Supplemental Material

Methods:

To assess how the models incorporating imaging improve the prediction of outcome (identification of patients who subsequently had an event as high risk [**true positive]**, or did not have an event as low risk [**true negative**], we generated contingency tables. The contingency tables are for models incorporating either MEWS alone, or the combination of MEWS and either heart or lung imaging. They display the frequency distribution for true positive (depicted in red), false positive, false negative, and true negative (depicted in blue) for all the models with or without imaging. Based on these contingency tables we calculated sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and accuracy for each model, for either mortality, or need for mechanical ventilation separately, with, or without imaging. In each model MEWS was categorized as high risk (≥5), or low risk (<5)[1] . For lung and heart imaging the patients were categorized as high risk or low risk based on the cutoffs described in Table 2. For each event we assessed models with high sensitivity (patients were categorized as high risk if having either high risk MEWS or high risk LUS/heart imaging features), or with high specificity (patients were categorized as high risk if having both high risk MEWS and high risk LUS/heart imaging features).

Sommers' Dxy [2], is a measure of ordinal association between two possibly dependent random variables X and Y, and measures the agreement between the two variables. In the context of the regression in the article it is used to assess the predictive ability of the cox regression in predicting its outcome (overall mortality and mortality or intubation). As Sommers' Dxy is a score of a model's predictive ability it is closely

related to models' C-statistic (AUC) by the following formula C = (Dxy + 1) / 2. As overfitting is a concern, measuring Sommer's Dxy (or it's derivative the C-statistic) in bootstrapped validation models should inform whether the models' predictive ability is unique to the current set of cases and predictors' value or it is more generalizable to the tested population.

Results:

Combined lung and echocardiographic evaluation

We stratified the patients into 4 groups: “good lungs-good heart” (93 patients with neither LUS or echocardiographic parameters associated with adverse outcome); “good lungs-bad heart” (49 patients with LUS score≤ 18 but at least one echocardiographic parameter associated with adverse outcome); “bad lungs-good heart” (33 patients with LUS score> 18 but no echocardiographic parameters associated with adverse outcome); and “bad lungs-bad heart” (25 patients with LUS score> 18 and at least one echocardiographic parameter associated with adverse outcome). Patients with "good lungs-bad heart" had higher mortality rate (HR 3.1 [1.04-10.2]; p =0.04) compared to patients with "good lungs-good heart". Patients with "good lungs-bad heart" had higher composite event rate (HR 4.03 [1.5-11.5]; p=0.003) compared to patients with "good lungs-good heart". Survival curves (Figures 1A, 1B) showed that patients with "bad lungs-bad heart" had the worst outcome, and that the patients with "good lungs-good heart" had the best. Baseline characteristics of these groups are presented in Supplemental Table 3. Interestingly, routine clinical evaluation, physical examination, oxygen saturation, chest X-ray findings and laboratory evaluation (apart from slightly higher troponin levels) were similar between the groups of patients with "good lungs" irrespective of heart

function, thus only the addition of echocardiography could differentiate the "good lungs-good heart" patients from the patients with "good lungs-bad heart".

Supplemental Table 1. COVID-19 modified early warning score (COVID-19 MEWS) calculation

	3	2	1	0	1	2	3
Age (years)				<65			≥65
Respiration rate (breaths/min)	≤8		9-11	12-20		21-24	≥25
Ambient O_2 saturation (%)	≤91	92-93	94-95	≥96			
Any supplemental oxygen		yes		no			
Systolic blood pressure (mmHg)	≤90	91-100	101-110	111-219			≥220
Heart rate (beats/min)	≤40		41-50	51-90	91-110	111-130	≥131
consciousness				alert			Drowsiness lethargy coma confusion
Temperature (Celsius)	≤35.0		35.1-36.0	36.1-38.0	38.1-39.0	≥39.1	

Supplemental Table 2. Univariate analysis of lung ultrasound (LUS) prediction of clinical events

