

Dyspnea is severe and associated with a higher intubation rate in *de novo* acute hypoxemic respiratory failure

Online Supplement

Figure E1. Study flow chart

Table E1. Factors associated with a decrease of dyspnea visual analog scale (Dyspnea-VAS) between baseline (patient randomization) and 1 hour after treatment initiation

Table E2. Factors associated with a decrease of dyspnea visual analog scale (dyspnea-VAS) between baseline (patient randomization) and 1 hour after treatment initiation (n=253)

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Figure E2. Cumulative incidence of survival up to 90 days in patients with moderate-to-severe dyspnea at baseline (dashed red line) and no or mild dyspnea (solid blue line)

Figure E1. Study flow chart

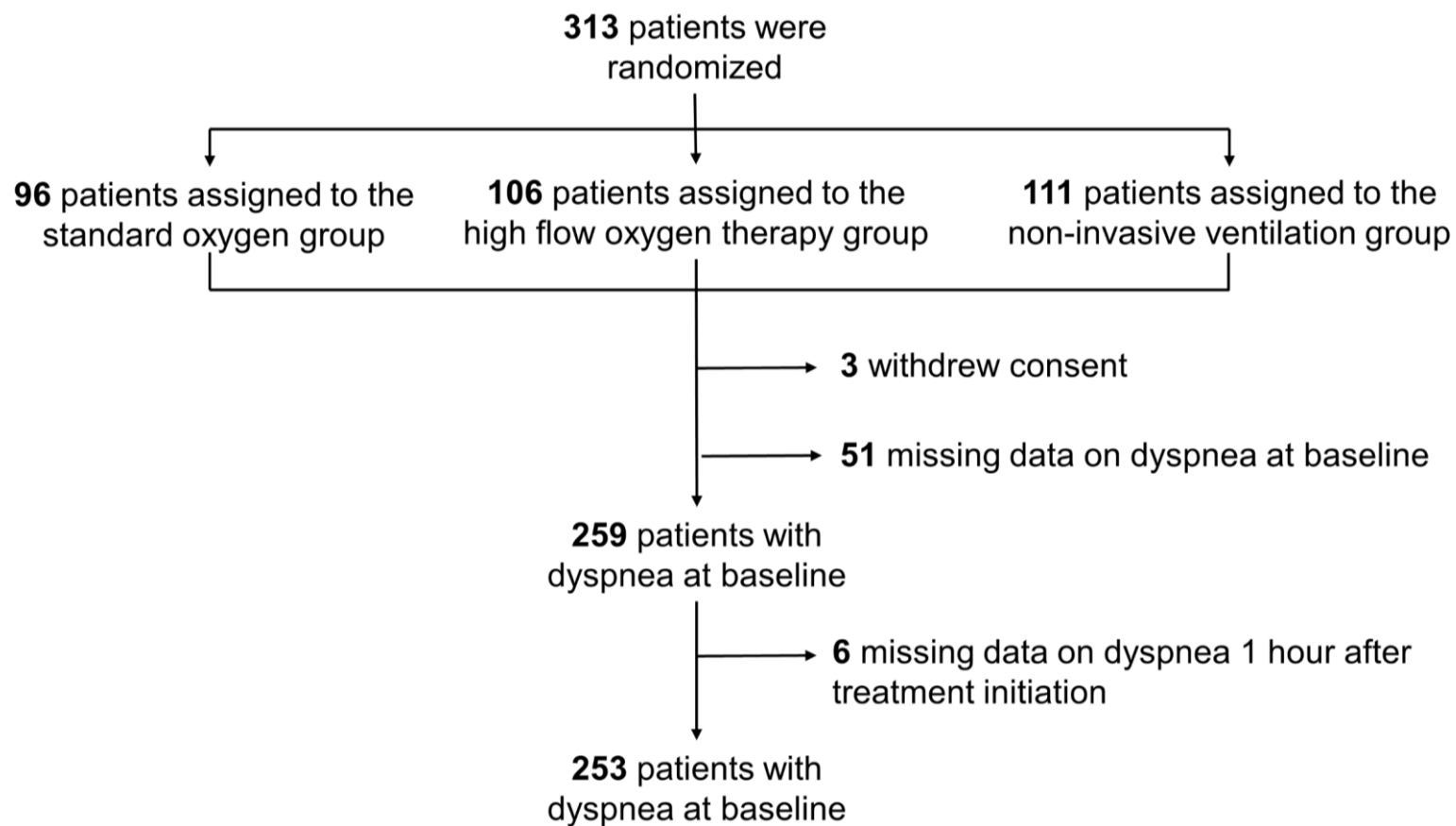


Table E1. Factors associated with a decrease of dyspnea visual analog scale (Dyspnea-VAS) between baseline (patient randomization) and 1 hour after treatment initiation

	Univariate analysis		Multivariate analysis	
	Linear regression coefficient $\pm$ SE	P value	Estimate $\pm$ SE	P value
Patient characteristics				
Age > 60 years	5.40 $\pm$ 3.00	0.073		
Gender <i>male</i>	3.52 $\pm$ 3.31	0.288		
BMI		0.343		
25-30 <i>kg.m⁻²</i>	2.41 $\pm$ 3.51			
>30 <i>kg.m⁻²</i>	5.88 $\pm$ 4.03			
Current or past smoking	3.76 $\pm$ 3.10	0.227		
Pre-existing cardiac failure	3.79 $\pm$ 6.25	0.544		
Immunosuppression	4.33 $\pm$ 3.41	0.205		
McCabe 2 or 3	5.80 $\pm$ 3.71	0.119		
SAPS II, <i>per 10 points</i>	0.27 $\pm$ 0.16	0.097		
SOFA at inclusion, <i>per points</i>	1.05 $\pm$ 0.81	0.194		
Bilateral pulmonary infiltrates	3.13 $\pm$ 3.72	0.402		
