

# THE LANCET

## Respiratory Medicine

### Supplementary appendix 2

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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**Supplementary material for: “Feasibility and physiological effects of prone positioning in non-intubated patients with acute respiratory failure due to CoViD-19 (PRON-COVID) : a prospective cohort study”**

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**Table of contents**

Video 1	Page 2
Table E1	Page 2
Table E2	Page 2
Table E3	Page 3
Table E4	Page 5
Table E5	Page 6
Table E6	Page 7
Table E7	Page 9
Table E8	Page 10
Table E9	Page 13
Table E10	Page 16
Table E11	Page 18

## VIDEO LEGEND

**Video 1** – Tutorial on prone positioning with helmet continuous positive airway pressure device – Video performed with a volunteer. Codec: H.265/HVEC

## TABLES

Age (y)	67.2 ± 10.9
C-reactive protein (mg/dL)	11.7±9.4
PaO <sub>2</sub> /FiO <sub>2</sub> (mmHg)	205.8 ± 106.2

FiO <sub>2</sub>	49.6±25.7
PEEP (cmH <sub>2</sub> O)	8.3±2.6
Arterial Blood Gas	
pH	7.49±0.1
PaO <sub>2</sub> (mmHg)	80.4±50.5
PaCO <sub>2</sub> (mmHg)	31.1±4.7
SaO <sub>2</sub> (%)	93.8±4.0
White blood cells (10 <sup>3</sup> /μL)	7.5±3.1
Platelets (10 <sup>3</sup> /μL)	230.2±92.0
Haemoglobin (g/dL)	13.9±1.8
INR	1.2±0.3
aPTTr	1.1±0.1
Bilirubin (mg/dL)	0.6±0.4
C-reactive protein (mg/dL)	10.8±9.2
Procalcitonin	0.4±0.5
Na <sup>+</sup> (mmol/L)	137.0±4.7
K <sup>+</sup> (mmol/L)	4.0±0.6
Cl <sup>-</sup> (mmol/L)	100.6±4.2
Creatinine(mg/dL)	1.0±0.2
Lactic dehydrogenase (U/L)	423.9±201.2
D-dimer (ng/dL)	512.3±603.7
AST/GOT (U/L)	60.7±49.6
ALT/GPT (U/L)	58.8±52.1

ALT/GPT: alanine aminotransferase/glutamic-pyruvic transaminase; AST/GOT: aspartate aminotransferase/glutamic-oxalacetic transaminase; Cl<sup>-</sup>: Chloride; FiO<sub>2</sub>: fraction of inspired oxygen; K<sup>+</sup>: potassium; Na<sup>+</sup>: sodium; PaCO<sub>2</sub>: arterial carbon dioxide partial pressure; PaO<sub>2</sub>: arterial oxygen partial pressure; PEEP: positive end-expiratory pressure; SaO<sub>2</sub>: arterial oxygen saturation of haemoglobin.

Age (years)	57.4 ± 7.4
Sex	
Female	12 (26.3%)
Male	44 (73.7%)
BMI (kg/m <sup>2</sup> )	27.5 ± 3.2
Time between symptom onset and hospitalization (days)	7.8 ± 4.2
Time between hospitalization and prone positioning (days)	3.4 ± 3.1
Time between symptom onset and prone positioning (days)	11.2 ± 4.5
Comorbidities	
Previous myocardial infarction	4 (7.1%)
Congestive heart failure	0 (0%)
Hypertension	23 (41.1%)
Vascular disease	3 (5.4%)
Chronic bronchopulmonary disease	2 (3.6%)
Gastric or liver disease	3 (5.4%)
Diabetes	8 (14.3%)
Moderate-severe Chronic Kidney Disease (eGFR<59)	0 (0%)
Solid malignancy	3 (5.4%)
Smoking history	
Active smoker	1 (1.8%)
Former smoker (<1 year)	1 (1.8%)
Former smoker (≥ 1 year)	20 (35.7.0%)
Never smoked	29 (51.8%)
Not declared	5 (8.9%)
Baseline blood values	
Na <sup>+</sup> (mmol/L)	138.4 ± 3.2
K <sup>+</sup> (mmol/L)	4.1 ± 0.7
Cl <sup>-</sup> (mmol/L)	101.2 ± 3.5
Creatinine (mg/dL)	0.9 ± 0.2

Urea (mg/dL)	32.6 ± 9.7
White blood cells (10 <sup>3</sup> /μL)	7.7 ± 3.7
Platelets (10 <sup>3</sup> /μL)	279.0 ± 114.1
Haemoglobin (g/dL)	12.7 ± 1.6
Haematocrit (%)	37.3 ± 4.5
Bilirubin (mg/dL)	0.6 ± 0.4
C-reactive protein (mg/L)	11.1 ± 7.1
Procalcitonin (ng/mL)	0.7 ± 1.6
Lactate dehydrogenase (U/L)	411.0 ± 162.2
AST/GOT (U/L)	57.2 ± 40.9
ALT/GPT (U/L)	61.1 ± 52.0
INR	1.2 ± 0.4
aPTT ratio	1.0 ± 0.2
D-dimer (ng/mL)	640.9 ± 521.5
Arterial blood gas at SP1	
pH	7.46 ± 0.0
PaO <sub>2</sub> (mmHg)	117.1 ± 47.4
PaCO <sub>2</sub> (mmHg)	35.3 ± 4.9
SaO <sub>2</sub> (%)	97.2 ± 2.0
Respiratory rate	24.5 ± 5.5
Arterial blood gas at PP1	
pH	7.46 ± 0.0
PaO <sub>2</sub> (mmHg)	200.4 ± 110.9
PaCO <sub>2</sub> (mmHg)	35.6 ± 4.5
SaO <sub>2</sub> (%)	98.4 ± 1.3
Arterial blood gas at SP2	
pH	7.46 ± 0.0
PaO <sub>2</sub> (mmHg)	121.4 ± 69.6
PaCO <sub>2</sub> (mmHg)	35.5 ± 4.4
SaO <sub>2</sub> (%)	97.1 ± 2.0
Outcomes	
Tracheal intubation	19 (33.9%)
Time to intubation	2.0 [2.0-4.0]
Duration of prone positioning	3.0 [3.0-4.0]
Prone positioning for > 3 hours	26 (46.4%)

