Supplementary Appendix

EXCLUSION CRITERIA

1- patients requiring ≥ 15 L/min additional oxygen to maintain SpO_2 ≥ 92% for hypoxemic and ≥ 92% for hypercapnic patients ($PaCO_2$ on inclusion > 45 mmHg);
2- patients presenting any clinical signs of ventilatory assistance requirement, previously defined as respiratory rate > 30 b/min or < 10 b/min, loss of consciousness (Glasgow coma scale ≤ 12), ventricular cardiac arrhythmia, hemodynamic instability (systolic blood pressure <80 mm Hg and/or the use of vasopressor), cardiac or respiratory arrest, severe respiratory acidosis with pH < 7.30 and $PaCO_2$ > 55 mm Hg;
3- Patients requiring emergent surgery or coronarography;
4- Pregnant or breastfeeding women;
5- Patients under administrative protective measures.

CRITERIA FOR ENDOTRACHEAL INTUBATION

The pre-determined criteria for endotracheal intubation and mechanical ventilation (MV) were established as follows to avoid delayed intubation: (1) signs of persisting or worsening respiratory failure, defined by at least two of the following criteria: a respiratory rate above 40 cycles/min, lack of improvement of signs of respiratory-muscle fatigue, development of copious tracheal secretions, acidosis with a pH below 7.35, SpO_2 below 90% for more than 5 min without technical dysfunction, or intolerance to NIV; or one of the following (2) hemodynamic instability defined by a SBP below 90 mmHg, MBP below 65 mmHg or requirement for vasopressor, (3) deterioration of neurologic status with a Glasgow coma scale below 12 points.

Table S1: Adverse events rate, according to the study group *

		FreeO$_2$ *(N=93)*	*Manual* *(N=94)*	*Total* *(N=187)*
Adverse events		43(23.0)	32 (17.1)	75 (40.1)
Serious adverse events		18 (9.6)	15 (8.0)	28 (17.6)
Premature interruption of treatment		6 (3.2)	1 (0.5)	7 (3.7)
Ventilatory assistance		17 (9.1)	18 (9.6)	35 (18.7)
	Invasive	3	5	8
	Noninvasive	14	13	27
Transfer to the ICU		19 (10.2)	18 (9.6)	37 (19.8)
	Hypoxemic	14	11	25
	Hypercapnic	5	7 #	12
Death at day 28		10 (5.3)	4 (2.4)	14 (7.5)

* Results are presented as number of patients (percentage). No adverse event and/or death were considered as related to the study device or the protocol, but always to the underlying pathological process. Premature arrest of treatment in the FreeO2 group was mainly related to weaning. There were no significant differences among the study groups in any of the

events listed, except for transfer to the ICU for the hypercapnic subgroup, that was significantly higher in the Manual group (Risk difference -7.0 percentage points; 95% confidence interval, -14 to -1; # p=0.033).

Table S2: Characteristics of the deceased patients at baseline, according to the study group and stratification *

	Total **(N=14)**		**Hypoxemic** **(N=12)**		**Hypercapnic** **(N=2)**	
Characteristics	***FreeO$_2$*** (N=10)	***Manual*** (N=4)	***FreeO$_2$*** (N=9)	***Manual*** (N=3)	***FreeO$_2$*** (N=1)	***Manual*** (N=1)
Age – yr.	74.6 ± 9.5	79.5 ± 9.02	75.2 ± 9.8	80.3 ± 10.8	69	77
Male sex – no. (%)	8 (80.0)	3 (75.0)	7 (77.8)	2 (66.7)	1 (100)	1 (100)
COPD – no. (%)	2 (20.0)	2 (50.0)	2 (22.2)	1 (33.3)	0 (0.0)	1 (100)
Immunodeficiency – no. (%)	9 (90.0)	1 (25.0) **#**	8 (88.9)	0 (0.0) **#**	1 (100)	1 (100)
Do-not-intubate order – no. (%)	3 (30.0)	0 (0.0)	3 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)
LTOT – no. (%)	0 (0.0)	1 (25.0)	0 (0.0)	1 (33.3)	0 (0.0)	0 (0.0)
HMV – no. (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (00)	0 (0)
O_2 flow – L/min.	7.8 ± 3.2	7.0 ± 3.4	8.0 ± 3.4	7.7 ± 3.8	6.0	5.0
Respiratory Rate – breaths/min	29 ± 7	24 ± 4	30 ± 7	24 ± 5	23	24

SpO_2 - %	94.2 ± 5.2	93.8 ± 5.5	93.8 ± 5.3	95.3 ± 5.5	98	89
Heart Rate – beats/min	92 ± 18	81 ± 32	94 ± 18	82 ± 40	74	78
Systolic arterial pressure - mmHg	120 ± 24	120 ± 11	119 ± 26	119 ± 16	123	121
Mean arterial pressure - mmHg	87 ± 19	84 ± 10	85 ± 20	85 ± 14	101	82
pH §	7.40 ± 0.04	7.38 ± 0.03	7.40 ± 0.04	7.39 ± 0.04	7.40	7.36
PCO_2 – mmHg **§**	34.3 ± 10.0	43.3 ± 4.3	32.4 ± 8.6	41.7 ± 3.5	51	48

