

Supplementary material for

Clinical frailty, and not features of acute infection, is associated with late mortality in COVID-19: a retrospective cohort study

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Table S1. Description of the Clinical Frailty Scale*		
1	Very fit	Among the fittest people for their age.
2	Fit	Fit, occasionally active exercise.
3	Managing well	Well controlled medical problems, not regularly active.
4	Living with very mild frailty	Independent, but often symptoms limit their activities.
5	Living with mild frailty	Needing help with high order instrumental activities of everyday life.
6	Living with moderate frailty	Needing help with all outdoor activities and with housekeeping.
7	Living with severe frailty	Completely dependent on others for personal care.
8	Living with very severe frailty	Approaching end of life.
9	Terminally ill	People with <6 months life expectancy due to underlying conditions, but who do not have severe frailty.
*Adapted from <i>Can Geriatr J.</i> 2020 Sep 1;23(3):210-215.		

Table S2. Description of the 4C Mortality Score*

Variable	Variable value (4C mortality scoring)
Age (years)	<50 (0) 50-59 (2) 60-69 (4) 70-79 (6) ≥80 (7)
Sex	Female (0) Male (1)
Number of comorbidities according to Charlson comorbidity index & physician-assessed obesity	0 (0) 1 (1) ≥2 (2)
Respiratory rate (breaths/minute)	<20 (0) 20-29 (1) ≥30 (2)
Peripheral oxygen saturation (%) on room air	≥92 (0) <92 (2)
Glasgow Coma Scale	15 (0) ≤15 (2)
Urea (mmoL/L)	<7 (0) 7-14 (1) >14 (3)
C-reactive protein (mg/L)	<50 (0) 50-99 (1) ≥100 (2)
	Range: 0-21
*Adapted from <i>BMJ</i> . 2020 Sep 9;370:m3339.	

Table S3: Measures of explained variation for different sets of confounders in the final multivariable model

	Adjusted R squared index (%)*
In hospital	
Core model (clinical)	18.6
Core model (clinical)+CFS	21.3
Core model (laboratory)	15.6
Core model (laboratory)+CFS	19.9
Late mortality	
Core model (clinical)	12.6
Core model (clinical)+CFS	23.4
Core model (laboratory)	7.1
Core model (laboratory)+CFS	21.6
<p>*Adjusted R squared index is a measure of explained variation. Higher R squared index indicates better model fit to observed data.</p> <p>Clinical model for 28-day mortality included age>65 years, shortness of breath, myalgia, confusion, respiratory rate>20 (breaths/min.), hypoxia (SpO2<92%), congestive heart failure, chronic kidney disease, hypertension and dementia.</p> <p>Laboratory model for 28-day mortality included white blood cells (WBCs)<4 or WBCs>12 ($\times 10^9/L$), neutrophil number, urea, estimated glomerular filtration rate (eGFR), alkaline phosphatase (ALP), C-reactive protein (CRP), albumin and sodium.</p> <p>Clinical model for late mortality included age>65 years, confusion, active cancer, ischemic heart disease and dementia.</p> <p>Laboratory model for late mortality included haemoglobin, neutrophil number, estimated glomerular filtration rate (eGFR), alkaline phosphatase (ALP) and albumin.</p> <p>Abbreviations: CFS: clinical frailty scale.</p>	

Table S4. Additive value of CFS over the core models for 28-day and late mortality		
	AIC	P-value
28-day mortality		
Clinical model	437.1	
Clinical model + CFS	424.9	<0.001
Clinical model + CFS \geq 5	429.1	0.002
Laboratory model	418.1	
Laboratory model + CFS	395.3	<0.001
Laboratory model + CFS \geq 5	400.5	<0.001
Late mortality		
Clinical model	220.0	
Clinical model + CFS	191.6	<0.001
Clinical model + CFS \geq 5	200.0	<0.001
Laboratory model	206.5	
Laboratory model + CFS	173.1	<0.001
Laboratory model + CFS \geq 5	179.2	<0.001
<p>Clinical model for 28-day mortality included age>65 years, shortness of breath, myalgia, confusion, respiratory rate>20 (breaths/min.), hypoxia (SpO₂<92%), congestive heart failure, chronic kidney disease, hypertension and dementia.</p> <p>Laboratory model for 28-day mortality included white blood cells (WBCs)<4 or WBCs>12 ($\times 10^9/L$), neutrophil number, urea, estimated glomerular filtration rate (eGFR), alkaline phosphatase (ALP), C-reactive protein (CRP), albumin and sodium.</p> <p>Clinical model for late mortality included age>65 years, confusion, active cancer, ischemic heart disease and dementia.</p> <p>Laboratory model for late mortality included haemoglobin, neutrophil number, estimated glomerular filtration rate (eGFR), alkaline phosphatase (ALP) and albumin.</p> <p>Abbreviations: AIC: Akaike information criterion; CFS: clinical frailty scale.</p>		

