Essai FLORALI : *High* **FL***ow* **O***xygen therapy for the* **R***esuscitation of patients with* **A***cute* **L***ung* **I***njury*

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groupe FLORALI
soutien du réseau REVA

Conflits d’intérêts

- Fisher&Paykel

The New England
Journal of Medicine

Volume 333 SEPTEMBER 28, 1995 Number 13

NONINVASIVE VENTILATION FOR ACUTE EXACERBATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Laurent Brochard, M.D., Jordi Mancebo, M.D., Marc Wysocki, M.D., Frédéric Lofaso, M.D., Giorgio Conti, M.D., Alain Rauss, M.D., Gérald Simonneau, M.D., Salvador Benito, M.D., Alessandro Gasparetto, M.D., François Lemaire, M.D., Daniel Isabey, Ph.D., and Alain Harf, M.D.

Noninvasive Ventilation in Severe Hypox… Respiratory Failure

A Randomized Clinical Trial

Miquel Ferrer, Antonio Esquinas, Miguel Leon, Gumersindo Gonzalez, Antonio Alar…

Unitat de Vigilància Intensiva Respiratòria, Institut Clínic de Pneumologia i Cirurgia Toràcica, Institut d'In… Pi i Sunyer, Hospital Clínic, Universitat de Barcelona, Barcelona; Unidad de Cuidados Intensivos, Hospital… Unidad de Cuidados Intensivos, Hospital Arnau de Vilanova, Lleida, Spain

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Noninvasive Positive-Pressure Ventilation for Respiratory Failure after Extubation

Andrés Esteban, M.D., Ph.D., Fernando Frutos-Vivar, M.D., Niall D. Ferguson, M.D., Yaseen Arabi, M.D.,

Noninvasive Ventilation and Weaning in Patients with Chronic Hypercapnic Respiratory Failure

A Randomized Multicenter Trial

Christophe Girault[1,2], Michael Bubenheim[3], Fekri Abroug[4], Jean Luc Diehl[5], Souheil Elatrous[6], Pascal Beuret[7], Jack Richecoeur[8], Erwan L'Her[9], Gilles Hilbert[10], Gilles Capellier[11], Antoine Rabbat[12], …[13], Claude Guérin[14], Philippe Guiot[15], Jacques Bénichou[3,16], and Guy Bonmarchand[1,2], …al Group*

…al Intensive Care, Rouen University Hospital, Rouen, France; [3]Department of Biostatistics, Rouen University Hospital, Rouen, …30-IFRMP.23, Institute for Biomedical Research, Rouen University, Rouen, France; [4]Medical Intensive Care Unit, Monastir …onastir, Tunisia; [5]Medical Intensive Care Unit, Georges Pompidou University Hospital, Paris, France; [6]Medical Intensive Care …y Hospital, Mahdia, Tunisia; [7]Medico-surgical Intensive Care Unit, Roanne Hospital, Roanne, France; [8]Medico-surgical …ontoise Hospital, Pontoise, France; [9]Medical Intensive Care Unit, Brest University Hospital, Brest, France; [10]Medical Intensive …niversity Hospital, Bordeaux, France; [11]Medical Intensive Care Unit, Besançon University Hospital, Besançon, France; …ical Intensive Care Unit, Hôtel-Dieu University Hospital, Paris, France; [13]Medical Intensive Care Unit, Ariana University …ia; [14]Medical Intensive Care Unit, Lyon University Hospital, Lyon, France; [15]Medical Intensive Care Unit, Mulhouse Hospital, … [16]INSERM U 657, Rouen University, Rouen, France

Outcomes of Patients With Acute Respiratory Failure After Abdominal Surgery Treated With Noninvasive Positive Pressure Ventilation*

Samir Jaber, MD, PhD; Jean-Marc Delay, MD; Gérald Chanques, M… Mustapha Sebbane, MD; Eric Jacquet, MD; Bruno Souche, MD; Pierre-François Perrigault, MD; and Jean-Jacques Eledjam, MD, PhI…

NONINVASIVE VENTILATION IN IMMUNOSUPPRESSED PATIENTS WI… PULMONARY INFILTRATES, FEVER, AND ACUTE RESPIRATORY FAILU…

Gilles Hilbert, M.D., Didier Gruson, M.D., Fréderic Vargas, M.D., Ruddy Valentino, M.D., Georges Gbikpi-Benissan, M.D., Michel Dupon, M.D., Josy Reiffers, M.D., and Jean P. Cardinaud, M…

Research

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Noninvasive Ventilation vs Oxygen Therapy on Mortality Among Immunocompromised Patients With Acute Respiratory Failure

A Randomized Clinical Trial

Virginie Lemiale, MD; Djamel Mokart, MD; Matthieu Resche-Rigon, MD, PhD; Frédéric Pène, MD, PhD; Julien Mayaux, MD; Etienne Faucher, MD; Martine Nyunga, MD; Christophe Girault, MD, PhD; Pierre Perez, MD; Christophe Guitton, MD, PhD; Kenneth Ekpe, MD; Achille Kouatchet, MD; Igor Théodose, MS; Dominique Benoit, MD, PhD; Emmanuel Canet, MD; François Barbier, MD, PhD; Antoine Rabbat, MD; Fabrice Bruneel, MD; Francois Vincent, MD; Kada Klouche, MD, PhD; Kontar Loay, MD; Eric Mariotte, MD; Lila Bouadma, MD, PhD; Anne-Sophie Moreau, MD; Amélie Seguin, MD; Anne-Pascale Meert, MD, PhD; Jean Reignier, MD, PhD; Laurent Papazian, MD, PhD; Ilham Mehzari, MD; Yves Cohen, MD, PhD; Maleka Schenck, MD; Rebecca Hamidfar, MD; Michael Darmon, MD, PhD; Alexandre Demoule, MD, PhD; Sylvie Chevret, MD, PhD; Elie Azoulay, MD, PhD; for the Groupe de Recherche en Réanimation Respiratoire du patient d'Onco-Hématologie (GRRR-OH)

Indications de la ventilation non-invasive dans l'insuffisance respiratoire aiguë

- Œdème aigu pulmonaire
- Exacerbation de BPCO

Bersten NEJM 1991; 325:1825-30
Brochard. NEJM 1995;333:8817-22

The New England
Journal of Medicine

Volume 325 DECEMBER 26, 1991 Number 26

TREATMENT OF SEVERE CARDIOGENIC PULMONARY EDEMA WITH CONTINUOUS POSITIVE AIRWAY PRESSURE DELIVERED BY FACE MASK

ANDREW D. BERSTEN, M.B., B.S., ANDREW W. HOLT, M.B., B.S., ALNIS E. VEDIG, M.B., B.S., GEORGE A. SKOWRONSKI, M.B., B.S., AND CHRISTOPHER J. BAGGOLEY, M.B., B.S.

