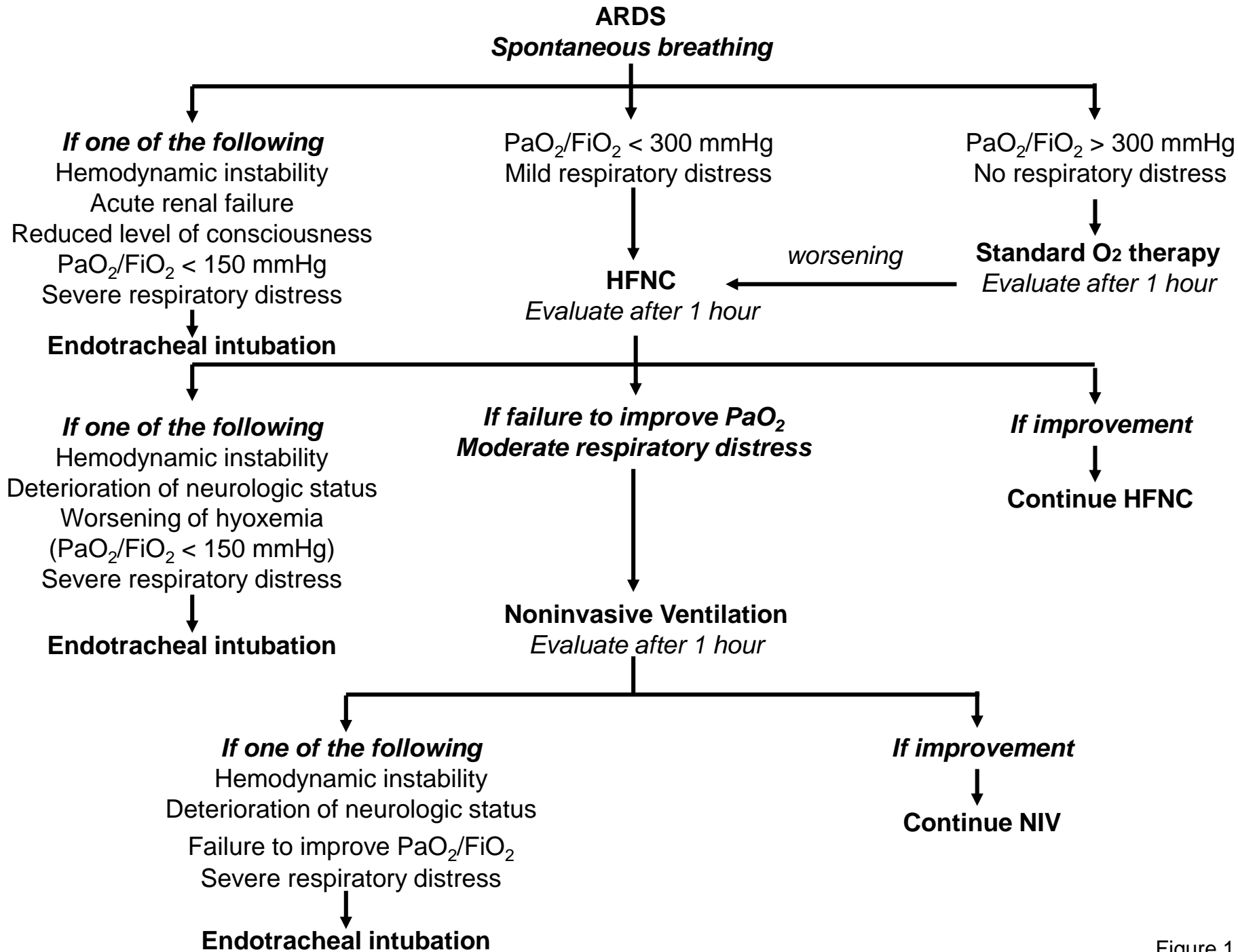


Figure 1