

## Supplemental material

### ***Successful versus failed transition from controlled ventilation to pressure support ventilation in COVID-19 patients: a retrospective cohort study.***

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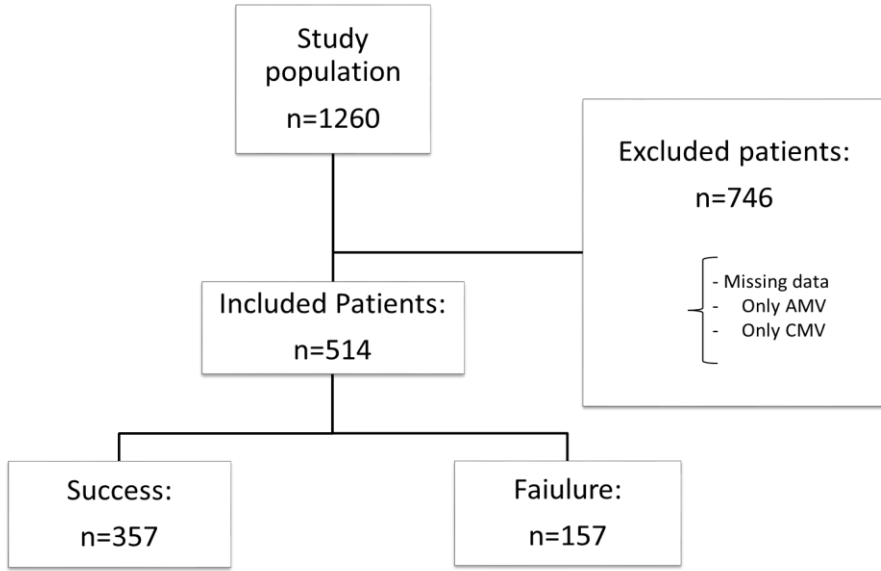
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### Data collection

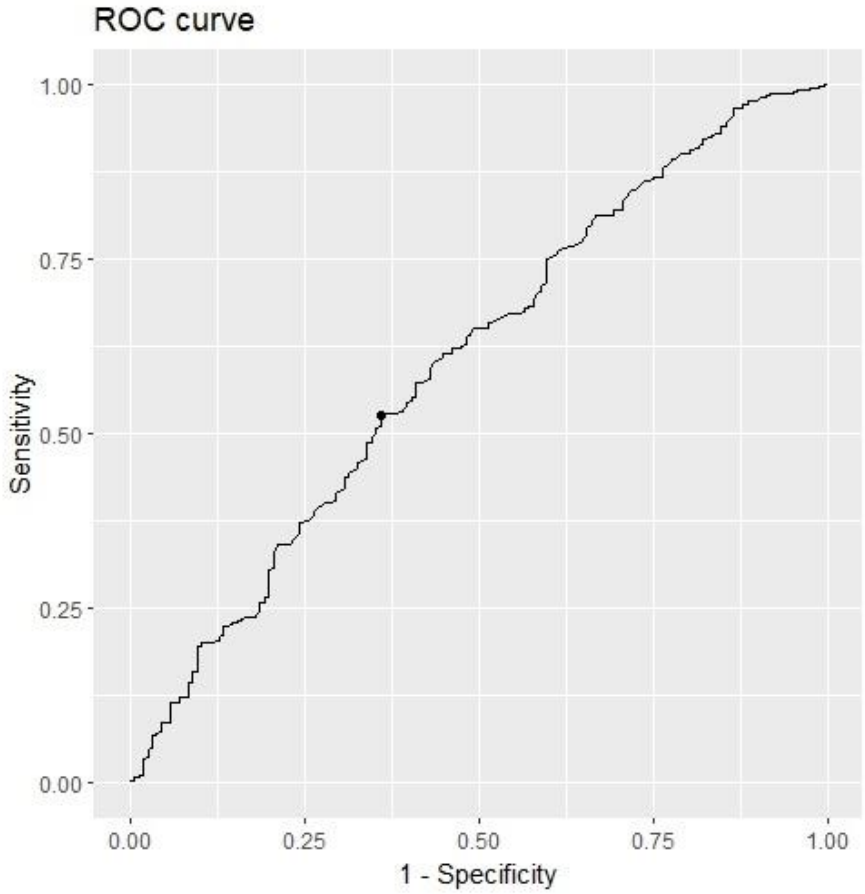
A COVID-19 retrospective/prospective multicentric registry included patient clinical data daily recorded on an electronic database (REDCap. Research Electronic Data Capture; Vanderbilt University. Nashville. TN. USA).

