Physiological effects and subjective tolerability of prone positioning in COVID-19 pneumonia and healthy hypoxic challenge

Supplementary materials

Supplementary Table 1 Change in SpO_2 (all values) in different positions compared to baseline supine position in COVID-19 cohort

Supplementary Table 2 Change in SpO_2 (median value in each position for every individual) in different positions compared to baseline supine position in COVID-19 cohort

Supplementary Table 3 Change in SpO2 (all values) in different positions compared to baseline supine position in participants from the COVID-19 cohort who were in the prone position for at least 30 minutes.

Supplementary Table 4 Change in respiratory rate in different positions compared to baseline supine position in COVID-19 cohort

Supplementary Table 5 Change in heart rate in different positions compared to baseline supine position in COVID-19 cohort

Supplementary Table 6 Change in SpO2 in different positions compared to baseline supine position in hypoxic challenge cohort

Supplementary Table 7 Effect of selected clinical variables on SpO_2 in prone and supine positions in COVID-19 cohort

Supplementary Table 8 Patient reports and investigator observations of experience and factors that helped or hindered tolerability of prone position

Supplementary Figure 1 Dot plot and LOESS smooth curve of SpO_2 change across time at individual level

Supplementary Figure 2 Dot plot of mean SpO_2 in supine, prone and resupination position at individual level

Supplementary Figure 3 Effect of body position on respiratory rate

Supplementary Figure 4 Effect of body position on heart rate

Position	Estimate	Standard Error	p value
Supine	93.12	0.377	-
Lateral	+0.358	0.533	0.505
Prone	+1.62	0.533	0.0030
Resupination	-0.335	0.533	0.531

Supplementary Table 1 Change in SpO_2 (all values) in different positions compared to baseline supine position in COVID-19 cohort. This shows the effect of the four positions on the SpO_2 estimate compared to initial supine. All SpO_2 values recorded during the study are included in the model (n = 50719). *P*-values are calculated using two tailed t-tests and Satterthwaite's method to estimate the degrees of freedom.

Position	Estimate	Standard Error	p value
Supine	93.17	0.355	-
Lateral	+0.500	0.295	0.0943
Prone	+1.88	0.295	1.64×10^{-8}
Resupination	-0.292	0.295	0.3259

Supplementary Table 2 Change in SpO_2 (median value in each position for every individual) in different positions compared to baseline supine position in COVID-19 cohort. This shows the effect of the four positions on the SpO_2 estimate compared to initial supine. A single SpO_2 (median) in each position for every individual was taken as the outcome variable, resulting in 96 SpO_2 values included in the model. *P*-values are calculated using two tailed t-tests and Satterthwaite's method to estimate the degrees of freedom.

Position	Estimate	Standard Error	p value
Supine	93.51	0.381	-
Lateral	+0.045	0.539	0.933
Prone	+1.45	0.539	0.0096
Resupination	-0.358	0.539	0.510

Supplementary Table 3 Change in SpO_2 (all values) in different positions compared to baseline supine position in participants from the COVID-19 cohort who were in the prone position for at least 30 minutes (n = 16). This shows the effect of the four positions on the SpO_2 estimate compared to initial supine. All SpO_2 values recorded during the study are included in the model (n = 32061). *P*-values are calculated using two tailed t-tests and Satterthwaite's method to estimate the degrees of freedom.

Position	Estimate	Standard Error	p value
Supine	20.613	1.069	-
Lateral	+1.222	1.511	0.421
Prone	-1.2341	1.511	0.416
Resupination	+0.5147	1.511	0.734

Supplementary Table 4 Change in respiratory rate in different positions compared to baseline supine position in COVID-19 cohort. This shows the effect of the four positions on the respiratory rate estimate compared to initial supine. All respiratory rate values recorded during the study are included in the model (n = 42264). *P*-values are calculated using two tailed t-tests and Satterthwaite's method to estimate the degrees of freedom.

Position	Estimate	Standard Error	p value
Supine	79.149	2.287	-
Lateral	+0.148	3.234	0.964
Prone	+1.910	3.234	0.556
Resupination	+1.373	3.234	0.672

Supplementary Table 5 Change in heart rate in different positions compared to baseline supine position in COVID-19 cohort. This shows the effect of the four positions on the heart rate estimate compared to initial supine. All heart rate values recorded during the study are included in the model (n = 50718). *P*-values are calculated using two tailed t-tests and Satterthwaite's method to estimate the degrees of freedom.

