Con il patrocinio di

Associazione Italiana Pneumologi Ospedalieri

Ospedale San Giuseppe
MultiMedica S.p.A.

PNEUMOLOGIA 2016

Milano, 16 – 18 giugno 2016 · Centro Congressi Palazzo delle Stelline

PNEUMOLOGIA 2016
Milano, 16 – 18 giugno 2016 · Centro Congressi Palazzo delle Stelline

Quando la NIV non basta

Andrea Vianello
Fisiopatologia e Terapia Intensiva Respiratoria
Ospedale-Università di Padova

British Journal of Anaesthesia 110 (6): 896–914 (2013)
Advance Access publication 5 April 2013 · doi:10.1093/bja/aet070

BJA

REVIEW ARTICLES

Complications of non-invasive ventilation techniques: a comprehensive qualitative review of randomized trials

M. Carron[1], U. Freo[1]*, A. S. BaHammam[2], D. Dellweg[3], F. Guarracino[4], R. Cosentini[5], P. Feltracco[1], A. Vianello[6], C. Ori[1] and A. Esquinas[7]

Sixty-two RCTs including a total of 5870 patients

Overall NIV failure: 16.3%

Study	Site	Interface*	Ventilation mode*	Patients (n)*	Failure (%)*,†	Minor complications (%)
COPD						
Bott and colleagues[10]	Ward	Nasal mask	CPAP/SC	30/30	10/30	NR
Brochard and colleagues[11]	ICU	Facial mask	PSV/SC	43/42	26/74	NL: 2
Barbé and colleagues[12]	Ward	Nasal mask	IPAP+EPAP/SC	14/10	29/NR	NR
Plant and colleagues[13]	ED	Facial-nasal mask	PSV+PEEP/SC	118/118	15/23	NR
Conti and colleagues[14]	ICU	Facial mask/TI	PSV/ACV+PEEP	23/26	52/NR	NR
Keenan and colleagues[15]	ICU	Facial mask	IPAP+EPAP/SC	25/27	8/7	I: 12
Kirakli and colleagues[16]	ICU	Facial mask	PS			
Carrera and colleagues[17]	ED	Facial mask	IP			
Maggiore and colleagues[18]	ICU	Facial mask	P			
ACPO						
Bersten and colleagues[19]	ED-ICU	facial mask	C			
Mehta and colleagues[20]	ED-ICU	Nasal mask	IP			
Masip and colleagues[21]	ICU	Facial mask	P			
Levitt[22]	ED	Facial mask	IP			
Nava and colleagues[23]	ED	Facial mask	P			
Bellone and colleagues[24]	ED	Facial mask	P			
Crane and colleagues[25]	ED	Facial mask	IP			
Bellone and colleagues[26]	ED	Facial mask	P			
Moritz and colleagues[27]	ED	Facial mask	IP			
Ferrari and colleagues[28]	HDU	Facial mask	P			
Gray and colleagues[29]	ED	Facial mask	C			
Rusterholtz and colleagues[30]	ICU	Facial mask	P			
Ferrari and colleagues[31]	ED	Facial mask	PSV+PEEP/CPAP	40/40	8/0	NR
Nouira and colleagues [32]	ED	Facial mask	PSV+PEEP/CPAP	99/101	7/10	NR
Hypoxic ARF						
Wysocki and colleagues[33]	ICU	Facial mask	PSV+PEEP/SC	21/20	62/70	NR
Antonelli and colleagues[34]	ICU	Facial mask/TI	PSV+PEEP/SC	32/32	31/47	NL: 5
Delclaux and colleagues[35]	ICU	Facial mask	CPAP/SC	62/61	34/39	I: 14; NL: 3; GI: 2
Hilbert and colleagues[36]	ICU	Facial mask	PSV+PEEP/SC	26/26	46/77	NL: 23
Ferrer and colleagues[37]	ICU	Facial mask	PSV+PEEP/SC	51/54	25/52	NL: 25; GI: 2; EL: 6
Cosentini and colleagues[38]	HDU	Helmet	CPAP/SC	20/27	0/0	I: 5
Fartoukh and colleagues[39]	ED-ward	Facial mask	PSV+PEEP-IPAP+EPAP/SC	35/36	6/NR	NR
Gupta and colleagues[40]	ICU	Facial mask	PSV+PEEP/SC	28/25	7/16	NR
Wermke and colleagues[41]	Ward	Facial mask	PSV+PEEP/SC	43/44	14/25	NR
Hypoxic–hypercapnic ARF						
Kramer and colleagues[42]	ICU	Nasal mask	IPAP+EPAP/SC	16/15	31/73	NL: 13; AL: 13; I: 13
Wood and colleagues[43]	ED	Nasal mask	IPAP+EPAP/SC	11/16	31/68	PNX: 6
Celikel and colleagues[44]	ICU	Facial mask	PSV+PEEP/SC	15/15	7/40	NL: 46; GI: 6
Confalonieri and colleagues[45]	ICU	Nasal mask	PSV+PEEP/SC	28/28	21/61	GI: 4
Antonelli and colleagues[46]	ICU	Facial mask	PSV+PEEP/SC	20/20	20/70	NL: 5

Study	Site	Interface*	Ventilation mode*	Patients (n)*	Failure (%)*,†	Minor complications (%)
Martin and colleagues[47]	ICU	Facial mask	IPAP+EPAP/SC	32/29	28/59	NR
Gay and colleagues[48]	ICU	Facial mask	PSV+PEEP/PAV+PEEP	23/21	4/10	NL: 26; C: 11
Kwok and colleagues[49]	ICU	Nasal/facial mask	IPAP+EPAP/ IPAP+EPAP	35/35	23/23	I: 34(NM) - 11 (FM)
Fernández-Vivas and colleagues[50]	ICU	Facial mask	PSV+PEEP/ACV+PEEP	59/58	37/34	NL: 26; GI: 6 EL: 9; I: 13
			V+PEEP	31/33	58/100	NL: 13
			AP+EPAP	17/17	6/0	CFM: 6; GI: 6; EL: 6
			+PEEP	46/44	20/14	AL: 68 (NM)
				42/44	24/27	NR
				24/24	21/50	I: 13
				99/105	1/5	NL: 4; I: 9
				105/104	1/10	NR
				47/46	28/15	NR
				39/42	72/69	NR
Esteban and colleagues[60]	ICU	Facial mask	PSV+PEEP/SC	114/104	48/48	I: 3
Nava and colleagues[61]	ICU	Facial mask	IPAP+EPAP/SC	48/49	8/24	I: 8; NL: 29; EL: 4; NC: 4;OD: 2
Kindgen-Milles and colleagues[62]	ICU	Nasal mask	CPAP/SC	25/25	4/16	NR
Ferrer and colleagues[63]	ICU	Facial mask	IPAP+EPAP/SC	79/83	11/22	NL: 6; GI: 1
Ferrer and colleagues[64]	ICU	Facial mask	IPAP+EPAP/SC	54/54	11/19	NR
Zarbock and colleagues[65]	POICU	Nasal mask	CPAP/SC	232/236	1/3	NR
Khilnani and colleagues[66]	ICU	Facial mask	PSV+PEEP/SC	20/20	15/25	?
Weaning						
Nava and colleagues[67]	ICU	Facial mask/TI	PSV+PEEP/PSV+PEEP	25/25	12/32	NL: 56; GI: 2
Girault and colleagues[68]	ICU	Facial mask	PSV+PEEP/PSV+PEEP	16/17	24/25	NR
Ferrer and colleagues[69]	ICU	Facial mask	PSV+PEEP/PSV+PEEP	21/22	14/27	NL: 29; GI: 5
Trevisan and colleagues[70]	ICU	Facial mask	PSV+PEEP/ PSV+PEEP	21/22	21/NR	NL: 4
Girault and colleagues[71]	ICU	Facial mask	PSV+PEEP/SC	68/70	32/29	GI: 7; I: 7

