Longitudinal Analysis of Disease Progression Using Image and Laboratory Data for Covid-19 Patients

Additional Material

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1 List of features

1.1 Demografic features

Sex categories: male [0], female [1]
Age in years

1.2 Clinical features

Hospital stay	in days - Duration of the complete in-house hospital stay; sum of "Stationary stay" and "ICU stay"
Stationary stay	in days - Duration of the stationary in-house hospital stay
ICU stay	in days - Duration of the in-house intensive care unit (ICU) stay
Duration of intubation	in days - Period during which the patient was intubated
Duration of invasive ventilation	in days - Period during which the patient was invasively ventilated through a tube or tracheostoma.
Time: symptoms to hospital admission	in days
Time: symptoms to ICU admission	in days
Time: hospital admission to ICU admission	in days
Outcome (30 days)	categories: the patient passed away [1], the patient is hospitalized with extracorporal membrane oxygenation (ECMO) therapy [2],

	the patient is hospitalized with invasive ventilation support[3], the patient is hospitalized with non-invasive ventilation support [4], the patient is hospitalized without oxygen requirement [5], the patient was meanwhile moved to another health care facility [6], the patient was meanwhile discharged home [7] - Description of the patient's health care status 30 days after Covid-19 disease has been diagnosed
Death	categories: the patient did not die during the observed hospital stay [0], the patient died during the observed hospital stay [1]
SpO2	in % - All measurements were performed at the time of hospital admission when the patients did not experience any additional ventilation; data imputation of 6%, missing values were replaced by cohort's (gender- and wave-specific) median
Use of invasive ventilation	categories: no [0], yes [1]
Use of ECMO	categories: no [0], yes [1]; ECMO = extracorporal membrane oxygenation
Use of proning	categories: no [0], yes [1]
Use of tracheotomy	categories: no [0], yes [1]
Use of hemodialysis	categories: no [0], yes [1]
Use of ADVOS	categories: no [0], yes [1]; ADVOS = advanced organ support
Use of catecholamine treatment	categories: no [0], yes [1]
Use of dexamethasone treatment	categories: no [0], yes [1]

1.3 Laboratory features

For each listed laboratory parameter we collected values at two times, namely ± 1 day to the corresponding lung CT scan at T_0 (initial CT) and T_1 (follow up CT). The Δ of the values was computed by subtracting the initial value from the follow up value. If a value was not analyzed for a patient at the required time we applied data imputation and replaced the missing value by the cohort's (gender- and wave-specific) mean.

Hemoglobin	in g/dl for T_0/ T_1/Δ; data imputation of 1%
Leukocytes	in G/l for T_0/ T_1/Δ; data imputation of 1%
Neutrophiles	in % of leukocytes for T_0/ T_1/Δ; data imputation of 14%
Lymphocytes	in % of leukocytes for T_0/ T_1/Δ; data imputation of 13%
Monocytes	in % of leukocytes for T_0/ T_1/Δ; data imputation of 14%

Thrombocytes in G/l for T_0/ T_1/Δ; data imputation of 1%

ALT in U/l for T_0/ T_1/Δ; data imputation of 5%, Alanine Aminotransferase
Creatinine in mg/dl for T_0/ T_1/Δ; data imputation of 1%
CK-MB in U/l for T_0/ T_1/Δ; data imputation of 30%, CK-MB = Creatine Kinase Myocardial Band
LDH in U/l for T_0/ T_1/Δ; data imputation of 10%, LDH = Lactate Dehydrogenase
Troponin T in ng/ml for T_0/ T_1/Δ; data imputation of 27%

CRP in mg/dl for T_0/ T_1/Δ; data imputation of 1%
IL-6 in pg/ml for T_0/ T_1/Δ; data imputation of 23%, IL-6 = Interleukin-6
Procalcitonin in ng/ml for T_0/ T_1/Δ; data imputation of 6%

APTT in seconds for T_0/ T_1/Δ; data imputation of 3% , Activated Partial Thromboplastin Time
Fibrinogen in mg/dl for T_0/ T_1/Δ; data imputation of 34%
INR no unit for T_0/ T_1/Δ; data imputation of 2%, INR = Prothrombin Time International Normalized Ratio
D-dimer in μg/ml for T_0/ T_1/Δ; data imputation of 13%

1.4 Image-derived features

We computed the volume of the following five CT labels at two times, namely T_0 (initial CT) and T_1 (follow up CT) and computed their Δ by subtracting the first volume from the follow up volume.