Table S5. Cross validation of AUC for the main multivariable models		
	Training set (50%)	Validation set (50%)
	AUC (95% CI)	AUC (95% CI)
28-day mortality		
Clinical model	0.795 (0.791-0.798)	0.795 (0.790-0.796)
Laboratory model	0.784 (0.764-0.794)	0.783 (0.768-0.794)
Late mortality		
Clinical model	0.710 (0.638-0.748)	0.719 (0.604-0.768)
Laboratory model	0.843 (0.779-0.861)	0.893 (0.802-0.864)
<p>Clinical model for 28-day mortality included age>65 years, shortness of breath, myalgia, confusion, respiratory rate>20 (breaths/min.), hypoxia (SpO₂<92%), congestive heart failure, chronic kidney disease, hypertension and dementia.</p> <p>Laboratory model for 28-day mortality included white blood cells (WBCs)<4 or WBCs>12 (x10⁹/L), neutrophil number, urea, estimated glomerular filtration rate (eGFR), alkaline phosphatase (ALP), C-reactive protein (CRP), albumin and sodium.</p> <p>Clinical model for late mortality included age>65 years, confusion, active cancer, ischemic heart disease and dementia.</p> <p>Laboratory model for late mortality included haemoglobin, neutrophil number, estimated glomerular filtration rate (eGFR), alkaline phosphatase (ALP) and albumin.</p> <p><u>Note:</u> Close concordance in AUCs of the two datasets (training and validation) indicates absence of overfitting.</p> <p>Abbreviations: AUC: area under the curve; CI: confidence interval.</p>		

Table S6. Univariate associations of clinical characteristics with early (28-day) and late mortality						
	Early mortality			Late mortality		
	Survived (n=351)	Died (n=120)	P-value*	Survived (n=310)	Died (n=41)	P-value*
Demographics						
Age (years)	69 (24)	82 (15)	<0.001	66 (24)	83 (18)	<0.001
Male sex	181 (51.6)	67 (55.8)	0.459	162 (52.3)	19 (46.3)	0.509
Symptoms and signs at presentation						
T>38°C or T<36°C	82 (24.5)	31 (26.5)	0.710	71 (24.1)	11 (26.8)	0.701
Cough	237 (68.5)	76 (63.3)	0.311	211 (69.2)	26 (63.4)	0.476
Sputum	85 (24.6)	21 (17.5)	0.130	76 (24.9)	9 (22.0)	0.847
Shortness of breath	201 (58.1)	82 (68.3)	0.051	180 (59.0)	21 (51.2)	0.400
Haemoptysis	11 (3.2)	0 (0)	0.074	10 (3.3)	1 (2.4)	1.000
Rhinorrhea	15 (4.3)	2 (1.7)	0.260	13 (4.3)	2 (4.9)	0.694
Pharyngitis	36 (10.4)	0 (0)	<0.001	34 (11.1)	2 (4.9)	0.284
Myalgia	74 (21.4)	11 (9.2)	0.002	70 (23.0)	4 (9.8)	0.066
Arthralgia	9 (2.6)	0 (0)	0.120	8 (2.6)	1 (2.4)	1.000
Fatigue	132 (38.2)	46 (38.3)	1.000	117 (38.4)	15 (36.6)	0.866
Headache	37 (10.7)	8 (6.7)	0.281	37 (12.1)	0 (0)	0.013
Confusion	69 (19.9)	48 (40.0)	<0.001	54 (17.7)	15 (36.6)	0.011
Anosmia	21 (6.1)	4 (3.3)	0.348	19 (6.2)	2 (4.9)	1.000
Abdominal pain	44 (12.7)	11 (9.2)	0.330	40 (13.1)	4 (9.8)	0.802
Diarrhea	69 (19.9)	16 (13.3)	0.131	63 (20.7)	6 (14.6)	0.532
Heart rate (bpm)	89 (28)	90 (31)	0.415	90 (29)	85 (24)	0.272
Heart rate > 90 bpm	154 (46.1)	57 (49.1)	0.591	141 (48.0)	13 (32.5)	0.090
Systolic BP (mmHg)	126 (33)	126 (27)	0.975	126 (33)	124 (36)	0.806
Diastolic BP (mmHg)	73 (17)	70 (14)	0.068	74 (17)	70 (19)	0.039
RR (breaths/min)	20 (6)	22 (10)	<0.001	20 (6)	20 (6)	0.780
RR > 20 (breaths/min)	144 (43.2)	71 (61.2)	0.001	126 (43.0)	18 (45.0)	0.866
Hypoxia (SpO2<92%)	134 (40.1)	70 (59.8)	<0.001	116 (39.6)	18 (43.9)	0.613
Mean BP (mmHg)	94 (20)	94 (19)	0.362	95 (20)	92 (26)	0.365
Co-morbidities						
Active cancer	37 (10.6)	19 (16.0)	0.140	27 (8.8)	10 (24.4)	0.005
Asthma	45 (12.9)	10 (8.3)	0.249	42 (13.6)	3 (7.3)	0.328
COPD	52 (14.9)	19 (15.8)	0.883	42 (13.6)	10 (24.4)	0.098
Other ILD	16 (4.6)	7 (5.8)	0.625	14 (4.6)	2 (4.9)	1.000
Ischemic heart disease	67 (19.2)	28 (23.3)	0.357	52 (16.9)	15 (36.6)	0.005
Congestive heart failure	37 (10.6)	31 (25.8)	<0.001	30 (9.8)	7 (17.1)	0.175
Chronic kidney disease	72 (20.6)	41 (34.2)	0.004	60 (19.5)	12 (29.3)	0.153
DM diet-controlled	31 (8.9)	15 (12.5)	0.285	28 (9.1)	3 (7.3)	1.000
DM tabs-controlled	37 (10.6)	14 (11.7)	0.736	31 (10.1)	6 (14.6)	0.415
DM- insulin	21 (6.0)	8 (6.7)	0.826	19 (6.2)	2 (4.9)	1.000
Hypertension	124 (35.5)	65 (54.2)	0.001	108 (35.1)	16 (39.0)	0.607
Liver disease	19 (5.4)	2 (1.7)	0.122	16 (5.2)	3 (7.3)	0.477
Dementia	51 (14.6)	37 (30.8)	<0.001	33 (10.7)	18 (43.9)	<0.001
WHO ordinal scale at admission (>4)	156 (44.8)	36 (30.0)	0.005	139 (45.3)	17 (41.5)	0.739
WHO ordinal scale at discharge (>4)	335 (98.8)	0 (0)	<0.001	297 (99.3)	38 (95.0)	0.070
Continuous variables are presented as median (inter-quartile range) and categorical variables as absolute count (valid percentage).						
*P-values are derived from Mann Whitney U test for continuous variables and Fisher's exact test for categorical variables.						