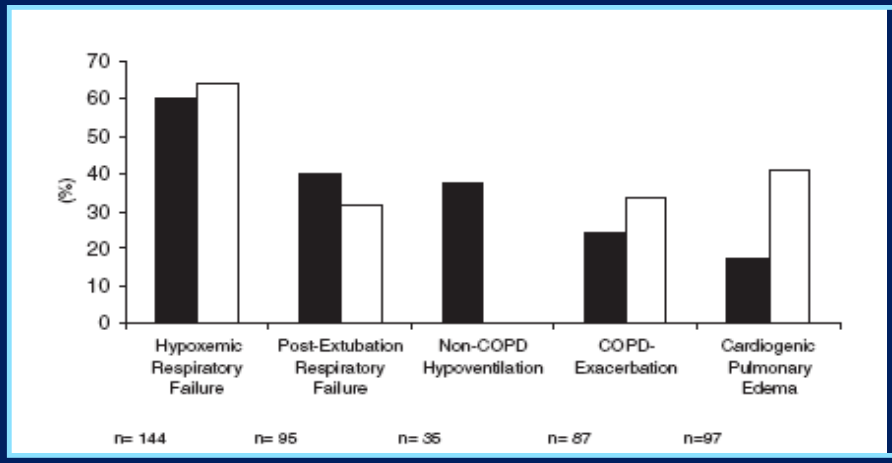
NIV – Real Life

Evaluation of all 449 patients receiving NPPV for a 1-yr period for acute or acute on chronic RF

- CPE (n=97)
- AECOPD (n=87)
- non-COPD acute hypercapnic RF (n=35)
- postextubation RF (n=95)
- acute hypoxemic RF (n=144)

Intubation rate was 18%, 24%, 38%, 40%, and 60%, respectively

Hospital mortality for patients with acute hypoxemic RF who failed NPPV was 64%



No. of Patients	COPD Exacerbation (n = 87)	Non-COPD Hypercapnic Respiratory Failure (n = 35)	Acute Hypoxemic Respiratory Failure (n = 144)	Cardiogenic Pulmonary Edema (n = 97)	Postextubation Respiratory Failure (n = 95)
Mask intolerance			1	1	
Refractory hypoxemia	1		43	1	17
Refractory respiratory acidosis	8	4	8	1	4
Depressed mental status	5	5	11	1	5
Secretion accumulation			2		
Vomiting/aspiration			1		1
Severe arrhythmia			2	1	1
Hemodynamic instability			7	3	1
Cardiorespiratory arrest or risk for arrest	4	3	2	3	4
Surgical procedure	1		5	4	
Other/unknown	2	1	5	2	5
Total, *n*	21	13	87	17	38
Intubation rate, %	24	37	60	18	40

Schettino G. *Crit Care Med* 2008; 36:441-7

Use of Noninvasive Ventilation in Patients with Acute Respiratory Failure, 2000–2009

A Population-Based Study

Allan J. Walkey[1] and Renda Soylemez Wiener[2,3]

AnnalsATS Volume 10 Number 1 | February 2013

- **Rationale:** evidence supporting use of NIV varies widely for different causes of ARF.
- **Population:** 11,659,668 cases of ARF from the Nationwide Inpatient Sample during years 2000 to 2009;
- **Objectives:** To compare utilization trends and outcomes associated with NIV in patients with and without COPD.

Use of Noninvasive Ventilation in Patients with Acute Respiratory Failure, 2000–2009

A Population-Based Study

Allan J. Walkey[1] and Renda Soylemez Wiener[2,3]

AnnalsATS Volume 10 Number 1 | February 2013

Acute respiratory failure-associated diagnosis

COPD	344,707 (40.9)	597,022 (35.7)
Cardiogenic pulmonary edema	155,396 (18.5)	293,862 (17.6)
Asthma	12,067 (1.4)	54,877 (3.3)
Pneumonia	121,682 (14.5)	314,339 (18.8)
Sepsis	24,763 (2.9)	79,744 (4.8)
Neurological condition	35,463 (4.3)	91,995 (5.5)
Other/unknown	146,777 (17.4)	241,634 (14.4)

Changing etiologies of ARF among patients receiving NIV

Use of Noninvasive Ventilation in Patients with Acute Respiratory Failure, 2000–2009

A Population-Based Study

Allan J. Walkey[1] and Renda Soylemez Wiener[2,3]

AnnalsATS Volume 10 Number 1 | February 2013

- 20% of patients without a COPD diagnosis who received NIV ⟶ IMV;
- 13.4% of patients with COPD who received NIV ⟶ IMV;
- Patients experiencing NIV failure before transition to IMV had greater hospital mortality than those initially on IMV.