VARIABLE	OXYGEN (N = 20)	OXYGEN PLUS CPAP (N = 19)	P VALUE†
Intubation and mechanical ventilation — no. (%)	7 (35)	0 (0)	0.005
Stay in ICU (days)			
All patients	2.7±2.0	1.2±0.4	0.006
Excluding 7 ventilated patients	1.7±0.8	—	0.066
Hospital stay (days)			
All patients	7.9±4.1	8.7±8.3	0.68
Survivors only	8.9±3.6	9.5±8.5	0.79
In-hospital deaths — no. (%)	4 (20)	2 (10)	0.36
Predicted in-hospital mortality (%)‡	29±10	28±11	—

Œdème aigu pulmonaire cardiogénique

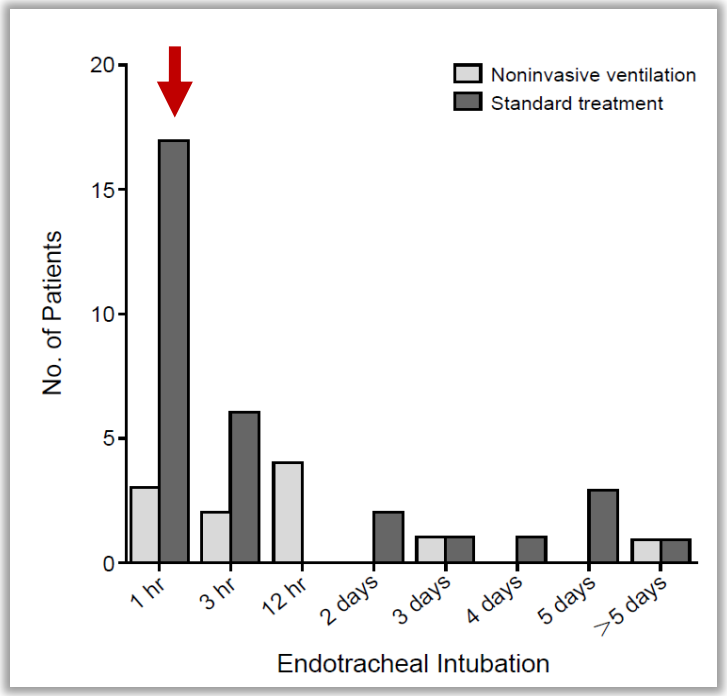
Bersten NEJM 1991; 325:1825-30

The New England
Journal of Medicine

Volume 333 SEPTEMBER 28, 1995 Number 13

NONINVASIVE VENTILATION FOR ACUTE EXACERBATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

LAURENT BROCHARD, M.D., JORDI MANCEBO, M.D., MARC WYSOCKI, M.D., FRÉDÉRIC LOFASO, M.D., GIORGIO CONTI, M.D., ALAIN RAUSS, M.D., GÉRALD SIMONNEAU, M.D., SALVADOR BENITO, M.D., ALESSANDRO GASPARETTO, M.D., FRANÇOIS LEMAIRE, M.D., DANIEL ISABEY, PH.D., AND ALAIN HARF, M.D.



Exacerbation de BPCO

CHARACTERISTIC	STANDARD TREATMENT		NONINVASIVE VENTILATION		P VALUE†
	INTUBATION NOT REQUIRED (N = 11)	INTUBATION REQUIRED (N = 31)	INTUBATION NOT REQUIRED (N = 32)	INTUBATION REQUIRED (N = 11)	
Length of hospital stay — days	20±16	41±36‡	17±9	40±22§	<0.001
Deaths — no. of patients (%)	2 (18)	10 (32)	1 (3)	3 (27)	

VNI dans l'insuffisance respiratoire aiguë *de novo ?*

	Patients	n	Objective	Intubation rate VNI / O_2 (%)	Study interests	Drawbacks
Wysocki Chest 1995 107:761-8	ARF non COPD	41	Intubation rate	**62 / 70**	COPD exclusion	Multiple causes, sub-groups
Confalonieri AJRCCM 1999 160:1585-91	ARF with comunity-acquired pneumonia	56	Intubation rate	**21 / 61**	Pneumonie communautaire sévère	Many COPD
Martin AJRCCM 2000 161:807-13	ARF All causes	61	Hospital stay Intubation rate	**28 / 59**		COPD hypercapnia
Ferrer Chest 2005 128:3916-24	Hypoxemic ARF non COPD non hyperCO_2	105	Intubation rate	**25 / 52**	Exclusion BPCO et hypercapnie	1/3 CPE

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Maria Elena Martinez-Quintana
Antonia Lopez-Martinez
Noemi Llamas
Maravillas Alcazar
Antoni Torres

Non-invasive ventilation in community-acquired pneumonia and severe acute respiratory failure

n=184, VNI première ligne
dont 102 IRA « de novo »

	"De novo" ARF			Previous cardiac or respiratory disease		
	NIV success ($n = 55$)	NIV failure ($n = 47$)	p value	NIV success ($n = 61$)	NIV failure ($n = 21$)	p value
ICU mortality, n (%)	0 (0%)	34 (50%)	<0.001	0 (0%)	12 (57%)	<0.001
Hospital mortality, n (%)	5 (9%)	23 (49%)	<0.001	5 (8%)	14 (67%)	<0.001
Among intubated patients, n (%)[a]	–	16 (40%)	–	–	12 (63%)	–

Mortalité élevée
après échec de VNI

Carillo et al. Intensive Care Med 2012;38:458-66

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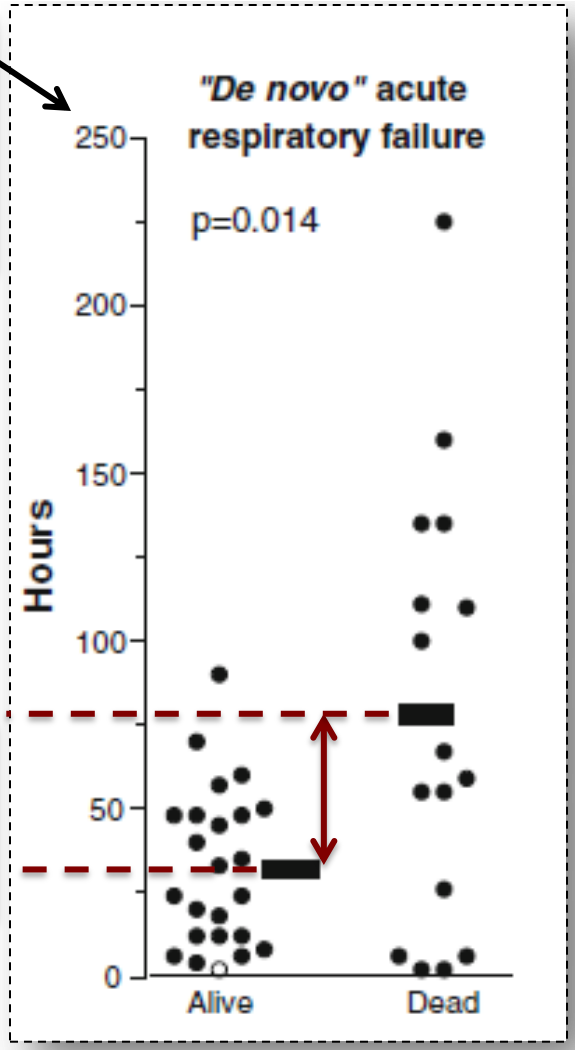
Non-invasive ventilation in community-acquired pneumonia and severe acute respiratory failure

durée moyenne de VNI avant intubation



32 ± 24 vs 78 ± 65 h, *p = 0,014*

n=184, VNI première ligne dont 102 IRA « de novo »

