

Quantitative CT scan and response to pronation in COVID-19 ARDS

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Online supplementary materials

Supplementary methods

The CT scan measures the density (ρ_{Lung}). The lung is assumed to comprise two compartments: tissue, $\rho=1$, Hounsfield units, HU =0, and gas, $\rho=0$, HU = -1000. According to these premises, it is possible to calculate, in each voxel, both density and mass (density = ρ):

$$\rho = \frac{CT + 1000}{1000}$$

$$\text{Voxel tissue mass} = \rho_{\text{voxel}} \cdot V_{\text{voxel}}$$

The total lung volume (V_{lung}) was computed as

$$V_{\text{lung}} = V_{\text{voxel}} * \text{No of Voxels}$$

where V_{voxel} equals the volume of a single voxel.

The total tissue mass of the lung was computed as the product of the density multiplied by lung volume:

$$\text{Lung tissue mass} = \rho \cdot V_{\text{lung}}$$

While the gas volume was computed as

$$\text{Total gas volume} = (1 - \rho) * \text{Total lung volume}$$

Supplementary Tables

Table S1. Population demographic characteristics at ICU admission divided by the oxygen response to pronation

Variables	Total (N = 125)	Oxygen Non- responders (N = 62)	Oxygen Responders (N = 63)	p-value
Sex, Female n (%)	30 (24)	14 (23)	16 (25)	.44
Age, years	62 ± 11	62 ± 10	61 ± 11	.50
Weight, kg	86 ± 19	85 ± 19	87 ± 19	.63
Height, cm	171 ± 9	171 ± 8	170 ± 9	.38
BMI, kg/m²	30 ± 6	29 ± 7	30 ± 6	.40
Comorbidities:				
Hypertension, n (%)	64 (51)	32 (52)	32 (51)	.93
Diabetes, n (%)	22 (18)	11 (18)	11 (17)	.97
Active Smoke, n (%)	5 (4)	3 (5)	2 (3)	.68
Obesity, n (%)	38 (30)	16 (26)	22 (35)	.27
Cancer, n (%)	14 (11)	11 (18)	3 (5)	.025
CKD, n (%)	9 (7)	6 (10)	3 (5)	.32
COPD, n (%)	13 (10)	6 (10)	7 (11)	.79
Atrial Fibrillation, n (%)	8 (6)	6 (10)	2 (3)	.16
CAD, n (%)	15 (12)	9 (15)	6 (10)	.39
Liver disease, n (%)	10 (8)	2 (3)	8 (13)	.10
SOFA	5 [4, 6]	5 [4, 6]	5 [3, 7]	.77
SAPS II	38 [33, 43]	40 [34, 45]	37 [33, 43]	.34
Days between the onset of symptoms and CT scan, days	10±6	12 ± 7	9 ± 5	.009
Days between the onset of symptoms and first pronation, days	11±6	12±7	9±4	.004

The median PaO₂/FiO₂ ratio increase observed during prone ventilation was used as cut-off, defining Oxygen Responders subjects with a PaO₂/FiO₂ ratio above the median value and Oxygen Non Responders when below. *Acronyms: BMI body mass index; CAD coronary arterial disease; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; CT computed tomography; ICU: intensive care unit; SAPS: Simplified Acute Physiology Score; SOFA: Sequential Organ Failure Assessment.*

Table S2. Ventilatory parameters of the population divided by oxygen response to pronation in supine position before the first pronation

Variables	Total (N = 125)	Oxygen Non- responders (N = 62)	Oxygen Responders (N = 63)	p-value
ARDS Severity				.60
Mild n (%)	1 (0.8)	0 (0.0)	1 (2)	
Moderate n (%)	65 (52.0)	33 (53)	32 (51)	
Severe n (%)	59 (47.2)	29 (47)	30 (47)	
Ventilator setting:				
Tidal Volume/PBW, ml/kg	6.7 ± 0.9	6.6 ± 1.0	6.8 ± 0.8	.31
RR, breath/minute	19 ± 3	19 ± 4	19 ± 3	.84
PEEP, cm H ₂ O	12 ± 2	12 ± 2	12 ± 2	.85
Plateau Pressure, cm H ₂ O	24 ± 3	24 ± 3	23 ± 3	.44
Crs, ml/cm H ₂ O	41 ± 11	39 ± 10	42 ± 12	.19
Driving Pressure, cm H ₂ O	11 ± 3	11 ± 3	11 ± 3	.31
Arterial blood Gas:				
pH	7.36 ± 0.07	7.36 ± 0.07	7.37 ± 0.07	.41
PaCO₂, mm Hg	47 ± 9	49 ± 10	46 ± 8	.064
Ventilatory Ratio	1.6 ± 0.5	1.7 ± 0.5	1.6 ± 0.4	.56
PaO₂, mm Hg	77 ± 16	77 ± 16	77 ± 16	.77
FiO₂, %	77 ± 2	75 ± 2	79 ± 2	.19
PaO₂/FiO₂	103 [82, 123]	105 [82, 133]	101 [76, 120]	.42

