

## SUPPLEMENTARY INFORMATION

**Supplementary Table S1: Characteristics of the patients included in derivation and validation cohorts**

Variable	Development and internal validation (n=1568)	External validation (n=956)	p-value	missing
<b><i>Sociodemographics</i></b>				
Sex (male)			0.01	
Male	933(59.50)	520(54.39)		
Female	635(40.50)	436(45.61)		
Age*	67.42(16)	65.75(20)	0.03	
<b><i>Comorbidities</i></b>				
Myocardial infarction	30(1.91)	16(1.67)	0.66	
Congestive heart failure	22(1.28)	19(2)	0.26	
Peripheral vascular disease	74(4.72)	37(3.87)	0.31	
Cerebrovascular disease	89 (5.68)	63 (6.59)	0.35	
Dementia	37(2.36)	40(4.18)	0.01	
Chronic pulmonary disease	181(11.54)	110(11.51)	0.98	
Rheumatic disease	22 (1.40)	13(1.36)	0.93	
Liver disease (mild)	42(2.68)	21(2.20)	0.45	
Diabetes without chronic complication	142(9.06)	98(10.25)	0.32	
Diabetes with chronic complication	39(2.49)	25(2.62))	0.84	
Renal disease	149(9.50)	83(8.68)	0.49	
Neoplasia	200(12.76)	101 (10.56)	0.1	
Metastatic solid tumor	18(1.15)	12(1.26)	0.81	
<b><i>Basal treatments</i></b>				
Antidiabetics	211(13.46)	198(20.71)	<0.0001	
Antiacids	274 (17.47)	246 (25.73)	<0.0001	
Antihypertensives	24(1.53)	25(2.62)	0.05	
Diuretics	195(12.44)	212(22.18)	>0.0001	
Beta-blockers	133(8.48)	113(11.8)	0.0061	

Calcium channel blockers	129(8.23)	120(12.55)	0.0004	
Renin angiotensin aldosterone system inhibitors	362(23.09)	278(29.1)	0.0008	
Lipid lowering drugs	235(14.99)	209(20.86)	<0.0001	
NSAIDs	718(45.8)	597(62.45)	<0.0001	
Anticoagulants	374(23.85)	326 (34.10)	<0.0001	
Immunosuppressants	29(1.85)	20(2.1)	0.67	
Chronic systemic steroids	373(23.79)	310(32.43)	<0.0001	
Neuroleptics	259 (16.52)	233(24.37)	<0.0001	
<b>Vital signs *</b>				
Temperature MAX	37.28 (0.92)	37.07(0.87)	<0.0001	193/160
Systolic Blood pressure MIN	124(19.18))	125.6(21.36)	0.08	227/157
Systolic Blood pressure MAX	132.3(19.69)	132 (22.03)	0.60	227/157
Diastolic blood pressure MIN	72.20(10.72)	73.12(11.73)	0.07	227/157
Diastolic blood pressure MAX	77.54(10.85)	77(11.56)	0.22	227/157
Cardiac rate MIN	75.80(13.63)	77(15)	0.07	220/152
Cardiac rate MAX	83.75(14.83))	82.85(15.77)	0.18	220/152
SpO2 MIN	94.27 (2.87)	95.18 (2.42)	<0.0001	815/458
<b>Laboratory test*</b>				
PaO2	74.61(21.60)	73.85 (23.86)	0.51	457/376
Glucose	122(44.29)	131.6(59.17)	<0.0001	3/12
Urea	45.55(35)	45(34.2)	0.60	4/15
Creatinine	1.06(0.72)	1.08(0.87)	0.62	4/10
ALT	34.84(32.9)	35.26(36.71)	0.78	15/81
Creatine kinase	163(322)	193(635)	0.29	712/346
Sodium	137.5(4.27)	138.3(4.21)	<0.0001	10/14
Potassium	4.13(0.51)	4.06(0.51)	0.0017	46/36
Dimer D	1777(4793)	1317(2590)	0.0049	316/153
Prothrombin time	83.7(21.07)	85.33(19.64)	0.05	106/23
Ferritin	754(919)	715(838.5)	0.49	1155/329
Fibrinogen	601(141)	584.2(163)	0.1	1067/532
LDH	308(127)	277(269)	<0.0001	237/170