Mortalité associée au retard d'intubation

Carillo et al. Intensive Care Med 2012;38:458-66

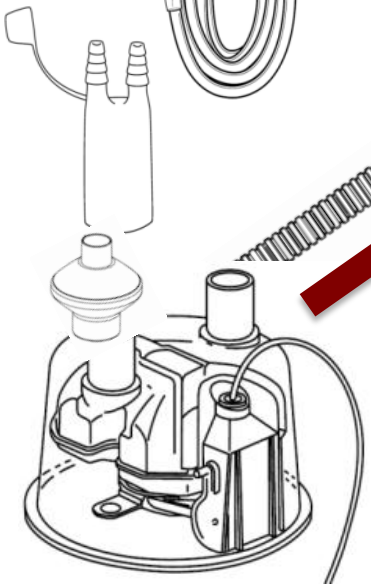
Mélangeur air-oxygène

Canule patient

Circuit vers le patient

Humidificateur-réchauffeur

- 37° C
- H_2O 44 mg/l



L'oxygénothérapie nasale humidifiée et réchauffée à haut débit (OHD)

- Technique récente : 2006…
- Effets physiologiques :
  - FiO_2 élevée, jusqu'à 100%
  - Pression positive dans les voies aériennes
  - Lavage espace mort
- Impact clinique :
  - Bonne tolérance
  - Amélioration de l'oxygénation et des signes de détresse respiratoire aiguë
- Mais aucun essai clinique

Parke. BJA 2009; 103: 886-90
Roca. Resp Care 2010; 55: 408-13
Sztrimf. Int Care Med 2011; 37:1780-86
Frat et al. Resp Care 2014; oct 7

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic Respiratory Failure

Jean-Pierre Frat, M.D., Arnaud W. Thille, M.D., Ph.D., Alain Mercat, M.D., Ph.D., Christophe Girault, M.D., Ph.D., Stéphanie Ragot, Pharm.D., Ph.D., Sébastien Perbet, M.D., Gwénael Prat, M.D., Thierry Boulain, M.D., Elise Morawiec, M.D., Alice Cottereau, M.D., Jérôme Devaquet, M.D., Saad Nseir, M.D., Ph.D., Keyvan Razazi, M.D., Jean-Paul Mira, M.D., Ph.D., Laurent Argaud, M.D., Ph.D., Jean-Charles Chakarian, M.D., Jean-Damien Ricard, M.D., Ph.D., Xavier Wittebole, M.D., Stéphanie Chevalier, M.D., Alexandre Herbland, M.D., Muriel Fartoukh, M.D., Ph.D., Jean-Michel Constantin, M.D., Ph.D., Jean-Marie Tonnelier, M.D., Marc Pierrot, M.D., Armelle Mathonnet, M.D., Gaëtan Béduneau, M.D., Céline Delétage-Métreau, Ph.D., Jean-Christophe M. Richard, M.D., Ph.D., Laurent Brochard, M.D., and René Robert, M.D., Ph.D., for the FLORALI Study Group and the REVA Network*

N Engl J Med. 2015 Jun 4;372(23):2185-9

Insuffisance respiratoire aiguë hypoxémique
FR >25 c/min ; PaO_2/FiO_2 ≤300,
$PaCO_2$ ≤45 mmHg

Information et recueil consentement
Randomisation et Stratification
antécédent Insuffisance cardiaque

Oxygène Standard

Oxygène Haut-Débit

VNI/ Oxygène Haut-Débit

Standard oxygen
SpO_2 ≥92%

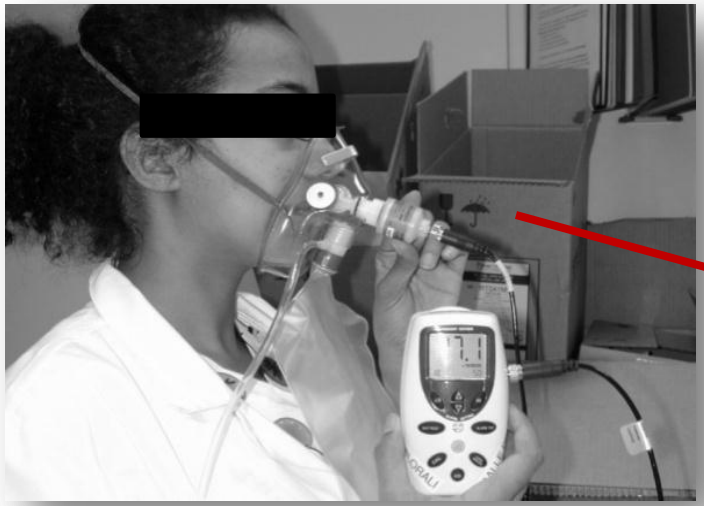
High-Flow oxygen
SpO_2 ≥92%

NIV
SpO_2 ≥92%
avec VNI ≥8 h/j

FLORALI

Insuffisance respiratoire aiguë hypoxémique

FR >25 c/min ; PaO_2/FiO_2 ≤300, $PaCO_2$ ≤45 mm Hg



FiO_2 déterminée par un analyseur d'oxygène portable

FLORALI

Critères d'**Exclusion** :

- Contre-indications à la VNI
- BPCO, Ins. Resp. chronique
- OAP
- choc
- Score de Glasgow <12 pts
- Indication à intubation urgente
- Neutropénie profonde (<500/mm^3)

Critères prédéterminés d'intubation

défaillance **respiratoire***

- ✓ *signes de détresse respiratoire persistant ou se majorant après*
- ✓ *encombrement bronchique,*
- ✓ *pH <7,35,*
- ✓ *SpO2 <90% non expliquée par des problèmes techniques,*
- ✓ *intolérance VNI, dépendance de la VNI > 12h*

défaillance **neurologique**

- ✓ *trouble de la conscience*
- ✓ *agitation*

défaillance **hémodynamique**

- ✓ *PAS <90 mmHg, PAM <65 mmHg*
- ✓ *amines vasopressives,*

FLORALI

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Objectif primaire :

Taux d'intubation

Calcul effectif

N= 300 (100 patients/groupe)

α=0.05, 1-β=0.8

Hypothèse: taux d'intubation

- dans groupe O_2 standard : 60%
- dans groupe OHD ou VNI/OHD : 40%

Essai FLORALI

Objectif primaire :