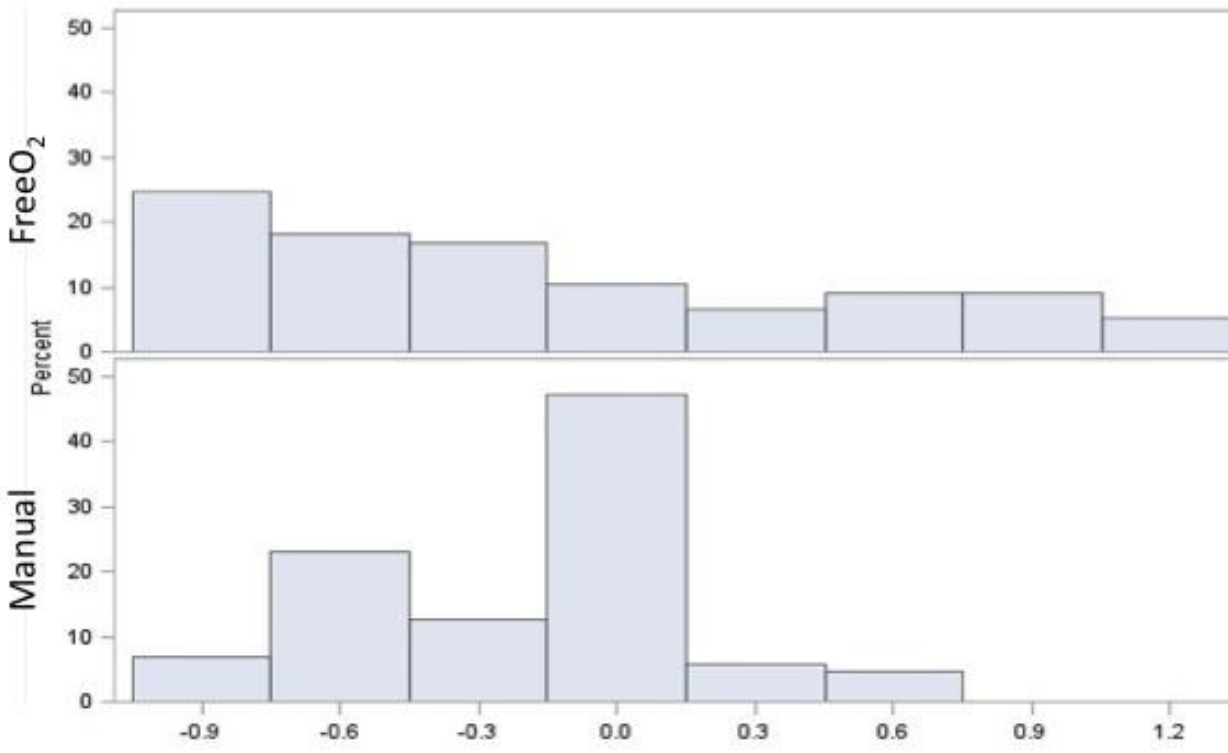
*Plus-minus values are means ± SD, unless specified otherwise. There were no significant differences among the study groups in any of the characteristics listed, except for immunodeficiency. $FreeO_2$ indicates patients assigned to the automated oxygen administration group, and Manual patients assigned to the standard oxygen administration control group. Hypoxemic indicates the stratification group of patients with $PCO_2 \leq 45$ mmHg that were assigned to a SpO_2 range of 92-96%. Hypercapnic indicates the stratification group of patients with $PCO_2 > 45$ mmHg that were assigned to a SpO_2 range of 90-94%. Patients who were assigned to receive automated oxygen were connected to the $FreeO_2$ system set on the automated mode. Patients assigned to Manual were also connected to the $FreeO_2$ system for monitoring purposes, but the system was set to the recording mode solely.

COPD: chronic obstructive pulmonary disease; Immunodeficiency: active cancer or hemopathy, chemotherapy, severe neutropenia, long-term steroid therapy; Treatment limitation and do-not-intubate order: it was systematically assessed on admission by either the emergency physician or the intensivist, according to patient's health status; LTOT: long-term oxygen therapy; HMV: home mechanical ventilation (noninvasive ventilation); SpO_2: pulse oximetry value.

O_2 flow was the value measured immediately after enrollment and before randomization.

§: Blood gas results were obtained from either capillary or arterial blood sample.

Figure S1



Supplementary Figure legend

Figure S1 : Oxygen flow variations within groups

Diagram represents the percentage of oxygen flow variations among groups. While flow variations mainly involved a decrease in the Manual group, flow variations , either decrease or increase, were more homogeneously distributed within the FreeO2 group depending on the patient's status.