C-reactive protein	83(76)	73.6(69.35)	0.0022	13/27
Procalcitonine	0.37(2.58)	0.52(4.12)	0.37	230/189
hs-cTnT	28(51)	19(21)	0.001	1128/877
Red blood cells	4.60(0.63)	4.46(0.66)	0.12	3/8
Haemoglobin	13.7(1.85)	13.47(1.93)	0.0044	3/7
Haematocrit	42(5.4)	41(5.55)	<0.0001	3/8
Mean corpuscular volume	91.7(6.2)	90.22(6.39)	<0.0001	3/8
RDW	13.35(1.7)	13.63(1.84)	0.0002	3/6
Platelets	194.5(79.7)	200(82)	0.10	3/7
Leukocytes	6.94	6.89(3.5)	0.72	3/7
Lymphocytes	1.21(2.38)	1.17(0.65)	0.46	8/28
Neutrophils	5.14(2.80)	5(3)	0.19	8/28
Basophils	0.02(0.03)	0.02(0.02)	0.59	8/28
Monocytes	0.52(0.35)	0.52(0.33)	0.78	8/28
Eosinophils	365(23.3)	191(20)	0.05	8/28
<b>Outcome</b>	<b>365 (23.28)</b>	<b>191(19.98)</b>	<b>0.05</b>	
VMK 100%	255(16.26)	79(8.26)	<0.0001	
Optiflow	87(5.55)	73(7.64)	0.04	
NIMV	45(2.87)	15(1.57)	0.0374	
ICU admission	78(4.97)	54(5.65)	0.46	
Death	180(11.48)	110(11.51)	0.98	

NSAIDS: non-steroidal anti-inflammatory drugs; MAX: maximum value; MIN: minimum value; SpO2: pulse oximetric saturation; PaO2: partial arterial oxygen concentration; ALT: alanine aminotransferase; LDH: Lactate dehydrogenase; hs-cTnT: high-sensitivity cardiac troponin T ; RDW: Red blood cell distribution width; VMK100%: standard-high-flow-oxygen-facemask with reservoir-bag at least during six hours and need for more intensive therapy afterwards; Optiflow (TM)-high-flow-nasal-cannula; NIMV: non-invasive mechanical ventilation; ICU : intensive care unit.

Data are given as frequencies and percentages except for \*, expressed as means and standard deviation.

**Supplementary Table S2: Univariate analysis, relationship between predictors and outcome in development-internal validation and external validation datasets**

Variable	DEVELOPMENT DATASET				EXTERNAL VALIDATION DATASET			
	Missing	Deteroration no (n=1203)	Deteroration Yes (n=365)	p-value	Missing	Deteroration no (n=765)	Deteroration yes (n=191)	p-value
<b><i>Sociodemographics</i></b>								
Sex (male)		681(56.61)	252(69.04)	<0.0001		406(53.07)	114(59.7)	0.10
Age*		65.29(16)	74.53(14)	<0.0001		62.94(19.8)	77(14.7)	<0.0001
<b><i>Comorbidities</i></b>								
Myocardial infarction		24(2)	6(1.64)	0.67		11(1.44)	5(2.62)	0.25
Congestive heart failure		14(1.16)	6(1.64)	0.47		14(1.83)	5(2.62)	0.48
Peripheral vascular disease		46(3.82)	28(7.67)	0.0024		29(3.79)	8(4.19)	0.8
Cerebrovascular disease		55(4.57)	34(9.32)	0.0006		42(5.49)	21(11)	0.006
Dementia		25(2.08)	12(3.29)	0.18		27(3.53)	13(6.81)	0.04
Chronic pulmonary disease		114(9.48)	67(18.36)	<0.0001		80(10.46)	30(15.71)	0.04
Rheumatic disease		18(1.50)	4(1.10)	0.57		11(1.44)	2(1.05)	0.67
Liver disease (mild)		31(2.58)	11(3.01)	0.65		15(1.96)	6(3.14)	0.32
Diabetes without chronic complication		87(7.23)	55(15.07)	<0.0001		69(9.02)	29(15.18)	0.01
Diabetes with chronic complication		27(2.24)	12(3.29)	0.26		17(2.22)	8(4.19)	0.13
Renal disease		85(7.07)	64(17.53)	<0.0001		57(7.45)	26(13.61)	0.007
Neoplasia		131(10.9)	69(18.9)	<0.0001		69(9.02)	32(16.75)	0.0019
Metastatic solid tumor		11(0.91)	7(1.92)	0.11		9(1.18)	3(1.57)	
<b><i>Basal treatments</i></b>								
Antidiabetics		134(11.14)	77(21.10)	<0.0001		131(17.12)	67(35.08)	<0.0001