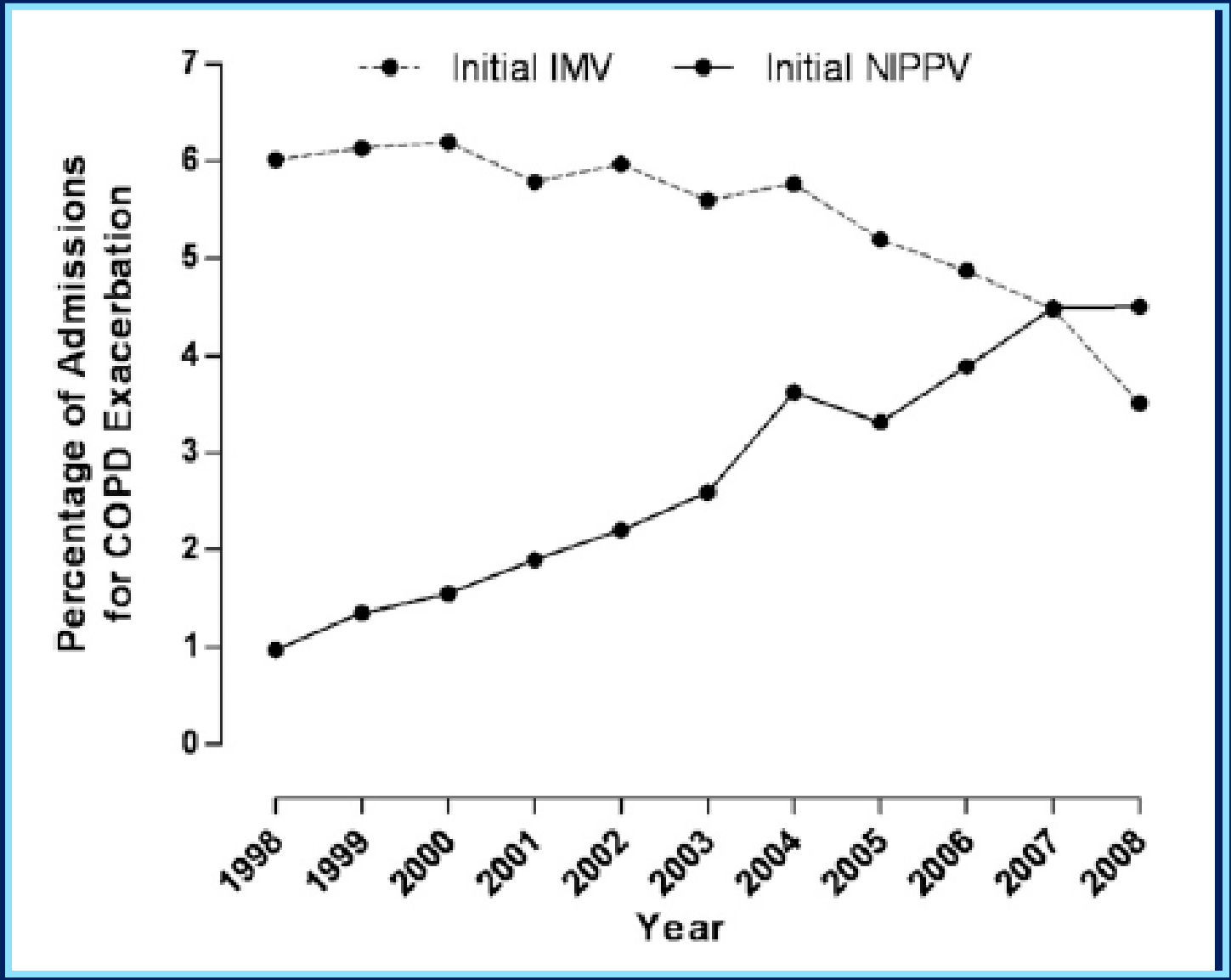
Outcomes of Noninvasive Ventilation for Acute Exacerbations of Chronic Obstructive Pulmonary Disease in the United States, 1998–2008

Divay Chandra[1]*, Jason A. Stamm[1]*, Brian Taylor[2], Rose Mary Ramos[1], Lewis Satterwhite[2], Jerry A. Krishnan[3], David Mannino[4], Frank C. Sciurba[1], and Fernando Holguín[1]

[1]University of Pittsburgh, Pittsburgh, Pennsylvania; [2]Emory University, Atlanta, Georgia; [3]University of Illinois at Chicago, Chicago, Illinois; and [4]University of Kentucky, Lexington, Kentucky

- **Rationale:** The patterns and outcomes of NIV use in patients hospitalized for AECOPD nationwide are unknown.
- **Population:** 7,511,267 admissions for acute AE occurred from 1998 to 2008;
- **Objectives:** To determine the prevalence and trends of NIV in AECOPD.

AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE VOL 185 2012



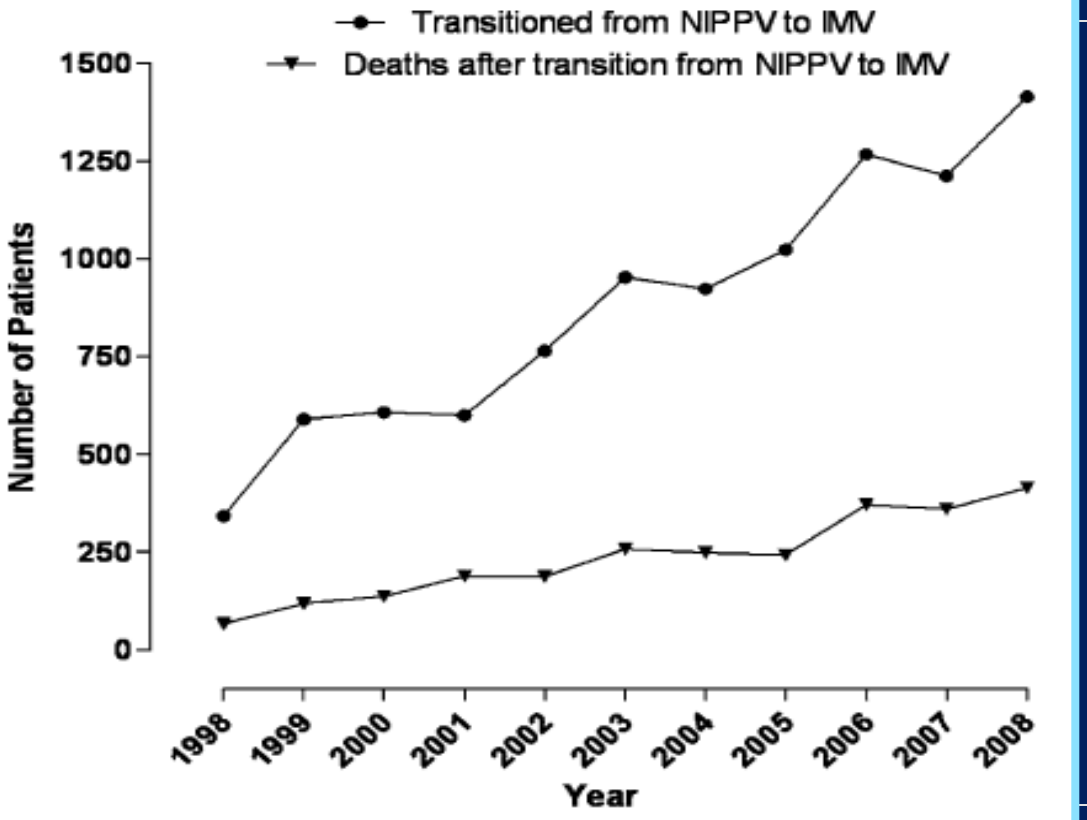
Use of NIPPV or IMV as first-line respiratory support in patients hospitalized with AECOPD

AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE VOL 185 2012

Outcomes of Noninvasive Ventilation for Acute Exacerbations of Chronic Obstructive Pulmonary Disease in the United States, 1998–2008