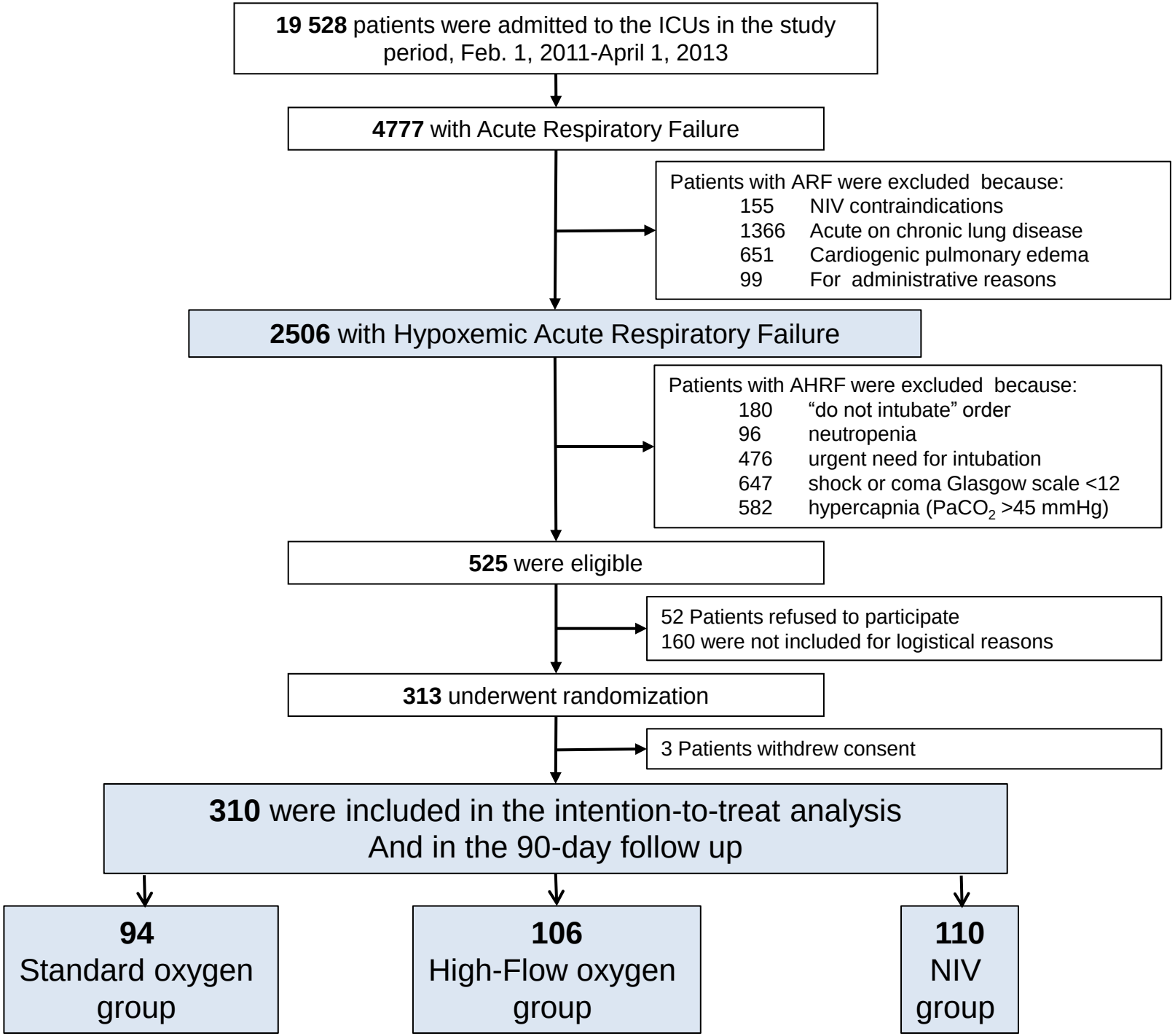
Taux d'intubation

Objectifs secondaires principaux:

- **mortalité en réanimation et à J90**
- nombre de jours sans ventilation à J28
- Durée de séjour
- Complications

Analyse post-hoc de sous-groupe :

Taux d'intubation des patients avec PaO_2:FiO_2 ≤200


19 528 patients were admitted to the ICUs in the study period, Feb. 1, 2011-April 1, 2013
4777 with Acute Respiratory Failure
Patients with ARF were excluded because:
155 NIV contraindications
1366 Acute on chronic lung disease
651 Cardiogenic pulmonary edema
99 For administrative reasons
2506 with Hypoxemic Acute Respiratory Failure
Patients with AHRF were excluded because:
180 "do not intubate" order
96 neutropenia
476 urgent need for intubation
647 shock or coma Glasgow scale <12
582 hypercapnia ($PaCO_2$ >45 mmHg)
525 were eligible
52 Patients refused to participate
160 were not included for logistical reasons
313 underwent randomization
3 Patients withdrew consent
310 were included in the intention-to-treat analysis
And in the 90-day follow up
94
Standard oxygen group
106
High-Flow oxygen group
110
NIV group