Position	Estimate	Standard Error	p value
Supine	93.694	0.907	-
Lateral	-1.530	1.282	0.240
Prone	-2.467	1.282	0.0615
Resupination	-0.128	1.283	0.921

Supplementary Table 6 Change in SpO_2 in different positions compared to baseline supine position in hypoxic challenge cohort. This shows the effect of the four positions on the SpO_2 estimate compared to initial supine. *P*-values are calculated using two tailed t-tests and Satterthwaite's method to estimate the degrees of freedom.
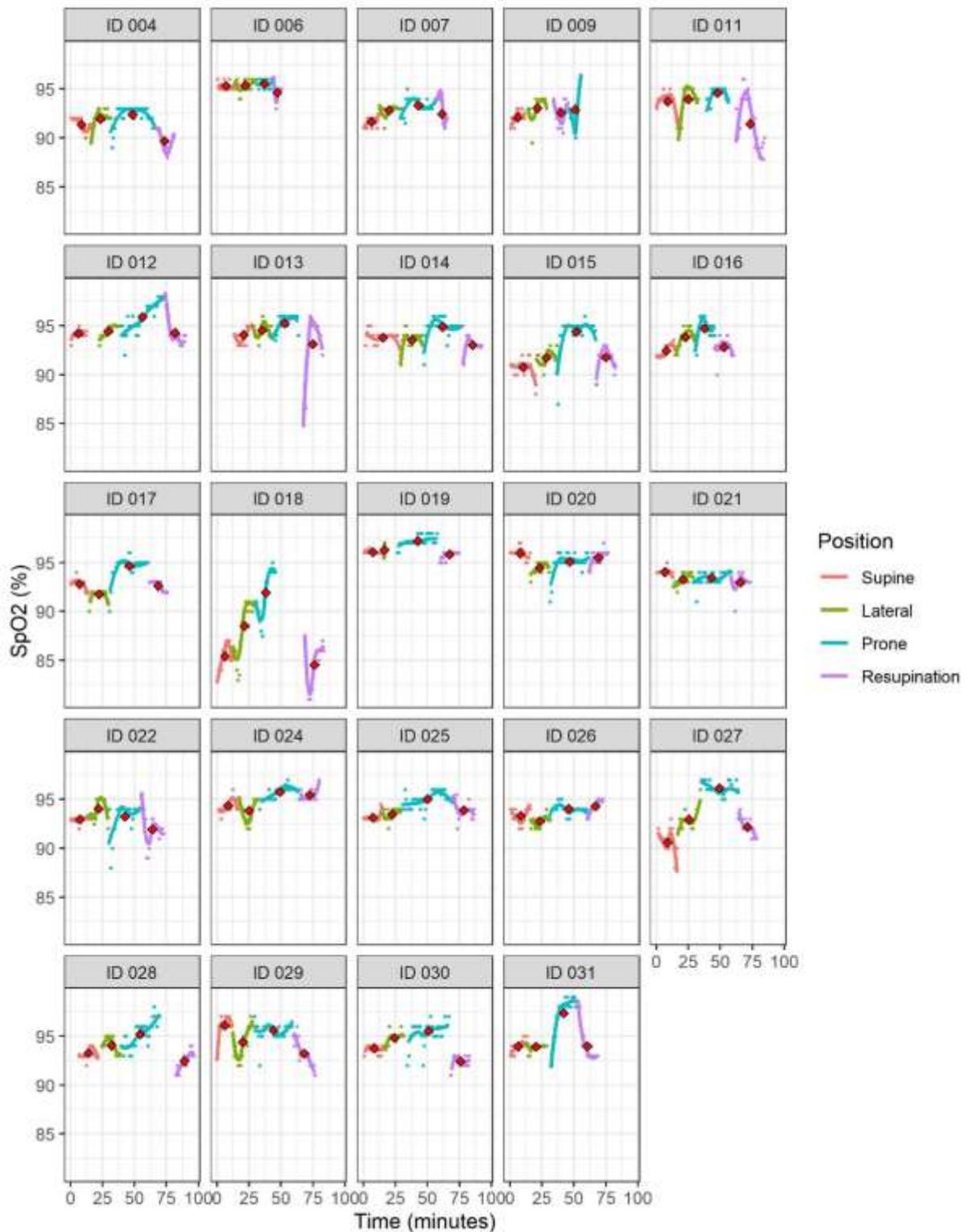
Term	Estimate	Standard error	p value
Age	-0.030	0.009	0.013
BMI	-0.067	0.044	0.156
Radiographic severity score	0.036	0.078	0.653
FiO$_2$	4.182	2.714	0.149
Duration in prone position	0.014	0.017	0.436
Baseline SpO$_2$	-0.228	0.061	0.003

Supplementary Table 7 Effect of selected clinical variables on the magnitude of SpO$_2$ change between prone and supine positions in COVID-19 cohort using linear modelling. *P*-values are calculated using two tailed t-tests.