Number of prone positioning cycles	1 [1-3]
Prone positioning cycles >1	21 (49.0%)

ALT/GPT: alanine aminotransferase/glutamic-pyruvic transaminase; AST/GOT: aspartate aminotransferase/glutamic-oxalacetic transaminase; BMI: body mass index; Cl<sup>-</sup>: Chloride; CPAP: continuous positive airway pressure; FiO<sub>2</sub>: fraction of inspired oxygen; K<sup>+</sup>: potassium Na<sup>+</sup>: sodium; PaCO<sub>2</sub>: arterial carbon dioxide partial pressure; PaO<sub>2</sub>: arterial oxygen partial pressure; PEEP: positive end-expiratory pressure; SaO<sub>2</sub>: arterial oxygen saturation of haemoglobin.

**Table E4 – Comparison between patients in whom prone positioning was feasible and not feasible**

	Feasible (n = 47)	Non-feasible (n = 9)	p	Difference	95% CI	
Age (years)	57.1 ± 7.2	58.9 ± 8.4	0.52	1.8	-3.7	7.2
BMI (kg/m <sup>2</sup> )	27.3 ± 3.6	28.4 ± 4.6	0.44	1.1	-1.8	4.0
Baseline blood values						
Na <sup>+</sup> (mmol/L)	138.3 ± 3.3	139.4 ± 2.9	0.32	1.2	-1.2	3.6
K <sup>+</sup> (mmol/L)	4.0 ± 0.5	4.5 ± 1.1	0.05	0.5	0.0	1.0
Cl <sup>-</sup> (mmol/L)	101.1 ± 3.6	101.3 ± 3.2	0.88	0.2	-2.4	2.8
Creatinine (mg/dL)	0.9 ± 0.2	1.0 ± 0.3	0.30	0.1	-0.1	0.3
Urea (mg/dL)	31.3 ± 9.0	38.8 ± 10.7	0.03	7.4	0.6	14.3
White blood cells (10 <sup>3</sup> /μL)	7.6 ± 3.3	8.1 ± 5.4	0.72	0.5	-2.2	3.1
Platelets (10 <sup>3</sup> /μL)	282.2 ± 116.7	262.3 ± 104.2	0.64	19.9	-103.6	64.0
Haemoglobin (g/dL)	12.6 ± 1.6	13.5 ± 1.2	0.14	0.9	-0.3	2.0
Haematocrit (%)	37.0 ± 4.7	39.3 ± 2.5	0.16	2.3	-1.0	5.6
Bilirubin (mg/dL)	0.6 ± 0.4	0.6 ± 0.4	0.73	0.0	-0.2	0.3
C-reactive protein (mg/L)	11.0 ± 7.4	11.2 ± 5.2	0.94	0.2	-5.0	5.4
Procalcitonin (ng/mL)	0.5 ± 0.8	1.8 ± 3.6	0.10	1.3	-0.3	2.8
Lactate dehydrogenase (U/L)	389.7 ± 157.1	508.1 ± 157.6	0.05	118.4	2.1	234.7
AST/GOT (U/L)	48.6 ± 24.8	111.7 ± 75.5	0.0002	63.1	32.2	94.1
ALT/GPT (U/L)	53.3 ± 36.7	110.0 ± 98.0	0.01	56.7	17.0	96.4
INR	1.2 ± 0.4	1.1 ± 0.1	0.58	0.1	-0.3	0.2
aPTT ratio	1.0 ± 0.1	1.0 ± 0.3	0.55	0.0	-0.2	0.1
D-dimer (ng/mL)	633.5 ± 451.3	673.2 ± 793.0	0.84	56.7	-352.5	432.0
FiO <sub>2</sub> (%)	68.5 ± 19.8	74.4 ± 15.9	0.40	5.9	-8.1	20.0
PEEP (mmHg)	8.2 ± 2.3	8.8 ± 1.9	0.96	0.6	-1.2	2.3
Arterial blood gas						
pH	7.46 ± 0.0	7.45 ± 0.0	0.35	0.0	0.0	0.0

PaO <sub>2</sub> (mmHg)	116.0 ± 47.5	132.6 ± 66.6	0.37	16.6	-20.4	53.7
PaO <sub>2</sub> /FiO <sub>2</sub> (mmHg)	179.5 ± 76.1	189.4 ± 104.0	0.74	10.0	-49.0	68.9
PaCO <sub>2</sub> (mmHg)	35.2 ± 4.8	36.6 ± 5.5	0.45	1.4	-2.2	4.9
SaO <sub>2</sub> (%)	97.1 ± 2.1	96.8 ± 2.7	0.75	0.3	-1.9	1.4
Respiratory rate	24.4 ± 5.5	28.4 ± 4.8	0.13	4.0	-1.2	9.2