Cause of ARF				
Community-acquired pneumonia	-1.26 $\pm$ 3.19	0.692		
Hospital-acquired pneumonia	3.66 $\pm$ 4.45	0.412		
Other	-1.99 $\pm$ 3.51	0.571		
At baseline, at randomization				
Dyspnea-VAS	-0.36 $\pm$ 0.04	<0.001	-0.38 $\pm$ 0.05	<0.001
Respiratory rate, <i>per cycles min⁻¹</i>	-0.09 $\pm$ 0.24	0.711		
Heart rate, <i>per 10 beat min⁻¹</i>	-0.01 $\pm$ 0.08	0.940		
Systolic arterial pressure, <i>per 10 mmHg</i>	0.09 $\pm$ 0.07	0.187		
Blood gases				
PaCO ₂ , <i>per 10 mmHg</i>	0.16 $\pm$ 0.27	0.559		
pH, <i>per 0.1 point</i>	7.22 $\pm$ 27.07	0.790		
Non-invasive respiratory support (randomization arm)		0.117		0.011
Standard oxygen therapy	1		1	
High flow oxygen therapy	-6.00 $\pm$ 3.71		-7.09 $\pm$ 3.35	
Noninvasive ventilation	0.97 $\pm$ 3.70		2.56 $\pm$ 3.36	

BMI, body mass index; SAPS 2, Simplified Acute Physiology Score; SOFA, Sequential Organ Failure Assessment score; VAS, visual analog scale.

Table E2. Dyspnea-VAS at baseline, one hour after treatment initiation and the change in dyspnea-VAS between baseline and the first hour after initiation of respiratory support in the three treatment groups

Variable	Standard O2	High flow oxygen therapy	Non-invasive ventilation	All patients	P value
Dyspnea-VAS at baseline, mm	45 (18 – 634)	40 (8 – 63)	50 (20 – 70)	47 (12 – 65)	0.210
Dyspnea-VAS one hour after treatment initiation, mm	37 (15 – 58)	25 (5 – 50)	45 (22 – 61)	35 (11 – 56)	0.002
Change in dyspnea-VAS between baseline and the first hour after treatment initiation	0 (-10 – 0.5)	-6 (-22 – 0)	0 (-18 – 10)	-2 (-19 – 2)	NA
P value, Student paired test	0.105	<0.001	0.360	<0.001	