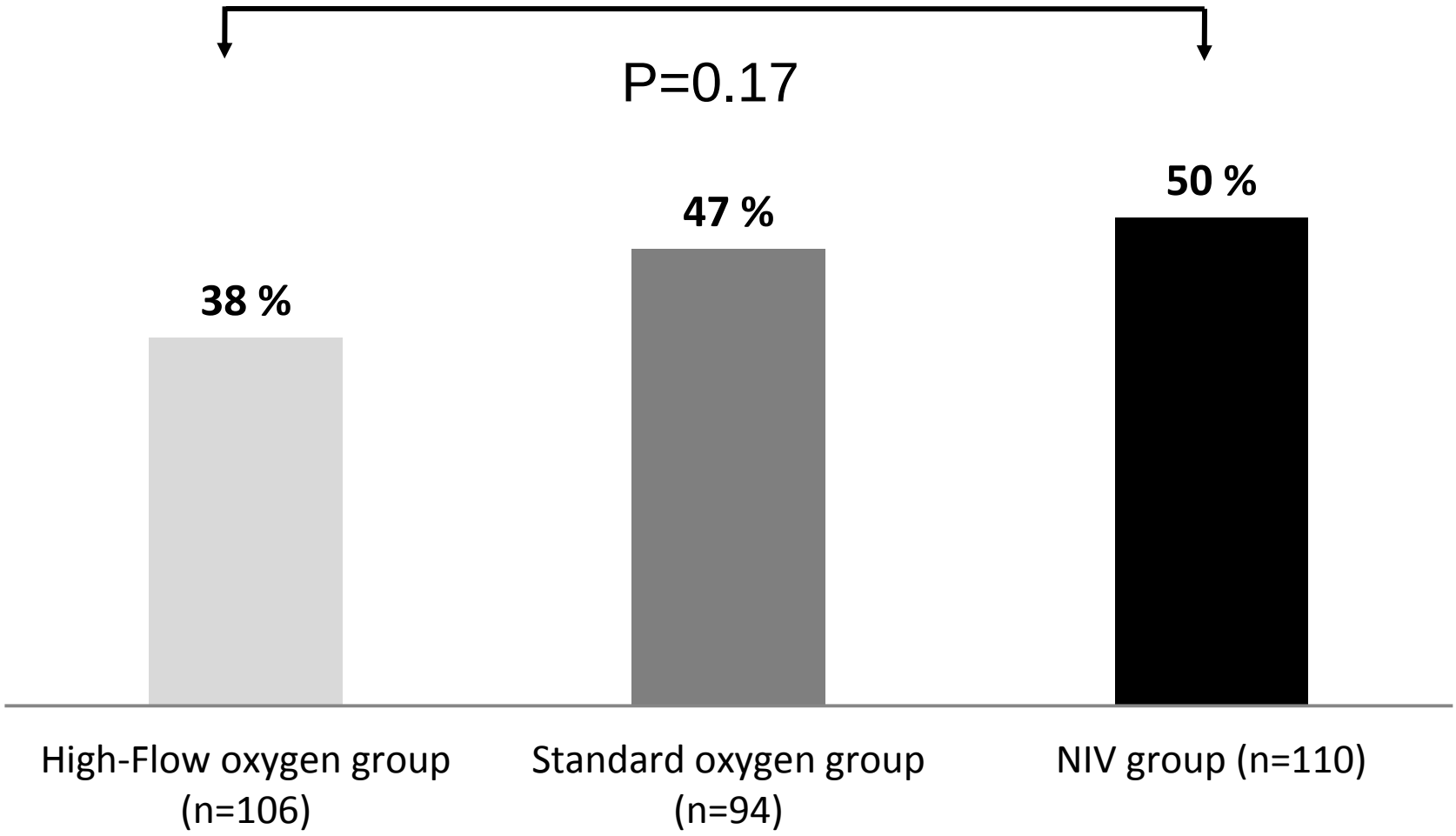
Caractéristiques des patients

Characteristics at inclusion	Standard oxygen Group (n=94)	High-Flow oxygen Group (n=106)	NIV Group (n=110)
Age – yr	59±17	61±16	61±17
Male sex – no. (%)	63 (67.0)	75 (70.7)	74 (67.3)
Body-mass index	26±5	25±5	26±6
SAPS II at inclusion	24±9	25±9	27±9
SOFA at inclusion	3.6±1.8	3.7±2.0	4.2±2.1
Preexisting cardiac failure - no. (%)	4 (4.3)	8 (7.5)	8 (7.3)
Immunodeficiency – no. (%):	30 (31.9)	26 (24.5)	26 (23.6)
Liver cirrhosis – no. (%)	5 (5.3)	6 (5.7)	5 (4.5)
Smoker – no. (%)	36 (38.3)	34 (32.1)	40 (36.4)
Reason for acute respiratory failure, no. (%)			
Community-acquired pneumonia	57 (60.6)	71 (67.0)	69 (62.7)
Hospital acquired pneumonia	13 (13.8)	12 (11.3)	12 (10.9)
other	24 (25.5)	23 (21.7)	29 (26.4)
Bilateral pulmonary infiltrates – no. (%)	80 (85.1)	79 (74.5)	85 (77.3)

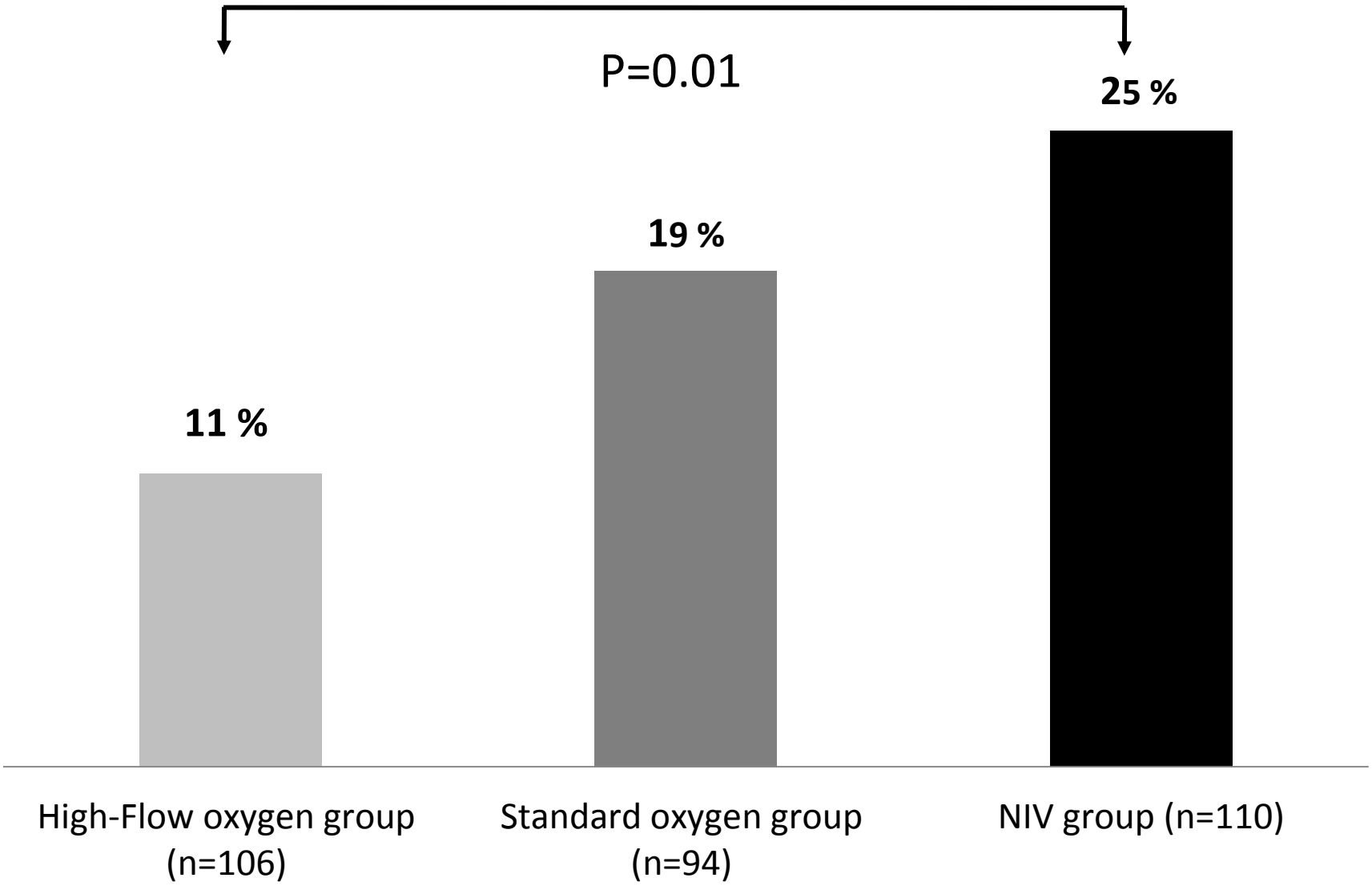
Caractéristiques des patients (2)

Characteristics at inclusion	Standard oxygen Group (n=94)	High-Flow oxygen Group (n=106)	NIV group (n=110)
Clinical parameters			
Respiratory rate - breath/min	32±6	33±6	33±7
Heart rate - beats/min	104±16	106±21	106±21
Systolic arterial pressure – mmHg	130±22	127±24	128±21
Mean arterial pressure – mmHg	89±15	87±17	86±16
Arterial blood gas			
pH	7.44±0.06	7.43±0.06	7.43±0.06
PaO_2 – mmHg	91±33	85±31	90±35
FiO_2	0.66±0.12	0.66±0.13	0.64±0.14
PaO_2:FiO_2 ratio– mmHg	146±53	137±56	150±62
$PaCO_2$ – mmHg	35±5	36±6	34±6