Abbreviations: T: temperature; mmHg: millimeters of mercury; bpm: beats per minute; BP: blood pressure; RR: respiratory rate; COPD: chronic obstructive pulmonary disease; ILD: interstitial lung disease; DM: diabetes mellitus; WHO: World Health Organization.

Table S7. Univariate associations of laboratory parameters with early (28-day) and late mortality						
	Early mortality			Late mortality		
	Survived (n=351)	Died (n=120)	P-value*	Survived (n=310)	Died (n=41)	P-value*
Laboratory parameters						
Haemoglobin (g/L)	131 (31)	128 (33)	0.242	133 (27)	113 (34)	<0.001
WBCs (x10 ⁹ /L)	7.3 (4)	8.1 (6)	0.003	7.1 (4)	7.9 (4)	0.015
WBCs<4 or WBCs>12 (x10 ⁹ /L)	58 (17.0)	35 (29.7)	0.005	50 (16.6)	8 (19.5)	0.658
Neutrophils (x10 ⁹ /L)	5.5 (3)	6.6 (5)	<0.001	5.3 (3)	5.9 (4)	0.067
Eosinophils (x10 ⁹ /L)	0.01 (0)	0.01 (0)	0.073	0.01 (0)	0.01 (0)	0.401
Lymphocytes (x10 ⁹ /L)	0.96 (0.7)	0.85 (0.8)	0.027	0.96 (0.7)	0.97 (0.8)	0.818
Platelets (x10 ⁹ /L)	222 (112)	223 (122)	0.959	217 (109)	246 (166)	0.254
Urea (mmol/L)	6.5 (6)	9.8 (10)	<0.001	6.3 (5)	8.3 (6)	0.027
Creatinine (µmol/L)	81 (39)	104 (72)	<0.001	81 (37)	82 (54)	0.605
eGFR (mL/min/1.73 m ²)	76 (39)	49 (44)	<0.001	77 (37)	59 (38)	0.021
ALP (IU/L)	79 (41)	88 (45)	0.003	78 (37)	98 (103)	0.013
Bilirubin (µmol/L)	8 (5)	8 (7)	0.453	8 (5)	7.5 (6)	0.608
CRP (mg/L)	58 (100)	92 (135)	<0.001	57 (99)	79 (106)	0.834
Albumin (g/L)	39 (7)	36 (6)	<0.001	39 (6)	35 (8)	0.001
Sodium (mmol/L)	137 (6)	138 (8)	0.008	137 (6)	137 (5)	0.980
Potassium (mmol/L)	4.1 (1)	4.3 (1)	0.047	4.1 (1)	4.15 (1)	0.865
Risk scores						
Clinical Frailty Scale	3 (4)	6 (3)	<0.001	3 (3)	6 (2)	<0.001
4C mortality score	10 (6)	14 (4)	<0.001	9 (6)	12.5 (4)	<0.001
Continuous variables are presented as median (inter-quartile range) and categorical variables as absolute count (valid percentage).						
*P-values are derived from Mann Whitney U test for continuous variables and Fisher's exact test for categorical variables.						
Abbreviations: WBCs; white blood cells; eGFR: estimated glomerular filtration rate; ALP: alkaline phosphatase; CRP: C-reactive protein.						