The median PaO₂/FiO₂ ratio increase observed during prone ventilation was used as cut-off, defining Oxygen Responders subjects with a PaO₂/FiO₂ ratio above the median value and Oxygen Non Responders when below. *Acronyms: ARDS: acute respiratory distress syndrome; Crs: compliance of the respiratory system; FiO₂ inspiratory fraction of oxygen; PaCO₂ arterial*

partial pressure of carbon dioxide; PaO₂ arterial partial pressure of oxygen; PBW: predicted body weight, PEEP: positive end-expiratory pressure; RR: respiratory rate.

Table S3. Clinical outcomes of the population divided by oxygen response to pronation

Variables	Total (N = 125)	Oxygen Non- responders (N = 62)	Oxygen Responders (N = 63)	p-value
Number of Pronation, n	4 [2, 6]	4 [2, 6]	4 [2, 7]	.56
Total Pronation Time, hour	80 [46, 146]	76 [41, 148]	90 [48, 146]	.67
iNO, n (%)	32 (26)	22 (35)	10 (16)	.01
Days of Ventilation	30 [17, 41.5]	33 [19, 43]	28 [16, 36]	.19
Tracheostomy, n (%)	76 (61)	36 (58)	40 (63)	.53
Hospital LOS, days	45 [26, 65]	47 [25, 63]	43 [26, 65]	.91
ICU LOS days	33 [19, 45]	35 [19, 47]	32 [19, 42]	.54
ICU Outcome				.54
Deceased n (%)	51 (41)	27 (44)	24 (38)	
Discharged n (%)	74 (59)	35 (56)	39 (62)	

The median PaO₂/FiO₂ ratio increase observed during prone ventilation was used as cut-off, defining Oxygen Responders subjects with a PaO₂/FiO₂ ratio above the median value and Oxygen Non Responders when below. *Acronyms: ICU: intensive care unit; iNO: inhaled nitric oxide; LOS: length of stay.*

Table S4. Baseline quantitative CT parameters of the population divided for the oxygen response to pronation.

Variables	All patients (N = 125)	Oxygen Non- responders (N = 62)	Oxygen Responders (N = 63)	p-value
Bilateral Lung				
Volume, ml	3526 ±1009	3534 ± 997	3518 ± 1028	.93
Density, HU	-545 ±106	-534 ± 102	-557 ± 110	.22
Tissue mass, g	1541 ±390	1593 ± 409	1490 ± 366	.14
Hyper inflated lung				
Volume, ml	160 ±157	163 ± 168	157 ± 147	.84
Density, HU	-968 ±2	-968 ± 3	-968 ± 2	.46
Tissue mass, g	5 ±5	5 ± 5	5 ± 4	.96
Well aerated lung				
Volume, ml	2092 ±895	2037 ± 843	2145 ± 947	.50
Density, HU	-740 ±31	-740 ± 31	-740 ± 32	.90
Tissue mass, g	530 ±208	518 ± 201	542 ± 216	.52
Poorly aerated lung				
Volume, ml	891 ±324	902 ± 351	879 ± 297	.69
Density, HU	-343 ±20	-342 ± 18	-344 ± 22	.72
Tissue mass, g	584 ±210	593 ± 227	576 ± 193	.67
Non aerated lung				
Volume, ml	319 ±192	353 ± 196	285 ± 184	.050
Density, HU	-51 ±8	-49 ± 9	-53 ± 5	.004
Tissue mass, g	303 ±185	337 ± 190	271 ± 176	.047

The median PaO₂/FiO₂ ratio increase observed during prone ventilation was used as cut-off, defining Oxygen Responders subjects with a PaO₂/FiO₂ ratio above the median value and Oxygen Non Responders when below. *Acronyms: CT: computed tomography.*

Table S5. Population demographic characteristics at ICU admission divided by CO₂ response to pronation.

