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Supplemental information

The value of longitudinal clinical data and paired CT scans in predicting the deterioration of COVID-19 revealed by an artificial intelligence system

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Supplementary Information

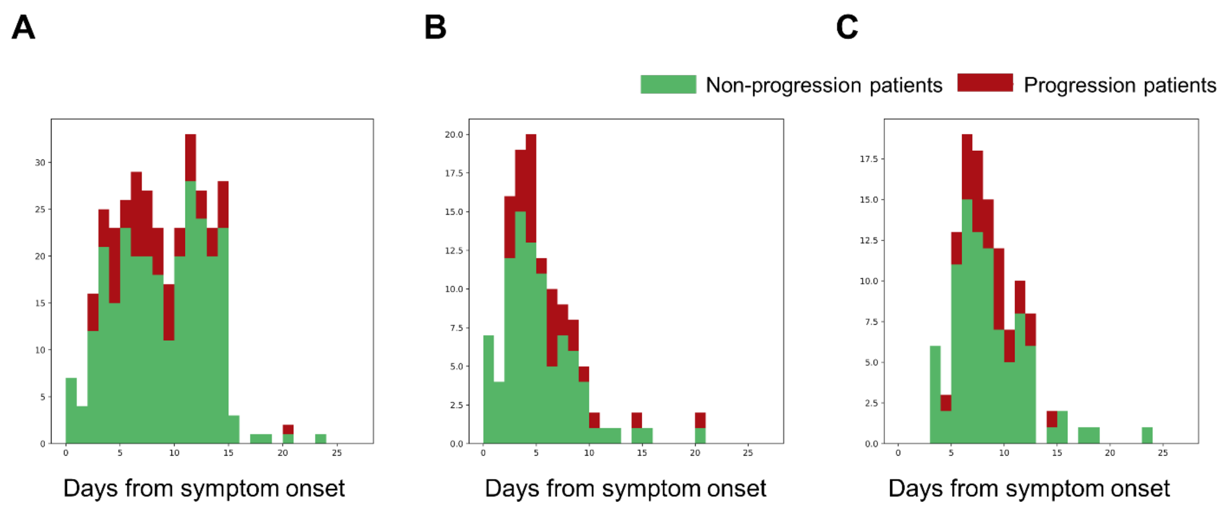

Figure S1. The distribution of days when CT scanned from symptom onset, Related to Figure 2. (**a)** All dates of 341 CT scanned from symptom onset. (**b)** Dates of first scanned CT for 119 patients after admission to hospital from symptom onset. (**c)** Dates of second scanned CT from symptom onset.