At the ICU admission, a trained investigator of each center collected demographical data (age, weight, height, body mass index (BMI), predicted body weight (Pbw), sex, comorbidities, SOFA Score, Acute Physiology, and Chronic Health Evaluation (APACHE) II score, SAPS Score, Charlson comorbidity index, clinical frailty scale), ventilation support or O<sub>2</sub> therapy before ICU admission, ventilator settings and respiratory parameters (mode of ventilation, fraction of inspired oxygen [FiO<sub>2</sub>], positive end-expiratory pressure [PEEP], respiratory rate, tidal volume, peak inspiratory pressure, plateau pressure, driving pressure, compliance of respiratory system [C<sub>RS</sub>], the arterial partial pressure of oxygen [PaO<sub>2</sub>], the arterial partial pressure of carbon dioxide [PaCO<sub>2</sub>], PaO<sub>2</sub>/FiO<sub>2</sub> ratio); prone positioning.

During the ICU stay, the investigators collected daily: the mode of respiratory support (oxygen mask, non-invasive mechanical ventilation, invasive mechanical ventilation); ventilator settings and respiratory parameters; medications; prone positioning. To describe the clinical course of the subject included in the analysis, we considered the following clinical outcomes: ICU mortality, ICU length of stay, duration of mechanical ventilation, defined as the number of days between intubation and extubation or death, and probability of breathing without assistance, defined as the time until the patient was found to be free from any respiratory support.



**Figure 1** Study population



**Figure 2** ROC curve representing the  $\text{PaO}_2/\text{FiO}_2$  ratio in determining the successful transition to PSV. Area Under the Curve = 0.604, optimal cut-off point at  $\text{PaO}_2/\text{FiO}_2$  ratio = 186.5 mmHg.

	<b>Global n = 514</b>	<b>Success n = 357</b>	<b>Failure n = 157</b>	<b>p value</b>
<b>Paralysis (%)</b>	39.9 (200/501)	40.8 (141/346)	38.1(59/155)	0.570
<b>Neuromuscular blockade (days)</b>	5 ± 5	5 ± 4	5 ± 5	0.466
<b>Length of controlled ventilation (days)</b>	7 ± 6	7 ± 6	7 ± 6	0.803
<b>Tracheostomy (%)</b>	<b>36.2 (181/500)</b>	<b>29.8 (103/346)</b>	<b>50.6 (78/154)</b>	<b>&lt; 0.001</b>
<b>Prone Position (days)</b>	2 ± 2	2 ± 2	2± 2	0.628
<b>Ventilatory parameters</b>				
<b>Respiratory Rate (breaths/min)</b>	20 ± 4	20 ± 4	20 ± 4	0.729
<b>TV/PBW (ml/kg)</b>	7.1± 1.3	7.1± 1.3	7.0 ± 1.3	0.848
<b>PEEP (cmH<sub>2</sub>O)</b>	11.5 ± 2.6	11.5 ± 2.5	11.5 ± 2.7	0.944
<b>FiO<sub>2</sub> (%)</b>	<b>52± 13 (512)</b>	<b>51 ± 12 (355)</b>	<b>55 ± 14 (157)</b>	<b>0.010</b>
<b>Compliance Respiratory System (mL/cmH<sub>2</sub>O)</b>	44 ± 14	44 ± 14	43± 15	0.527
<b>Plateau Pressure (cmH<sub>2</sub>O)</b>	22.9± 3.1	22.7 ± 3.0	23.4 ± 3.2	0.074
<b>Driving Pressure (cmH<sub>2</sub>O)</b>	<b>11.0± 2.6</b>	<b>10.7± 2.8</b>	<b>11.6 ± 3.1</b>	<b>0.015</b>
<b>PaO<sub>2</sub>/FiO<sub>2</sub> ratio (mmHg)</b>	<b>193 ± 64</b>	<b>200 ± 64</b>	<b>177 ± 63</b>	<b>&lt; 0.001</b>
<b>pH</b>	<b>7.42 ± 0.06</b>	<b>7.42 ± 0.05</b>	<b>7.41 ± 0.07</b>	<b>0.010</b>
<b>PaCO<sub>2</sub> (mmHg)</b>	50 ± 10	49 ± 10	51 ± 11	0.088
<b>Ventilatory ratio * (mL*mmHg/min*kg)</b>	1.81 ± 0.63	1.79 ± 0.55	1.84 ± 0.62	0.490
<b>Minute Ventilation (L/min)</b>	9.3 ± 2.4	9.2 ± 2.4	9.5 ±2.5	0.277