Variables	Total (N = 125)	CO₂ Non-responders (N = 74)	CO₂ Responders (N = 51)	p-value
Sex, Female n(%)	30 (24)	17 (23)	13 (25)	.75
Age, years	62 ± 11	62 ± 11	62 ± 10	.98
Weight, kg	86 ± 19	86 ± 21	87 ± 17	.44
Height, cm	171 ± 9	171 ± 9	171 ± 9	.68
BMI, kg/m²	30 ± 6	30 ± 7	30 ± 6	.57
Comorbidities:				
Hypertension, n(%)	64 (51)	36 (49)	28 (55)	.49
Diabetes, n(%)	22 (18)	12 (16)	10 (20)	.63
Active Smoke, n(%)	5(4)	1 (1)	4 (8)	.07
Obesity, n(%)	38 (30)	21 (28)	17 (33)	.55
Cancer, n(%)	14 (11)	10 (14)	4 (8)	.32
CKD, n(%)	9 (7)	6 (8)	3 (6)	.64
COPD, n(%)	13 (10)	6 (8)	7 (14)	.31
Atrial Fibrillation, n(%)	8 (6)	4 (5)	4 (8)	.58
CAD, n(%)	15 (12)	4 (5)	11 (22)	.007
Liver disease, n(%)	10 (8)	6 (8)	4 (8)	1.00
SOFA	5 [4, 6]	5 [3, 6]	5 [4, 6]	.37
SAPS II	38 [33, 43]	40 [33, 44]	37 [33, 41]	.25

Acronyms: BMI body mass index; CAD coronary arterial disease; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; CT computed tomography; ICU: intensive care unit; SAPS: Simplified Acute Physiology Score; SOFA: Sequential Organ Failure Assessment.

Table S6. Ventilatory parameters of the population divided by carbon dioxide response to pronation in supine position before the first pronation cycle.

Variables	Total (N = 125)	CO₂ Non-responders (N = 74)	CO₂ Responders (N = 51)	p-value
ARDS Severity				.40
Mild n(%)	1 (0.8)	0 (0)	1 (2)	
Moderate n(%)	65 (52.0)	37 (50)	28 (55)	
Severe n(%)	59 (47.2)	37 (50)	22 (43)	
Ventilator setting:				
Tidal Volume/PBW, ml/kg	6.7 ± 0.9	6.6 ± 0.8	6.9 ± 1.0	.019
RR, breath/minute	19 ± 3	18 ± 3	21 ± 4	<0.001
PEEP, cm H₂O	12 ± 3	12 ± 2	12 ± 3	.80
Plateau Pressure, cm H₂O	24 ± 3	24 ± 3	24 ± 3	.96
Crs, ml/cm H₂O	41 ± 11	39 ± 10	43 ± 13	.09
Driving Pressure, cm H₂O	11 ± 3	11 ± 3	11 ± 3	.78
Arterial blood Gas:				
pH	7.36 ± 0.07	7.37 ± 0.07	7.35 ± 0.07	.026
PaCO₂, mm Hg	47 ± 9	46 ± 9	49 ± 9	.09
Ventilatory Ratio	1.6 ± 0.5	1.5 ± 0.4	1.9 ± 0.5	<0.001
PaO₂, mm Hg	77 ± 16	77 ± 17	77 ± 14	.96
FiO₂, %	0.8 ± 0.2	0.8 ± 0.2	0.8 ± 0.2	.47
PaO₂/FiO₂	103 [82, 123]	100 [82, 120]	107 [81, 130]	.44

Acronyms: ARDS: acute respiratory distress syndrome; Crs: compliance of the respiratory system; FiO₂ inspiratory fraction of oxygen; PaCO₂ arterial partial pressure of carbon dioxide; PaO₂ arterial partial pressure of oxygen; PBW: predicted body weight, PEEP: positive end-expiratory pressure; RR: respiratory rate.

Table S7. Clinical outcomes of the population divided by carbon dioxide response to pronation

Variables	Total (N = 125)	CO₂ Non-responders (N = 74)	CO₂ Responders (N = 51)	p-value
Number of Pronation, n	4 [2, 6]	4 [2, 6]	3 [2, 6]	.82
Total Pronation Time, hour	80 [46, 146]	83 [46, 146]	76 [41, 150]	.94
iNO, n(%)	32 (26)	23 (31)	9 (18)	.07
Days of Ventilation	30 [17, 41.5]	29 [16, 39]	33 [19, 42]	.40
Tracheostomy, n(%)	76 (61)	41 (55)	35 (69)	.10
Hospital LOS, days	45 [26, 65]	40 [22, 63]	49 [33, 65]	.14
ICU LOS days	33 [19, 45]	33 [16, 43]	36 [19, 46]	.43
ICU Outcome				.46
Deceased n(%)	50 (40)	32 (43)	18 (35)	
Discharged n(%)	75 (60)	42 (57)	33 (64)	

Acronyms: ICU: intensive care unit; iNO: inhaled nitric oxide; LOS: length of stay.