Divay Chandra[1]*, Jason A. Stamm[1]*, Brian Taylor[2], Rose Mary Ramos[1], Lewis Satterwhite[2], Jerry A. Krishnan[3], David Mannino[4], Frank C. Sciurba[1], and Fernando Holguín[1]

[1]University of Pittsburgh, Pittsburgh, Pennsylvania; [2]Emory University, Atlanta, Georgia; [3]University of Illinois at Chicago, Chicago, Illinois; and [4]University of Kentucky, Lexington, Kentucky



The percentage of patients transitioned from NIV to IMV ≈ 5% and did not increase from 1998 to 2008

AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE VOL 185 2012

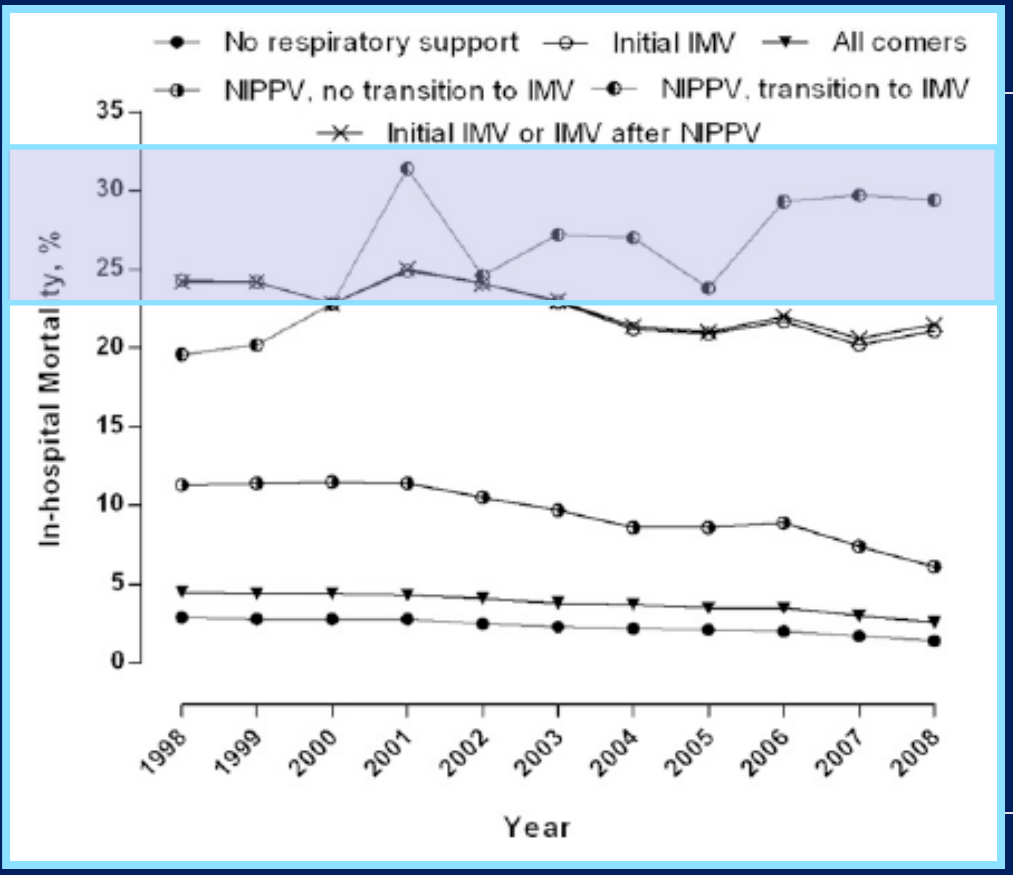
Reasons for low rate of IMV use after NPPV, compared to clinical trial:

- End of life decision to not accept IMV
- Patients died before IMV could be started
- Good selection of appropriate patients

Outcomes of Noninvasive Ventilation for Acute Exacerbations of Chronic Obstructive Pulmonary Disease in the United States, 1998–2008

Divay Chandra[1]*, Jason A. Stamm[1]*, Brian Taylor[2], Rose Mary Ramos[1], Lewis Satterwhite[2], Jerry A. Krishnan[3], David Mannino[4], Frank C. Sciurba[1], and Fernando Holguín[1]

[1]University of Pittsburgh, Pittsburgh, Pennsylvania; [2]Emory University, Atlanta, Georgia; [3]University of Illinois at Chicago, Chicago, Illinois; and [4]University of Kentucky, Lexington, Kentucky



- High mortality rate (≈30%) ;↑ over time
- OR for death:1.63, compared to those initially on IMV
- ↑hospital stay

AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE VOL 185 2012

Aetiology of NIV failure

A. Failure to adequately ventilate/oxygenate
    A. Delayed NIV treatment
    B. Inappropriate ventilatory technique
    C. Patient's clinical condition
B. Dependence on non-invasive support
    Lack of improvement of acute illness
C. Complications

NIV reasons for failure

	ACPE	COPD	Non COPD	ALI/ARDS
Hypoxemia	+	+		+++
Hypercapnia	+	++	+	
Leak/Mask intol	+	+	++	++
Secretion		+	+	+
Mentation	+	+	+	+
Agitation		+		++
Progression			+	+++
Failure Rate	18%	24%	37%	60%

Schettino G. *Crit Care Med* 2008; 36:441-7

Transition to IMV: when is in the interest of a patient?

- **Hospital mortality: 64% *(Schettino, 2008)***
- **Mortality rate: 30%; prolonged hospitalization *(Chandra, 2011)***
- **Great hospital mortality *(Walkey, 2013)***

Transition to IMV
(personal experience, 2011-2014)

Number of subjects	62
Age (mean ± SD) , yrs	65.4±19.3
Gender (males, females)	26, 36
Ineffective NIV, n (%) Severe hypercapnia Severe hypoxemia	52 (83.8) 25 (42.4) 21 (35.6)
Dependence on NIV, n (%)	8 (13.3)
NIV complication, n (%)	2 (3.4)
Tracheotomy, n (%)	16 (28.8)
Outcome , n (%) Died during hosp Discharged from hosp	 41 (66.1) 21 (33.9)

Remarks

- **Mortality rate among patients transitioned to IMV is very high;**
- **The outcome of patients with ILD and COPD is extremely poor.**