**Supplements Table 1.** Ventilator settings and respiratory mechanics and blood gas parameters before switching from CMV to PSV

<b>Ventilator settings and respiratory mechanics before switching for patients with early transition from CMV to PSV (<math>\leq 7</math> days)</b>				
<b>Variables</b>	<b>Global (n=)</b>	<b>Success (n=)</b>	<b>Failure (n=)</b>	<b>p value</b>
<b>Respiratory Rate (respirations/ min)</b>	20 $\pm$ 4 (321)	20 $\pm$ 4 (222)	20.16 $\pm$ 3.57 (99)	0.989
<b>FiO<sub>2</sub> (%)</b>	<b>52 <math>\pm</math> 13 (322)</b>	<b>51 <math>\pm</math> 13 (223)</b>	<b>54 <math>\pm</math> 15 (99)</b>	<b>0.045*</b>
<b>SpO<sub>2</sub> (%)</b>	<b>97 [95;98]</b>	<b>97 [96; 99]</b>	<b>97 [95; 98]</b>	<b>0.013*</b>
<b>PEEP (cmH<sub>2</sub>O)</b>	11.4 $\pm$ 2.4(322)	11.3 $\pm$ 2.4 (223)	11.6 $\pm$ 2.5 (99)	0.307
<b>PaO<sub>2</sub>/FiO<sub>2</sub> ratio (mmHg)</b>	<b>200 <math>\pm</math> 68 (322)</b>	<b>201 <math>\pm</math> 66 (223)</b>	<b>184 <math>\pm</math> 69 (99)</b>	<b>0.004*</b>
<b>Tidal Volume (mL)</b>	458 $\pm$ 71(245)	452 $\pm$ 67 (164)	469 $\pm$ 77 (81)	0.094
<b>TV/PBW (ml/kg)</b>	7.0 $\pm$ 1.0 (228)	7.0 $\pm$ 1.0 (153)	7.0 $\pm$ 1.0 (75)	0.816
<b>Peak Pressure (cmH<sub>2</sub>O)</b>	26.5 $\pm$ 5.0(88)	26.5 $\pm$ 5.3 (58)	26.5 $\pm$ 4.4 (30)	0.999
<b>Plateau Pressure (cmH<sub>2</sub>O)</b>	<b>22.4 <math>\pm</math> 2.9(175)</b>	<b>22.0 <math>\pm</math> 2.9 (115)</b>	<b>23.1 <math>\pm</math> 2.7 (60)</b>	<b>0.019*</b>
<b>Driving Pressure (cmH<sub>2</sub>O)</b>	10.5 $\pm$ 2.8(175)	10.2 $\pm$ 2.6 (115)	11.1 $\pm$ 3.1 (60)	0.047
<b>Compliance Respiratory System (mL/cmH<sub>2</sub>O)</b>	46 $\pm$ 15 (174)	46 $\pm$ 14 (114)	45 $\pm$ 16 (60)	0.714
<b>EtCO<sub>2</sub> (mmHg)</b>	38.8 $\pm$ 7.7 (78)	39.3 $\pm$ 7.9 (59)	37.2 $\pm$ 6.9 (19)	0.286
<b>pH</b>	<b>7.41 <math>\pm</math> 0.06(319)</b>	<b>7.42<math>\pm</math> 0.05 (220)</b>	<b>7.40 <math>\pm</math> 0.08 (99)</b>	<b>0.017*</b>
<b>PaO<sub>2</sub> (mmHg)</b>	98 $\pm$ 36(322)	100 $\pm$ 33 (223)	94 $\pm$ 40 (99)	0.192
<b>PaCO<sub>2</sub> (mmHg)</b>	49 $\pm$ 10 (320)	48 $\pm$ 9 (221)	50 $\pm$ 11 (99)	0.280
<b>Ventilatory ratio * (mL*mmHg/min*kg)</b>	1.75 $\pm$ 0.49(222)	1.75 $\pm$ 0.49 (149)	1.75 $\pm$ 0.51 (73)	0.961
<b>Minute Ventilation (L/min)</b>	9.1 $\pm$ 2.0 (243)	9.1 $\pm$ 2.1 (162)	9.1 $\pm$ 2.0 (81)	0.748
<b>Dead Volume (%)</b>	22.7 $\pm$ 11.9(67)	23.6 $\pm$ 13.0 (49)	20.3 $\pm$ 8.3 (18)	0.328