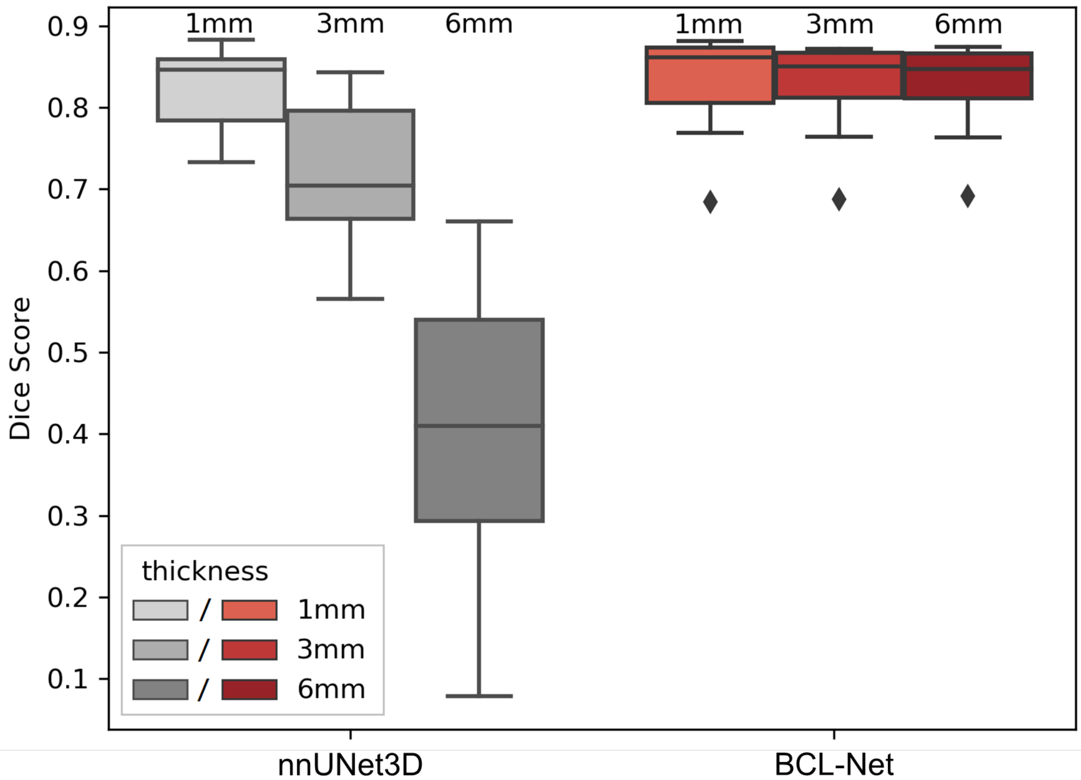

Figure S2. Compared to nnUNet3D, BCL-Net is more robust to various CT thickness, Related to Figure 4 and Table 3. To evaluate the effects of CT volume thickness, we tested 1mm, 3mm and 6mm CT scans using different methods. 3mm and 6mm volumes are uniformly-spaced sampling from 1mm volumes. The performance of nnUNet3D remarkably suffers from the increasing slice thickness, while the performance of our BCL-Net remains stable, suggesting its robustness to different slice thickness.

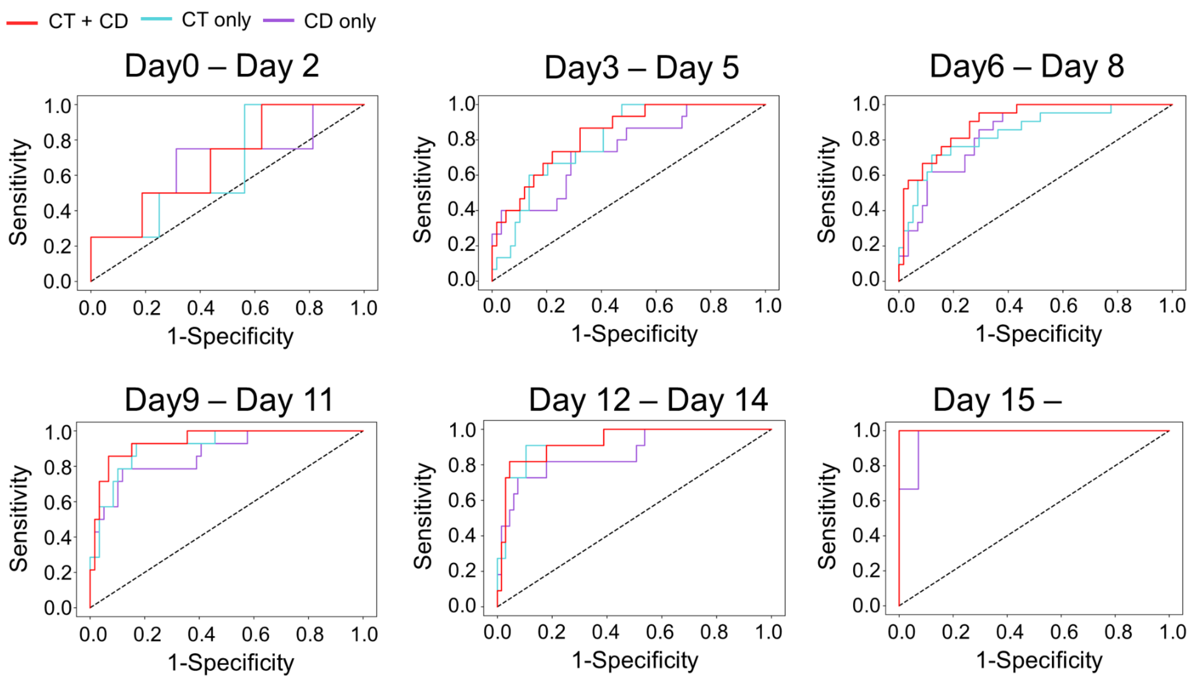

Figure S3. Time-dependent AUC with different time group combinations, Related to Figure 6. CT: computed tomography; CD: clinical data.