**Table E5 – Comparison of patients undergoing different prone positioning cycles at five days**

	PP Cycles = 1 (n=21)	PP Cycles = 2 or 3 (n=15)	PP Cycles ≥ 4 (n=8)
PEEP (cmH <sub>2</sub> O)	7.6±2.5	7.7±2.5	7.7±2.5
FiO <sub>2s</sub>	50.7±26.6	57.7±19.2	50.6±17.9
PaO <sub>2</sub> (mmHg)	128.8±60.6	140.02±54.4	121.8±43.3
PaO <sub>2</sub> /FiO <sub>2</sub> (mmHg)	251.4±108.5	242.9±47.6	258.7±88.5
PaCO <sub>2</sub> (mmHg)	35.4±5.1	39.6±3.6	34.3±4.2
pH	7.5±0.0	7.4±0.0	7.5±0.0
Na <sup>+</sup> (mmol/L)	139.9±2.5	137.0±1.0	139.0±1.8
K <sup>+</sup> (mmol/L)	4.4±0.5	4.2±0.8	4.2±0.7
Cl <sup>-</sup> (mmol/L)	104.0±3.4	101.7±2.1	101.7±4.3
Creatinine (mg/dL)	0.8±0.2	0.6±0.1	0.9±0.2
Urea (mg/dL)	35.8±8.3	N/A	28.6±2.6
White blood cells (103/μL)	6.7±2.2	7.3±2.8	6.7±3.7
Platelets (103/μL)	407.9±148.5	402.3±80.4	427.1±63.1
Haemoglobin (g/dL)	11.8±1.0	10.9±1.2	11.9±1.0
Haematocrit (%)	35.1±2.6	32.4±3.9	35.4±3.3
Bilirubin (mg/dL)	0.4±0.1	0.3±0.1	0.4±0.1
C-reactive protein (mg/dL)	4.87±6.8	2.7±3.8	2.5±3.1
Procalcitonin (ng/mL)	0.1±0.1	0.22 (single datum)	0.15 (single datum)
Lactate dehydrogenase (U/L)	310.3±117.1	296.5±76.4	264.7±52.0
AST/GOT (U/L)	48.5±25.8	26.7±10.3	36.6±12.6
ALT/GPT (U/L)	80.1±64.4	38.3±17.5	64.0±41.0
INR	1.1±0.1	1.1±0.1	1.1±0.1
aPTTr	1.02±0.1	0.9±0.1	0.9±0.1
D-dimer (ng/mL)	907.70±925.6	522.7±342.0	882.8±853.0

ALT/GPT: alanine aminotransferase/glutamic-pyruvic transaminase; AST/GOT: aspartate aminotransferase/glutamic-oxalacetic transaminase; BMI: body mass index; Cl<sup>-</sup>: Chloride; CPAP: continuous positive airway pressure; FiO<sub>2</sub>: fraction of inspired oxygen; GFR: glomerular filtration rate; K<sup>+</sup>: potassium Na<sup>+</sup>: sodium; PaCO<sub>2</sub>: arterial carbon dioxide partial pressure; PaO<sub>2</sub>: arterial oxygen partial pressure; PEEP: positive end-expiratory pressure; SaO<sub>2</sub>: arterial oxygen saturation of haemoglobin; SP1: baseline supine position; PP1: after prone positioning; SP2: one hour after resuming supine position; SpO<sub>2</sub>: peripheral oxygen saturation of haemoglobin.

**Table E6 – Study timepoints in patients with baseline PaO<sub>2</sub>/FiO<sub>2</sub><300 mmHg (N=42)**

	Supine (SP1)	At prone positioning (PP1)	One hour after supine positioning (SP2)	p (SP1 vs PP1)	Difference (SP1 vs PP1)	95% CI		p (SP1 vs SP2)	Difference (SP1 vs SP2)	95% CI	
FiO <sub>2</sub> (%)	70.0 ± 20.0	70.0 ± 20.0	66.7 ± 20.6	1.0	0.0	0.0	0.0	0.11	3.3	-7.4	0.8
PEEP (cmH <sub>2</sub> O)	8.4 ± 2.2	8.4 ± 2.2	8.4 ± 2.2	1.0	0.0	0.0	0.0	0.33	0.1	-0.1	0.2
Arterial blood gas											
pH	7.46 ± 0.00	7.46 ± 0.00	7.46 ± 0.00	0.66	0.0	0.0	0.0	0.13	0.0	0.0	0.0
PaO <sub>2</sub> (mmHg)	109.1 ± 38.7	192.2 ± 109.8	112.7 ± 52.8	<0.0001	83.1	-53.5	112.6	0.67	3.6	-13.2	20.4
PaO <sub>2</sub> /FiO <sub>2</sub> (mmHg)	164.3 ± 56.7	256.8 ± 96.5	178.5 ± 83.7	<0.0001	101.5	-69.9	133.0	0.18	14.2	-6.6	35.0
PaCO <sub>2</sub> (mmHg)	35.5 ± 4.9	35.6 ± 4.6	35.5 ± 4.5	0.86	0.1	-1.1	0.9	0.98	0.0	-1.2	1.2
SaO <sub>2</sub> (%)	97.0 ± 2.0	98.4 ± 1.4	96.9 ± 2.1	<0.0001	-1.3	-1.9	0.9	0.46	0.1	-1.0	0.5
SpO <sub>2</sub> (%)	96.9 ± 2.9	98.0 ± 2.2	97.0 ± 1.9	0.01	-1.1	-2.2	-0.3	0.67	0.1	-0.8	1.2
Respiratory rate	24.8 ± 5.7	25.0 ± 7.0	24.2 ± 6.6	0.97	-0.2	-1.4	1.4	0.39	0.6	-2.2	0.9
Use of accessory respiratory muscles	9 (21.4%)	7 (16.7%)	5 (11.9%)	0.32	4.8%	-6.8%	16.3%	0.16	9.5%	-5.7%	24.8%
Dyspnoea	7 (16.7%)	4 (9.5%)	2 (4.8%)	0.26	7.2%	-7.3%	21.7%	0.06	11.9%	-2.2%	26.1%
Comfort				0.32				0.10			
Unacceptable	0 (0%)	0 (0%)	0 (0%)								
Acceptable	9 (21.4%)	13 (31.0%)	4 (9.5%)								
Good	22 (52.4%)	19 (45.1%)	22 (52.4%)								
Excellent	11 (26.2%)	10 (23.8%)	15 (35.7%)								