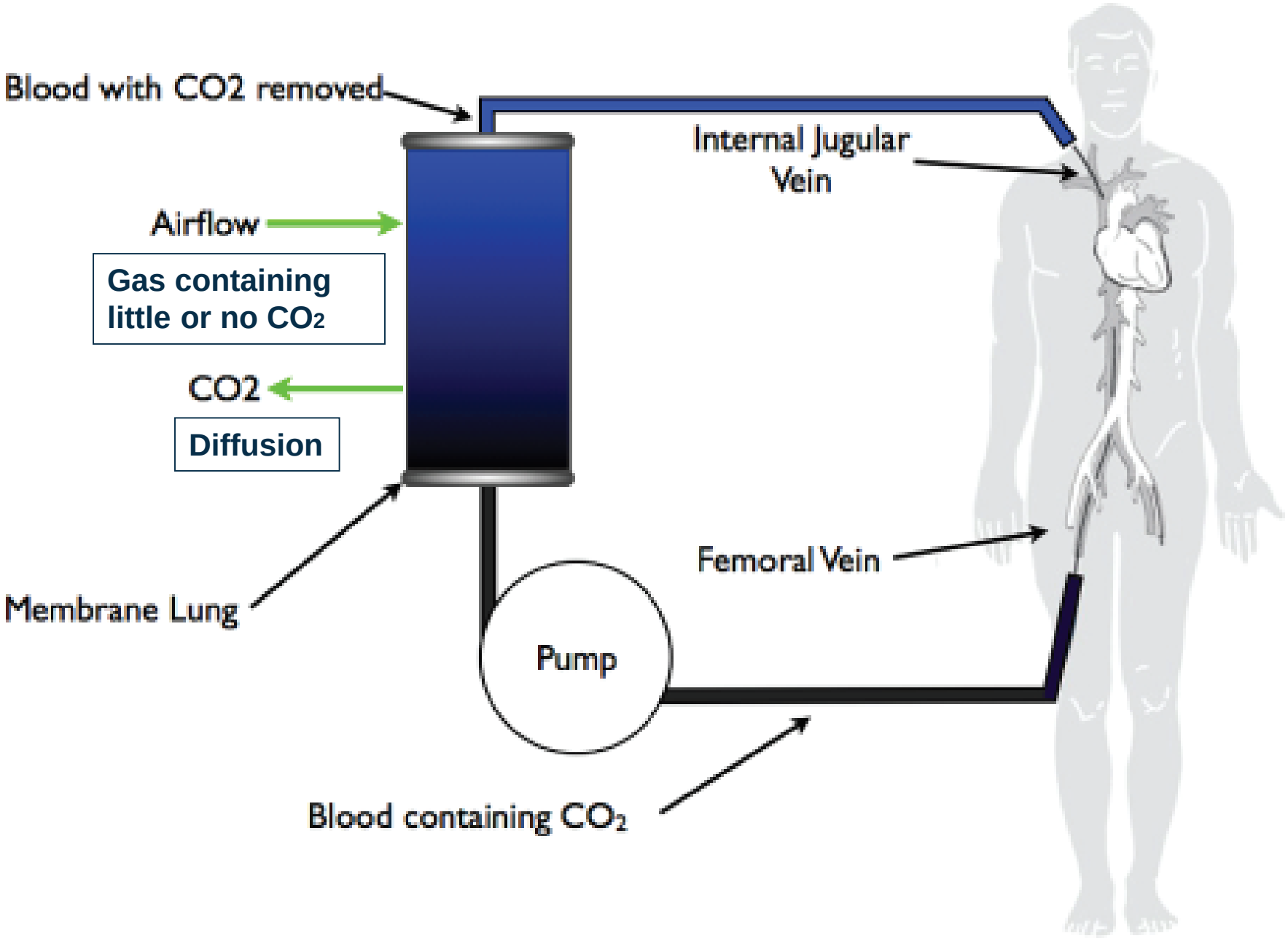
→ **Should IPF/COPD patients be excluded from IMV after failing a NIV trial?**

NIV reasons for failure

	ACPE	COPD	Non COPD	ALI/ARDS
Hypoxemia	+	+		+++
Hypercapnia	+	++	+	
Leak/Mask intol	+	+	++	++
Secretion		+	+	+
Mentation	+	+	+	+
Agitation		+		++
Progression			+	+++
Failure Rate	18%	24%	37%	60%

Schettino G. *Crit Care Med* 2008; 36:441-7

A requirement to effectively counteract hypercapnia!


Blood with CO2 removed
Internal Jugular Vein
Airflow
Gas containing little or no CO2
CO2
Diffusion
Membrane Lung
Femoral Vein
Pump
Blood containing CO2