Table S8. Association of disease features with early (28-day) and late mortality after adjustment for age, sex and eGFR

	Early mortality		Late mortality	
	OR (95% CI)	P-value*	OR (95% CI)	P-value*
Symptoms and signs at presentation				
Shortness of breath	2.23 (1.35-3.66)	0.002	0.92 (0.46-1.85)	0.825
Myalgia	0.79 (0.38-1.67)	0.545	0.83 (0.26-2.61)	0.747
Confusion	1.23 (0.74-2.06)	0.428	1.28 (0.59-2.77)	0.538
Respiratory rate (breaths/min.)	1.08 (1.04-1.13)	<0.001	1.02 (0.95-1.08)	0.646
RR>20 (breaths/min.)	2.51 (1.54-4.08)	<0.001	1.24 (0.62-2.49)	0.539
Hypoxia (SpO ₂ <92%)	2.49 (1.54-4.04)	<0.001	1.29 (0.64-2.57)	0.478
Co-morbidities				
Active Cancer	1.56 (0.81-3.00)	0.186	3.18 (1.33-7.60)	0.009
Ischemic heart disease	0.79 (0.46-1.36)	0.396	1.79 (0.86-3.75)	0.122
Congestive heart failure	1.94 (1.09-3.43)	0.023	1.23 (0.48-3.12)	0.666
Chronic kidney disease	0.70 (0.38-1.27)	0.237	0.85 (0.33-2.21)	0.747
Hypertension	1.35 (0.85-2.14)	0.210	0.71 (0.35-1.44)	0.342
Dementia	1.09 (0.63-1.91)	0.749	2.95 (1.30-6.70)	0.010
Adapted WHO ordinal scale at admission	0.50 (0.37-0.69)	<0.001	0.91 (0.56-1.49)	0.714
Laboratory parameters				
Haemoglobin (g/L)	0.999 (0.988-1.009)	0.826	0.975 (0.959-0.992)	0.004
WBCs<4 or WBCs>12 (x10 ⁹ /L)	1.92 (1.12-3.27)	0.017	1.20 (0.50-2.85)	0.687
Neutrophils (x10 ⁹ /L)	1.12 (1.05-1.20)	<0.001	1.10 (0.99-1.22)	0.063
Urea (mmol/L)	1.02 (0.98-1.06)	0.321	0.99 (0.92-1.06)	0.762
ALP (IU/L)	1.002 (1.000-1.005)	0.076	1.006 (1.002-1.010)	0.005
CRP (mg/L)	1.005 (1.003-1.008)	<0.001	0.999 (0.995-1.004)	0.764
Albumin (g/L)	0.94 (0.90-0.99)	0.015	0.92 (0.86-0.99)	0.020
Sodium (mmol/L)	1.035 (0.998-1.073)	0.060	0.97 (0.90-1.03)	0.305
Risk scores				
Clinical Frailty Scale	1.25 (1.08-1.44)	0.003	1.96 (1.51-2.53)	<0.001
4C mortality score	1.25 (1.14-1.38)	<0.001	1.14 (0.99-1.31)	0.066
*Odds ratios are derived from binary logistic regression with early (28-day) mortality or late mortality as the dependent variable, and per one unit increase for continuous variables, or versus the reference category for categorical variables plus age, sex and eGFR as independent variables.				
Abbreviations: eGFR: estimated glomerular filtration rate; OR: odds ratio; CI: confidence intervals; RR: respiratory rate; WHO: World Health Organization; WBCs: white blood cells; ALP: alkaline phosphatase, CRP: C-reactive protein.				

Table S9. Clinical and laboratory features as predictors of total 9-month long-term COVID-19 mortality (combined early and late mortality)

	OR (95% CI)*	P-value
Demographics		
Age (years)	1.08 (1.06-1.10)	<0.001
Age> 65 years	7.01 (4.13-11.88)	<0.001
Male sex	1.05 (0.72-1.53)	0.811
Symptoms and signs at presentation		
T>38°C or T<36°C	1.14 (0.73-1.77)	0.569
Cough	0.77 (0.52-1.15)	0.203
Sputum	0.69 (0.43-1.11)	0.125
Shortness of breath	1.23 (0.83-1.83)	0.298
Haemoptysis	0.18 (0.02-1.45)	0.108
Rhinorrhea	0.57 (0.18-1.78)	0.336
Pharyngitis	0.10 (0.02-0.42)	0.002
Myalgia	0.34 (0.19-0.63)	<0.001
Arthralgia	0.23 (0.03-1.87)	0.170
Fatigue	0.98 (0.66-1.45)	0.920
Headache	0.38 (0.17-0.83)	0.016
Confusion	2.99 (1.94-4.60)	<0.001
Anosmia	0.58 (0.23-1.49)	0.259
Abdominal pain	0.68 (0.36-1.27)	0.229
Diarrhea	0.61 (0.36-1.03)	0.065
Heart rate (bpm)	1.00 (0.99-1.01)	0.947
Heart rate> 90 bpm	0.88 (0.60-1.30)	0.532
Systolic BP (mmHg)	1.00 (0.99-1.01)	0.727
Diastolic BP (mmHg)	0.99 (0.97-1.00)	0.061
Respiratory rate (breaths/min)	1.05 (1.02-1.09)	0.001
RR > 20 (breaths/min)	1.76 (1.19-2.61)	0.005
Hypoxia (SpO ₂ <92%)	1.92 (1.30-2.84)	0.001
Mean BP (mmHg)	0.99 (0.98-1.01)	0.400
Co-morbidities		
Active Cancer	2.30 (1.31-4.05)	0.004
Asthma	0.56 (0.29-1.07)	0.079
COPD	1.39 (0.83-2.33)	0.211
Other ILD	1.24 (0.52-2.93)	0.625
Ischemic heart disease	1.79 (1.13-2.84)	0.013
Congestive heart failure	2.85 (1.69-4.82)	<0.001
Chronic kidney disease	2.03 (1.32-3.13)	0.001
DM diet-controlled	1.26 (0.67-2.35)	0.471
DM tabs-controlled	1.27 (0.70-2.30)	0.437
DM- insulin	1.01 (0.46-2.23)	0.979
Hypertension	1.88 (1.27-2.76)	0.001
Liver disease	0.58 (0.21-1.63)	0.304
Dementia	4.32 (2.66-7.03)	<0.001
Adapted WHO ordinal scale at admission	0.70 (0.55-0.88)	0.003
Adapted WHO ordinal scale at discharge	0.28 (0.21-0.36)	<0.001
Laboratory parameters		
Haemoglobin (g/L)	0.986 (0.977-0.995)	0.002
WBCs (x10 ⁹ /L)	1.00 (0.99-1.02)	0.772

