

Non-invasive ventilation for SARS-COV2 related acute respiratory failure: a sub-analysis from the HOPE COVID-19 registry

SUPPLEMENTAL MATERIAL

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	Overall population (1933)	Oxygen only (1437)	NIV w/wo intubation (390)	Invasive ventilation (106)	p-value
Demographic data and baseline characteristics					
Age, year median (IQR)	71 (58-80) n=1928	71 (58-81) n=1435	70 (58-79) n=390	67 (57-73) n=102	0.18
Female sex n (%)	703 (36.4)	538 (37.4%)	133 (34.1)	32 (30.2)	0.19
Obesity n (%)	365/1429 (25.5)	263/1067 (24.6)	70/273 (25.6)	32/89 (36)	0.06
Hypertension n (%)	1070/1924 (55.6)	784/1435 (56.4)	222/383 (58.0)	64 (60.4%)	0.3
Dyslipidemia n (%)	757/1911 (39.6)	574/1425 (40.3)	141/380 (37.1)	42 (39.6)	0.53
Current or previous Smoker n (%)	471/1721 (27.4)	330/1286 (25.7) *	113/338 (33.4) *	28/97 (28.9)	0.02
DM n (%)	389/1831 (21.2)	292/1378 (21.2)	70/354 (19.8)	27/99 (27.3)	0.27
Prior stroke n (%)	188/1867 (10.1)	142/1402 (10.1)	41/361 (11.4)	5/104 (4.8%)	0.15
Heart disease, any n (%)	548 (28.3)	407 (28.3)	113 (29)	28 (26.4)	0.87
Lung Disease, any n (%)	428 (22.1)	318 (22.1)	85/390 (21.8)	25 (23.6)	0.93
Asma n (%)	97 (5)	73 (5.1)	18 (4.6)	6 (5.7)	0.98
COPD n (%)	172 (8.9)	124 (8.6)	37 (9.5)	11 (10.4)	0.75
Restrictive n (%)	21 (1)	15 (1)	5 (1.3)	1(0.9)	0.98
Liver disease n (%)	64/1842 (3.5)	44/1391 (3.2)	16/347 (4.6)	4/104 (3.8)	0.41
Chronic kidney disease CL<30 n (%)	154/1833 (8.4)	109/1378 (7.9)	31/352 (8.8)	14/103 (13.6)	0.13
Cancer history n (%)	280/1866 (15)	207/1397 (14.8)	62/366 (16.9)	11/103 (10.7)	0.27
Connective disease n (%)	67/1867 (3.6)	48/1402 (3.4)	17/361 (4.7)	2/104 1.9)	0.32
Any immunosuppressive condition n (%)	145/1707 (8.5)	102/1290 (7.9)	32/320 (10.0)	11/97 (11.3)	0.28
Prior therapies					