FiO<sub>2</sub>: fraction of inspired oxygen; PaCO<sub>2</sub>: arterial carbon dioxide partial pressure; PaO<sub>2</sub>: arterial oxygen partial pressure; PEEP: positive end-expiratory pressure;  
SaO<sub>2</sub>: arterial oxygen saturation of haemoglobin; SP1: baseline supine position; PP1: after prone positioning; SP2: one hour after resuming supine position;  
SpO<sub>2</sub>: peripheral oxygen saturation of haemoglobin;

	Supine (SP1)	At prone positioning (PP1)	One hour after supine positioning (SP2)	p- value SP1 vs PP1	95% Confidence intervals	p- value SP1 vs SP2	95% CI
FiO2	69.5±19.4	69.5±19.4	69.2±19.5	1.0	0.0 0.0	0.10	-6.08 0.63
PEEP (cmH <sub>2</sub> O)	8.4±2.2	8.4±2.2	8.3±2.2	1.0	0.0 0.0	0.03	-0.05 0.16
Arterial blood gas						0.76	
pH	7.4±0.00	7.4±0.0	7.5±0.0	0.94	0.0 0.0	0.08	-.00 .01
PaO <sub>2</sub> (mmHg)	118.7±50.7	202.2±113.7	124.0±71.1	<0.0001	-109.9 -58.0	0.61	-12.04 20.44
PaO <sub>2</sub> /FiO <sub>2</sub> (mmHg)	181.1±80.1	287.6±125.5	194.4±103.1	<0.0001	-137.20 -77.92	0.28	-9.95 33.43
PaCO <sub>2</sub> (mmHg)	35.5±4.9	35.9±4.6	35.9±4.5	0.22	-1.50 .36	0.41	-.65 1.56
SaO <sub>2</sub> (%)	97.1±2.1	98.3±1.6	97.1±2.1	<0.0001	-1.76 -.78	0.45	-.90 .40
SpO <sub>2</sub> (%)	96.9±2.8	98.0±2.3	97.1±1.9	0.00	-1.96 -.40	0.92	-.81 .89
Use of accessory respiratory muscles	12(21.4%)	9(16.1%)	7(12.5%)	0.18	-.04 .15	0.10	-.03 .21
Dyspnoea	9(16.1%)	6(10.71%)	3(5.36%)	0.26	-.06 .16	0.03	-.01 .22

FiO<sub>2</sub>: fraction of inspired oxygen; PaCO<sub>2</sub>: arterial carbon dioxide partial pressure; PaO<sub>2</sub>: arterial oxygen partial pressure; PEEP: positive end-expiratory pressure; SaO<sub>2</sub>: arterial oxygen saturation of haemoglobin; SP1: baseline supine position; PP1: after prone positioning; SP2: one hour after resuming supine position; SpO<sub>2</sub>: peripheral oxygen saturation of haemoglobin.

**Table E8 – Comparison between responders and non-responders (PaO<sub>2</sub>/FiO<sub>2</sub> improvement >10%)**

	Responders (n = 19)	Non-responders (n = 27)	p	Difference	95% CI	
Age (years)	58.2 ± 7.4	56.5 ± 7.3	0.44	1.7	-6.2	2.7
Sex						
Female	5 (26.3%)	27 (25.6%)	0.98			
Male	14 (73.7%)	20 (74.1%)				
BMI (kg/m <sup>2</sup> )	26.5 ± 3.2	27.9 ± 3.8	0.23	1.4	-0.9	3.6
Time between symptom onset and hospitalization (days)	8.7 ± 5.0	7.0 ± 4.0	0.22	1.6	-4.3	1.0
Time between hospitalization and prone positioning (days)	2.5 ± 2.0	4.5 ± 3.6	0.03	2.0	0.2	3.9
Time between symptom onset and prone positioning (days)	11.2 ± 5.1	11.6 ± 4.3	0.78	0.4	-2.4	3.2
Comorbidities						
Previous myocardial infarction	1 (5.3%)	1 (3.7%)				
Congestive heart failure	0 (0%)	0 (0%)				
Hypertension	7 (36.8%)	11 (40.7%)				
Vascular disease	0 (0%)	3 (11.1%)				
Chronic bronchopulmonary disease	1 (5.3%)	0 (0%)				
Gastric or liver disease	0 (0%)	2 (7.4%)				
Diabetes	4 (21.1%)	2 (7.4%)				
Moderate-severe Chronic Kidney Disease (eGFR<59)	0 (0%)	0 (0%)				
Solid malignancy	1 (5.3%)	2 (7.4%)				
Smoking history						
Active smoker	0 (0%)	1 (3.7%)				
Former smoker (<1 year)	0 (0%)	1 (3.7%)				
Former smoker (≥ 1 year)	7 (37.0%)	9 (33.3%)				
Never smoked	10 (52.6%)	15 (55.9%)				
Not declared	2 (10.5%)	1 (3.7%)				
Baseline blood values						
Na <sup>+</sup> (mmol/L)	137.9 ± 2.3	138.4 ± 3.9	0.62	0.5	-1.5	2.5
K <sup>+</sup> (mmol/L)	3.9 ± 0.5	4.1 ± 0.6	0.23	0.2	-0.1	0.5
Cl <sup>-</sup> (mmol/L)	101.8 ± 3.5	100.5 ± 3.5	0.21	1.4	-3.5	0.8
Creatinine (mg/dL)	0.9 ± 0.2	0.8 ± 0.2	0.45	0.0	-0.2	0.1