Supplementary Table 8: Patient reports and investigator observations of experience and factors that helped or hindered tolerability of prone position

|	POSITIVE		NEGATIVE	
	Patient experience report	Investigator observation	Patient experience report	Investigator observation
Comfort	Eight patients found the position comfortable [14, 15, 18, 20, 21, 22, 28, 29]. For two of these it was less comfortable than supine and lateral but became easier over time [18, 20]. For one, it took effort to get into position but became more relaxing with time [14]. For five of these [14, 18, 20, 21, 29] plus one other [12] the position became easier over time. One noted it was how they were at home [28].	Four patients were calm and comfortable [14, 18, 19, 24]. For two it was a natural sleeping position [11,15].	Five said it was uncomfortable, not a position of choice [7, 9, 27, 30, 31] though one said they would do it if they had to [7]. For three of these [9, 27, 30] plus five others [10, 11, 16, 22, 26] it became more uncomfortable over time with patient [27] reporting discomfort in arms and neck and patient [9] burning energy holding themselves up. Patients [10] and [11] had shoulder pain. One became hot and uncomfortable on the face over time [26]. Patient [22] reported slightly more murmur and strain in heart. Patient [16] had to discontinue due to discomfort even though their breathing improved.	Four had difficulty moving into the position, moving was difficult and effortful [6, 19, 31, 28]. One was heavy and unable to support his own weight [31]. Three were unable to maintain the position [7, 9, 29]. Two had neck pain [6, 7]. One patient was less settled than previous position (Lateral) and needed to readjust position frequently at the beginning of proning[10]. One patient with high discomfort and breathlessness scores, couldn't get fully flat (arms raised to level of pillow made it appear upper body a bit raised from bed) [30].
Breathing	Three patients said it felt easier to breathe [12, 17, 19], for one because pressure on lungs was removed [19]. For three their breathing improved over time [12, 20, 29].	Patient [19]'s breathing improved.	Three found it more difficult to breathe [13, 24, 26]. One felt they had to work slightly harder [26] and another that breathing was difficult due to trying to lift own weight when breathing in [24]. For one there was no difference to breathing [10].	
Throat/coughing	One hadn't been coughing in this position [16].		One could not lie fully prone; the position made him cough [4]. For one it was harder to clear throat than when lateral [14]. One person got hotter, had a sore dry throat [13] and another's throat became sore over time [22].	
Devices			Three reported face hot and stuffy, nasal cannula digging in or not comfortable with mask on [10, 11, 16]. For one the devices became more uncomfortable over time [11].	
Other	One noted it was better for their heel [26].		One person needed to go to the toilet [13]. One said that they might struggle to go to the toilet [28]. Three reported that lying on their back was easier [13, 18, 19].	In one patient the position pressed on the bladder [13].