The membrane lung

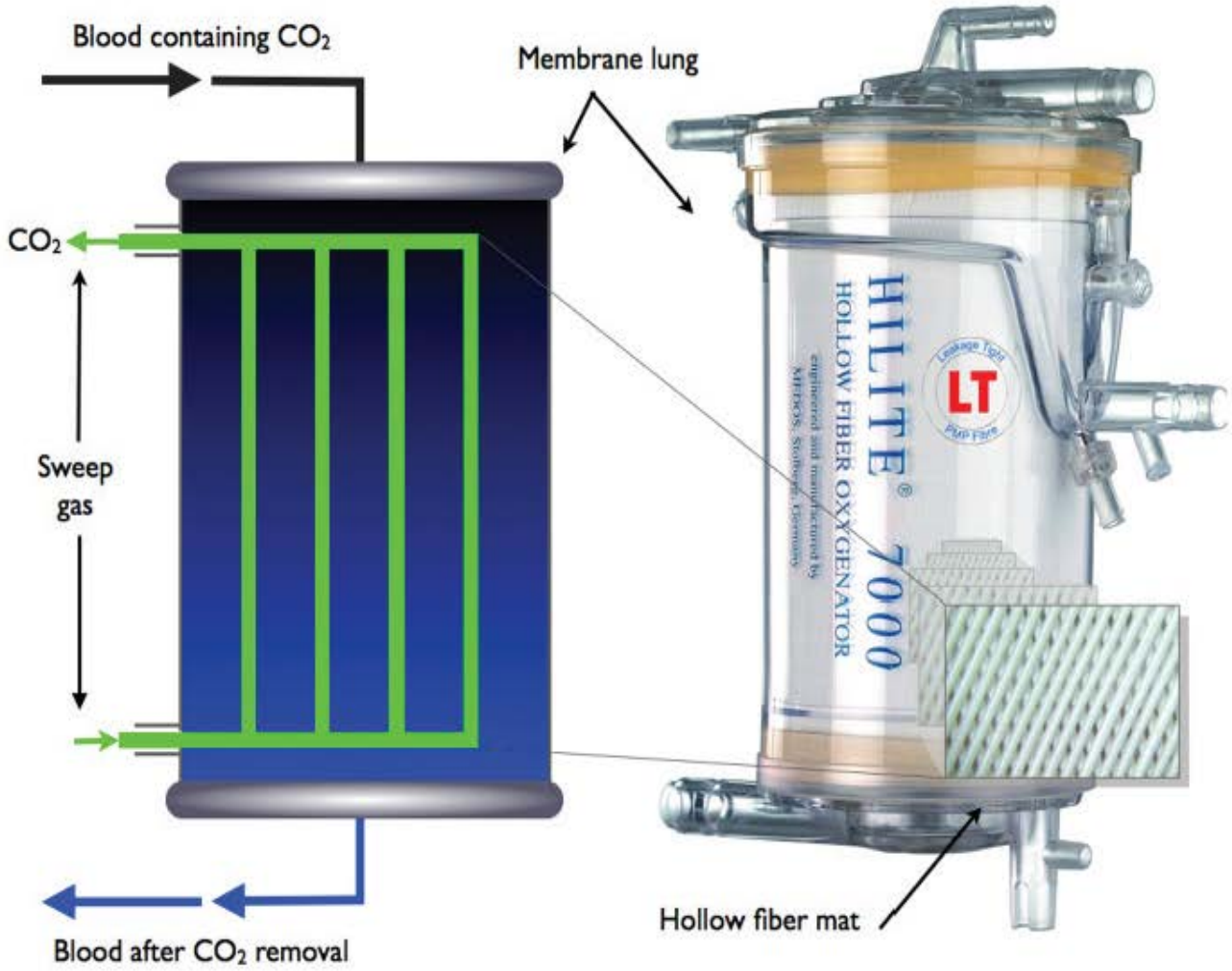
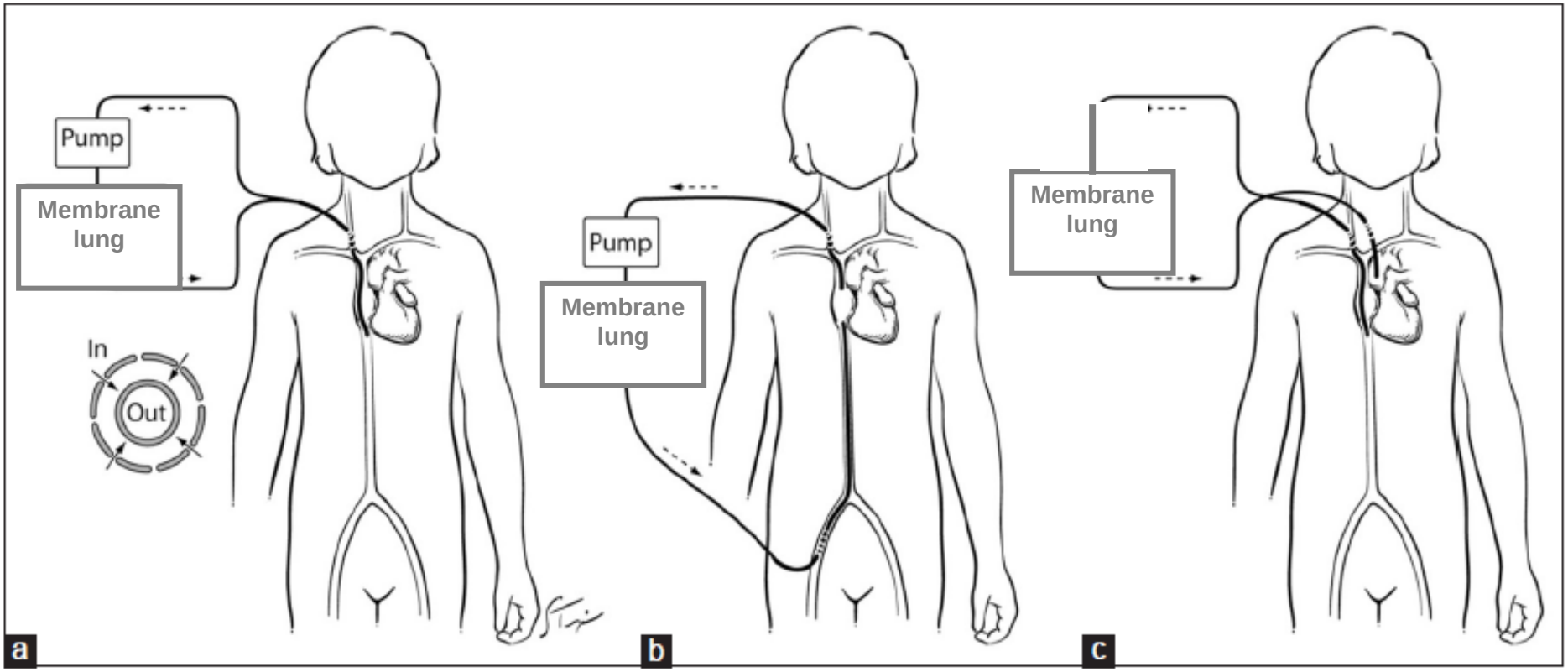
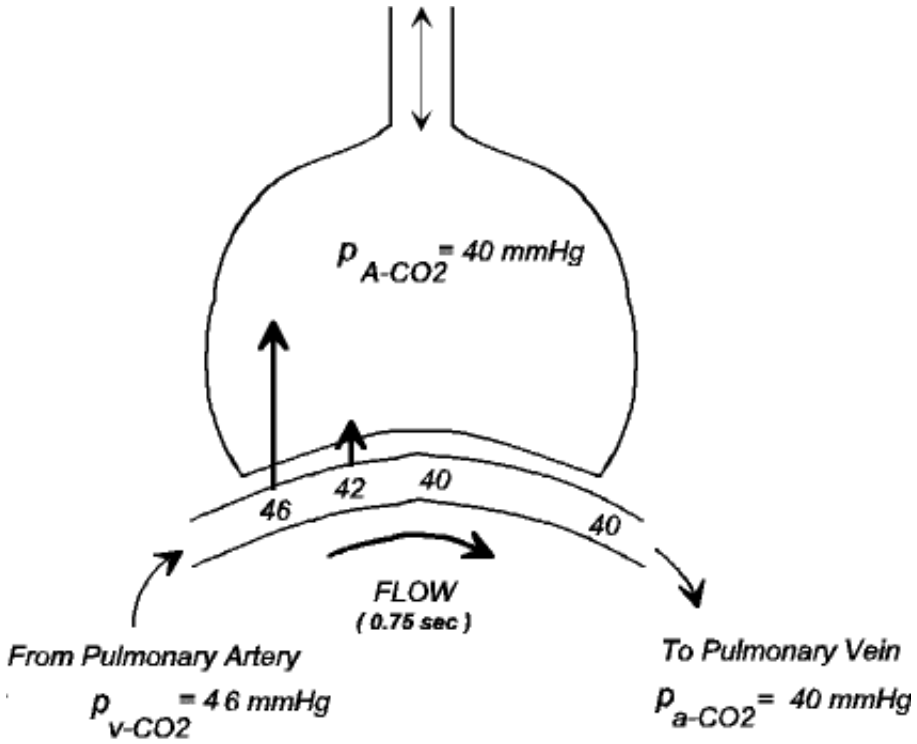