Urea (mg/dL)	30.5 ± 7.4	30.8 ± 8.6	0.93	0.2	-5.0	5.4
White blood cells (10 <sup>3</sup> /μL)	7.6 ± 2.8	7.4 ± 3.6	0.80	0.3	-2.2	1.7
Platelets (10 <sup>3</sup> /μL)	251.7 ± 105.5	300.7 ± 122.9	0.17	48.9	-21.1	119.0
Haemoglobin (g/dL)	12.9 ± 2.1	12.4 ± 1.2	0.30	0.5	-1.5	0.5
Haematocrit (%)	37.7 ± 5.9	36.4 ± 3.8	0.36	1.3	-4.2	1.6
Bilirubin (mg/dL)	0.7 ± 0.5	0.5 ± 0.2	0.14	0.2	-0.4	0.1
C-reactive protein (mg/L)	12.7 ± 7.0	9.1 ± 6.5	0.08	3.7	-7.7	0.4
Procalcitonin (ng/mL)	0.3 ± 0.3	0.7 ± 1.1	0.31	0.34	-0.3	1.0
Lactate dehydrogenase (U/L)	457.6 ± 209.2	350.8 ± 111.4	0.04	106.8	-208.9	-4.8
AST/GOT (U/L)	52.5 ± 28.2	46.4 ± 23.0	0.47	6.1	-23.2	11.0
ALT/GPT (U/L)	52.1 ± 40.3	54.9 ± 35.5	0.81	2.8	-20.8	26.4
INR	1.3 ± 0.6	1.1 ± 0.1	0.18	0.2	-0.4	0.1
aPTT ratio	1.1 ± 0.1	1.0 ± 0.1	0.37	0.4	-0.1	0.0
D-dimer (ng/mL)	614.1 ± 472.3	604.2 ± 411.8	0.95	9.8	-310.0	290.4
Arterial blood gas at SP1						
pH	7.45 ± 0.0	7.46 ± 0.0	0.76	0.0	0.0	0.0
PaO <sub>2</sub> (mmHg)	120.5 ± 51.7	114.7 ± 45.0	0.70	5.8	-34.6	23.1
PaCO <sub>2</sub> (mmHg)	34.3 ± 4.9	36.0 ± 4.8	0.24	1.7	-1.2	4.6
SaO <sub>2</sub> (%)	97.3 ± 2.1	97.1 ± 2.0	0.84	0.12	-1.3	1.1
Arterial blood gas at PP1						
pH	7.46 ± 0.0	7.46 ± 0.0	0.99	0.0	0.0	0.0
PaO <sub>2</sub> (mmHg)	230.0 ± 110.1	179.6 ± 108.8	0.13	50.4	-116.4	15.6
PaCO <sub>2</sub> (mmHg)	34.3 ± 5.2	36.5 ± 3.8	0.10	2.2	-0.5	4.9
SaO <sub>2</sub> (%)	98.6 ± 1.3	98.3 ± 1.4	0.58	0.23	-1.1	0.6
Arterial blood gas at SP2						
pH	7.46 ± 0.0	7.47 ± 0.0	0.57	0.0	0.0	0.0
PaO <sub>2</sub> (mmHg)	167.4 ± 87.5	88.9 ± 21.0	<0.0001	78.5	-113.6	-43.3
PaCO <sub>2</sub> (mmHg)	34.4 ± 4.6	36.3 ± 4.2	0.16	1.9	-0.7	4.5
SaO <sub>2</sub> (%)	98.1 ± 2.1	96.5 ± 1.8	0.01	1.6	-2.8	-0.4
Outcomes						
Tracheal intubation	4 (21.1%)	9 (33.3%)	0.36		-0.1	0.4
Time to intubation	2 [2-4]	2 [1-5]	1.0			
Duration of prone positioning	3.5 [3-4]	3.5 [3-4]	0.85			
Prone positioning for > 3 hours	10 (52.6%)	15 (55.6%)	0.85	3.0%	-26.6%	32.2%

Number of prone positioning cycles	4 [3-4]	2 [1-4]	0.72			
Prone positioning cycles >1	10 (52.6%)	13 (48.1%)	0.72	4.5%	-35.5%	24.4%

ALT/GPT: alanine aminotransferase/glutamic-pyruvic transaminase; AST/GOT: aspartate aminotransferase/glutamic-oxalacetic transaminase; BMI: body mass index; Cl<sup>-</sup>: Chloride; CPAP: continuous positive airway pressure; FiO<sub>2</sub>: fraction of inspired oxygen; GFR: glomerular filtration rate; K<sup>+</sup>: potassium Na<sup>+</sup>: sodium; PaCO<sub>2</sub>: arterial carbon dioxide partial pressure; PaO<sub>2</sub>: arterial oxygen partial pressure; PEEP: positive end-expiratory pressure; SaO<sub>2</sub>: arterial oxygen saturation of haemoglobin; SP1: baseline supine position; PP1: after prone positioning; SP2: one hour after resuming supine position; SpO<sub>2</sub>: peripheral oxygen saturation of haemoglobin.