|	HELPED TOLERABILITY		HINDERED TOLERABILITY	
	Patient report	Investigator observation	Patient report	Investigator observation
Pillows for support	Pillows in the right places, e.g. to help neck [16, 26]. A doughnut pillow [10] or 'toilet seat' could help [9].	Pillows helped seven patients to be more comfortable: arms on pillow beside head [12], arms raised on pillow [29], arms under pillow [28], flat bed with pillow under face [10] and under head [17], head turned to left and pillow under right side of head [22], under chest and forehead [9].	Lack of support for head and shoulders. One reported neck pulling [7] and lack of design for the head - need shoulders supported so head is looking down and free [9]. Pillows on the face were uncomfortable [31].	
Body position	Raising arms or having them by the side [14, 24]. Raising arms takes pressure off the body weight pressing on chest [14].	One patient became comfortable after lifting arm above head while in a slight prone/left lateral position [24].	What to do with arms [26], hand being stuck under body [31]. 90kg, has whole body weight pushing down, almost as if need to do a press up to get up [28].	
Devices			Devices made it uncomfortable for five patients [4, 10, 11, 21, 26]: CO2 probe [4], nasal cannula [10, 11], tubes [21, 26].	Seven patients had problems with equipment and probes getting in the way [9,11,14,29] or falling out [12,19,24].
Bed	Flat bed [18]. Raising bed 15-20 degrees [24].	Incline of the bed was helpful at 10 degrees for one patient [19]. Two needed a flat bed [10, 20].		
Other	More comfortable with gown half off (as neck of gown was digging into neck) [14].	Patient talked less in this position which may have helped breathlessness [16].	Had just eaten [28]. Difficult to move bedding, had to kick blankets off [28].	In one patient talking raised the respiratory rate [7].
Summary	17 patient-reported problems [4, 7, 9, 10, 11, 13, 14, 16, 18, 19, 20, 24, 26, 27, 28, 30, 31]. Investigators noted 15 patients who had problems [6, 7, 9, 10, 11, 12, 13, 14, 19, 24, 27, 28, 29, 30, 31]. 15/25 patients reported some discomfort including discomfort in arms, neck and shoulders and becoming hot. For some it became more comfortable over time as they settled into it. 8/25 said they found the position comfortable. Some found it easier to breathe and some found it more difficult, some were more prone to coughing. Implications for practice to help make patients more comfortable: • Support with pillows for the head, neck and limbs could be helpful and a 'doughnut' pillow to avoid neck strain could help. • Raising the arms could help. • Devices getting in the way were a source of discomfort. • The angle of the bed was important for some and the preferred angle varied between individuals.			