Antiacids	167(13.88)	107(29.32)	<0.0001	158 (20.65)	88(46.07)	<0.0001
Antihypertensives	15(1.25)	9(2.47)	0.09	13(1.70)	12(6.28)	0.0004
Diuretics	112(9.31)	83(22.74)	<0.0001	143(18.69)	69(36.13)	<0.0001
Cardiovascular	83(6.90)	32(8.77)	0.23	50(6.54)	18(9.42)	0.16
Beta-blockers	84(7)	49(13.42)	0.0001	79(10.33)	34(17.80)	0.0042
Calcium channel blockers	83(7)	46(12.60)	0.0005	79(10.33)	41(21.47)	<0.0001
Renin-angiotensin aldosterone system inhibitors	244(21)	118(32.33)	<0.0001	184(24.05)	94(49.21)	<0.0001
Lipid lowering drugs	155(13)	80(22)	<0.0001	128(16.73)	81(42.41)	<0.0001
NSAIDs	570(47.38)	148(40.55)	0.02	477(62.35)	120(62.83)	0.90
Anticoagulants	254(21)	120(33)	<0.0001	224(29.28)	102(53.40)	<0.0001
Immunosuppressants	23(2)	6(1.64)	0.74	17(2.22)	3(1.57)	0.57
Chronic systemic steroids	270(22.44)	103 (28)	0.02	241(31.50)	69(36.13)	0.22
Neuroleptics	164(13.63)	95(26.03)	<0.0001	150 (19.61)	83(43.46)	<0.0001

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***Vital signs***

Temperature MAX	153/40	37.23(0.9)	37.46(1)	0.0002	127/33	37.07(0.83)	37.04(1.02)	0.75
Systolic Blood pressure MIN	176/51	123.3(18.8)	126.3(20.26)	0.01	127/30	125.7(21.72)	124.9(19.84)	0.67
Systolic Blood pressure MAX	176/51	131.4(19.2)	135(21)	0.005	127/30	131.6(22.22)	132.5(21.35)	0.62
Dyastolic blood pressure MIN	176/51	72.38(1.48)	71.61(11.46)	0.28	127/30	73.69(12.06)	70.84(10.03)	0.0022
Dyastolic blood pressure MAX	176/51	77.57(10.37)	77.44(12.27)	0.86	127/30	77.25(11.86)	75.59(10.19)	0.07
Cardiac rate Min	177/43	75.2(12.7)	77.75(16.14)	0.0096	123/29	76.77(12.69)	77.78(16.04)	0.47
Cardiac rate Max	177/43	83.07(14.3)	85.92(16.24)	0.005	123/29	82.42(15.22)	84.55(17.74)	0.16
SpO2 Min	539/276	94.53(2.5)	92.3(4.33)	<0.0001	322/136	95.35(2.3)	93.70(2.62)	<0.0001