Parameter	**HR mortality**	**P value**	**HR ventilation**	**P value**	**HR Composite Event**	**P value**
Pleural effusion	5.1 (1.7-12.7)	0.006	1.18(0.05-4)	0.86	3.2 (1.06-7.4)	0.04
Pleural thickening	4.3 (1.00-77)	0.05	5.1(2.4-12)	0.004	7.9 (1.66-140)	0.004
Lung consolidation	1.6 (0.61-5.5)	0.36	4.8 (3.4-11)	0.0007	2.6 (1.03-8.8)	0.04
LUS score, per 10 points	2.6 (1.5-4.6)	0.0005	7.5 (3.3-19)	<0.0001	3.8 (2.3-6.5)	<0.0001
Dichotomous LUS score>20, 18 points	2.78 (1.27-5.82)	0.01	3.5(1.4-8.9)	0.006	3.4 (1.8-6.3)	0.0001

Supplemental Table 3. Patients stratified by baseline cardiac and lung ultrasound

Parameter	Good lungs Good heart N=93	Bad lungs Good heart N=33	Good lungs Bad heart N=49	Bad lungs Bad heart N=25	P value	P value Good lungs-Good heart vs Good lungs-Bad heart
Clinical evaluation						
Age, mean±SD, years	64.4±23	66.0±17	64.6±21	77.9±13	0.03	0.92
Male gender, n (%)	56 (60)	23 (70)	27 (55)	15 (60)	0.61	0.55
Modified Early Warning Score, median (IQR)	3 (0- 4)	5 (3-7)	3.5 (2-6)	7 (6-11)	<0.0001	0.06
Temperature, mean±SD, Celsius	37.2±0.8	37.5±0.7	37.2±1.1	37.3±1.2	0.45	0.87
O_2 saturation, mean±SD, %	95.6±3	88.3±7	94.8±5	89.3±7	<0.0001	0.76
Heart Rate, mean±SD, beats/minute	80.8±15	88.6±20	90.6 ±20	87.7±18	0.0006	0.01
Systolic blood pressure, mean±SD, mm Hg	134±22	137±22	127±20	132±21	0.29	0.11
Diastolic blood pressure, mean±SD, mm Hg	75±14	72±16	76±16	69±16	0.24	0.70
Lung crepitation, n (%)	15 (16)	11 (33)	6 (12)	7 (28)	0.10	0.54
Leg edema, n (%)	4 (4)	5 (15)	4 (8)	4 (16)	0.15	0.47
C-reactive protein, mean±SD, mg/L	46±59	126±60	62±66	111±75	<0.0001	0.08
D-dimer, median (IQR), mg/L	0.5 (0.3-1.2)	0.8 (0.6-2.1)	0.8 (0.5-1.0)	2.0 (0.9- 4.6)	<0.0001	0.13
Troponin-I, median (IQR), ng/L	6 (3-11)	11(5-21)	9 (5-21)	30 (16-81)	<0.0001	0.04
BNP, median (IQR), pg/mL	25 (11-74)	45 (18-73)	36 (16-190)	183 (71-442)	0.0002	0.24
Chest X ray						
Lobar infiltrate, n (%)	17 (18)	1 (3)	9 (18)	6 (24)	0.15	0.99
Bilateral infiltrate, n (%)	23 (25)	25 (76)	9 (18)	15 (60)	<0.0001	0.75
Hilar congestion, n (%)	5 (5)	5 (15)	6 (12)	2 (8)	0.22	0.10
Echocardiographic evaluation						
Ejection fraction, mean±SD, %	58.2±7	59.3±5	56.1±6	54.0±8	0.008	0.05
Left ventricle S', mean±SD, cm/sec	7.9±2.2	8.0±2.8	6.5±1.6	5.8±1.8	0.004	0.007
Left ventricle end-diastolic diameter, mean±SD, mm	44.3±6	43.6±10	39.9±11	41.1±10	0.03	0.01
Left ventricle end-systolic diameter, mean±SD, mm	28.7±5	27.3±7	26.4±9	28.8±11	0.26	0.08
Left ventricle mass index, mean±SD, gram/m^2	74.8±24	79.8±23	69.1±30	83.4±25	0.15	0.30
Left atrial volume index, mean±SD, ml/m^2	30.3±11	30.0±14	31.4±15	31.2±12	0.95	0.68
E wave velocity, mean±SD, cm/sec	67.4±22	61.3±15	66.1±23	69.3±16	0.49	0.73
A wave velocity, mean±SD, cm/sec	66.1±23	67.0±16	62.0±22	63.4±13	0.70	0.34
E/A ratio, mean±SD	1.08±0.4	0.92±0.2	1.12±0.6	1.05±0.4	0.27	0.73
e' septal, mean±SD, cm/sec	6.9±2.2	6.6±1.8	6.0±1.6	5.7±2.5	0.03	0.01
e' lateral, mean±SD, cm/sec	9.3±3.4	8.0±2.1	8.0±2.5	7.1±1.9	0.003	0.02
E/e' average ratio, mean±SD	9.7±6	8.8±2.5	10.6±6.4	12.1±5.1	0.15	0.46
Right atrium pressure, mean±SD, mm Hg	8.0±4	7.4±4	8.8±4	9.5±5	0.24	0.35
Stroke volume index, mean±SD ,ml/m^2	36.1±8	36.5±11	24.2±8	27.1±8	<0.0001	<0.0001
Cardiac index, mean±SD, L/min/m^2	3.0±3.0	2.9±0.9	2.0±0.6	2.2±0.8	0.12	0.03
Pulmonary acceleration time, mean±SD, msec	99.2±29	84.2±25	87.4±32	76.6±27	0.008	0.05
RV end-diastolic area index, mean±SD, cm^2/m^2	11.8±2.3	10.1±2.1	10.7±3.4	12.2±3.6	0.02	0.06
RV end-systolic area index, mean±SD cm^2/m^2	6.5±2	5.9±1	6.5±3	7.6±4	0.11	0.96