Anticoagulation n (%)	267/1885 (14.2)	192/1411 (13.6)	61/370 (16.5)	14/104 (13.5)	0.36
Antiplatelet n (%)	349/1894 (18.4)	254/1417 (17.9)	73/372 (19.6)	22/105 (21)	0.6
ACEI/ARB n (%)	765/1907 (40.1)	554/1418 (39.1)	158/383 (41.3)	53 (50)	0.08
Beta-blockers n (%)	392/1889 (20.8)	289/1419 (20.4)	82/365 (22.5)	21/105 (20)	0.67
Beta-2 agonists n (%)	241/1884 (12.8)	170/1413 (12)	59/368 (16)	12/103 (11.7)	0.12
Inhaled Corticosteroids n (%)	207/1889 (11)	150/1417 (10.6)	41/367 (11.2)	16/105 (15.2)	0.34
Home Oxygen therapy n (%)	87/1909 (4.6)	6/14242 (4.3)	20/381 (5.2)	5/104 (4.8)	0.75
Antidepressant n (%)	276/1886 (14.6)	213/1410 (15.1)	55/371 (14.8)	8/105 (7.6)	0.11
Clinical presentation					
Fever n (%)	1600/1912 (83.7)	1182/1426 (82.9)	325/380 (85.5)	93 (87.7)	0.24
Dyspnea, any entity n (%)	1204/1889 (63.7)	856/1410 (60.7) *	259/374 (66.4) *	89/105 (84.8) *	<0.001
Tachypnea n (%)	609/1814 (33.6)	404/1356 (29.8) *	143/354 (40.4) *	62/104 (59.6) *	<0.001
O2 saturation < 92% n (%)	851/1876 (45.4)	584/1399 (41.7) *	189/373 (50.7) *	78/104 (75) *	<0.001
Diarrhea n (%)	342/1811 (18.9)	269/1362 (19.8)	52/350 (14.9)	21/99 (21.2)	0.09
Vomiting n (%)	140/1811 (7.7)	11/1355 (8.2)	23/356 (6.5)	6/100 (6)	0.44
Hypo/anosmia n (%)	99/1724 (5.7)	68/1285 (5.3) *	17/343 (5.0) °	14/96 (14.6) *°	0.001
Dysgeusia n (%)	118/1723 (6.8)	81/1286 (6.3) °	23/342 (6.7) *	14/95 (14.7) *°	0.007
Cough n (%)	1336/1891 (70.7)	999/1412 (10.8)	254/375 (67.7)	83/104 (79.8)	0.06
Max temperature at presentation (°C) median(IQR)	37,7 (36.8-38.5) n=930	37.6 (36.8-38.5) * n=705	37.7 (36.9-38.4) ° n = 180	38.2 (37.6-38.6) *° n=45	0.002
Blood pressure abnormality n (%)	166/1909 (8.7)	107/1420 (7.5) *	43/383 (11.2)	16 (15.1) *	0.004

Table S1. Overall HOPE REGISTRY population baseline characteristics according to ventilation and oxygen support type. ACEi: Angiotensin converting enzymes inhibitors, ARB: angiotensin receptor blocker, DM: diabetes mellitus, COPD: chronic obstructive pulmonary disease.

* and ° mark the groups with a statistically significant difference

	Overall population (1933)	Oxygen only (1437)	NIV w/wo intubation (390)	Invasive ventilation (106)	p-value
<i>Laboratory data</i>					
Leucocytes, 10⁹/L median (IQR)	6.2 (4.7-8.7) n=1883	6.1(4.5-8.5) * n=1405	6.5 (5-9.3) ° n=376	7.3 (5.3-12) *° n=102	0.02
Lymphocytopenia (<1.5 10⁹/L) n (%)	1472/1824 (80.7)	1107/1366 (81)	292/358 (81.6)	74/100 (74)	0.22
Thrombocytopenia (<150k) n (%)	544/1877 (29)	414/1401 (29.6)	98/372 (26.3)	32/104 (30.8)	0.44
Anemia at presentation n (%)	485/1868 (26)	339/1393 (24.3) *	116/373 (31.1) *	30/102 (29.4)	0.022
Creatinine (mg/dl) median (IQR)	0.95 (0.75-1.24) n=1592	0.94 (0.75-1.21) * n=1198	0.96 (0.75-1.35) n=315	1.08 (0.8-1.6) * n=79	0.01
High levels of D-dimer n (%)	1167/1641 (71.1)	847/1217 (69.6) *	245/335 (73.1)	75/89 (84.3) *	0.009
High levels of troponin n (%)	180/918 (19.6)	86/602 (14.3) *°	66/243 (27.2) *	28/73 (38.4) °	<0.001
High transaminase level n (%)	849/1756 (48.3)	603/1315 (45.9) *	176/343 (51.3) °	70/98 (71.4) *°	<0.001
High levels of LDH n (%)	1403/1724 (81.4)	1028/1283 (80.1)	300/355 (84.5)	75/86 (87.2)	0.06
High levels of ferritin n (%)	686/1073 (63.9)	486/756 (64.3)	146/244 (59.8)	54/72 (74)	0.08
High levels of CRP n (%)	1799/1893 (95)	1333/1411(94.5)	366/380 (96.3)	100/102 (98)	0.12
High levels of procalcitonin n (%)	407/1480 (27.5)	270/1077 (25.1) *	95/312 (30.4) °	42/91 (46.2) *°	<0.001
<i>Imaging</i>					
Bilateral chest x-rays abnormality n (%)	1260 (65.2)	923 (64.2)	263 (67.4)	74 (69.8)	0.14
<i>In-hospital therapy</i>					
Corticosteroids n (%)	555/1869 (29.7)	351/1403 (25) *°	161/370 (43.5) °	43/96 (44.9) *	<0.001
Chloroquine n (%)	1594/1893 (84.2)	1192/1417 (84.1)	311/372 (83.6)	91/104 (87.5)	0.62
Antivirals n (%)	1299/1898 (68.4)	936/1416 (66.1) *°	276/377 (73.2) *	87/105 (82.9) °	<0.001
Interferon n (%)	320/1857 (17.2)	206/1389 (14.8) °	67/366 (18.3) *	47/102 (46.1) *°	<0.001