**Supplements Table 2.** Ventilator settings and respiratory mechanics before switching for patients with early transition from CMV to PSV ( $\leq 7$  days)

<b>Ventilator settings and respiratory mechanics before switching for patients with late transition from CMV to PSV (&gt; 7 days)</b>				
<b>Variables</b>	<b>Global (n=)</b>	<b>Success (n=)</b>	<b>Failure (n=)</b>	<b>p value</b>
<b>Respiratory Rate (respirations/ min)</b>	20 ± 5 (189)	20 ± 5 (132)	21 ± 5 (57)	0.634
<b>FiO<sub>2</sub> (%)</b>	53 ± 12 (190)	52 ± 12 (132)	55 ± 13 (58)	0.107
<b>SatO<sub>2</sub> (%)</b>	97 [95; 98]	97 [96; 98]	97 [95; 98]	0.057
<b>PEEP (cmH<sub>2</sub>O)</b>	11.7 ±2.8(190)	11.8 ± 2.7 (132)	11.3 ± 3.1 (58)	0.305
<b>PaO<sub>2</sub>/FiO<sub>2</sub> ratio (mmHg)</b>	<b>181 ±56 (189)</b>	<b>187 ± 58 (131)</b>	<b>166 ± 51 (58)</b>	<b>0.016*</b>
<b>Tidal Volume (mL)</b>	474 ±110(160)	471 ± 111 (113)	481 ± 109 (47)	0.589
<b>TV/PBW (ml/kg)</b>	7.1 ±1.7 (147)	7.2 ± 1.6 (106)	7.0 ± 1.2 (41)	0.717
<b>Peak Pressure (cmH<sub>2</sub>O)</b>	26.3 ±4.8(45)	26.7 ± 3.8 (34)	25.2 ± 7.1(11)	0.358
<b>Plateau Pressure (cmH<sub>2</sub>O)</b>	23.9 ±3.3(100)	23.8 ± 3.0 (68)	24.0 ± 3.9 (32)	0.794
<b>Driving Pressure (cmH<sub>2</sub>O)</b>	11.9 ±3.0(100)	11.6 ± 3.0 (68)	12.6 ± 3.0 (32)	0.098
<b>Compliance Respiratory System (mL/cmH<sub>2</sub>O)</b>	40 ± 13(97)	40 ± 14 (66)	38 ± 12 (31)	0.452
<b>EtCO<sub>2</sub> (mmHg)</b>	39.04 ± 9.95(58)	39.69 ± 10.47 (43)	37.20 ± 8.32 (15)	0.409
<b>pH</b>	7.43 ± 0.05(186)	7.43 ± 0.05 (129)	7.42 ± 0.05 (57)	0.309
<b>PaO<sub>2</sub> (mmHg)</b>	92 ± 24 (189)	94 ± 26 (131)	87 ± 19 (58)	0.061
<b>PaCO<sub>2</sub> (mmHg)</b>	51 ± 11(186)	50 ± 11 (129)	53 ± 12 (57)	0.169
<b>Ventilatory ratio * (mL*mmHg/min*kg)</b>	1.92 ± 0.79(144)	1.90 ± 0.78 (103)	1.96 ± 0.83 (41)	0.689
<b>Minute Ventilation (L/min)</b>	9.6 ± 2.9(159)	9.4 ± 2.8 (113)	10.1 ± 3.0 (46)	0.181
<b>Dead Volume (%)</b>	23.98 ± 13.53(50)	23.07 14.53 (37)	26.56 10.23 (13)	0.428