Supplemental Figure 1 Dot plot and LOESS smooth curve of SpO₂ change across time at individual level. Colours indicate the position (supine, lateral, prone, resupination). The red diamond represents the mean SpO₂ for each position. The thirty SpO₂ readings within each minute are averaged and plotted. Subject 009 became tired in the lateral position and therefore needed to resupinate before attempting the prone position.
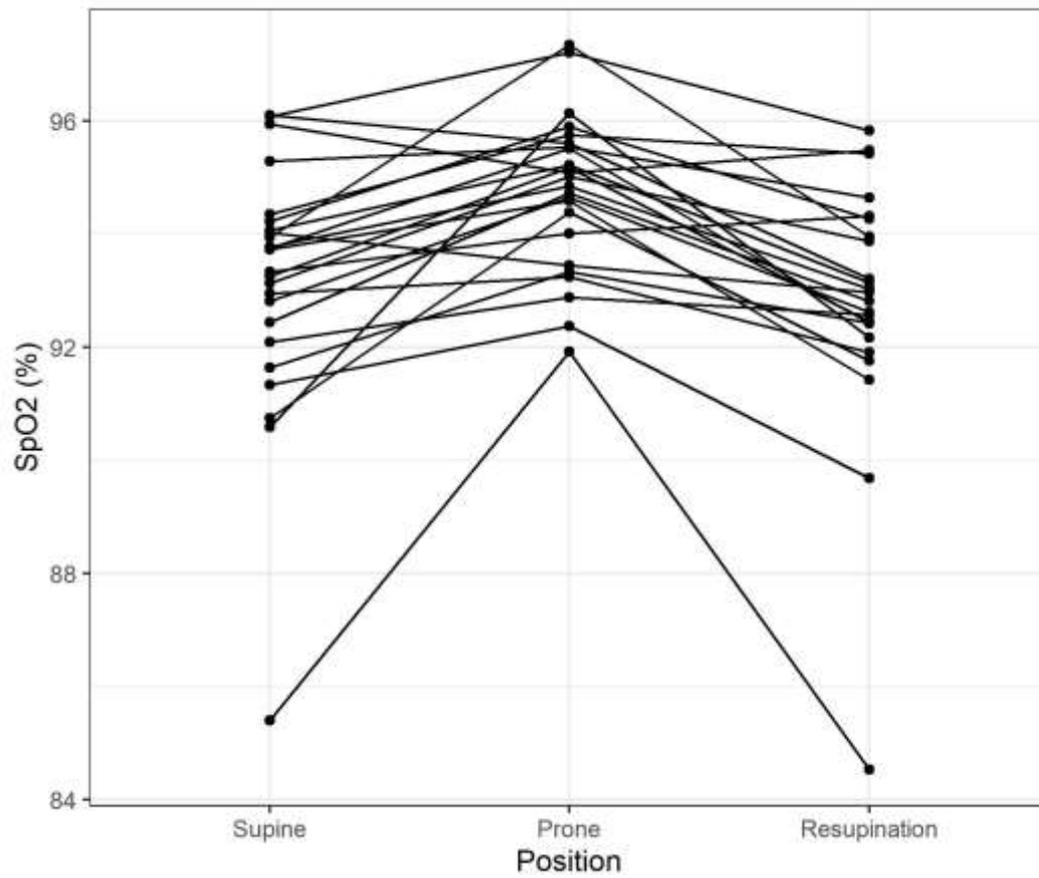
Supplementary Figure 2 Dot plot of mean SpO$_2$ in supine, prone and resupination position at individual level. Lines connect values from the same individual.
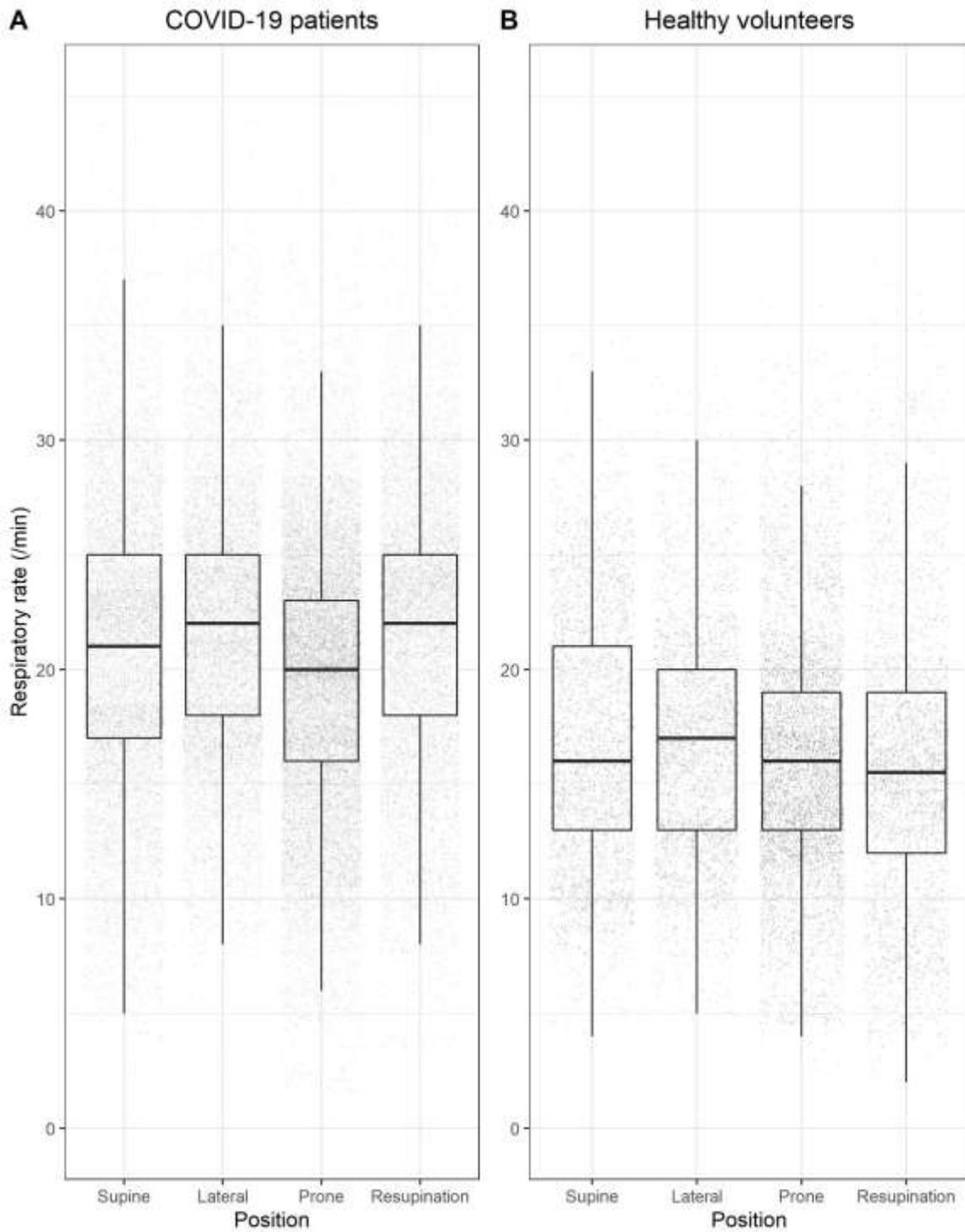
Supplementary Figure 3 Effect of body position on respiratory rate. Boxplots showing the respiratory rate measured in COVID-19 patients (A) and healthy volunteers (B) in the different positions. Boxes represent 25th percentile, median and 75th percentile. The lower and upper whiskers extend to 1.5 times the interquartile range from the 25th and 75th percentile respectively. The overlaid dot plots show each respiratory rate that was recorded every 2 seconds.
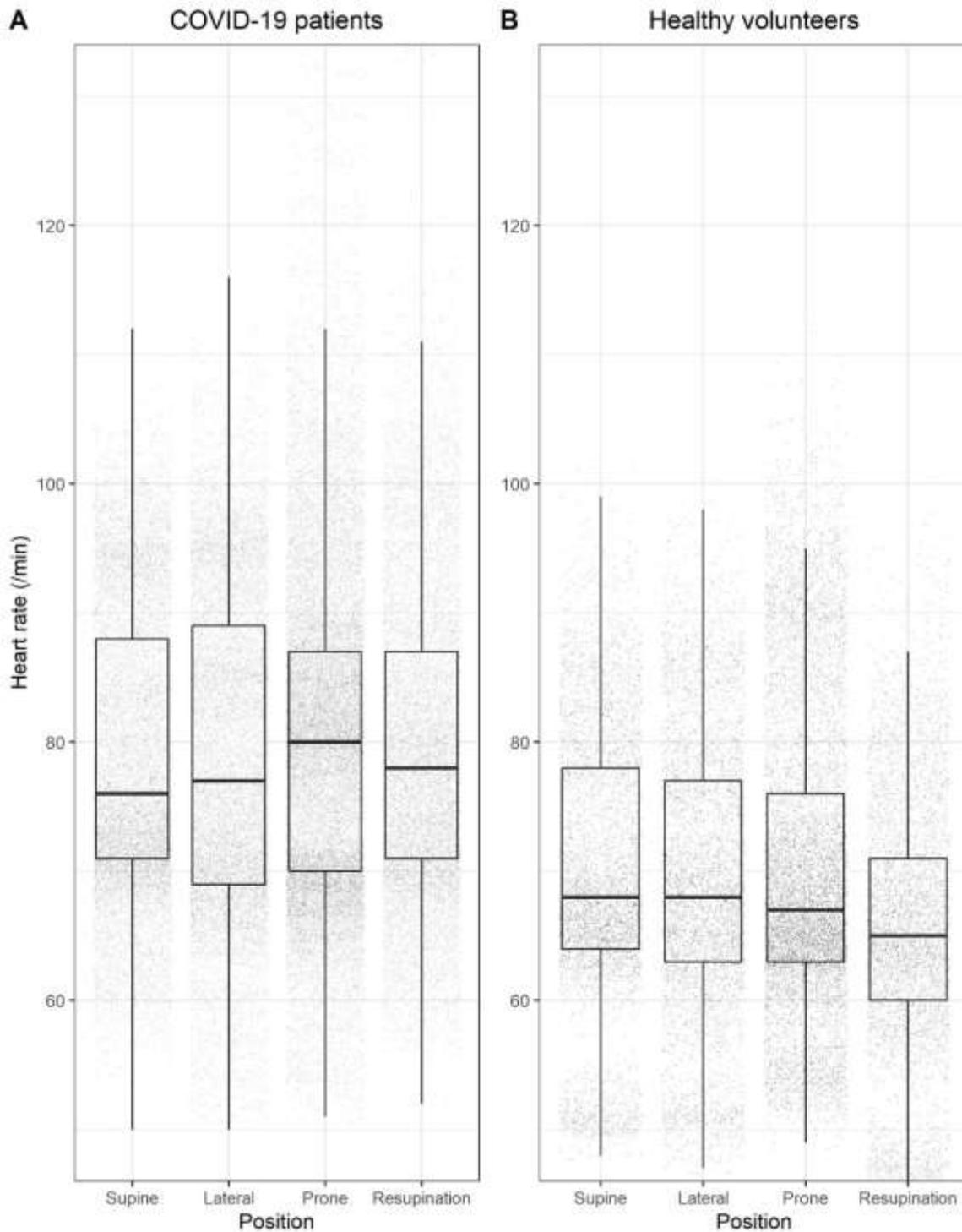
Supplementary Figure 4 Effect of body position on heart rate. Boxplots showing the heart rate measured in COVID-19 patients (A) and healthy volunteers (B) in different positions. Boxes represent 25th percentile, median and 75th percentile. The lower and upper whiskers extend to 1.5 times the interquartile range from the 25th and 75th percentile, respectively. The overlaid dot plots show each heart rate that was recorded every 2 seconds.