Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. List of Centers and Investigators

Study centers	Principal investigator
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4. Division of Cardiology, ASST Santi Paolo e Carlo, University of Milan, Milan, Italy.	Prof Stefano Carugo
5. Division of Cardiology, ASST Cremona, Cremona	Dr Gian battista Danzi
6. Coronary Care Unit and Laboratory of Clinical and Experimental Cardiology- Fondazione IRCCS Policlinico San Matteo, University of Pavia, Pavia, Italy.	Dr Sergio Leonardi
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8. Department of Cardiology, Istituti Clinici Scientifici Maugeri IRCCS, Institute of Montescano, Pavia, Italy	Dr Maria Teresa La Rovere
9. Cardiovascular Department, Azienda Sanitaria Universitaria Integrata di Trieste (ASUITS), University of Trieste, Trieste, Italy	Prof Gianfranco Sinagra
10. Cardiovascular Disease Unit, IRCCS Ospedale Policlinico San Martino, Genova, Italy	Prof Pietro Ameri
11. Heart Failure Unit, Cardiology, G. da Saliceto Hospital, Piacenza, Italy	Dr Massimo Piepoli
12. Cardiology Rehabilitation Unit, S. Raffaele IRCCS, Rome, Italy.	Dr Maurizio Volterrani
13. Division of Cardiology, Buccheri La Ferla-Fatebenefratelli Hospital, Palermo, Italy	Dr Maurizio Volterrani Dr.Saullo

eTable 1. Laboratory findings of the study population at admission stratified by baseline troponin level (N=614).

		Normal troponin (N=336)		*Elevated troponin (N=278)*		
	Reference Range	N		N		*p-value*
Red blood cell count (x10^6/µL)	4.0-5.2	331	4.46 (4.03-4.83)	277	4.35 (3.90-4.78)	*0.040*
Hemoglobin (g/dl)	12.0-16.0	330	13.3 (11.9-14.4)	275	13.1 (11.2-14.2)	*0.118*
Hematocrit (%)	37.0-47.0	330	38.8 (35.4-42.0)	274	38.5 (33.9-42.1)	*0.371*
White blood cell count (per µL)	4000-10800	332	6630 (5000-8525)	277	7650 (5200-10600)	*0.001*
Lymphocytes absolute (per µL)	900-4000	300	973 (630-1400)	242	880 (600-1140)	*0.008*
Platelets count, (x10^3/µL)	130-400	330	208 (158-269)	275	203 (156-275)	*0.880*
Serum creatinine (mg/dl)	0.60-1.00	328	0.92 (0.75-1.11)	271	1.12 (0.89-1.67)	*<0.001*
eGFR (CKD-EPI) mL/min	>80	328	83 (64-96)	271	61 (37-82)	*<0.001*
Serum sodium (mEq/L)	136-145	327	138 (135-140)	271	138 (136-141)	*0.034*
Serum potassium (mEq/L)	3.4-4.5	328	4.0 (3.7-4.4)	269	4.0 (3.6-4.4)	*0.555*
Serum chloride (mEq/L)	98-107	213	101 (98-103)	214	100 (97-104)	*0.287*
CRP (mg/dL)	<5.0	324	46 (13-118)	270	70 (18-160)	*0.007*
Procalcitonin (ng/mL)	<0.5	135	46 (13-118)	270	70 (18-160)	0.007
Ferritin (µg/L)	30-400	137	626 (318-1392)	130	788 (401-1557)	*0.080*
D-dimer (ng/mL)	<232	232	789 (426-1699)	169	1038 (496-3299)	*0.020*
Interleukin-6 (pg/mL)	<7.0	50	39 (14-111)	35	44 (14-103)	*0.662*
NT-proBNP (pg/mL)	<93	64	204 (85-554)	100	882 (196-3170)	*<0.001*
Bilirubin (mg/dL)	<1.2	289	0.6 (0.4-0.8)	251	0.6 (0.4-0.8)	*0.489*
Aspartate transaminase (U/L)	18-39	325	38 (25-57)	271	47 (29-74)	*0.001*
Alanine transaminase (U/L)	10-50	323	33 (21-56)	272	31 (20 -52)	*0.483*
Lactate dehydrogenase (U/L)	135-225	274	362 (239-568)	219	368 (260-514)	*0.959*
Creatine phosphokinase (U/L)	39-308	151	106 (49-306)	162	114 (62-343)	*0.457*
Serum albumin (g/L)	45-52	164	33 (28-36)	163	31 (28-36)	*0.075*
INR	0.9-1.2	302	1.1 (1.0-1.2)	251	1.1 (1.0-1.3)	*0.008*
ABG test pH	7.37-7.45	302	7.47 (7.43-7.50)	240	7.46 (7.42-7.50)	*0.677*
ABG test lactate (mmol/L)	0.5-2.2	249	1.1 (0.8-1.5)	203	1.3 (1.0-1.8)	*<0.001*

Data shown as median (IQR) or count (%).