Tocilizumab n (%)	174/1858 (9.4)	82/1391 (5.9) *	58/363 (16) *	34/104 (32.7) *	<0.001
Antibiotic n (%)	1457/1833 (79.5)	1085/1361 (79.7) *	277/368 (75.3) °	95/104 (91.3) *°	0.001
ACEI/ARB n (%)	341/1800 (18.9)	261/1334 (19.6)	63/368 (17.1)	17/98 (17.3)	0.52
Pronation during admission n (%)	244/1854 (13.2)	102/1386 (7.4) *	87/372 (23.4) *	55/96 (57.3) *	<0.001
<i>In-hospital Complications</i>					
Sepsis n (%)	332/1866 (17.8)	138/1394 (9.9) *	143/375 (38.1) *	51/97 (52.6) *	<0.001
Relevant bleedings n (%)	43/1826 (2.4)	21/1378 (1.5) *°	15/354 (4.2) *	7/94 (7.4) °	<0.001
Embolic event n (%)	34/1833 (1.9)	18/1376 (1.3) *°	12/361 (3.3) *	4/96 (4.2) °	0.009
Renal failure during admission n (%)	414/1880 (22)	245/1405 (17.4) *	113/376 (30.1) *	56/99 (56.6) *	<0.001
Heart failure during admission n (%)	170/1870 (9.1)	97/1398 (6.9) *	43/373 (11.5) *	30/99 (30.3) *	<0.001
Circulatory or ECMO support n (%)	61/1850 (3.3)	1/468 (0.2) *	33/361 (9.1) *	27/97 (27.8) *	<0.001
Length of hospital stay (days) mean ±SD	9.19 ±6.7, n=1741	8.9 ±6.4, n=1329*	9.9 ± 7.3, n=331	11.5 ± 8.0, n=81*	<0.001

Table S2. Overall HOPE REGISTRY population laboratory characteristics and in-hospital outcomes according to ventilation and oxygen support type.

ACEi: Angiotensin converting enzymes inhibitors, ARB: angiotensin receptor blocker, DM: diabetes mellitus, COPD: chronic obstructive pulmonary disease. CRP: C-reactive protein, LDH: lactic dehydrogenase, ECMO: Extracorporeal membrane oxygenation

* and ° mark the groups with a statistically significant difference

	Overall NIV population (390)	Alive (243)	Dead (147)	p-value
<i>Demographic data and baseline characteristics</i>				
Age, year median (IQR)	70 (58-79) n= 390	63 (53-73) n=243	78 (70-85) n=147	<0.001
Female sex n (%)	133/390 (34.1)	86/243 (35.4)	47/147 (32.0)	0.5
BMI n (%)	27 (25-31) n=219	27 (25-31) n=142	27 (25-31) n=77	0.1
Obesity n (%)	70/273 (25.6)	45/179 (25.1)	25/94 (26.6)	0.9
Hypertension n (%)	222/383 (58.0)	117/239 (49.0)	105/144 (72.9)	<0.001
Dyslipidemia n (%)	141/380 (37.1)	71/238 (29.8)	70/142 (49.3)	<0.001
Current or previous Smoker n (%)	103/338 (30.5)	51/210 (29.1)	52/128 (40.7)	0.004
DM n (%)	70/354 (19.8)	39/225 (17.3)	31/129 (24.0)	0.1
Prior stroke n (%)	41/361 (11.4)	19/225 (8.4)	22/136 (16.2)	0.04