Table S8. Quantitative CT characteristics dividing the population based on the ARDS severity

Variables	Total (N = 124)	Moderate (N = 65)	Severe (N = 59)	p-value
Bilateral Lung				
Volume, ml	3514 ±1005	3470 ±952	3563 ±1066	.61
Density, HU	-544 ±106	-551 ±104	-537 ±108	.46
Tissue mass, g	1542 ±391	1502 ±380	1586 ±402	.23
Hyper inflated lung				
Volume, ml	159 ±157	171 ±178	145 ±130	.36
Density, HU	-968 ±2	-968 ±2	-968 ±3	.46
Tissue mass, g	5 ±5	5 ±5	4 ±4	.38
Well aerated lung				
Volume, ml	2079 ±887	2054 ±861	2106 ±921	.75
Density, HU	-740 ±31	-741 ±32	-738 ±30	.64
Tissue mass, g	528 ±208	518 ±192	539 ±225	.57
Poorly aerated lung				
Volume, ml	892 ±324	878 ±310	907 ±342	.62
Density, HU	-343 ±20	-344 ±20	-342 ±20	.58
Tissue mass, g	585 ±211	576 ±204	596 ±219	.61
Non-aerated lung				
Volume, ml	320 ±193	305 ±191	337 ±195	.36
Density, HU	-51 ±8	-51 ±9	-50 ±6	.66
Tissue mass, g	305 ±185	291 ±184	321 ±186	.37

Acronyms: CT: computed tomography.

Supplementary Figures

Figure S1. Antero-posterior regional lung tissue distribution in intubated patients divided by the O₂ response to pronation.