Legend: ABG: arterial blood gas, CKD-EPI: chronic kidney disease epidemiology collaboration formula, CRP: C-reactive protein, eGFR: estimated glomerular filtration rate, INR International Normalized Ratio, NT-proBNP: N-terminal fragment of the prohormone brain natriuretic peptide.

eTable 2. Multivariable logistic regression model for elevated level of troponin (N=533).

		Multivariable	
	Level/Units	OR (95% CI)	*p-value*
Sodium	+1 mEq/L	1.06 (1.02-1.10)	*0.004*
CRP	+10 mg/L	1.03 (1.01-1.05)	*0.002*
eGFR (CKD-EPI)	+10 mL/min	0.82 (0.76-0.88)	*<0.001*
Heart failure	Yes vs No	2.01 (1.07-3.79)	*0.030*
Coronary artery disease	Yes vs No	2.04 (1.27-3.29)	*0.003*
Prior anticoagulant therapy	Yes vs No	2.01 (1.16-3.50)	*0.013*

Legend: CKD-EPI: chronic kidney disease epidemiology collaboration formula; CRP: C reactive protein; eGFR: estimated glomerular filtration rate.

eTable 3. In-hospital management and outcomes of the study population stratified by baseline troponin level (N=614).

	Normal troponin (N=336)		*Elevated troponin (N=278)*		
	N		N		*p-value*
Hospital length of stay (days)	336	14.0 (9.0-25.0)	278	13.0 (8.0-21.0)	*0.030*
Pharmacological treatment					
Lopivanir/Ritonavir	335	91 (27.2)	274	88 (32.1)	*0.213*
Darunavir/Ritonavir	335	93 (27.8)	274	74 (27.0)	*0.908*
Remdesivir	335	3 (0.9)	274	2 (0.7)	*1.000*
Corticosteroid	335	152 (45.4)	274	119 (43.4)	*0.691*
Tocilizumab	335	24 (7.2)	274	22 (8.0)	*0.804*
Hydroxychloroquine	335	293 (87.5)	274	215 (78.5)	*0.004*
Antibiotics	335	286 (85.4)	274	245 (89.4)	*0.173*
Ventilatory support					
Oxygen support with FiO_2 <50%	333	147 (44.1)	273	132 (48.4)	*0.341*
Oxygen support with FiO_2 ≥50%	330	153 (46.4)	267	163 (61.0)	*<0.001*
Non-invasive ventilation	334	134 (40.1)	274	112 (40.9)	*0.916*
Intubation	334	56 (16.8)	276	36 (13.0)	*0.244*
Complication					
ARDS	299	82 (27.4)	242	71 (29.3)	*0.692*
Sepsis	328	21 (6.4)	265	31 (11.7)	*0.034*
Acute renal insufficiency	209	13 (6.2)	197	41 (20.8)	*<0.001*
Multiorgan failure	205	6 (2.9)	192	21 (10.9)	*0.003*
STEMI	330	3 (0.9)	271	8 (3.0)	*0.073*
NSTEMI	243	1 (0.4)	229	16 (7.0)	*<0.001*
Heart Failure	243	7 (2.9)	229	44 (19.2)	*<0.001*
Ventricular arrhythmia	330	2 (0.6)	271	5 (1.8)	*0.253*
Pulmonary embolism	330	17 (5.2)	272	27 (9.9)	*0.037*
Other embolism	330	5 (1.5)	272	11 (4.0)	*0.096*
Stroke	330	2 (0.6)	272	1 (0.4)	*1.000*
Major bleeding	244	4 (1.6)	229	16 (7.0)	*0.008*
Delirium	204	3 (1.5)	192	13 (6.8)	*0.015*
Outcome					
Death	336	44 (13.1)	278	104 (37.4)	*<0.001*
Cause of death					
Respiratory insufficiency	42	36 (85.7)	103	81 (78.6)	*0.455*
Myocardial infarction	42	0 (0.0)	103	5 (4.9)	*0.322*
Pulmonary embolism	42	2 (4.8)	103	9 (8.7)	*0.511*
Stroke	42	1 (2.4)	103	3 (2.9)	*1.000*
Multiorgan failure	42	7 (16.7)	103	36 (35.0)	*0.047*
Bleeding	42	1 (2.4)	103	3 (2.9)	*1.000*

Data shown as median (IQR), count (%)

Legend: ARDS: acute respiratory distress syndrome; FiO_2: fraction of inspired oxygen, NSTEMI: non-ST segment elevation myocardial infarction, STEMI: ST segment elevation myocardial infarction.

eTable 4. Univariable and multivariable Cox regression model for death.