Heart disease, any n (%)	113/390 (29)	57/243 (23.5)	56/147 (38.1)	0.002
Lung Disease, any n (%)	85/390 (21.8)	48/243 (19.8)	37/147 (25.2)	0.3
Asma n (%)	18/390 (4.6)	14/243 (5.8)	4/147 (2.7)	0.3
COPD n (%)	37/390 (9.5)	16/243 (6.6)	21/147 (14.3)	0.02
Restrictive lung disease n (%)	5/390 (1.3)	4/243 (1.6)	1/147 (0.7)	0.7
Liver disease n (%)	16/347 (4.6)	9/217 (4.1)	7/130 (5.4)	0.6
Chronic kidney disease CL<30 n (%)	31/352 (8.8)	7/220 (3.2)	24/132 (18.2)	<0.001
Cancer history n (%)	62/366 (16.9)	34/229 (14.8)	28/137 (20.4)	0.2
Connective disease n (%)	17/361 (4.7)	6/225 (2.7)	11/136 (8.1)	0.02
Any immunosuppressive condition n (%)	32/320 (10.0)	16/202 (7.9)	16/118 (13.6)	0.1
<i>Prior therapies</i>				
Anticoagulation n (%)	61/370 (16.5)	30/231 (13.0)	31/139 (22.3)	0.02
Antiplatelet n (%)	73/372 (19.6)	32/232 (13.8)	41/140 (29.3)	<0.001
ACEI/ARB n (%)	158/383 (41.3)	85/239 (35.6)	73/144 (50.7)	0.004
B-blockers n (%)	82/365 (22.5)	42/229 (18.3)	40/136 (29.4)	0.01
B-2 agonists n (%)	59/368 (16)	28/230 (12.2)	31/138 (22.5)	0.01
Inhaled Corticosteroids n (%)	41 (11.2)	20/229 (8.7)	21/138 (15.2)	0.06
Home Oxygen therapy n (%)	20/381 (5.2)	10/236 (4.2)	10/145 (6.9)	0.3
Antidepressant n (%)	55/371 (14.8)	25/230 (10.9)	30/141 (21.3)	0.01
<i>Clinical presentation</i>				
Fever n (%)	325/380 (85.5)	209/236 (88.6)	116/144 (80.6)	0.03
Dyspnea, any entity n (%)	259 (66.4)	155/232 (64.8)	104/142 (73.0)	0.2
Tachypnea n (%)	143/354 (40.4)	74/219 (33.8)	69/135 (51.1)	0.001
O2 saturation below 92% n (%)	189/373 (50.7)	86/229 (37.6)	103/144 (71.5)	<0.001
Diarrhea n (%)	52/350 (14.9)	39/220 (17.7)	13/130 (10.0)	0.05
Vomiting n (%)	23/356 (6.5)	19/225 (8.4)	4/131 (3.1)	0.05
Hypo/anosmia n (%)	17/343 (5.0)	15/216 (6.9)	2/127 (1.6)	0.03
Dysgeusia n (%)	23/342 (6.7)	22/214 (10.3)	1/128 (0.8)	0.001
Cough n (%)	254/375 (67.7)	162/238 (68.1)	92/137 (67.2)	0.9
Max temperature at presentation (°C) n (%)	37.7 (36.9-38.4) n = 180	37.6 (36.9-38.5) n=107	37.7 (36.9-38.4) n=73	0.9
Blood pressure abnormality n (%)	43/383 (11.2)	17/242 (7.0)	26/141 (18.4)	0.001
<i>Laboratory data</i>				
Leucocytes, 10 ⁹ /L median (IQR)	6.5 (5-9.3) n=376	6.6 (4.9-9.4) n=237	7.2 (5.2-9.9) n=139	0.2
Platelets count (<1.5 10 ⁹ /L) n (%)	292/358 (81.6)	171/227 (75.3)	121/131 (92.4)	<0.001
Thrombocytopenia (<150k) n (%)	98/372 (26.3)	58/238 (24.4)	40/134 (29.9)	0.3
Anemia at presentation n (%)	116/373 (31.1)	60/238 (25.2)	56/135 (41.5)	0.001
Creatinine (mg/dl) median (IQR)	0.96 (0.75-1.35) n=315	0,9 (0,7-1.19) n=193	1.13 (0.85-1.58) n=122	0.01
High levels of D-dimer n (%)	245/335 (73.1)	150/216 (69.4)	95/119 (79.8)	0.04
High levels of troponin n (%)	66/243 (27.2)	29/152 (19.1)	37/91 (40.7)	<0.001
High transaminase level n (%)	176/343 (51.3)	105/215 (48.8)	71/128 (55.5)	0.2
High levels of LDH n (%)	300/355 (84.5)	183/223 (82.1)	117/132 (88.6)	0.1