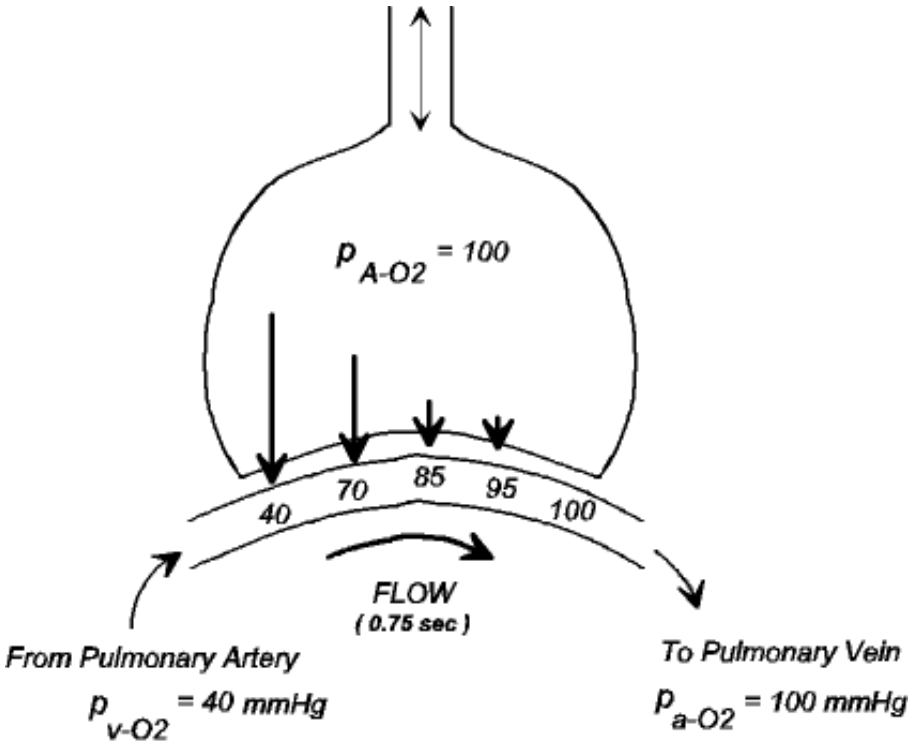
Figure 2. Diagram showing the basic principle of a membrane lung. Sweep gas passes through the hollow fibres. Hollow fibers are arranged in a complex mat. Image courtesy of Medos Medizintechnik AG (Stolberg, Germany).

The pump

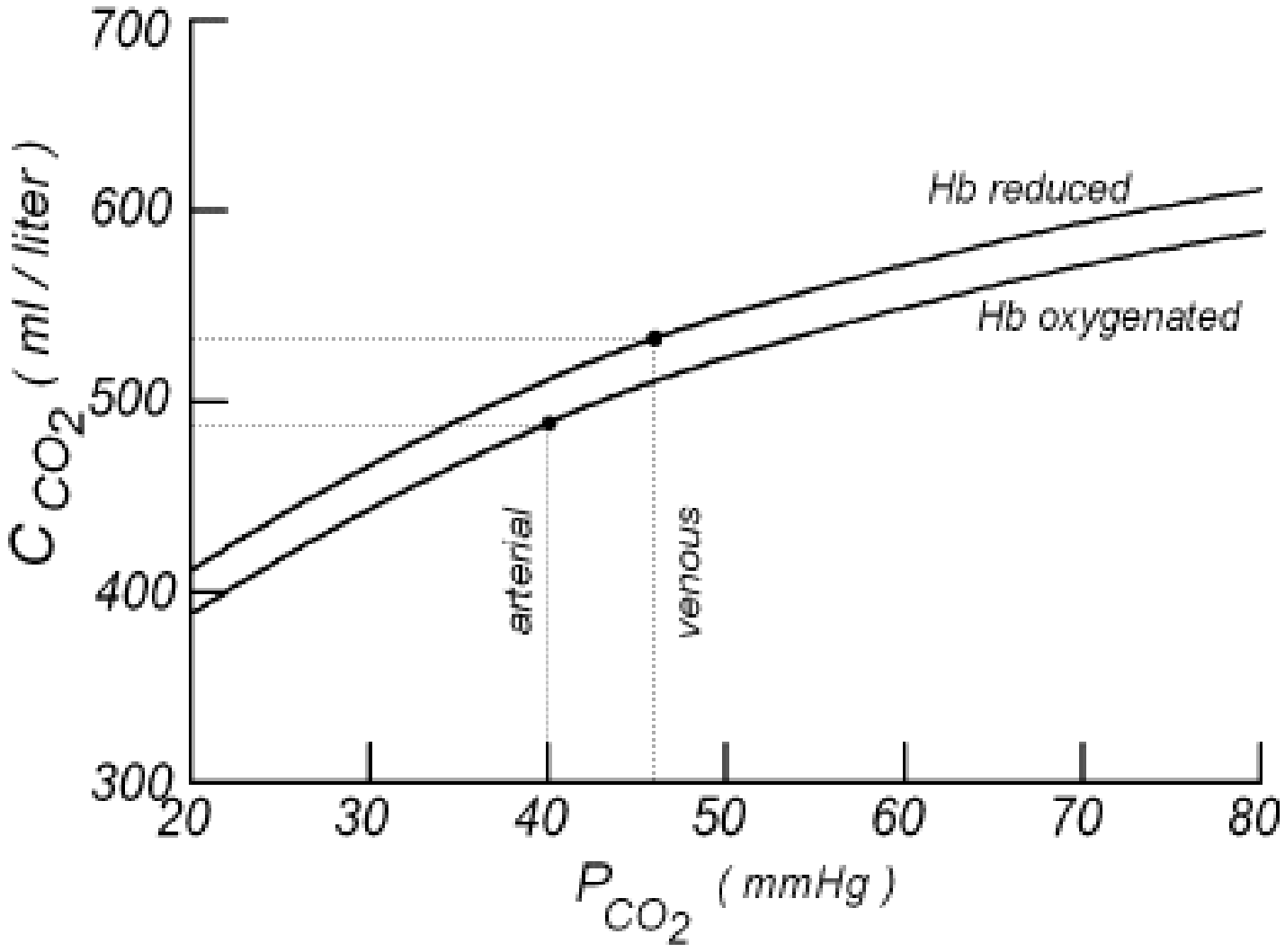


Three configurations of extracorporeal blood flow (a) single-site double lumen veno-venous (VV), (b) two-site VV, and (c) arterio-venous





Greater diffusibility of CO_2 compared to O_2 across extracorporeal membranes because of higher solubility.