		Univariable		***Multivariable N=510****	
	Level/Units	HR (95% CI)	*p-value*	HR (95% CI)	*p-value*
Age	+5 years	1.33 (1.24-1.44)	*<0.001*	1.29 (1.16-1.44)	*<0.001*
Sex	M vs F	1.44 (0.97-2.14)	*0.073*	1.58 (0.99-2.51)	*0.054*
Respiratory rate	≥22 vs <22	1.69 (1.12-2.55)	*0.012*		
Body mass index	+1 kg/m^2	1.01 (0.97-1.04)	*0.687*		
SBP	+10 mmHg	0.95 (0.88-1.03)	*0.186*		
Oxygen saturation	+5 %	0.83 (0.77-0.90)	*<0.001*	0.87 (0.78-0.97)	*0.013*
RBC	+0.5 $x10^6/\mu L$	0.84 (0.75-0.95)	*0.004*		
WBC	+1000 U/µL	1.03 (1.00-1.06)	*0.053*		
Lymphocytes	+100 U/µL	0.93 (0.89-0.96)	*<0.001*		
CRP	+10 mg/L	1.03 (1.01-1.04)	*<0.001*	1.03 (1.01-1.05)	*0.006*
Troponin	Elevated vs Normal	3.22 (2.26-4.59)	*<0.001*	1.71 (1.13-2.59)	*0.012*
NT-proBNP	+1000 ng/L	1.03 (1.00-1.05)	*0.026*		
LDH	+1000 mg/dL	1.11 (1.04-1.18)	*0.001*		
Bilirubin	+0.3 mg/dL	1.07 (0.96-1.19)	*0.249*		
D-dimer	+1000 ng/mL	1.02 (0.99-1.05)	*0.271*		
Creatinine	+1 mg/dL	1.12 (1.05-1.20)	*<0.001*		
eGFR (CKD-EPI)	+10 mg/L	0.83 (0.78-0.87)	*<0.001*	0.95 (0.86-1.04)	*0.263*
INR	+1	1.18 (0.98-1.41)	*0.075*		
ABG test lactate	+1 mmol/L	1.20 (1.12-1.29)	*<0.001*		
PaO_2/FiO_2	+50 mmHg/%	0.89 (0.82-0.96)	*0.003*	0.89 (0.80-0.99)	*0.030*
Interleukin-6	+10 pg/mL	1.00 (1.00-1.01)	*0.216*		
SOFA	+1 point	1.36 (1.26-1.47)	*<0.001*		
SOFA	3-4-5 vs 0-1-2	3.37 (2.00-5.68)	*<0.001*		
SOFA	≥6 vs 0-1-2	6.75 (3.65-12.48)	*<0.001*		
Heart failure	Yes vs No	2.54 (1.75-3.68)	*<0.001*	2.15 (1.28-3.63)	*0.004*
Coronary artery disease	Yes vs No	2.16 (1.54-3.04)	*<0.001*	1.12 (0.71-1.76)	*0.629*
Atrial fibrillation	Yes vs No	2.34 (1.62-3.38)	*<0.001*	1.14 (0.69-1.86)	*0.615*
Chronic obstructive pulmonary disease	Yes vs No	1.88 (1.20-2.97)	*0.006*	1.34 (0.78-2.32)	*0.286*
Diabetes	Yes vs No	1.41 (0.99-2.02)	*0.057*		
Obesity	Yes vs No	1.26 (0.85-1.85)	*0.25*		
Hypertension	Yes vs No	1.95 (1.37-2.78)	*<0.001*	1.26 (0.81-1.96)	*0.312*
Chronic kidney disease	Yes vs No	2.68 (1.90-3.79)	*<0.001*	1.03 (0.60-1.78)	*0.908*
Smoking	Ever vs Never smoker	1.33 (1.24-1.44)	*<0.001*		
Prior ACEi/ARB therapy	Yes vs No	1.62 (1.16-2.25)	*0.005*		
Prior statin therapy	Yes vs No	1.73 (1.23-2.43)	*0.002*		

*number of patients with complete data

Legend: ABG: arterial blood gas, ACEi: angiotensin converting enzyme inhibitor, ARB: angiotensin receptor blocker, , CKD-EPI: chronic kidney disease epidemiology collaboration formula, CRP: C-reactive protein, eGFR:

estimated glomerular filtration rate, FiO_2: fraction of inspired oxygen, INR International Normalized Ratio, NT-proBNP: N-terminal fragment of the prohormone brain natriuretic peptide, PaO_2: oxygen partial pressure at arterial gas analysis, RBC red blood cell, SBP Systolic blood pressure; SOFA: sequential organ failure assessment, WBC white blood cell.

eTable 5. Univariable and multivariable Cox regression model for death, including lymphocytes and respiratory rate.