High levels of ferritin n (%)	146/244 (59.8)	100/156 (64.1)	46/88 (52.3)	0.07
High levels of CRP n (%)	366/380 (96.3)	226/238 (95.0)	140/142 (98.6)	0.07
High levels of procalcitonin n (%)	95/312 (30.4)	42/196 (21.4)	53/116 (45.7)	<0.001
<i>Imaging</i>				
Bilateral chest XR abnormality n (%)	263/360 (73.1)	156/227 (68.7)	107/133 (80.5)	0.02
<i>In-hospital therapies</i>				
Corticosteroids n (%)	161/370 (43.5)	79/226 (35.0)	82/144 (56.9)	<0.001
Chloroquine n (%)	311/372 (83.6)	200/230 (87.0)	111/142 (78.2)	0.03
Antivirals n (%)	276/377 (73.2)	180/237 (75.9)	96/140 (68.6)	0.1
Interferon n (%)	67/366 (18.3)	42/228 (18.4)	25/138 (18.1)	1.0
Tocilizumab n (%)	58/363 (16)	34/228 (14.9)	24/135 (17.8)	0.5
Antibiotic n (%)	277/368 (75.3)	161/228 (70.6)	116/140 (82.9)	0.008
ACEI/ARB n (%)	63/368 (17.1)	42/234 (17.9)	21/134 (15.7)	0.7
<i>Ventilation therapy</i>				
Need for invasive mechanical ventilation n (%)	62/390 (15.9)	26/243 (10.7)	36/147 (24.5)	0.001
Pronation in NIV n (%)	63/372 (16.9)	30/230 (13.0)	33/142 (23.2)	0.011
<i>In-hospital complications</i>				
Sepsis n (%)	143/375 (38.1)	67/236 (28.4)	76 /139 (54.7)	<0.001
Relevant bleedings n (%)	15/354 (4.2)	8/223 (3.6)	7/131 (5.3)	0.4
Embolie event n (%)	12/361 (3.3)	7/230 (3.0)	5/131 (3.8)	0.7
Renal failure during admission n (%)	113/376 (30.1)	39/234 (16.7)	74/142 (52.1)	<0.001
Heart failure during admission n (%)	43/373 (11.5)	14/236 (5.9)	29/137 (21.2)	<0.001
Circulatory or ECMO support n (%)	33/361 (9.1)	8/227 (3.5)	25/134 (18.7)	<0.001
Length of in-hospital stay median (IQR)	8 (4-15) n=338	10 (6-16) n=232	6 (3-10) n=147	<0.001

Table S3. HOPE REGISTRY Cohort of patients treated with NIV according to death status.

ACEi: Angiotensin converting enzymes inhibitors, ARB: angiotensin receptor blocker, DM: diabetes mellitus, COPD: chronic obstructive pulmonary disease. CRP: C-reactive protein, LDH: lactic dehydrogenase, ECMO: Extracorporeal membrane oxygenation

	Univariate OR	95% CI		p-value
Age (OR per 5-year increase)	1.46	1.33	1.61	<0.001
Dyslipidemia	2.29	1.49	3.52	<0.001
Hypertension	2.81	1.80	4.39	<0.001
Heart Disease, any	2.0	1.29	3.14	0.002
CKD history	6.76	2.83	16.19	<0.001
Previous antiplatelet therapy	2.59	1.54	4.36	<0.001
Previous ACEI/ARB therapy	1.86	1.22	2.84	0.004
Previous Inhaled Beta-agonist Therapy	2.09	1.19	3.67	0.009
Previous Antidepressant therapy	2.22	1.24	3.95	0.006
O ₂ saturation below 92% at index evaluation	4.18	2.66	6.55	<0.001
Dysgeusia	0.07	0.01	0.52	<0.001
Blood pressure abnormalities	2.99	1.56	5.74	<0.001
Anemia	2.10	1.34	3.30	0.001
Elevated Troponin	2.90	1.63	5.20	<0.001
Lymphocytopenia (<1500/mm ³)	3.96	1.94	8.08	<0.001
In hospital corticosteroid use	2.46	1.60	3.78	<0.001
In hospital antibiotic use	2.01	1.19	3.40	0.008

Table S4. Unadjusted OR for death within NIV subgroup.