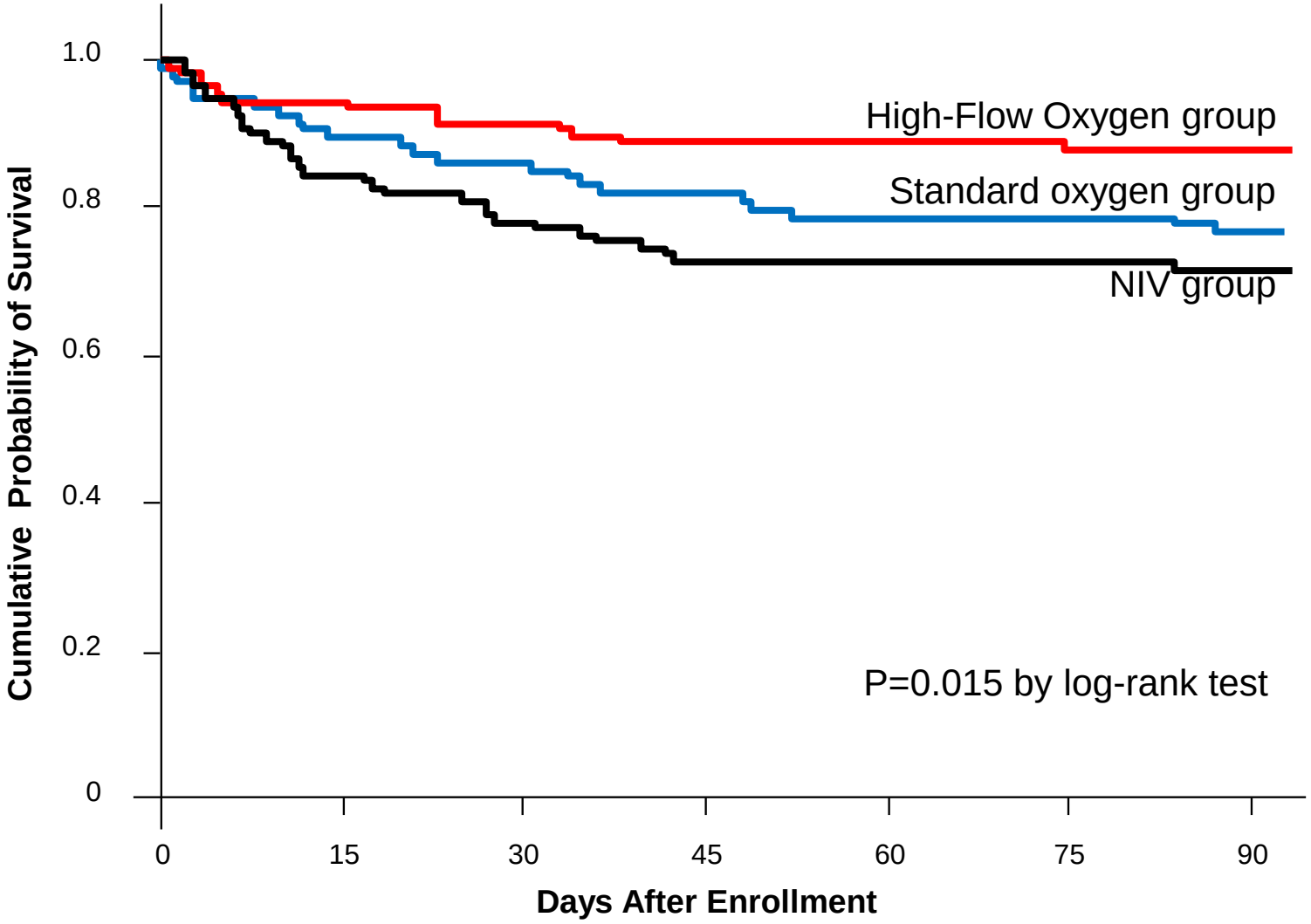
Taux d'intubation



Mortalité en réanimation



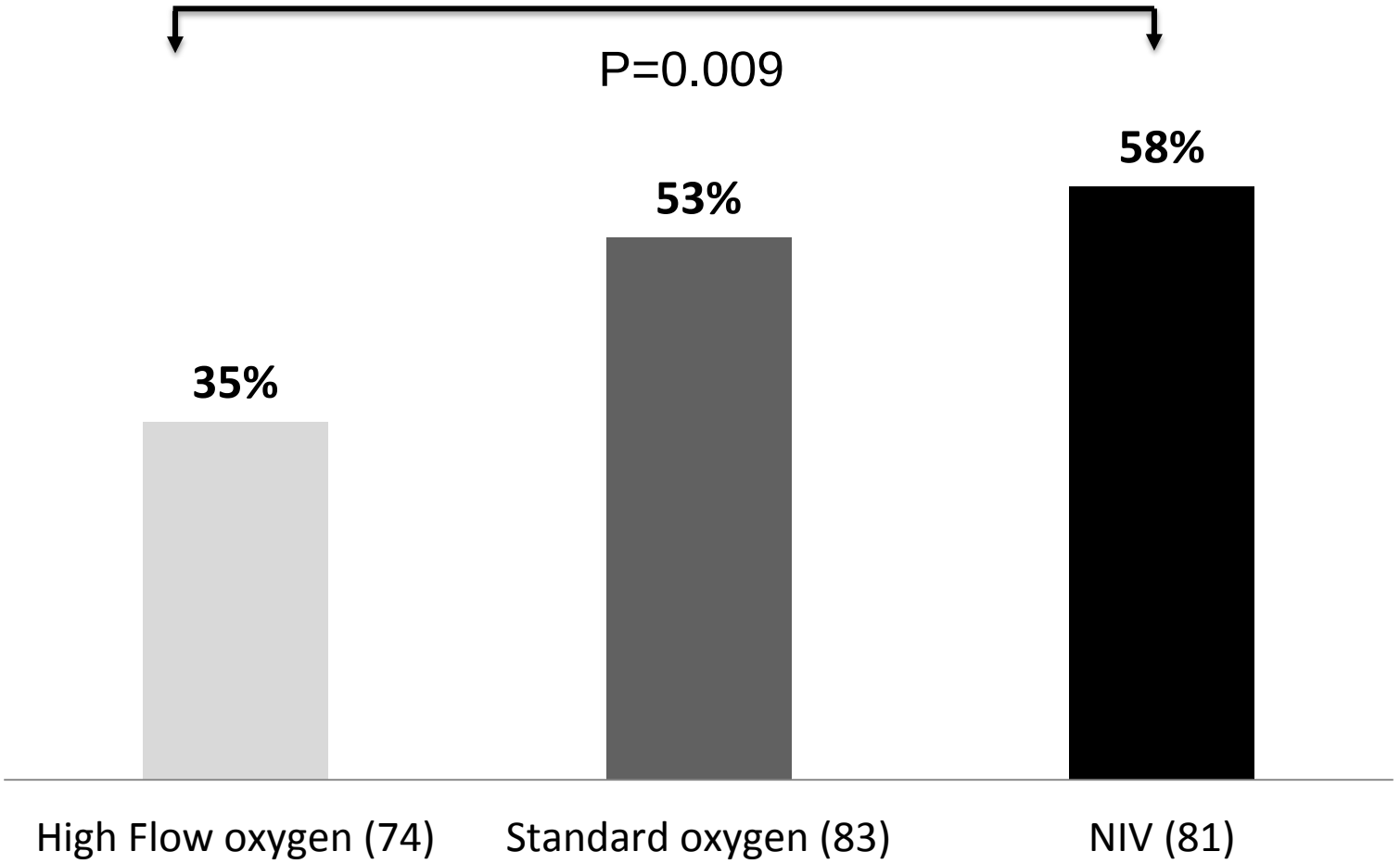
Survie à J90


1.0
0.8
0.6
0.4
0.2
0
Cumulative Probability of Survival
High-Flow Oxygen group
Standard oxygen group
NIV group
P=0.015 by log-rank test
0
15
30
45
60
75
90
Days After Enrollment