		Univariable		***Multivariable N=334****	
	Level/Units	HR (95% CI)	*p-value*	HR (95% CI)	*p-value*
Age	+5 years	1.33 (1.24-1.44)	*<0.001*	1.32 (1.16-1.51)	*<0.001*
Sex	M vs F	1.44 (0.97-2.14)	*0.073*	1.98 (1.11-3.52)	*0.020*
Respiratory rate	≥22 vs <22	1.69 (1.12-2.55)	*0.012*	1.35 (0.82-2.24)	*0.242*
Oxygen saturation	+5 %	0.83 (0.77-0.90)	*<0.001*	0.79 (0.70-0.90)	*<0.001*
Lymphocytes	+100 U/µL	0.93 (0.89-0.96)	*<0.001*	0.99 (0.94-1.04)	*0.610*
CRP	+10 mg/L	1.03 (1.01-1.04)	*<0.001*	1.03 (1.00-1.05)	*0.021*
Troponin	Elevated vs Normal	3.22 (2.26-4.59)	*<0.001*	1.65 (1.03-2.62)	*0.036*
eGFR (CKD-EPI)	+10 mL/min	0.83 (0.78-0.87)	*<0.001*	0.87 (0.78-0.98)	*0.021*
PaO_2/FiO_2	+50 mmHg/%	0.89 (0.82-0.96)	*0.003*	0.94 (0.83-1.07)	*0.350*
Comorbidities					
Heart failure	Yes vs No	2.54 (1.75-3.68)	*<0.001*	1.46 (0.75-2.81)	*0.263*
Coronary artery disease	Yes vs No	2.16 (1.54-3.04)	*<0.001*	1.13 (0.67-1.90)	*0.649*
Atrial fibrillation	Yes vs No	2.34 (1.62-3.38)	*<0.001*	1.12 (0.62-2.04)	*0.706*
Chronic obstructive pulmonary disease	Yes vs No	1.88 (1.20-2.97)	*0.006*	1.81 (1.00-3.26)	*0.051*
Hypertension	Yes vs No	1.95 (1.37-2.78)	*<0.001*	1.18 (0.70-2.00)	*0.542*
Chronic kidney disease	Yes vs No	2.68 (1.90-3.79)	*<0.001*	0.90 (0.48-1.69)	*0.749*

*number of patients with complete data

Legend: CKD-EPI: chronic kidney disease epidemiology collaboration formula, CRP: C-reactive protein, eGFR: estimated glomerular filtration rate, FiO_2: fraction of inspired oxygen, PaO_2: oxygen partial pressure at arterial gas analysis.

eTable 6. Univariable and multivariable Cox regression model for death, including lymphocytes, respiratory rate, prior ACEi/ARB therapy and prior statin therapy.