ACEi: Angiotensin converting enzymes inhibitors, ARB: angiotensin receptor blocker, CKD: chronic kidney disease.

	Overall NIV population (390)	No orotracheal intubation (328)	Orotacheal intubation (62)	p-value
Ventilation therapy				
Age, year	70 (58-79) n= 390	71 (57-80) n=328	68 (60-73) n=62	68 (60-73) n=62
Female sex	133/390 (34.1)	16/62 (25.8)	117/328 (35.7)	0.1
Obesity	70/273 (25.6)	11/55 (20.0)	59/218 (27.1)	0.3
Hypertension	222/383 (58.0)	182/322 (56.5)	40/61 (65.6)	0.2
Dyslipidemia	141/380 (37.1)	119/319 (37.3)	22/61 (36.1)	0.9
Current or previous Smoker	103/338 (30.5)	95/279 (34.1)	19/59 (32.2)	0.8
DM	70/354 (19.8)	56/295 (19.0)	14/59 (23.7)	0.4
Prior stroke	41/361 (11.4)	39/302 (12.9)	2/59 (3.4)	0.05
Heart disease	113/390 (29)	100/328 (30.5)	13/62 (21.0)	0.1
Lung Disease, any	85/390 (21.8)	72/328 (22.0)	13/62 (21.0)	0.9
Asma	18/390 (4.6)	17/328 (5.2)	17/328 (5.2)	0.3
COPD	37/390 (9.5)	33/328 (10.1)	4/62 (6.5)	0.4
Restrictive lung disease	5/390 (1.3)	17/328 (5.2)	17/328 (5.2)	0.03
Liver disease	16/347 (4.6)	14/289 (4.8)	2/58 (3.4)	0.6
Chronic kidney disease CL<30	31/352 (8.8)	23/293 (7.8)	8/59 (13.6)	0.16
Cancer history	62/366 (16.9)	57/308 (18.5)	5/58 (8.6)	0.07
Connective disease	17/361 (4.7)	17/303 (5.6)	0/58 (0.0)	0.09
Any immunosuppressive condition	32/320 (10.0)	30/264 (11.4)	2/56 (3.6)	0.08
Previous therapies				
Anticoagulation	61/370 (16.5)	52/310 (16.8)	9/60 (15.0)	0.7
Antiplatelet	73/372 (19.6)	61/312 (19.6)	12/60 (20.0)	0.9
ACEI/ARB	158/383 (41.3)	133/323 (41.2)	25/60 (41.7)	0.9
B-blockers	82/365 (22.5)	73/306 (23.9)	9/59 (15.3)	0.15
B-2 agonists	59/368 (16)	54/309 (17.5)	5/59 (8.5)	0.08
Inhaled Corticosteroids	41 (11.2)	34/307 (11.1)	7/60 (11.7)	0.9
Home Oxygen therapy	20/381 (5.2)	17/322 (5.3)	3/59 (5.1)	1.0
Antidepressant	55/371 (14.8)	46/311 (14.8)	9/60 (15.0)	1.0
Clinical presentation				
Fever	325/380 (85.5)	270/320 (84.4)	55/60 (91.7)	0.1
Dyspnea, any entity	259 (66.4)	214/313 (68.4)	45/61 (73.8)	0.4
Tachypnea	143/354 (40.4)	115/293 (39.2)	28/61 (45.9)	0.3
O2 saturation below 92%	189/373 (50.7)	150/312 (48.1)	39/61 (63.9)	0.02
Diarrhea	52/350 (14.9)	47/290 (16.2)	5/60 (8.3)	0.1
Vomiting	23/356 (6.5)	22/296 (7.4)	1/60 (1.7)	0.1
Hypo/anosmia	17/343 (5.0)	16/283 (5.7)	1/60 (1.7)	0.2
Dysgeusia	23/342 (6.7)	18/282 (6.4)	5/60 (8.3)	0.6
Cough	254/375 (67.7)	214/315 (67.9)	40/60 (66.7)	0.9
Max temperature at presentation (°C)	37.7 (36.9-38.4) n = 180	37.7 (36.8-38.4) n=149	37.9 (37.4-38.6)	0.2