WBCs<4 or WBCs>12 (x10 ⁹ /L)	1.86 (1.17-2.96)	0.009
Neutrophils (x10 ⁹ /L)	1.17 (1.10-1.24)	<0.001
Eosinophils (x10 ⁹ /L)	0.58 (0.04-9.09)	0.696
Lymphocytes (x10 ⁹ /L)	1.00 (1.00-1.00)	0.607
Platelets (x10 ⁹ /L)	1.00 (1.00-1.00)	0.261
Urea (mmol/L)	1.07 (1.04-1.10)	<0.001
Creatinine (μmol/L)	1.001 (0.999-1.003)	0.178
eGFR (mL/min/1.73 m ²)	0.977 (0.970-0.985)	<0.001
ALP (IU/L)	1.005 (1.002-1.008)	0.001
Bilirubin (μmol/L)	1.025 (0.999-1.053)	0.061
CRP (mg/L)	1.003 (1.001-1.005)	0.005
Albumin (g/L)	0.90 (0.86-0.94)	<0.001
Sodium (mmol/L)	1.05 (1.01-1.08)	0.004
Potassium (mmol/L)	1.25 (0.90-1.73)	0.180
Risk scores		
Clinical Frailty Scale	1.72 (1.54-1.93)	<0.001
4C mortality score	1.34 (1.26-1.44)	<0.001
<p>*Odds ratios are derived from univariable binary logistic regression with total 9-month mortality as the dependent variable, and per one unit increase for continuous variables, or versus the reference category for categorical variables, as the independent variable. Abbreviations: OR: odds ratio, CI: confidence intervals, T: temperature, mmHg: millimeters of mercury, bpm: beats per minute, BP: blood pressure, RR: respiratory rate, COPD: chronic obstructive pulmonary disease, ILD: interstitial lung disease, DM: diabetes mellitus, WHO: World Health Organization, WBC: white blood cells, eGFR: estimated glomerular filtration rate, ALP: alkaline phosphatase, CRP: C-reactive protein.</p>		

Table S10. Multivariable analysis of predictors for total 9-month long-term mortality (combined early and late mortality)

	OR (95% C.I.)*	P-value
a) Clinical characteristics		
CFS	1.57 (1.34-1.84)	<0.001
Age>65 years	2.27 (1.08-4.76)	0.030
Pharyngitis	0.31 (0.06-1.49)	0.143
Myalgia	1.46 (0.65-3.30)	0.364
Headache	1.42 (0.52-3.86)	0.491
Confusion	1.14 (0.63-2.08)	0.659
RR>20 (breaths/min.)	1.95 (1.17-3.25)	0.010
Hypoxia (SpO ₂ <92%)	1.61 (0.97-2.67)	0.065
Active cancer	3.03 (1.50-6.13)	0.002
Ischemic heart disease	0.97 (0.53-1.77)	0.923
Congestive heart failure	2.13 (1.09-4.16)	0.028
Chronic kidney disease	1.12 (0.66-1.91)	0.681
Hypertension	1.55 (0.94-2.56)	0.085
Dementia	1.61 (0.84-3.09)	0.156
b) Laboratory parameters		
CFS	1.58 (1.37-1.82)	<0.001
Haemoglobin	0.993 (0.980-1.005)	0.265
WBCs<4 or WBCs>12 (x10 ⁹ /L)	1.27 (0.67-2.43)	0.460
Neutrophils (x10⁹/L)	1.10 (1.01-1.20)	0.022
Urea (mmol/L)	1.00 (0.96-1.05)	0.913
eGFR (mL/min/1.73 m ²)	0.988 (0.975-1.000)	0.058
ALP (IU/L)	1.003 (1.000-1.006)	0.073
CRP (mg/L)	1.003 (1.000-1.006)	0.047
Albumin (g/L)	0.97 (0.92-1.03)	0.339
Sodium (mmol/L)	1.013 (0.972-1.055)	0.551
<p>*Odds ratios are derived from multivariable logistic regression with total 9-month long-term mortality as the dependent variable, and CFS as well as a) all clinical features, or b) all laboratory parameters associated at univariable analysis with total mortality, as independent variables.</p> <p>Abbreviations: OR: odds ratio, CI: confidence intervals, CFS: clinical frailty scale, RR: respiratory rate, WBCs: white blood cells, eGFR: estimated glomerular filtration rate, ALP: alkaline phosphatase, CRP: C-reactive protein.</p>		