		Univariable		***Multivariable N=299****	
	Level/Units	HR (95% CI)	*p-value*	HR (95% CI)	*p-value*
Age	+5 years	1.33 (1.24-1.44)	*<0.001*	1.31 (1.14-1.51)	*<0.001*
Sex	M vs F	1.44 (0.97-2.14)	*0.073*	2.19 (1.17-4.11)	*0.015*
Respiratory rate	≥22 vs <22	1.69 (1.12-2.55)	*0.012*	1.30 (0.76-2.21)	*0.335*
Oxygen saturation	+5 %	0.83 (0.77-0.90)	*<0.001*	0.80 (0.70-0.91)	*0.001*
Lymphocytes	+100	0.93 (0.89-0.96)	*<0.001*	0.99 (0.94-1.05)	*0.84*
CRP	+10 mg/L	1.03 (1.01-1.04)	*<0.001*	1.03 (1.01-1.05)	*0.015*
Troponin	Elevated vs Normal	3.22 (2.26-4.59)	*<0.001*	1.50 (0.92-2.45)	*0.108*
eGFR (CKD-EPI)	+10 mL/min	0.83 (0.78-0.87)	*<0.001*	0.85 (0.76-0.96)	*0.009*
PaO_2/FiO_2	+50 mmHg/%	0.89 (0.82-0.96)	*0.003*	0.95 (0.83-1.09)	*0.45*
Comorbidities					
Heart failure	Yes vs No	2.54 (1.75-3.68)	*<0.001*	1.20 (0.60-2.40)	*0.615*
Ischemic cardiomyopathy	Yes vs No	2.16 (1.54-3.04)	*<0.001*	1.06 (0.57-2.00)	*0.848*
Atrial fibrillation	Yes vs No	2.34 (1.62-3.38)	*<0.001*	1.18 (0.63-2.20)	*0.608*
Chronic obstructive pulmonary disease	Yes vs No	1.88 (1.20-2.97)	*0.006*	1.91 (1.02-3.59)	*0.043*
Hypertension	Yes vs No	1.95 (1.37-2.78)	*<0.001*	1.03 (0.57-1.86)	*0.934*
Chronic kidney disease	Yes vs No	2.68 (1.90-3.79)	*<0.001*	0.83 (0.43-1.63)	*0.595*
Prior ACEi/ARB therapy	Yes vs No	1.62 (1.16-2.25)	*0.005*	1.21 (0.69-2.11)	*0.501*
Prior statin therapy	Yes vs No	1.73 (1.23-2.43)	*0.002*	1.23 (0.69-2.21)	*0.484*

*number of patients with complete data

Legend: ACEi: angiotensin converting enzyme inhibitor, ARB: angiotensin receptor blocker, CKD-EPI: chronic kidney disease epidemiology collaboration formula, CRP: C-reactive protein, eGFR: estimated glomerular filtration rate, FiO_2: fraction of inspired oxygen, PaO_2: oxygen partial pressure at arterial gas analysis.

eTable 7. Univariable and multivariable Cox regression model, including prior ACEi/ARB therapy and prior statin therapy.

Variable		***Univariable***		***Multivariable N=473****	
	Level/Units	HR (95% CI)	*p-value*	HR (95% CI)	*p-value*
Age	+5 years	1.33 (1.24-1.44)	*<0.001*	1.30 (1.16-1.45)	*<0.001*
Sex	M vs F	1.44 (0.97-2.14)	*0.073*	1.59 (0.97-2.58)	*0.064*
Oxygen saturation	+5 %	0.83 (0.77-0.90)	*<0.001*	0.87 (0.78-0.97)	*0.012*
CRP	+10 mg/L	1.03 (1.01-1.04)	*<0.001*	1.03 (1.01-1.05)	*0.006*
Troponin	Elevated vs Normal	3.22 (2.26-4.59)	*<0.001*	1.61 (1.05-2.47)	*0.028*
eGFR (CKD-EPI)	+10 mL/min	0.83 (0.78-0.87)	*<0.001*	0.94 (0.85-1.04)	*0.228*
PaO_2/FiO_2	+50 mmHg/%	0.89 (0.82-0.96)	*0.003*	0.89 (0.80-1.00)	*0.053*
Comorbidities					
Heart failure	Yes vs No	2.54 (1.75-3.68)	*<0.001*	1.86 (1.07-3.21)	*0.027*
Coronary artery disease	Yes vs No	2.16 (1.54-3.04)	*<0.001*	1.31 (0.78-2.18)	*0.308*
Atrial fibrillation	Yes vs No	2.34 (1.62-3.38)	*<0.001*	1.21 (0.72-2.03)	*0.472*
Chronic obstructive pulmonary disease	Yes vs No	1.88 (1.20-2.97)	*0.006*	1.34 (0.76-2.38)	*0.314*
Hypertension	Yes vs No	1.95 (1.37-2.78)	*<0.001*	1.16 (0.71-1.90)	*0.547*
Chronic kidney disease	Yes vs No	2.68 (1.90-3.79)	*<0.001*	1.05 (0.59-1.87)	*0.857*
Prior ACEi/ARB therapy	Yes vs No	1.62 (1.16-2.25)	*0.005*	1.10 (0.72-1.69)	*0.646*
Prior statin therapy	Yes vs No	1.73 (1.23-2.43)	*0.002*	0.85 (0.53-1.37)	*0.506*

*number of patients with complete data

Legend: ACEi: angiotensin converting enzyme inhibitor, ARB: angiotensin receptor blocker, CKD-EPI: chronic kidney disease epidemiology collaboration formula, CRP: C-reactive protein, eGFR: estimated glomerular filtration rate, FiO_2: fraction of inspired oxygen, PaO_2: oxygen partial pressure at arterial gas analysis.