RV fractional area change, mean±SD, %	42.9±10	40.7±15	39.8±12	39.2±14	0.43	0.15
TAPSE, mean±SD, mm	2.4±0.5	2.6±0.5	2.0±0.5	1.7±0.4	<0.0001	0.002
RV S' , mean±SD, cm/sec	11.6±3	12.5±3	10.4±3	9.4±2	0.0002	0.02
Lung ultrasound evaluation						
Pleural effusion, n (%)	3 (3.2)	1 (3.0)	5 (10.2)	5 (20)	0.03	0.09
Pleural thickening, n (%)	79 (84)	33 (100)	41(83)	25(100)	0.001	0.84
Lung consolidation, n (%)	67 (72)	33 (100)	38 (77)	25 (100)	<0.0001	0.47
Lung ultrasound score, median (IQR)	10 (6-14)	21 (19-22)	12 (6-15)	23 (20-26)	<0.0001	0.44

BNP, brain natriuretic peptide; RV, right ventricle; TAPSE, tricuspid annular plane systolic excursion.

Supplemental Table 4. Inter-observer and intra-observer variability

Parameter	Mean difference	R^2	P value	Measurement variability
Inter-observer				
LUS points	0.5±0.3	0.97	0.13	4.6%
SV cc	0.4±0.9	0.98	0.61	1.4%
TAPSE cm	0.07±0.04	0.99	0.15	1.9%
Intra-observer				
LUS points		0.98	0.16	4.4%
SV cc		0.99	0.5	1.8%
TAPSE cm		0.99	0.75	1.0%

LUS, Lung Ultrasound; SV, Stroke Volume; TAPSE, tricuspid annular plane systolic excursion.

References

1) Liao X, Wang B, Kang Y. Novel coronavirus infection during the 2019-2020 epidemic: preparing intensive care units-the experience in Sichuan Province, China. *Intensive Care Med.*46(2):357-360.
2) Newson R. Parameters behind “nonparametric” statistics: Kendall's tau, Somers’ D and median differences." The Stata Journal (2001): 1-20.

Supplemental Figure 1. Examples of different patterns of lung ultrasound findings

(A) A-lines, normal reverberation artifacts of the pleural line that correspond to normal aeration of the lung. (**B**) A single B-line that represents reverberation artifact through mildly edematous interlobular septa or alveoli that correspond to moderate aeration lost. (**C**) Multiple coalescent B-lines that correspond to severe lung aeration loss. (**D**) Lung consolidation that correspond to complete aeration loss.