	Odds Ratio or Hazard Ratio (95% CI)	
	Standard Oxygen vs. High-Flow Oxygen	NIV vs. High-Flow Oxygen
Mortalité en réanimation – no. (%)		
Non ajustée	1.85 (0.84–4.09)	2.55 (1.21–5.35)
Ajustée (pour PaO_2, SAPS2 et insuffisance cardiaque)	**2.55** (1.07–6.08)	**2.60** (1.20–5.63)
Mortalité à J90 – no. (%)		
Non ajustée	**2.01** (1.01–3.99)	**2.50** (1.31–4.78)
Ajustée (pour SAPS2 et insuffisance cardiaque)	**2.36** (1.18–4.70)	**2.33** (1.22–4.47)

Effet délétère de la VNI vs OHD ?

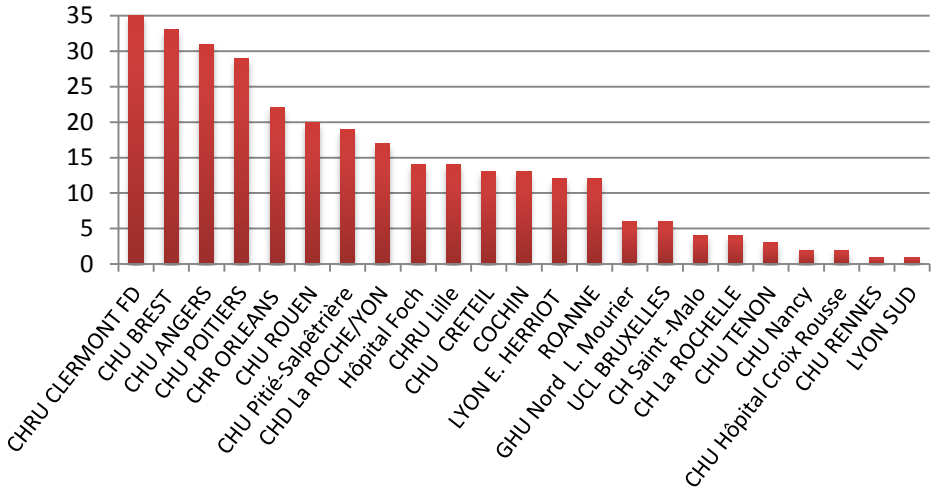
Taux d'intubation chez les patients avec PaO_2/FiO_2 ≤200 (n=238)



Conclusion

- Malgré l'absence de différence sur le taux d'intubation entre les groupes,
- La mortalité des patients en IRA hypoxémique traités par OHD est significativement plus basse comparativement aux deux autres groupes de patients
- Le taux d'intubation est significativement plus bas chez les patients avec une hypoxémie sévère traités par OHD.

- L'utilisation de la VNI doit être prudente dans la prise en charge de l'insuffisance respiratoire aiguë hypoxémique.
- Cependant il faut rester vigilant sur l'indication de l'OHD qui concerne les patients mono-défaillants respiratoires.



Alain Mercat, Angers;
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Saad Nseir, Lille;
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Louis Argaud, Lyon;
Jean-Damien Ricard, Colombes;
Jean Roeseler, Bruxelles;
Pascal Beuret, Roanne;
François Collet, Saint Malo;
Olivier Lesieur, La Rochelle;
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Eric Danin, Lyon;
Keyvan Razazi, Créteil;
Laurent Brochard, Toronto;

Stéphanie Ragot, CIC-1402;
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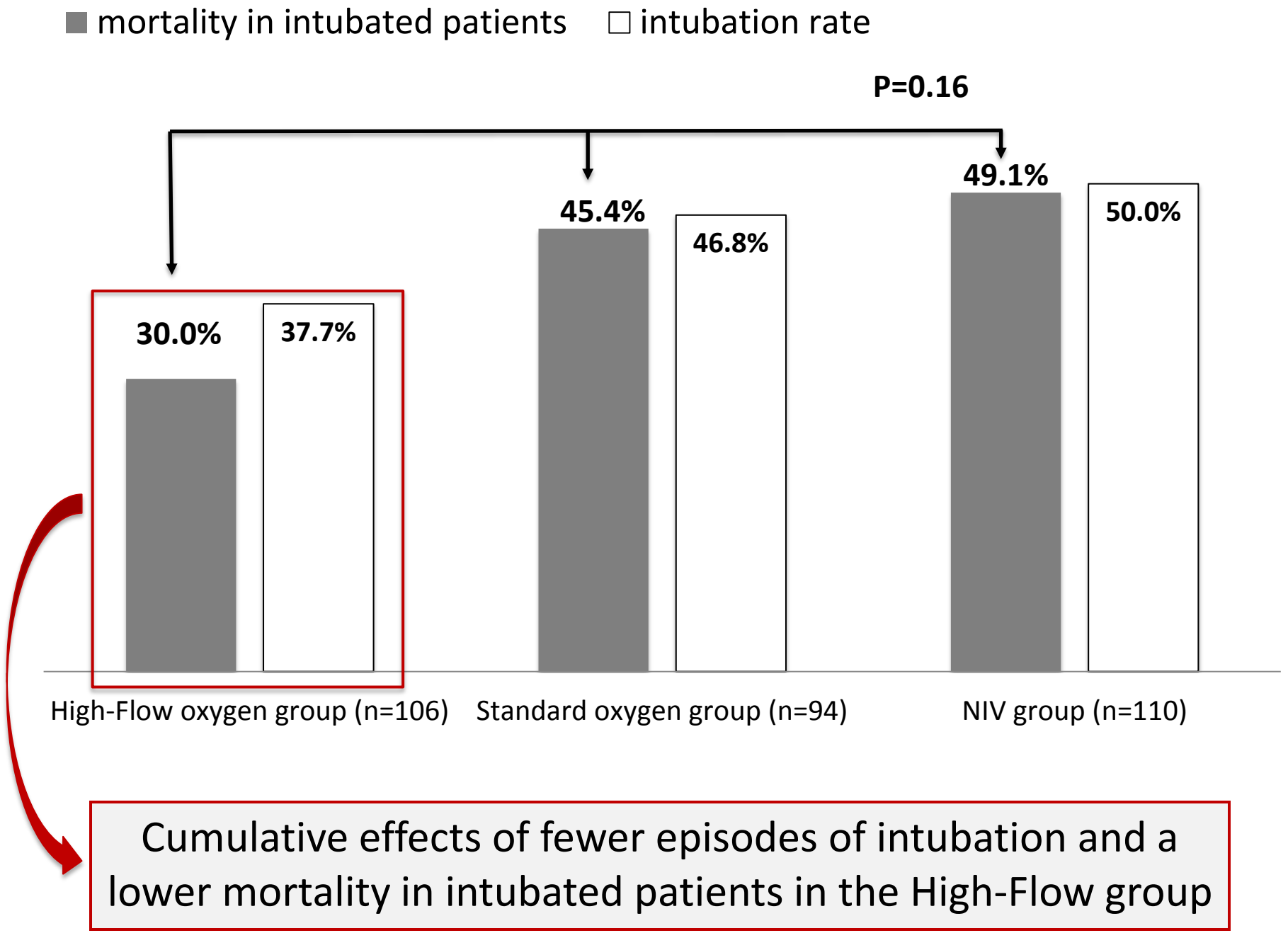