**Table E9 – Comparison between responders and non-responders (PaO<sub>2</sub>/FiO<sub>2</sub> improvement >20%)**

	<b>Responders (n = 15)</b>	<b>Non-responders (n = 31)</b>	<b>p</b>	<b>Difference</b>	<b>95% CI</b>	
Age (years)	58.6 ± 7.4	56.5 ± 7.3	0.37	2.1	-6.7	2.6
Sex						
Female	5 (33.3%)	7 (22.6%)	0.44			
Male	10 (66.7%)	24 (77.4%)				
BMI (kg/m <sup>2</sup> )	27.1 ± 3.4	27.5 ± 3.7	0.71	0.5	-1.9	2.9
Time between symptom onset and hospitalization (days)	8.4 ± 5.6	7.4 ± 3.9	0.48	1.0	-3.9	1.8
Time between hospitalization and prone positioning (days)	2.7 ± 2.1	4.1 ± 3.5	0.16	1.4	-0.6	3.4
Time between symptom onset and prone positioning (days)	11.1 ± 5.7	11.5 ± 4.1	0.79	0.4	-2.5	3.3
Comorbidities						
Previous myocardial infarction	1 (6.7%)	1 (3.2%)				
Congestive heart failure	0 (0%)	0 (0%)				
Hypertension	6 (40.0%)	12 (38.7%)				
Vascular disease	0 (0%)	3 (9.7%)				
Chronic bronchopulmonary disease	1 (6.7%)	0 (0%)				
Gastric or liver disease	0 (0%)	2 (6.5%)				
Diabetes	4 (26.7%)	2 (6.5%)				
Moderate-severe Chronic Kidney Disease (eGFR<59)	0 (0%)	0 (0%)				
Solid malignancy	1 (6.7%)	2 (6.5%)				
Smoking history						
Active smoker	0 (0%)	1 (3.2%)				
Former smoker (<1 year)	0 (0%)	1 (3.2%)				
Former smoker (≥ 1 year)	6 (40.0%)	10 (32.3%)				
Never smoked	8 (53.3%)	17 (54.8%)				
Not declared	1 (6.7%)	2 (6.5%)				
Baseline blood values						
Na <sup>+</sup> (mmol/L)	138.1 ± 2.3	138.3 ± 3.8	0.88	0.2	-2.0	2.3
K <sup>+</sup> (mmol/L)	3.9 ± 0.5	4.0 ± 0.6	0.66	0.1	-0.3	0.4
Cl <sup>-</sup> (mmol/L)	101.8 ± 3.8	100.57 ± 3.4	0.33	1.1	-3.4	1.2
Creatinine (mg/dL)	0.9 ± 0.2	0.9 ± 0.2	0.58	0.0	-0.2	0.1

Urea (mg/dL)	32.1 ± 7.8	30.0 ± 8.1	0.45	2.1	-7.5	3.4
White blood cells (10 <sup>3</sup> /μL)	7.2 ± 2.6	7.6 ± 3.6	0.72	0.4	-1.7	2.5
Platelets (10 <sup>3</sup> /μL)	257.3 ± 118.6	291.6 ± 117.0	0.36	34.3	-40.2	108.8
Haemoglobin (g/dL)	12.5 ± 2.0	12.6 ± 1.5	0.75	0.2	-0.9	1.2
Haematocrit (%)	36.6 ± 5.5	37.1 ± 4.5	0.74	0.5	-2.6	3.6
Bilirubin (mg/dL)	0.7 ± 0.6	0.5 ± 0.2	0.06	0.2	-0.5	0.0
C-reactive protein (mg/L)	12.3 ± 6.2	9.8 ± 7.1	0.25	2.5	-6.9	1.9
Procalcitonin (ng/mL)	0.4 ± 0.4	0.6 ± 1.0	0.49	0.2	-0.5	1.0
Lactate dehydrogenase (U/L)	469.9 ± 230.3	357.2 ± 112.0	0.04	112.7	-221.9	-3.5
AST/GOT (U/L)	52.7 ± 29.1	46.8 ± 22.9	0.50	5.9	-23.6	11.7
ALT/GPT (U/L)	51.0 ± 40.5	55.2 ± 35.9	0.73	4.2	-20.4	28.8
INR	1.4 ± 0.7	1.1 ± 0.1	0.09	0.2	-0.5	0.0
aPTT ratio	1.1 ± 0.2	1.0 ± 0.1	0.29	0.0	-0.1	0.0
D-dimer (ng/mL)	690.4 ± 511.8	578.0 ± 398.9	0.48	112.4	-433.6	208.9
Arterial blood gas at SP1						
pH	7.45 ± 0.0	7.46 ± 0.0	0.45	0.0	0.0	0.0
PaO <sub>2</sub> (mmHg)	123.3 ± 50.3	114.2 ± 46.5	0.55	9.1	-39.4	21.2
PaCO <sub>2</sub> (mmHg)	34.5 ± 5.2	35.6 ± 4.7	0.46	1.1	-1.9	4.2
SaO <sub>2</sub> (%)	97.6 ± 1.8	97.0 ± 2.1	0.40	0.5	-1.8	0.7
Arterial blood gas at PP1						
pH	7.46 ± 0.0	7.46 ± 0.0	0.83	0.0	0.0	0.0
PaO <sub>2</sub> (mmHg)	237.4 ± 110.3	182.5 ± 108.5	0.12	54.9	-124.0	14.3
PaCO <sub>2</sub> (mmHg)	34.7 ± 5.1	36.1 ± 4.3	0.32	1.4	-1.5	4.3
SaO <sub>2</sub> (%)	98.8 ± 0.9	98.2 ± 1.5	0.15	0.6	-1.5	0.2
Arterial blood gas at SP2						
pH	7.46 ± 0.0	7.46 ± 0.0	0.65	0.0	0.0	0.0
PaO <sub>2</sub> (mmHg)	182.3 ± 85.9	91.9 ± 32.7	<0.0001	90.4	-125.6	-55.3
PaCO <sub>2</sub> (mmHg)	34.6 ± 4.7	36.0 ± 4.3	0.34	1.3	-1.4	4.1
SaO <sub>2</sub> (%)	98.5 ± 1.5	96.4 ± 1.9	0.00	2.1	-3.3	-0.9
Outcomes						
Tracheal intubation	3 (20.0%)	10 (32.3%)	0.39		-0.1	0.4
Time to intubation	2 [2-4]	2 [2-4]	0.99			
Duration of prone positioning	3.5 [3-4]	3.5 [3-4]	0.85			
Prone positioning for > 3 hours	8 (53.4%)	17 (54.9%)	0.92	1.5%	-29.2%	32.2%