Blood pressure abnormality	43/383 (11.2)	33/321 (10.3)	10/62 (16.1)	0.18
Laboratory data				
Leucocytes, 10⁹/L	6.5 (5-9.3) n=376	0.95 (0.74-1.33) n=275	0.95 (0.74-1.33) n=275	0.1
Lymphocytopenia (<1.5 10⁹/L)	292/358 (81.6)	239/300 (79.7)	53/58 (91.4)	0.04
Thrombocytopenia (<150k)	98/372 (26.3)	81/316 (25.6)	17/56 (30.4)	0.5
Anemia at presentation	116/373 (31.1)	95/312 (30.4)	21/61 (34.4)	0.5
Creatinine (mg/dl)	0.96 (0.75-1.35) n=315	0.95 (0.74-1.33) n=275	0.95 (0.74-1.33) n=275	0.07
High levels of D-dimer	245/335 (73.1)	194/278 (69.8)	51/57 (89.5)	0.002
High levels of troponin	66/243 (27.2)	50/201 (24.9)	16/42 (38.1)	0.08
High transaminase level	176/343 (51.3)	141/283 (49.8)	35/60 (58.3)	0.2
High levels of LDH	300/355 (84.5)	248/298 (83.2)	52/57 (91.2)	0.1
High levels of ferritin	146/244 (59.8)	126/199 (63.3)	20/45 (44.4)	0.02
High levels of CRP	366/380 (96.3)	307/319 (96.2)	59/61 (96.7)	0.9
High levels of procalcitonin	95/312 (30.4)	71/252 (28.2)	24/60 (40.0)	0.07
Imaging				
Bilateral chest XR abnormality	263/360 (73.1)	212/300 (70.7)	51/60 (85.0)	0.02
In-hospital therapies				
Corticosteroids	161/370 (43.5)	122/310 (39.4)	39/60 (65.0)	<0.001
Chloroquine	311/372 (83.6)	254/311 (81.7)	57/61 (93.4)	0.02
Antivirals	276/377 (73.2)	223/316 (70.6)	53/61 (86.9)	0.008
Interferon	67/366 (18.3)	46/307 (15.0)	21/59 (35.6)	<0.001
Tocilizumab	58/363 (16)	38/303 (12.5)	20/60 (33.3)	<0.001
Antibiotic	277/368 (75.3)	219/307 (71.3)	58/61 (95.1)	<0.001
ACEI/ARB	63/368 (17.1)	56/307 (18.2)	7/61 (11.5)	0.2
Pronation during hospitalization	87/372 (23.4)	63/313 (20.1)	24/59 (40.7)	0.001
In-hospital complications				
Sepsis	143/375 (38.1)	111/315 (35.2)	32/60 (53.3)	0.008
Relevant bleedings	15/354 (4.2)	9/294 (3.1)	6/60 (10.0)	0.02
Embolic event	12/361 (3.3)	7/301 (2.3)	5/60 (8.3)	0.02
Renal failure during admission	113/376 (30.1)	80/314 (25.5)	33/62 (53.2)	<0.001
Heart failure during admission	43/373 (11.5)	35/312 (11.2)	8/61 (13.1)	0.7
Circulatory or ECMO support	33/361 (9.1)	2/301 (0.7)	31760 (51.7)	<0.001
TIME of in hospital stay	8 (4-15) n=338	10 (5-16) n=178	7 (3-12) n=160	0.006

Table S5. HOPE REGISTRY sub-analysis on patients treated with NIV and according to OTI.