mortality in intubated patients
intubation rate
P=0.16
30.0%
37.7%
45.4%
46.8%
49.1%
50.0%
High-Flow oxygen group (n=106)
Standard oxygen group (n=94)
NIV group (n=110)
Cumulative effects of fewer episodes of intubation and a lower mortality in intubated patients in the High-Flow group

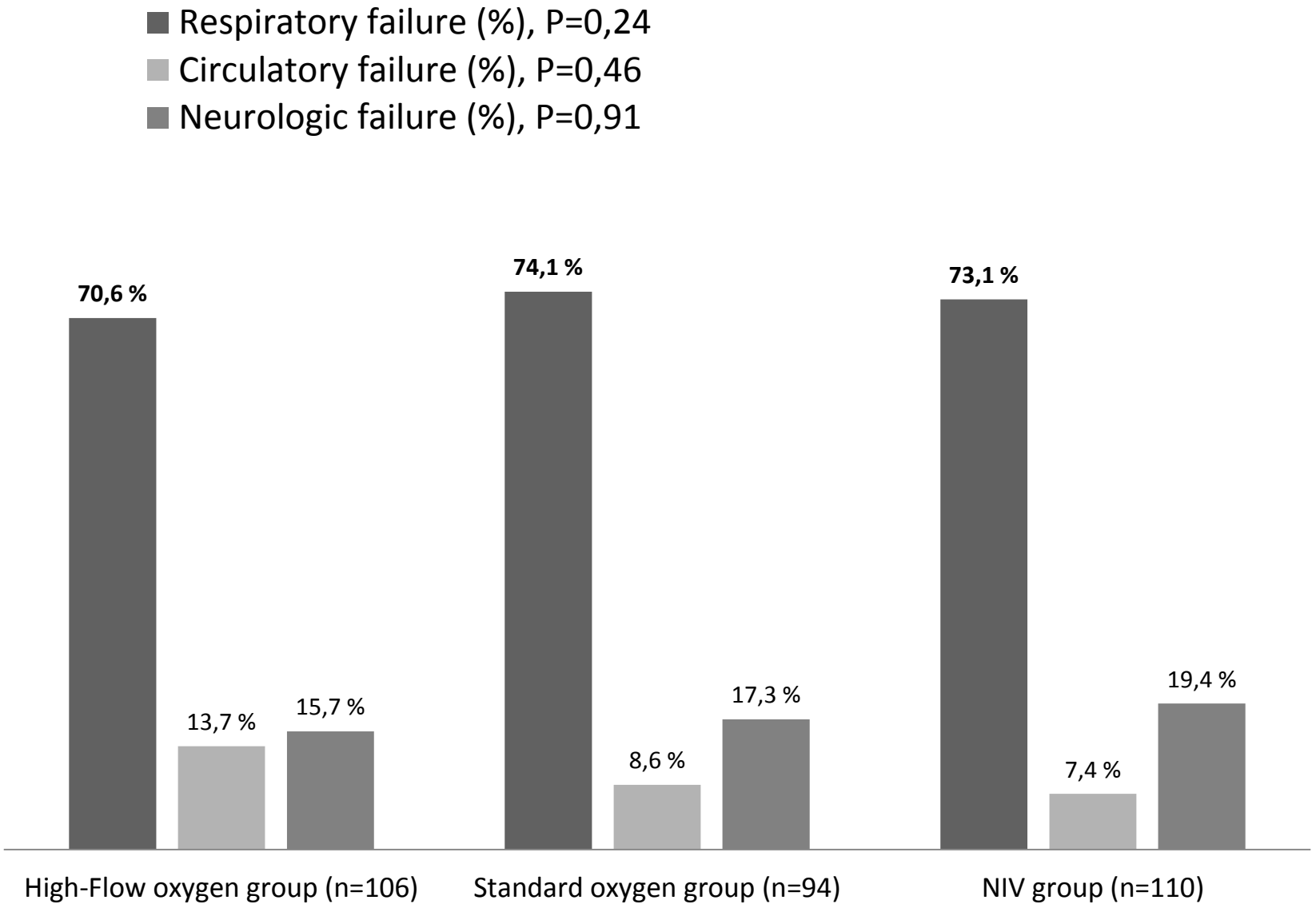
Benefits of High-Flow oxygen

Secondary outcomes	High-Flow group (n=86)	Standard oxygen group (n=74)	NIV group (n=91)	P Value
Respiratory patient-discomfort at H1– mm	29±26	40±29	43±29	<0.01
Grade of dyspnea at H1				<0.001
Marked improvement – no. (%)	19 (22.1)	5 (6.8)	13 (14.3)	
Slight improvement– no. (%)	46 (53.5)	26 (35.1)	40 (44.0)	
No change– no. (%)	18 (20.9)	33 (44.6)	23 (25.3)	
Slight deterioration – no. (%)	3 (3.5)	9 (12.2)	8 (8.8)	
Marked deterioration – no. (%)	0 (0.0)	1 (1.3))	7 (7.7)	
Respiratory rate at H1 – cycles/min	28±7	31±7	31±8	<0.01

Potential deleterious effect of NIV ?

High Tidal volume : 9.3 ±3 ml/kg of predicted body weight

Reason for intubation (%)



Outcomes	Study Group				Odds Ratio or Hazard Ratio (95% CI)	
	High-Flow Oxygen Group (N =106)	Standard Oxygen Group (N = 94)	NIV Group (N = 110)	P Value †	Standard Oxygen vs. High-Flow Oxygen	NIV vs. High-Flow Oxygen
ICU Stay						
Length of ICU stay, assessed at day 90 – days				0.57		
Survivors	10.7±15.8	9.1±11.7	11.0±11.6			
Non-survivors	14.9±13.6	21.6±19.9	15.7±13.7			
Complications during ICU-stay						
Cardiac dysrythmia – no. (%)	11 (10.4)	16 (17.0)	17 (15.4)	0.35		
Septic shock – no. (%)	19 (17.9)	26 (27.7)	34 (30.9)	0.08		
Cardio-respiratory arrest – no. (%)	5 (4.7)	7 (7.4)	6 (5.4)	0.70		
Nosocomial pneumonia – no. (%)	4 (3.8)	8 (8.5)	9 (8.2)	0.32		