Number of prone positioning cycles	2 [1-3]	2 [1-4]	0.72			
Prone positioning cycles >1	9 (60.0%)	14 (45.1%)	0.46	14.9%	-43.5%	19.0%

ALT/GPT: alanine aminotransferase/glutamic-pyruvic transaminase; AST/GOT: aspartate aminotransferase/glutamic-oxalacetic transaminase; BMI: body mass index; Cl: Chloride; CPAP: continuous positive airway pressure; FiO<sub>2</sub>: fraction of inspired oxygen; GFR: glomerular filtration rate; K<sup>+</sup>: potassium Na<sup>+</sup>: sodium; PaCO<sub>2</sub>: arterial carbon dioxide partial pressure; PaO<sub>2</sub>: arterial oxygen partial pressure; PEEP: positive end-expiratory pressure; SaO<sub>2</sub>: arterial oxygen saturation of haemoglobin; SP1: baseline supine position; PP1: after prone positioning; SP2: one hour after resuming supine position; SpO<sub>2</sub>: peripheral oxygen saturation of haemoglobin.



<b>Table E10 - Comparison between responders and non-responders (including patients who failed PP)</b>				
	<b>Responders (n=25)</b>	<b>Non-responders (n=31)</b>	<b>p</b>	<b>95% CI</b>
Sex				
Female	6 (24%)	6 (19.3%)		
Male	19 (76%)	25 (80.7%)	0.67	
Age (years)	58.8±8.2	56.3±6.6	0.21	-6.47 1.45
BMI (kg/m <sup>2</sup> )	27.3±3.4	27.6±4	0.73	-1.74 2.46
Baseline blood values				
Na <sup>+</sup> (mmol/L)	138.0±2.8	138.8±3.6	0.40	-1.02 2.49
K <sup>+</sup> (mmol/L)	4.0±0.7	4.1±0.7	0.55	-.26 .48
Cl <sup>-</sup> (mmol/L)	102.1±3.3	100.4±3.5	0.08	-3.52 .22
Creatinine (mg/dL)	0.9±0.2	0.9±0.2	0.51	-.17 .085
Urea (mg/dL)	32.4±9.2	32.9±10.2	0.87	
White blood cells (103/μL)	8.22±4.4	7.3±3.0	0.33	-2.95 1.02
Platelets (103/μL)	250.3±103	302.1±118.9	0.09	-8.63 112.24
Haemoglobin (g/dL)	12.8±1.9	12.7±1.3	0.74	-1.00 .71
Haematocrit (%)	37.6±5.3	37.2±3.9	0.75	-2.85 2.06
Bilirubin (mg/dL)	0.6±0.4	0.6±0.3	0.65	-.25 .16
C-reactive protein (mg/L)	12.9±6.6	9.6±7.2	0.09	-7.04 .50
Procalcitonin (ng/mL)	0.6±1.0	0.83±2	0.69	-.92 1.38
Lactate dehydrogenase (U/L)	459.8±190.9	378.5±133.6	0.08	-173.48 10.78
AST/GOT (U/L)	49.4±25.8	63.0±49.1	0.28	-11.34 38.76
ALT/GPT (U/L)	48.6±36.8	69.8±59.4	0.15	-8.17 50.60
INR	1.3±0.5	1.1±0.1	0.15	-.35 .056
aPTT ratio	1.1±0.1	1±0.2	0.13	-.16 .02
D-dimero (ng/mL)	673.8±646.7	619.4±431.8	0.73	-367.23 258.30
Comorbidities				
Previous myocardial infarction	1(4%)	3(10%)		
Congestive heart failure	0 (0%)	0 (0%)		
Hypertension	10(40%)	13(42%)		
Vascular disease	0 (0%)	3(10%)		
Chronic bronchopulmonary disease	1(4%)	1(3%)		
Gastric or liver disease	2(8%)	1(3%)		
Diabetes	4(16%)	4(13%)		
Moderate-severe Chronic Kidney Disease (eGFR<59)	0 (0%)	0 (0%)		
Solid malignancy	1(4%)	2(6%)		
Smoking history			0.57	
Active smoker	9(36%)	1(3%)		
Former smoker (<1 year)	14(56%)	1(3%)		
Former smoker (≥ 1 year)	2(8%)	11(35%)		
Never smoked		15(48%)		