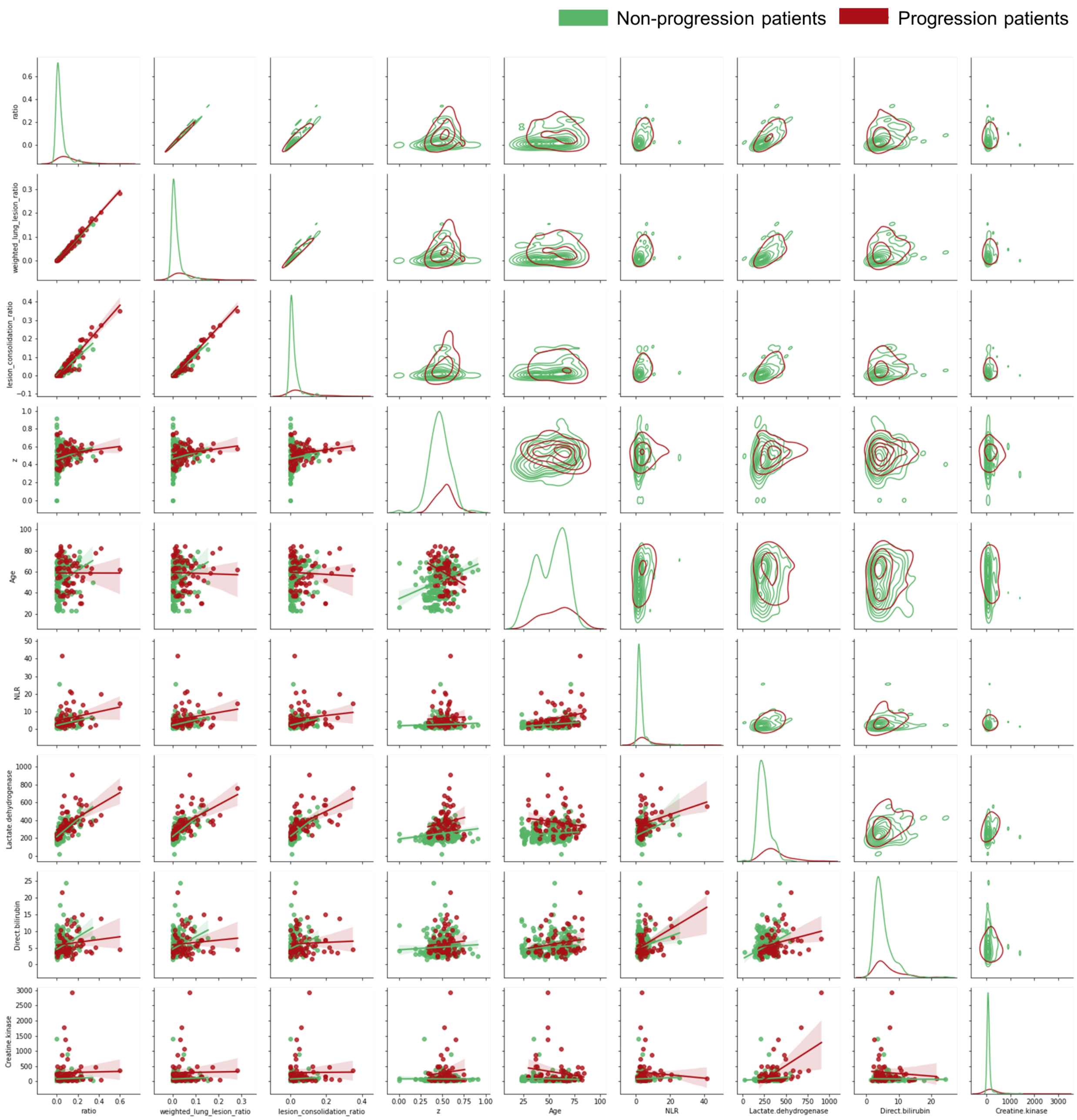

Figure S4. The univariate and bivariate distributions and the correlation of the features, Related to Figure 7. The diagonal of the grid diagram shows the univariate distribution of the features; the upper triangles represent the bivariate distribution of features; the lower triangles represent the correlations of features.

Table S1. The implementation details of base learners for ensemble learning, Related to Figure 3. The hyperparameters of base learners we used, including support vector machine (SVM), k-nearest neighbors (KNN), naive bayes (NB), multilayer perceptron (MLP), random forest (RF), gradient boost (GB), logistic regression (LR), adaptive boosting (Adaboost), and extreme gradient boosting (XGBoost).

Base learner	**Hpyerparameters(described in sklearn API, default value if not mentioned)**
SVM	kernel: 'rbf', C: 25, gamma: 1e-2
KNN	n_neighbors: 2
NB	Default as sklearn API
MLP	layers: (8, 32, 16), solvers: 'lbfgs', activation: 'relu'
RF	n_estimators: 64, max_features: 2
GB	n_estimators: 128
LR	C: 50
Adaboost	n_estimators: 4
XGBoost	n_estimators: 512, max_depth: 6, learning rate: 0.01, subsample: 0.8, colsample_bytree: 0.8, scale_pos_weight: 5.0

Table S2. The CT features included in the COVID-19 progression prediction data set, Related to Table 2. From the segmentation output of BCL-Net, Lung volume (LuV), lesion volume (LeV) and consolidation volume (CV) are quantified for left and right lung, respectively and. The percentage of consolidation (PCV) and lesion volume (PLV) are obtained by dividing by the corresponding lung volume. Additionally, we calculate the weighted volume from the inner product of the lesion and the intensity, and determine the related center of the lesion in the z-axis (z-position).