Table E3. Univariate analysis: factors associated with intubation 1 hour after treatment initiation (n=253)

	Univariate analysis		Multivariate analysis	
	Subdistribution hazard ratio (95 % confidence interval)	P value	Subdistribution hazard ratio (95 % confidence interval)	P value
Patient characteristics				
Age > 60 years	1.47 (1.02–2.11)	0.037		
Gender <i>male</i>	1.20 (0.80–1.81)	0.374		
BMI				
25-30 <i>kg.m⁻²</i>	1.02 (0.67–1.54)	0.561		
>30 <i>kg.m⁻²</i>	0.78 (0.48–1.27)			
Current or past smoking	1.12 (0.82–1.69)	0.428		
Pre-existing cardiac failure	1.03 (0.52–2.04)	0.938		
Immunosuppression	0.93 (0.64–1.36)	0.721		
McCabe 2 or 3	0.80 (0.52–1.23)	0.305		
SAPS II > 25	1.44 [1.01,2.07]	0.047		
SOFA at inclusion	1.03 (0.93–1.13)	0.562		
Bilateral pulmonary infiltrates	1.71 (1.04–2.83)	0.035		
Cause of ARF				
Community-acquired pneumonia	0.81 (0.56–1.15)	0.238		
Hospital-acquired pneumonia	1.28 (0.76–2.16)	0.346		
Other	1.19 (0.81–1.73)	0.370		
1 hour after treatment initiation				
Respiratory rate > 30 <i>min⁻¹</i>	2.02 (1.40–2.91)	<0.001	1.93 (1.21–3.09)	0.006
Dyspnea-VAS		<0.001		<0.001
16–39 <i>mm</i>	0.77 (0.42–1.40)		0.94 (0.52–1.70)	
40–64 <i>mm</i>	1.29 (0.80–2.07)		1.37 (0.80–2.36)	
≥65 <i>mm</i>	2.54 (1.49–4.34)		4.14 (2.04–8.41)	
Change in dyspnea intensity between baseline and 1 hour, <i>per 10 mm</i>	0.97 (0.89–1.07)	0.597	0.91 (0.83–1.01)	0.077
Heart rate > 100 <i>beat min⁻¹</i>	2.25 (1.53–3.31)	<0.001	2.43 (1.48–3.97)	<0.001
Systolic arterial pressure		0.019		0.003
120-140 <i>mmHg</i>	1.78 (1.13–2.79)		2.38 (1.42–3.98)	
>140 <i>mmHg</i>	1.86 (1.15–3.02)		1.86 (1.05–3.29)	
Blood gases				
PaO ₂ /FiO ₂		<0.001		<0.001
100–199 <i>mmHg</i>	0.49 (0.32–0.76)		0.48 (0.29–0.79)	
> 200 <i>mmHg</i>	0.34 (0.20–0.59)		0.31 (0.16–0.60)	
PaCO ₂ > 35 <i>mmHg</i>	1.17 (0.81–1.69)	0.414		
pH ≥ 7.40	0.58 (0.37–0.91)	0.019	0.59 (0.36–0.98)	0.041
Non-invasive respiratory support (randomization arm)				0.062
Standard oxygen therapy	1	0.078	1	
High flow oxygen therapy	0.61 (0.38–0.98)		0.57 (0.34–0.95)	

Noninvasive ventilation	0.94 (0.62–1.44)		0.93 (0.58–1.51)	
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BMI, body mass index; SAPS 2, Simplified Acute Physiology Score; SOFA, Sequential Organ Failure Assessment score; VAS, visual analog scale; PaO₂/FiO₂, ratio of arterial oxygen tension to inspired oxygen fraction.

The following variables were included in the initial complete model: SAPS 2, randomization arm, bilateral pulmonary infiltrates and heart rate, systolic arterial pressure, respiratory rate, dyspnea and PaO₂/FiO₂ at baseline.

The Area Under the Curve (AUC, 95% confidence interval) of the Fine and Gray model was 80 (73-86).

Figure E2. Cumulative incidence of survival up to 90 days in patients with moderate-to-severe dyspnea at baseline (dashed red line) and no or mild dyspnea (solid blue line)