Table S11. Multivariable analysis of predictors for early (28-day) mortality using a cutoff of CFS \geq 5

	OR (95% C.I.)*	P-value
a) Clinical characteristics		
Clinical Frailty Scale\geq5	2.47 (1.33-4.58)	0.004
Age>65 years	3.94 (1.79-8.70)	0.001
Shortness of breath	1.46 (0.82-2.60)	0.204
Myalgia	0.94 (0.41-2.14)	0.886
Confusion	1.63 (0.90-2.94)	0.104
RR>20 (breaths/min.)	2.07 (1.23-3.50)	0.006
Hypoxia (SpO ₂ <92%)	1.65 (0.95-2.84)	0.073
Congestive heart failure	2.10 (1.15-3.86)	0.016
Chronic kidney disease	1.21 (0.71-2.06)	0.477
Hypertension	1.71 (1.03-2.82)	0.036
Dementia	1.12 (0.60-2.09)	0.732
b) Laboratory parameters		
Clinical Frailty Scale\geq5	2.70 (1.52-4.79)	<0.001
WBCs<4 or WBCs>12 (x10 ⁹ /L)	1.42 (0.75-2.71)	0.286
Neutrophils (x10 ⁹ /L)	1.08 (0.999-1.17)	0.052
Urea (mmol/L)	1.01 (0.96-1.06)	0.729
eGFR (mL/min/1.73 m²)	0.985 (0.972-0.998)	0.023
ALP (IU/L)	1.002 (0.999-1.005)	0.147
CRP (mg/L)	1.004 (1.001-1.006)	0.017
Albumin (g/L)	0.98 (0.93-1.03)	0.395
Sodium (mmol/L)	1.045 (1.003-1.090)	0.036
*Odds ratios are derived from multivariable logistic regression with early mortality as the dependent variable, and CFS as well as a) all clinical features, or b) all laboratory parameters associated at univariable analysis with early mortality, as independent variables. Abbreviations: OR: odds ratio, CI: confidence intervals, RR: respiratory rate, WBC: white blood cells, eGFR: estimated glomerular filtration rate, ALP: alkaline phosphatase, CRP: C-reactive protein.		

Table S12. Multivariable analysis of predictors for late mortality using a cutoff of CFS \geq 5

	OR (95% C.I.)*	P-value
a) Clinical characteristics		
Clinical Frailty Scale\geq5	10.96 (3.50-34.27)	<0.001
Age>65 years	0.91 (0.29-2.84)	0.867
Confusion	0.56 (0.21-1.51)	0.252
Active Cancer	4.72 (1.75-12.76)	0.002
Ischemic heart disease	1.86 (0.82-4.20)	0.136
Dementia	3.82 (1.37-10.69)	0.011
b) Laboratory parameters		
Clinical Frailty Scale\geq5	11.45 (3.81-34.43)	<0.001
Haemoglobin (g/L)	0.980 (0.961-0.999)	0.041
Neutrophils (x10 ⁹ /L)	1.07 (0.96-1.20)	0.218
eGFR (mL/min/1.73 m ²)	0.996 (0.981-1.012)	0.643
ALP (IU/L)	1.003 (0.999-1.008)	0.156
Albumin (g/L)	0.97 (0.89-1.05)	0.420
*Odds ratios are derived from multivariable logistic regression with late mortality as the dependent variable, and CFS as well as a) all clinical features, or b) all laboratory parameters associated at univariable analysis with late mortality, as independent variables. Abbreviations: OR: odds ratio, CI: confidence intervals, eGFR: estimated glomerular filtration rate, ALP: alkaline phosphatase.		

Table S13. Association of disease features with early (28-day) and late mortality adjusted for Clinical Frailty Scale