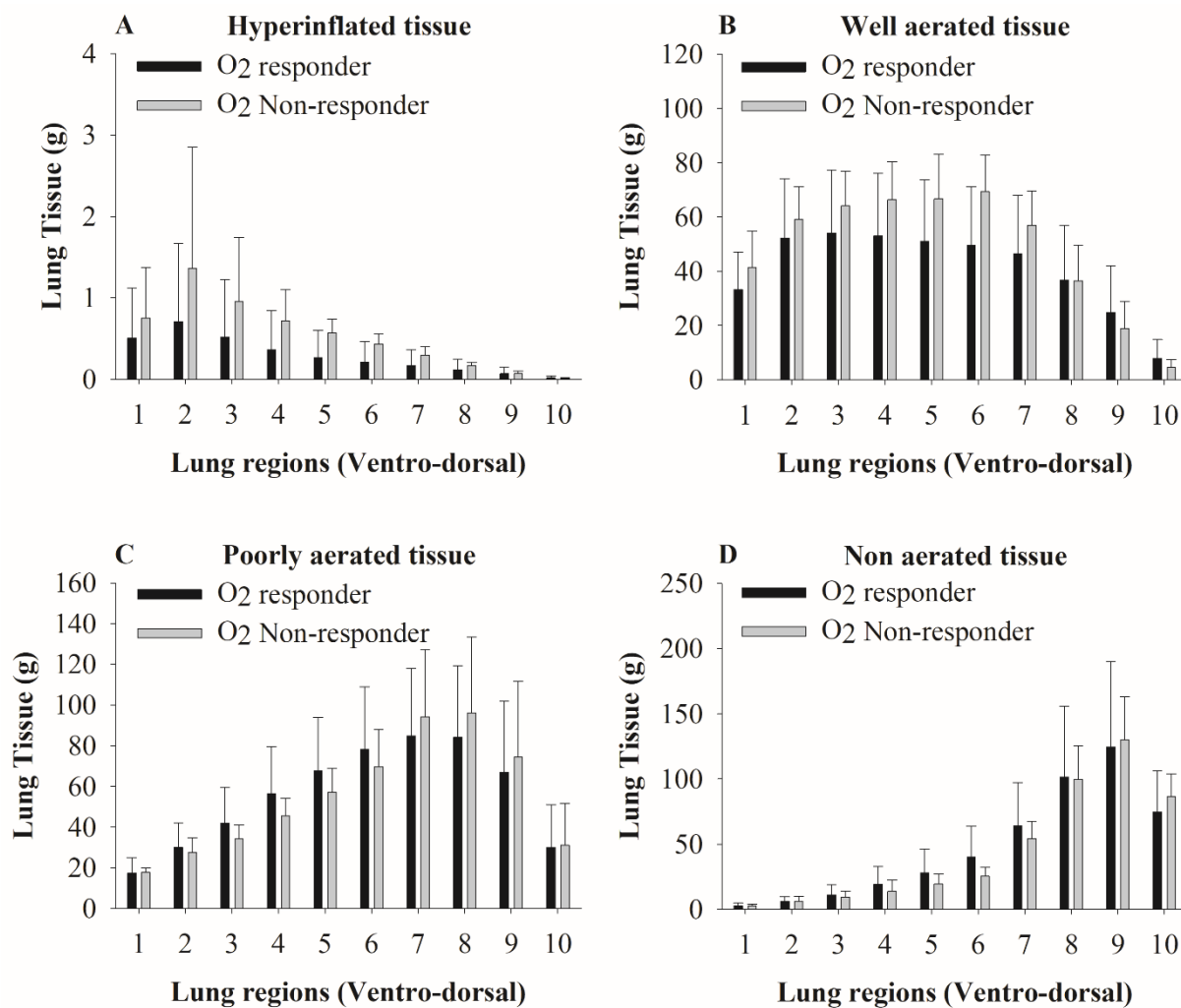


Figure S2. Antero-posterior regional lung tissue distribution in patients divided by the CO₂ response to pronation.