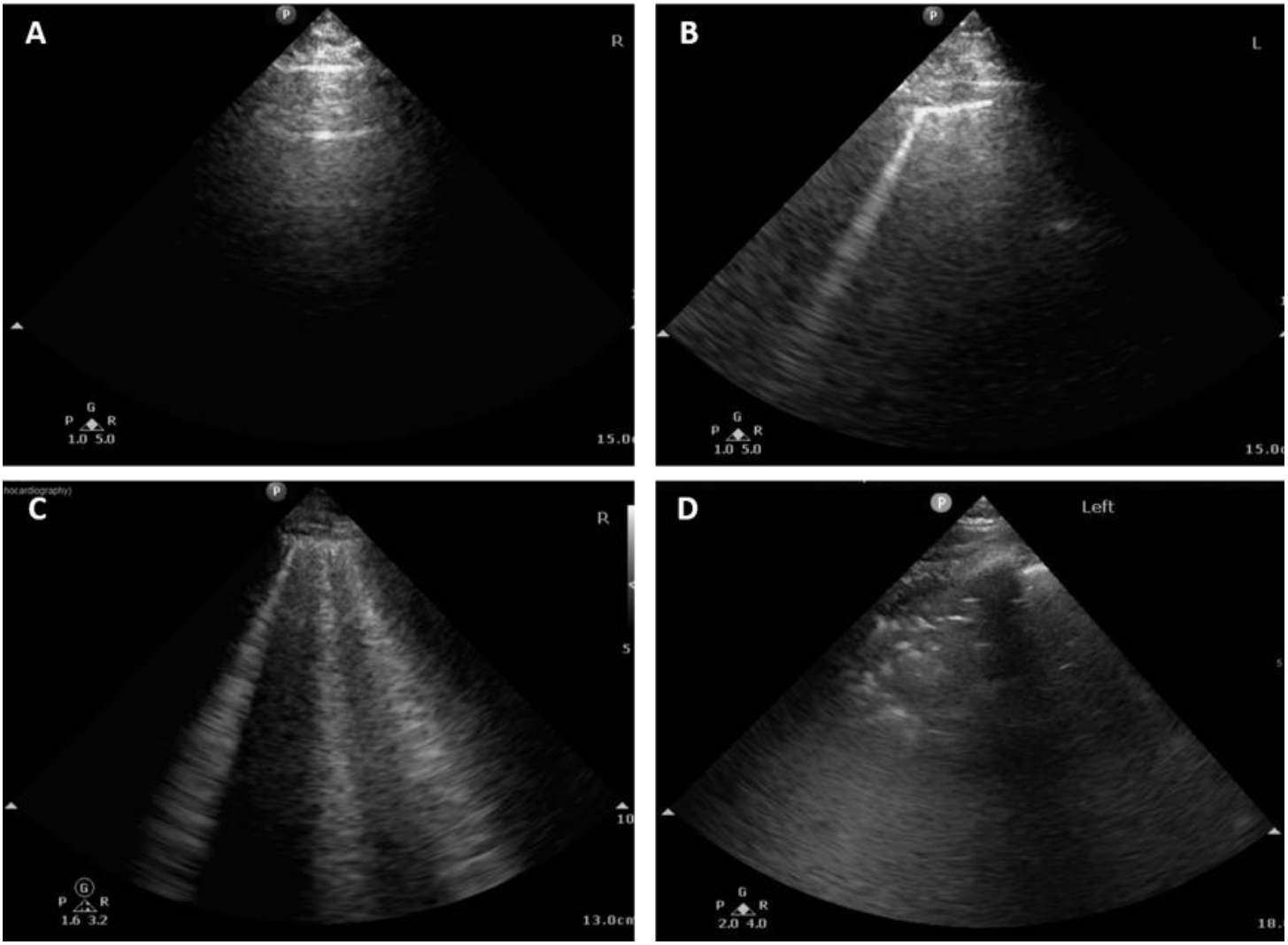
Supplemental Figure 2. Forest plots for association between imaging and outcome

A Forest plot for association of imaging with mortality. Impact of left ventricular, right ventricular, Doppler and lung ultrasound imaging parameters on mortality in patients with COVID-19 infection.

B Forest plot for association of imaging with the composite event. Impact of left ventricular, right ventricular, Doppler and lung ultrasound imaging parameters on mortality or need for invasive mechanical ventilation in patients with COVID-19 infection.

Abbreviations: EF, ejection fraction; SVI, stroke volume index; AT, pulmonic acceleration time; TAPSE, tricuspid annular plane systolic excursion; RV S', right ventricular systolic tricuspid lateral annular velocity; LUS score, lung ultrasound score.

Supplemental Figure 1



Supplemental Figure 2