	Early mortality		Late mortality	
	OR (95% CI)*	P-value	OR (95% CI)*	P-value
Age (years)	1.05 (1.03-1.07)	<0.001	1.01 (0.98-1.04)	0.403
Age > 65 years	3.29 (1.62-6.65)	0.001	1.15 (0.40-3.31)	0.788
Symptoms and signs at presentation				
Shortness of breath	2.30 (1.42-3.75)	0.001	1.09 (0.52-2.26)	0.819
Myalgia	0.81 (0.39-1.70)	0.581	1.64 (0.47-5.73)	0.438
Confusion	1.27 (0.76-2.11)	0.367	0.79 (0.36-1.75)	0.558
RR	1.08 (1.04-1.12)	<0.001	1.01 (0.94-1.08)	0.812
Hypoxia (SpO ₂ <92%)	2.06 (1.30-3.26)	0.002	1.00 (0.48-2.09)	0.994
Active Cancer	1.45 (0.77-2.74)	0.253	3.77 (1.41-10.04)	0.008
Ischemic heart disease	0.98 (0.58-1.67)	0.941	1.81 (0.83-3.94)	0.133
Congestive heart failure	2.14 (1.22-3.75)	0.008	0.98 (0.37-2.63)	0.968
Chronic kidney disease	1.42 (0.87-2.32)	0.156	0.99 (0.44-2.19)	0.974
Hypertension	1.93 (1.23-3.03)	0.004	1.04 (0.50-2.18)	0.918
Dementia	1.02 (0.58-1.79)	0.936	1.68 (0.75-3.76)	0.209
Adapted WHO ordinal scale at admission	0.55 (0.41-0.75)	<0.001	0.96 (0.55-1.67)	0.882
Laboratory parameters				
Haemoglobin (g/L)	1.002 (0.991-1.012)	0.774	0.981 (0.964-0.998)	0.033
WBCs<4 or WBCs>12 (x10 ⁹ /L)	1.87 (1.11-3.14)	0.019	0.98 (0.38-2.51)	0.961
Neutrophils (x10 ⁹ /L)	1.11 (1.04-1.19)	0.001	1.05 (0.94-1.17)	0.360
Urea (mmol/L)	1.05 (1.02-1.08)	0.002	1.01 (0.95-1.06)	0.854
eGFR (mL/min/1.73 m ²)	0.98 (0.97-0.99)	<0.001	1.00 (0.98-1.01)	0.572
ALP (IU/L)	1.002 (0.999-1.004)	0.124	1.005 (1.000-1.010)	0.070
CRP (mg/L)	1.005 (1.003-1.008)	<0.001	1.00 (0.995-1.004)	0.910
Albumin (g/L)	0.95 (0.90-0.99)	0.021	0.94 (0.87-1.01)	0.084
Sodium (mmol/L)	1.04 (1.004-1.077)	0.030	0.95 (0.89-1.01)	0.129
Risk scores				
4C mortality score	1.28 (1.18-1.39)	<0.001	1.06 (0.95-1.20)	0.300
*Odds ratios are derived from multivariable logistic regression with early (28-day) mortality or late mortality as the dependent variable, and per one unit increase for continuous variables, or versus the reference category for categorical variables plus Clinical Frailty Scale, as independent variables. Abbreviations: OR: odds ratio, CI: confidence intervals, eGFR: estimated glomerular filtration rate, CRP: C-reactive protein				

Table S14. Association of Clinical Frailty Scale with early (28-day) and late mortality according to age-group

≤65 years (n=169)				
	Early mortality (n=13)		Late mortality (n=6)	
	OR (95% CI)*	P-value	OR (95% CI)*	P-value
Clinical Frailty Scale	1.42 (1.08-1.86)	0.012	2.29 (1.44-3.65)	<0.001
>65 years (n=302)				
	Early mortality (n=107)		Late mortality (n=35)	
Clinical Frailty Scale	1.31 (1.14-1.51)	<0.001	1.89 (1.42-2.53)	<0.001
*Odds ratios are derived from binary logistic regression with early (28-day) mortality or late mortality as the dependent variable, and Clinical Frailty Scale as the independent variable. Abbreviations: OR: odds ratio, CI: confidence intervals.				