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***Laboratory test***

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Glucose	2/1	118.1(40.33)	134.3(53.56)	<0.0001	12/0	128.1(56.41)	145.5(67.32)	0.001
Urea	10/4	41(28)	60.65(47.33)	<0.001	3/0	40.21(27.53)	62.85(48.89)	<0.00011/0
Creatinine	3/1	1(0.65)	1.27(0.85)	<0.0001	1/0	0.97(0.50)	1.48(1.59)	<0.0001
ALT	82/23	34.8(32)	35(35.5)	0.89	67/14	36.13(38.73)	31.81(27.17)	0.08
Creatine kinase	526/186	157.6(346)	183(208)	0.22	274/72	182.9(655)	233.1(545)	0.39
Sodium	7/4	137.4(3.70)	137.5(5.77)	0.79	2/0	138.3(3.91)	138.2 (5.24)	0.73
Potassium	33/13	4.11(0.50)	4.19(0.55)	0.01	40/6	4.06(0.49)	4.07(0.57)	0.70
Dimer D	226/90	1516.2(3814.6)	2703.2(7207)	0.0090	133/20	1185.5(2264.3)	1803.2(3509.5)	0.03
PaO2	427/70	76.89(21.55)	68.62(20.57)	<0.0001	329/47	73.9 (23.7)	73.73(24.5)	0.94
Prothrombin time	79/27	85(20.31)	79.33(23)	<0.0001	21/2	86.39(18.94)	81.18(21.72)	0.0028
Ferritin	884/271	743.5 (957)	789.5(781.4)	0.63	263/66	696.4(826)	790(887)	0.26
Fibrinogen	801/266	597.1(139)	617(147.5)	0.21	418/114	582.8(165.5)	591(151.2)	0.70
LDH	176/61	291(95.61)	365(187)	<0.0001	148/22	269.1(96.66)	304.6(130.3)	0.001
C-reactive protein	12/1	71.07	120.6(87.3)	<0.0001	15/2	66.90(65.69)	99.64(76.93)	<0.0001
Procalcitonine	182/48	0.30(2.74)	0.60(1.95)	0.03	165/24	0.51(4.56)	0.56(1.76)	0.81
hs-cTnT	863/265	24.61(50.61)	39.23(5.24)	0.001	701/176	15.59(11.71)	34.67(38.69)	0.07
Red blood cells	3/0	4.63(0.61)	4.5(0.68)	0.0017	7/1	4.6(0.64)	4.42(0.73)	0.0018
Haemoglobin	3/0	13.74(1.79)	13.5(2.02)	0.0467	7/9	13.56(1.9)	13.11(2.02)	0.0038
Haematocrit	3/0	42.13(5.21)	41.79(6.03)	0.33	7/1	41.21(5.41)	40.13(6.03)	0.01
Mean corpuscular volume	3/0	91.26(5.96)	93.11(6.69)	<0.0001	7/1	89.94(6.30)	91.39(6.6)	0.0052
RDW	3/0	13.18(1.60)	13.91(1.89)	<0.0001	7/1	13.49(1.73)	14.18(2.13)	<0.0001
Platelets	3/0	201.5(82.43)	171.6(64.93)	<0.0001	7/1	206.3(82.70)	174.3(72.93)	<0.0001
Leucocytes	3/0	6.71(2.88)	7.7(6)	0.0023	7/0	6.81(3.43)	7.15(3.57)	0.24
Lymphocytes	6/2	1.18(0.62)	1.33(4.81)	<0.0001	22/6	1.22(0.65)	0.95(0.60)	<0.0001
Neutrophils	6/2	4.92(2.59)	5.85(3.33)	<0.0001	22/6	4.86(2.85)	5.48(3.16)	0.0098
Basophils	6/2	0.02(0.02)	0.02(0.04)	0.86	22/6	0.02(0.0006)	0.02(0.00148)	0.17
Monocytes	6/2	0.54(0.31)	0.48(0.47)	0.03	22/6	0.52(0.28)	0.50(0.47)	0.67
Eosinophils	6/2	0.04(0.14)	0.02(0.04)	<0.0001	22/6	0.05(0.27)	0.02(0.03)	0.0009

NSAIDS: non-steroidal anti-inflammatory drugs; MAX: maximum value; MIN: minimum value; SpO<sub>2</sub>: pulse oximetric saturation; PaO<sub>2</sub>: partial arterial oxygen concentration; ALT: alanine aminotransferase; LDH: Lactate dehydrogenase; hs-cTnT: high-sensitivity cardiac troponin T ; RDW: Red blood cell distribution width; VMK100%: standard-high-flow-oxygen-facemask with reservoir-bag at least during six hours and need for more intensive therapy afterwards; Optiflow (TM)-high-flow-nasal-cannula; NIMV: non-invasive mechanical ventilation; ICU : intensive care unit.