**Supplements Table 3.** Ventilator settings and respiratory mechanics before switching for patients with late transition from CMV to PSV (> 7 days)



Models for PaO<sub>2</sub>/FiO<sub>2</sub>, PaCO<sub>2</sub>, Peak inspiratory pressure, and Plateau pressure

Linear mixed model fit by maximum likelihood . t-tests use Satterthwaite's method

Formula: PaO<sub>2</sub>/FiO<sub>2</sub> ~ group \* time + (1 | id)

	Estimate	Std. Error	df	t-value	Pr(> t )	
(Intercept)	204.2886	2.738	519.11	74.613	< 2e-16	***
groupFailure	-30.7296	4.9353	514.9661	-6.227	9.90E-10	***
days	3.2509	0.7207	2397.38	4.511	6.77E-06	***
groupFailure:days	-5.6739	1.2805	2383.729	-4.431	9.80E-06	***

Significance codes: 0 = \*\*\*; 0.001 = \*\*; 0.01 = \*; 0.05 = .

Linear mixed model fit by maximum likelihood . t-tests use Satterthwaite's method

Formula: PaCO<sub>2</sub> ~ group \* time + (1 | id)

	Estimate	Std. Error	df	t value	Pr(> t )	
(Intercept)	47.2791	0.4106	524.4732	115.139	< 2e-16	***
groupFailure	3.5155	0.7397	518.88	4.752	2.61E-06	***
days	-1.1493	0.1035	2374.508	-11.099	< 2e-16	***
groupFailure:days	1.5148	0.1831	2360.06	8.274	< 2e-16	***

Significance codes: 0 = \*\*\*; 0.001 = \*\*; 0.01 = \*; 0.05 = .

Linear mixed model fit by maximum likelihood . t-tests use Satterthwaite's method

Formula: Peak\_pressure ~ group \* time + (1 | id)

	Estimate	Std. Error	df	t value	Pr(> t )	
(Intercept)	22.73434	0.21845	537.2561	104.069	< 2e-16	***
groupFailure	1.8102	0.40679	580.3732	4.45	1.03E-05	***
days	-1.42642	0.07882	1217.526	-18.096	< 2e-16	***
groupFailure:days	1.28276	0.15539	1184.792	8.255	4.01E-16	***

Significance codes: 0 = \*\*\*; 0.001 = \*\*; 0.01 = \*; 0.05 = .

Linear mixed model fit by maximum likelihood . t-tests use Satterthwaite's method

Formula: Plateau\_pressure ~ group \* time + (1 | id)

	Estimate	Std. Error	df	t value	Pr(> t )	
(Intercept)	22.22394	0.20734	319.7353	107.188	< 2e-16	***
groupFailure	1.41668	0.34579	279.8646	4.097	5.49E-05	***
days	-0.29792	0.07417	659.0935	-4.017	6.58E-05	***
groupFailure:days	0.28184	0.10567	622.0385	2.667	0.00785	**

Significance codes: 0 = \*\*\*; 0.001 = \*\*; 0.01 = \*; 0.05 = .

Adjusted model for ICU survival

coxph(formula = Surv(ICU\_LOS, ICU\_Outcome) ~ group + age + Charlson + SAPS + APACHE + pH)  
n= 503, number of events= 108 (11 observations deleted due to missingness)

	coef	exp(coef)	se(coef)	z	Pr(> z )	
group	0.65745	1.92986	0.19472	3.376	0.000735	***
age	0.04819	1.04937	0.01585	3.041	0.002356	**
charlson_tot	0.09935	1.10445	0.07456	1.333	0.182688	
saps_tot	0.01408	1.01418	0.01209	1.165	0.244123	
apache_tot	0.00933	1.00937	0.02693	0.346	0.728987	
ph_100	-0.0182	0.98196	0.01059	-1.719	0.085635	.

Significance codes: 0 = \*\*\*, 0.001 = \*\*, 0.01 = \*, 0.05 = .