Not declared		3(10%)		
Time between symptom onset and hospitalization (days)	8.0±4.6	7.6±3.9	0.76	-2.63 1.94
Time between enrollment and hospitalization (days)	2.7±2.0	4.0±3.6	0.11	-.33 2.95
Time between enrollment and symptom onset (days)	10.7±4.7	11.6±4.3	0.42	-1.44 3.37
Arterial blood gas at SP1				
pH	7.4±0.0	7.4±0.0	0.92	-.016 .017
PaO2 (mmHg)	114.8±49.7	121.8±52.1	0.61	-20.48 34.54
PaCO2 (mmHg)	35.2±5	35.7±4.9	0.72	-2.19 3.14
SaO2 (%)	97.0±2.3	97.1±2.0	0.80	-1.03 1.32
Arterial blood gas at PP1				
pH	7.4±0.0	7.5±0.0	0.70	-.02 .02
PaO2 (mmHg)	215.4±113.7	190.0±114.4	0.43	-88.98 38.23
PaCO2 (mmHg)	35.2±5.3	36.5±3.8	0.34	-1.33 3.76
SaO2 (%)	98.2±1.9	98.4±1.3	0.78	-.78 1.04
Arterial blood gas at SP2				
pH	7.5±0.0	7.5±0.0	0.50	-.01 .02
PaO2 (mmHg)	153.7±84.7	94.2±36.2	0.00	-96.59 -22.52
PaCO2 (mmHg)	35.4±4.8	36.3±4.4	0.50	-1.72 3.48
SaO2 (%)	97.7±2.2	96.5±1.9	0.06	-2.39 .06
Outcomes				
Tracheal intubation	7(28%)	12(39%)	0.40	-.14 .35
Time to intubation	2 [2-2]	3 [1-4]		
Number of prone positioning cycles	1.5 [1-3]	1 [1-3]		
Duration of prone positioning	3 [3-4]	3 [3-4]		

ALT/GPT: alanine aminotransferase/glutamic-pyruvic transaminase; AST/GOT: aspartate aminotransferase/glutamic-oxalacetic transaminase; BMI: body mass index; Cl<sup>-</sup>: Chloride; CPAP: continuous positive airway pressure; FiO<sub>2</sub>: fraction of inspired oxygen; GFR: glomerular filtration rate; K<sup>+</sup>: potassium Na<sup>+</sup>: sodium; PaCO<sub>2</sub>: arterial carbon dioxide partial pressure; PaO<sub>2</sub>: arterial oxygen partial pressure; PEEP: positive end-expiratory pressure; SaO<sub>2</sub>: arterial oxygen saturation of haemoglobin; SP1: baseline supine position; PP1: after prone positioning; SP2: one hour after resuming supine position; SpO<sub>2</sub>: peripheral oxygen saturation of haemoglobin.

<b>Table E11 – Trajectory of PaO2/FiO2 from SP1 to SP2 through a mixed model</b>					
	<b>Coefficient</b>	<b>Standard Error</b>	<b>95% Confidence intervals</b>		<b>P</b>
SP1 (intercept)	180.5	11.1	158.1	202.3	<0.0001
SP2	12.3	11.0	-9.3	34.0	0.26
Platelets (for each SD) effect at SP1	-6.4	11.2	-28.3	15.6	0.57
Additional effect of platelets (for each SD) at SP2	-19.3	11.1	-41.1	2.4	0.08
SP1 (intercept)	181.7	10.6	160.9	202.6	<0.0001
SP2	13.1	11.0	-8.4	34.6	0.23
C-reactive protein (for each SD) effect at SP1	-26.9	10.7	-47.8	-5.9	0.01
Additional effect of C-reactive protein (for each SD) at SP2	26.0	11.0	4.4	47.6	0.02
SP1 (intercept)	176.1	11.1	153.1	199.1	<0.0001
SP2	4.1	10.3	-16.0	24.3	0.69
Lactate dehydrogenase (for each SD) effect at SP1	-7.1	11.8	-30.3	16.0	0.55
Additional effect of lactate dehydrogenase (for each SD) at SP2	36.3	10.3	16.0	56.5	0.00
SP1 (intercept)	180.5	11.0	158.9	202.1	<0.0001
SP2	12.3	11.1	-9.4	34.1	0.27
Time between hospitalization and prone positioning (for each SD) effect at SP1	-12.6	11.1	-34.3	9.1	0.25
Additional effect of time between hospitalization and prone positioning (for each SD) at SP2	-17.1	11.2	-39.0	4.8	0.13
SP1 (intercept)	179.5	11.5	157.0	202.0	<0.0001
SP2	3.1	10.1	-16.8	22.9	0.76
Lactate dehydrogenase (for each SD) effect at SP1	3.1	12.5	-21.3	27.6	0.80
Additional effect of lactate dehydrogenase (for each SD) at SP2	27.9	11.0	6.3	49.4	0.01
C-reactive protein (for each SD) effect at SP1	-24.5	12.4	-48.8	-0.2	0.05
Additional effect of C-reactive protein (for each SD) at SP2	20.3	11.0	-1.1	41.8	0.06

Coefficients are expressed in mmHg SD. Standard Deviation SP1: Baseline supine position; SP2: one hour after resuming supine position