Steep slope in the CO_2 dissociation curve in the physiologic range of dissolved CO_2

Potential application of $ECCO_2R$ technology

- **$ECCO_2R$ for patients on IMV:**
  - to enable lung protective ventilation
  - to treat refractory hypercapnic RF
  - to support weaning and facilitate extubation
- **$ECCO_2R$ for patients on NIV:**
  - to avoid endotracheal intubation

Clinical use of $ECCO_2R$ in patients on NIV

- Chronic Obstructive Pulmonary Disease
- A bridge to Lung Transplant
- Other conditions

$ECCO_2R$ in COPD patients with hypercapnic ARF

Study details	N. of patients	Key efficacy findings	Key safety findings	Comments
Crotti (2012) [21]	1	Avoidance of ETI	-	V-V system
Kluge (2012) [12]	21	Success rate: 90% (19/21)	2 major and 7 minor bleeding complications; 1 pseudoaneurysm; 1 heparin-induced thrombocytopenia	A-V system
Brederlau (2012) [22]	3	Success rate: 66% (2/3)	-	A-V system cause of failure: NP
Burki (2013) [23]	9	Success rate: 89% (8/9)	-	V-V system cause of failure: worsening RF
Mani (2013) [24]	2	suCcess rate: 100% (2/2)	No complications	V-V system
Bonin (2013) [25]	1	Avoidance of ETI	Bleeding	V-V system
Del Sorbo (2015) [26]	25	ETI rate: 12%	13 patients (52%) experiencing adverse events (3 major and 1 minor bleedings, 9 technical drawbacks)	V-V system Historical controls; Risk of ETI 3 times higher in patients treated with *NIV* only

ARF: acute respiratory failure; COPD: chronic obstructive pulmonary disease; NIV: non-invasive ventilation; NP: nosocomial pneumonia; RF: respiratory failure.

Vianello et al, *Minerva Pneumol* 2015

Extracorporeal Co_2 Removal in Hypercapnic Patients At Risk of Noninvasive Ventilation Failure: A Matched Cohort Study With Historical Control*

Lorenzo Del Sorbo, MD[1]; Lara Pisani, MD[2]; Claudia Filippini, PhD[1]; Vito Fanelli, MD[1]; Luca Fasano, MD[2]; Pierpaolo Terragni, MD[1]; Andrea Dell'Amore, MD[3]; Rosario Urbino, MD[1]; Luciana Mascia, MD, PhD[1]; Andrea Evangelista, MD[4]; Camillo Antro, MD[5]; Raffaele D'Amato, MD[1]; Maria José Sucre, MD[1]; Umberto Simonetti, MD[1]; Pietro Persico, MD[1]; Stefano Nava, MD[2]; V. Marco Ranieri, MD[1]

Objectives: To assess efficacy and safety of NIV plus $ECCO_2R$ in comparison to NIV-only to prevent ETI in patients with exacerbated AECOPD

Design: Matched cohort study with historical control.

Methods: Primary endpoint: cumulative prevalence of ETI. 25 pts included in the study group. 21 patients selected for the control group

Results: Risk of being intubated 3 times higher in patients treated with NIV-only (hazard ratio, 0.27).

Intubation rate in NIVplus- $ECCO_2R$ 12% and in NIV-only 33% (not statistically different).

CCM, 2015

Extracorporeal Co_2 Removal in Hypercapnic Patients At Risk of Noninvasive Ventilation Failure: A Matched Cohort Study With Historical Control*

Lorenzo Del Sorbo, MD[1]; Lara Pisani, MD[2]; Claudia Filippini, PhD[1]; Vito Fanelli, MD[1]; Luca Fasano, MD[2]; Pierpaolo Terragni, MD[1]; Andrea Dell'Amore, MD[3]; Rosario Urbino, MD[1]; Luciana Mascia, MD, PhD[1]; Andrea Evangelista, MD[4]; Camillo Antro, MD[5]; Raffaele D'Amato, MD[1]; Maria José Sucre, MD[1]; Umberto Simonetti, MD[1]; Pietro Persico, MD[1]; Stefano Nava, MD[2]; V. Marco Ranieri, MD[1]

Limitations of the study:

- High number of pts who refused to give consent to "NIV-plus-$ECCO_2R$" $\rightarrow$ lack of clinical equipoise;
- Non-randomized design of the study;
- Decision to use $ECCO_2R$ made in an unblinded manner;
- Patients not representative of those commonly admitted to the ICU for treatment with NIV.

CCM, 2015

Extracorporeal Co_2 Removal in Hypercapnic Patients At Risk of Noninvasive Ventilation Failure: A Matched Cohort Study With Historical Control*

Lorenzo Del Sorbo, MD[1]; Lara Pisani, MD[2]; Claudia Filippini, PhD[1]; Vito Fanelli, MD[1]; Luca Fasano, MD[2]; Pierpaolo Terragni, MD[1]; Andrea Dell'Amore, MD[3]; Rosario Urbino, MD[1]; Luciana Mascia, MD, PhD[1]; Andrea Evangelista, MD[4]; Camillo Antro, MD[5]; Raffaele D'Amato, MD[1]; Maria José Sucre, MD[1]; Umberto Simonetti, MD[1]; Pietro Persico, MD[1]; Stefano Nava, MD[2]; V. Marco Ranieri, MD[1]

Conclusions: data provide the rationale for future RCT that are required to validate $ECCO_2R$ in patients with hypercapnic respiratory failure nonresponsive to NIV.

Removing extra CO_2 in AECOPD patients

- Reported studies are limited in size;
- Insufficient information regarding when $ECCO_2R$ should ideally be implemented;
- *However*, the ability to increase avoidance of IMV and trends in reduced hospital LOS $\rightarrow$ need for prospective, randomized, controlled studies.

Lund, *Curr Respir Care Rep* 2012

A bridge to Lung Transplant

Undergoing IMV before LT is an independent predictor of a longer time on MV and in the ICU during the post-transplantation period;

→ Growing interest in the use of $ECCO_2R$ as a bridge to LT for patients with severe, hypercapnic RF in the attempt to avoid or limit IMV.

$ECCO_2R$ in patients on waiting list for LT

Study details	N° of patients	Bridged to LT	Comments
Fisher, 2006	12	10	A-V system (8 still alive at the 1yr follow-up)
Ricci, 2010	12	3	Mean time on $ECCO_2R$: 13.5 days 8 died on the device, 1 recovered
Bartosik, 2011	2	1	1 recovered
Schellongowski, 2014	20	19	2 systems (A-V and V-V) (4 switched to ECMO) Complications in 6 pts

Removing extra CO_2 in patients on Waiting List

Bridging to LT with $ECCO_2R$ is feasible and associated with high successful transplantation and survival rates.

Sporadic case reports on the utilization of $ECCO_2R$

- Near-fatal pediatric and adult asthma (Conrad 2007, Elliot 2007, Jung 2011)
- Intracranial bleeding (Mallick 2007)
- Influenza infection (Twigg 2008)
- Chest/abdominal/head trauma (McKinlay 2008)
- Bronchopleural fistulae (Bombino 2011)
- Acute exacerbation of IPF (Vianello 2016)

Conclusions

- The boundaries for the use of NIV continue to expand; however, the risk of NIV failure is still present;
- Transitioning to IMV after NIV failure may not be in the interest of some categories of patients, including those with AECOPD;
- The future management of patients with COPD will routinely include “respiratory dyalisis”: only a fascinating hypothesis?