Figure S1

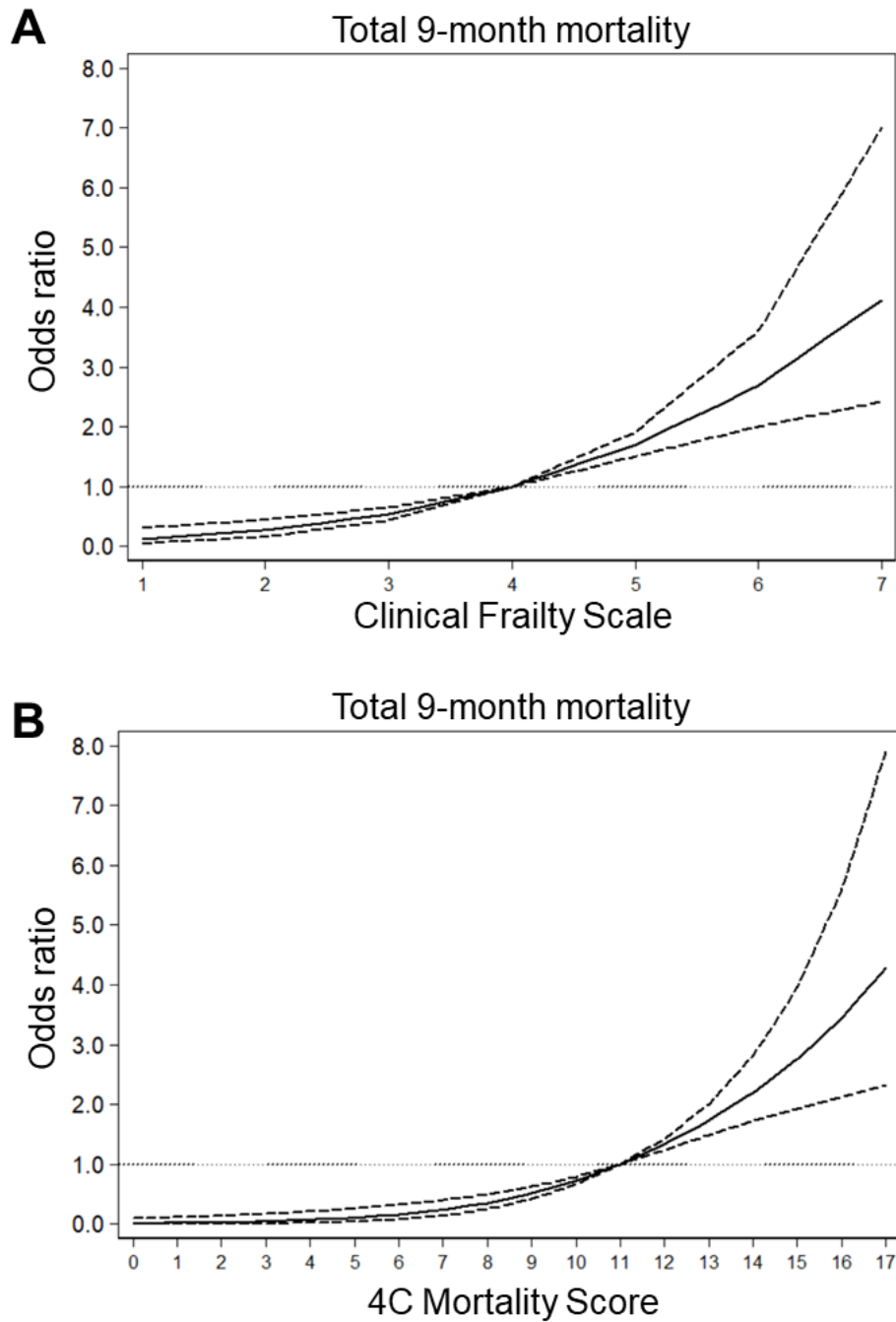


Figure S1. Smoothed restricted cubic spline plots of the odds ratio (OR) for overall mortality in patients with COVID-19 versus the baseline levels of **A.** Clinical Frailty Scale (CFS) and **B.** 4C mortality score. Depicted odds ratios indicate comparisons to the reference point (median value of CFS or 4C in our cohort). To enhance visual clarity, graphs were limited to the 95th percentile of corresponding scores. Three knots were fixed at the 10th, 50th, and 90th percentile of CFS and 4C distribution. The upper- and lower-most dashed curves represent the 95% CI of the predicted ORs (middle solid line).

Figure S2

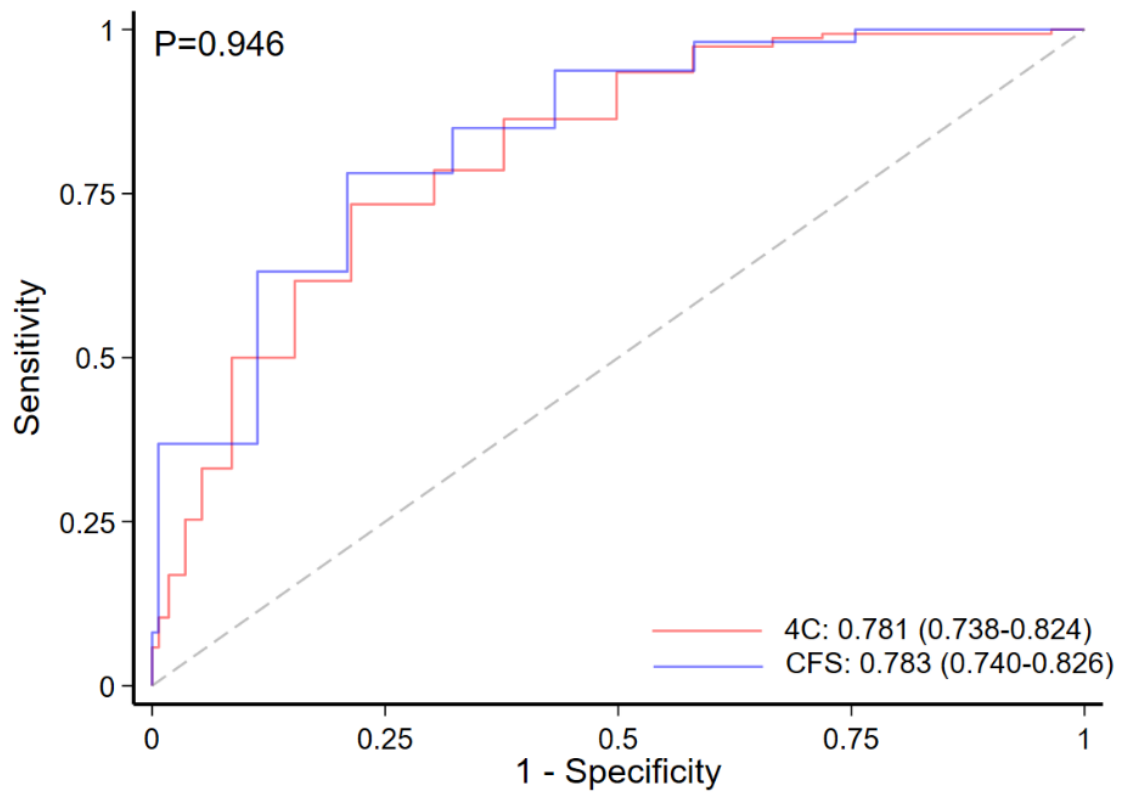


Figure S2: Receiver operating characteristic (ROC) curves and corresponding area(s) under the curve (AUC) for total 9-month mortality in patients hospitalized with COVID-19. The discriminatory performance of the 4C Mortality and the Clinical Frailty Scale score for the occurrence of death is graphically assessed by corresponding ROC curves and AUCs are compared to derive P-values using the chi-square distribution with one degree of freedom.