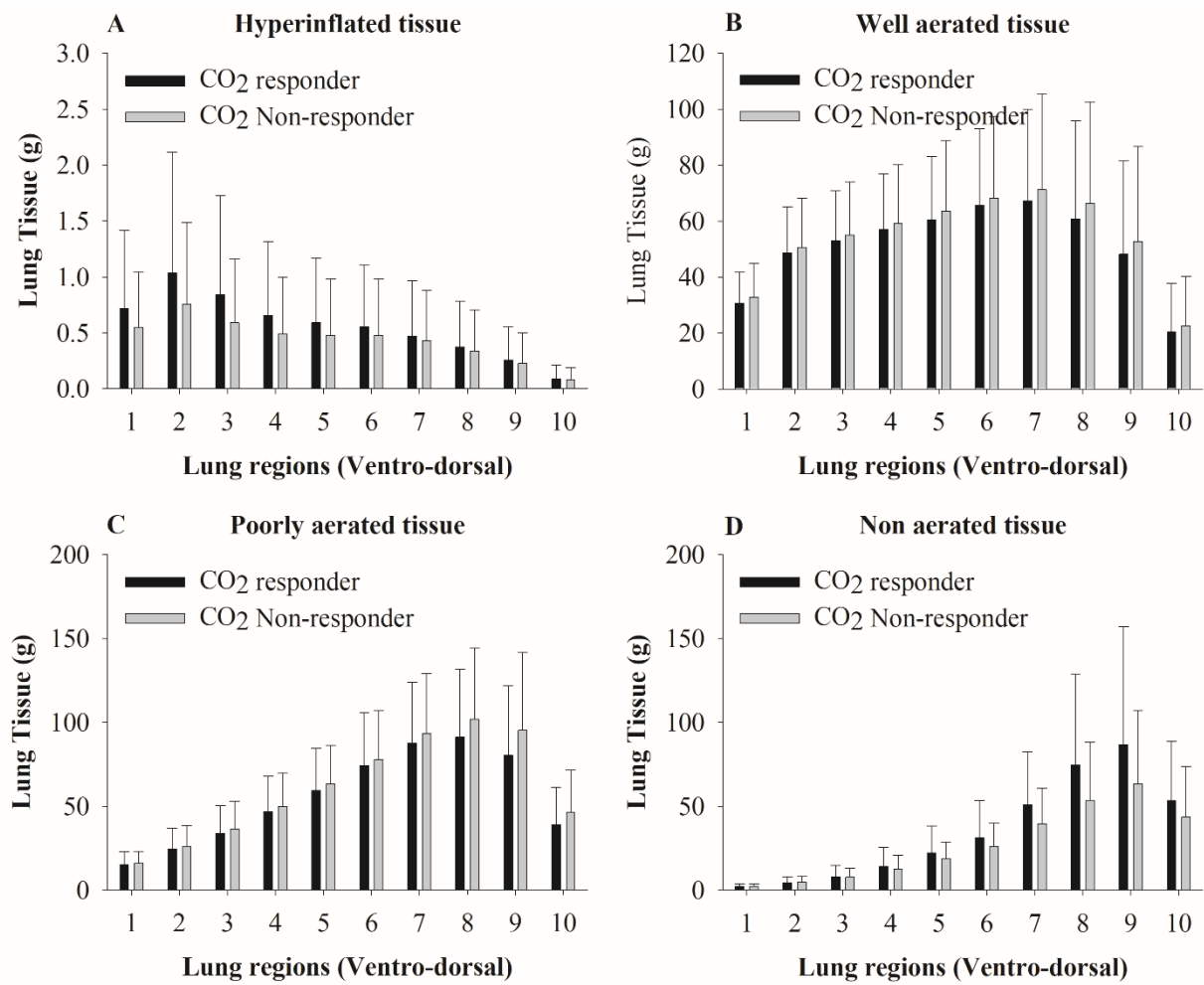


Figure S3. Association between the length of disease before pronation and response in PaO₂/FiO₂ ratio to pronation

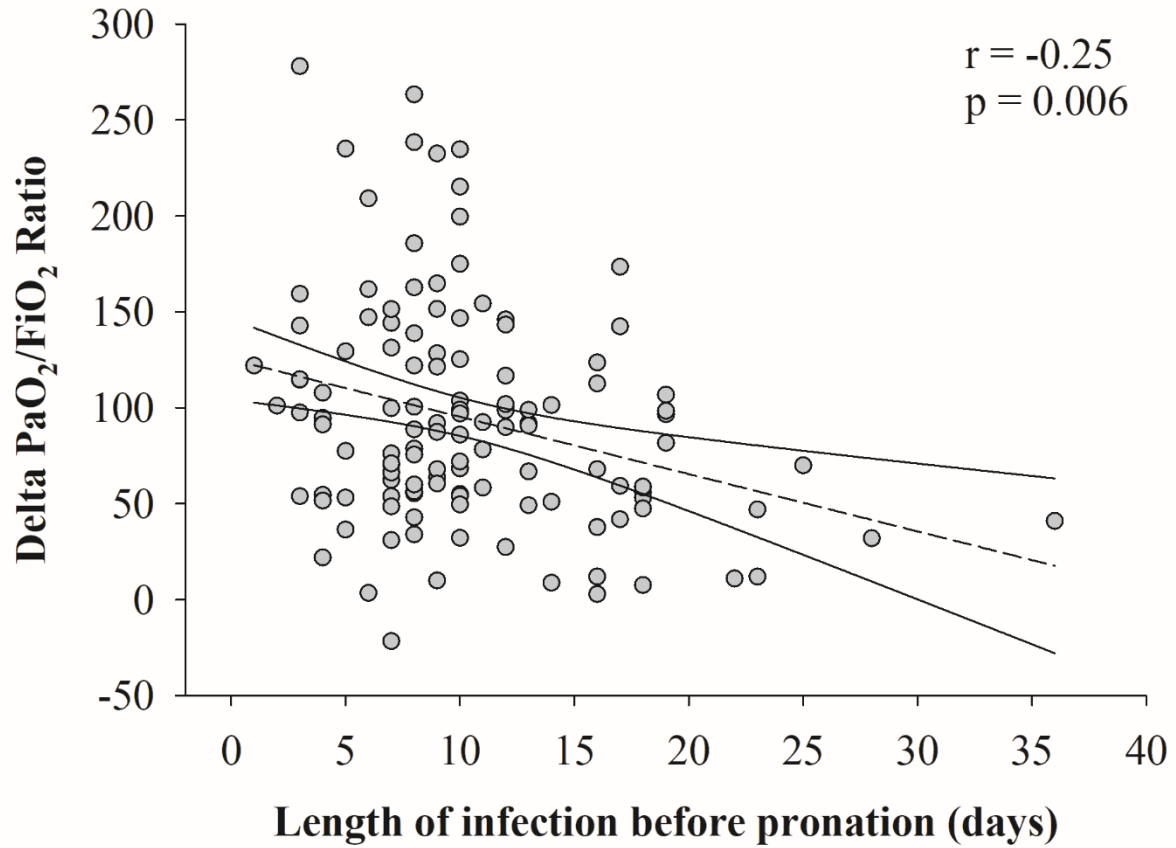


Figure S4. Association between the length of non-invasive ventilation before ICU pronation and response in PaO₂/FiO₂ ratio to pronation