ACEi: Angiotensin converting enzymes inhibitors, ARB: angiotensin receptor blocker, DM: diabetes mellitus, COPD: chronic obstructive pulmonary disease. CRP: C-reactive protein, LDH: lactic dehydrogenase, ECMO: Extracorporeal membrane oxygenation

	Univariate OR	95% CI		P value
Prior Stroke	0.24	0.06	1.00	0.05
O2 saturation below 92% at index evaluation	1.92	1.09	3.38	0.02
Elevated D-Dimer	3.68	1.52	8.91	0.002
Elevated ferritin	0.46	0.24	0.82	0.02
Lymphocytopenia (<1500/mm ³)	2.71	1.04	7.06	0.04
Bilateral Chest x-rays abnormalities	2.35	1.11	4.99	0.02
In-hospital corticosteroid use	2.86	1.61	5.09	<0.001
In-hospital Chloroquine use	3.20	1.11	9.17	0.02
In hospital antiviral use	2.76	1.26	6.04	0.008
In hospital Interferon use	3.14	1.69	5.82	<0.001
In hospital use of Tocilizumab	3.49	1.85	6.58	<0.001
In hospital antibiotic use	7.77	2.37	25.45	<0.001
Pronation during hospitalization	2.72	1.51	4.90	0.001

Table S6. Unadjusted OR for orotracheal intubation within NIV subgroup.

	Adjusted OR	95% CI		p-value
Age (OR per 5-year increase)	1.36	1.12	1.67	0.002
Dyslipidemia	-	-	-	-
Hypertension	2.49	0.78	8.01	0.13
Heart Disease	-	-	-	-
CKD history	-	-	-	-
Previous aspirin therapy	-	-	-	-
Previous Antidepressant therapy	-	-	-	-
O2 saturation below 92% at index evaluation	3.72	1.38	10.03	0.01
Anemia	-	-	-	-
Elevated D-Dimer	-	-	-	-
Elevated Troponin	-	-	-	-
Elevated Procalcitonin	-	-	-	-
Lymphocytopenia (<1500/mm ³)	3.60	0.97	13.4	0.055
In hospital corticosteroid use	-	-	-	-
In hospital antibiotic use	4.9	1.1	21.76	0.037
Obesity	1.87	0.58	6.04	0.29
Previous or current smoker	0.91	0.32	2.59	0.86

Table S7. Sensitivity multivariate logistic regression analysis forcing "obesity" and "Smoke habits" (previous or current smokers) in the model. Where not shown (i.e. "-") p value is higher than 0.05.

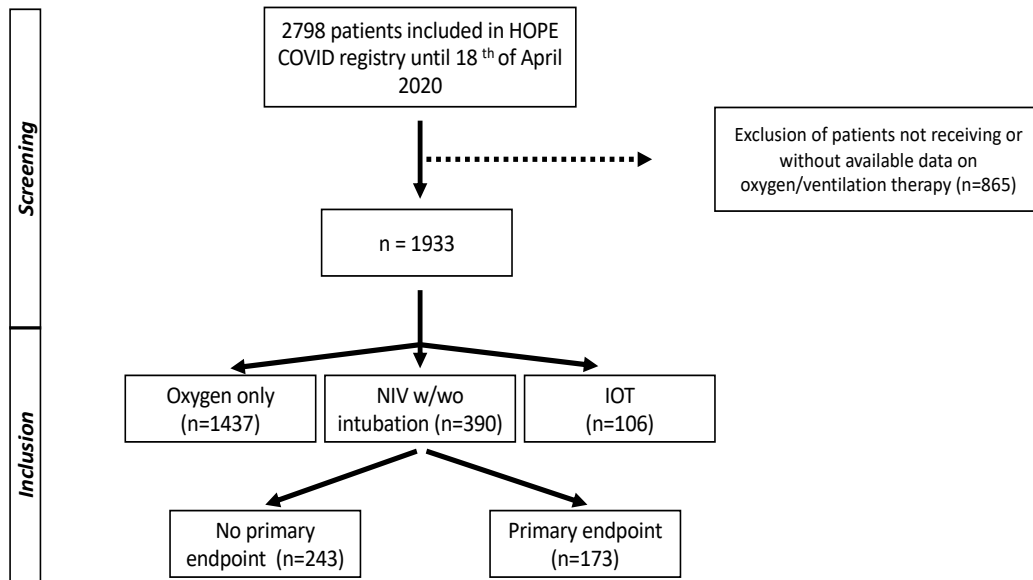


Figure S1. HOPE COVID sub-study flow-chart.