CT features		**All patients (n=119, s=341)**	**Severe group (n=29, s=68)**	**Non-severe group (n=90, s=273)**	**P values**
Lung volume, L	Total	6.31[5.10-7.86]	6.75[5.41-7.81]	6.25[5.04-7.86]	0.1949
	Left lung	2.93[2.41-3.70]	3.15[2.42-3.71]	2.92[2.41-3.68]	0.2375
	Right lung	3.37[2.68-4.18]	3.62[2.97-4.19]	3.34[2.68-4.16]	0.1613
Lesion volume, L	Total	0.15[0.00-3.00]	0.58[0.00-3.00]	0.12[0.00-1.35]	1.0e-16
	In left lung	0.05[0.00-1.32]	0.23[0.00-1.32]	0.03[0.00-0.66]	1.3e-16
	In right lung	0.09[0.00-1.67]	0.32[0.00-1.67]	0.06[0.00-0.89]	4.5e-14
Percent of lesion volume, %	Total	2.34[0.00-60.13]	9.17[0.04-60.13]	1.74[0.00-34.22]	3.9e-15
	In left lung	1.81[0.00-69.26]	8.47[0.02-69.26]	1.11[0.00-28.18]	6.5e-15
	In right lung	2.46[0.00-53.56]	9.97[0.00-53.56]	1.67[0.00-39.71]	3.6e-13
Weighted lesion volume, mL	Total	70.00[0.00-1459.13]	270.04[1.83-1459.13]	52.05[0.00-571.95]	1.2e-16
	In left lung	22.61[0.00-636.93]	105.84[0.29-636.93]	15.63[0.00-264.86]	2.8e-16
	In right lung	41.46[0.00-822.20]	152.63[0.08-822.20]	27.24[0.00-434.62]	2.4e-14
Consolidation volume, mL	Total	69.26[0.00-1941.83]	315.44[1.07-1941.83]	43.63[0.00-747.86]	3.3e-15
	In left lung	17.66[0.00-851.01]	101.36[0.18-851.01]	11.40[0.00-308.76]	4.4e-14
	In right lung	32.59[0.00-1090.82]	161.57[0.11-1090.82]	20.17[0.00-536.99]	9.0e-14
Percent of consolidation	Total	1.06[0.00-34.91]	4.00[0.01-34.91]	0.65[0.00-15.59]	2.0e-13

volume, %	In left lung	0.59[0.00-38.91]	3.02[0.00-38.91]	0.33[0.00-13.34]	1.7e-12
	In right lung	0.89[0.00-32.02]	4.44[0.00-32.02]	0.49[0.00-21.08]	2.7e-12
z-position, %	In lung	47.76[0.00-91.12]	53.70[33.43-75.82]	47.05[0.00-91.12]	8.7e-5
	In left lung	48.43[0.00-91.92]	53.92[26.54-82.45]	47.59[0.00-91.92]	0.0055
	In right lung	46.64[0.00-91.92]	53.95[34.81-91.92]	44.91[0.00-91.09]	1.9e-6

Table S3. The detailed time-dependent AUCs and F1 scores of the COVID-19 progression prediction, Related to Figure 6. Permutation test is performed on comparison of combination of CT scans and clinical data vs. CT scans only; combination of CT scans and clinical data vs. clinical data only; and CT scans only vs. clinical data only. The AUC and F1 score of the groups (Day15 -) reaching 1.00 are excluded from results.

	CT data	Clinical data	Day0-Day2	Day3-Day5	Day6-Day8	Day9-Day11	Day12-Day14
AUC		√	0.672	0.748	0.869	0.868	0.868
	√		0.641	0.800	0.842	0.915	0.932
	√	√	0.728	0.833	0.901	0.942	0.946
P values	Combination vs. CT		0.350	0.321	0.142	0.410	0.515
	Combination vs. CD		0.533	**0.033**	**0.043**	**0.014**	**0.025**
	CT vs. CD		0.613	0.250	0.531	0.266	0.070
F1 score		√	0.250	0.400	0.638	0.815	0.750
	√		0.286	0.424	0.694	0.815	0.889
	√	√	0.286	0.563	0.783	0.857	0.889
P values	Combination vs. CT		1.000	0.595	0.329	0.276	0.251
	Combination vs. CD		0.742	0.340	0.332	0.193	0.293
	CT vs. CD		0.634	0.393	0.492	0.464	0.511