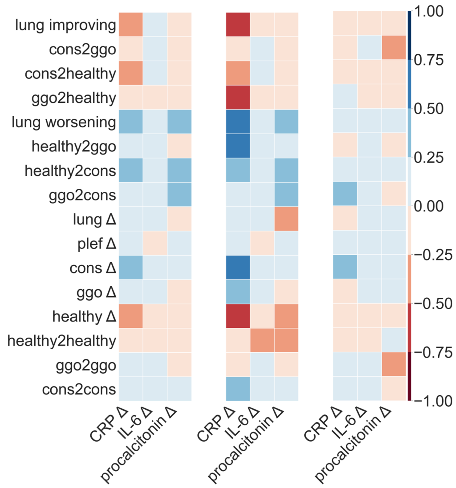
Lung in ml for T_0/ T_1/Δ; in % of initial lung volume for Δ
Healthy in ml for T_0/ T_1/Δ; in % of initial lung volume for T_0/Δ; in % of follow up lung volume for T_1]
GGO in ml for T_0/ T_1/Δ; in % of initial lung volume for T_0/Δ; in % of follow up lung volume for T_1], GGO = ground glas opacity
Consolidation in ml for T_0/ T_1/Δ; in % of initial lung volume for T_0/Δ; in % of follow up lung volume for T_1]
Pleural effusion in ml for T_0/ T_1/Δ; in % of initial pleural effusion volume for Δ

After registration we detected the status transition of the lung parenchyma from the the initial CT (T_0) to the follow up CT (T_1) voxel-wise. The status options are consolidation (cons), ggo (ggo) and healthy lung tissue (healthy). The different status transition options (see below) are named after the following system: “(voxel status at T_0) 2 (voxel status at T_1)” The number 2 is just seen as synonym of the word “(in)to”, like one status turns “into” another status. Summing up voxels with the same status transition we calculated the volume for each lung. As “common lung” we defined the intersection of the two label maps at T_0 and T_1 after their registration.

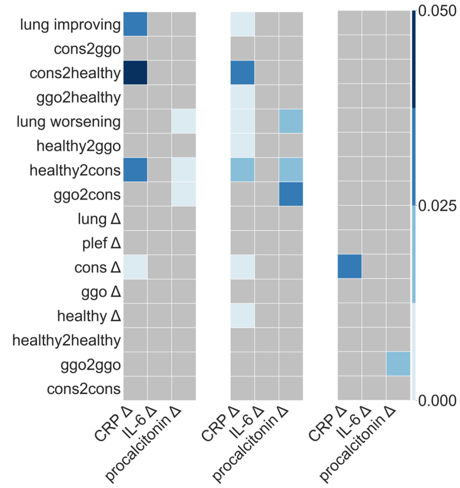
Healthy2Healthy in ml; in % of “common lung”
Healthy2GGO in ml; in % of “common lung”

Healthy2Cons	in ml; in % of "common lung"
GGO2GGO	in ml; in % of "common lung"
GGO2Cons	in ml; in % of "common lung"
GGO2Healthy	in ml; in % of "common lung"
Cons2Cons	in ml; in % of "common lung"
Cons2GGO	in ml; in % of "common lung"
Cons2Healthy	in ml; in % of "common lung"
Lung improving	in % of "common lung"; this feature is defined as the sum of status "Cons2GGO", "Cons2Healthy" and "GGO2Healthy"
Lung worsening	in % of "common lung"; this feature is defined as the sum of status "Healthy2GGO", "Healthy2Cons" and "GGO2Cons"

2 Correlation of longitudinal imaging and dynamic inflammatory data



(a) Correlation



(b) Significance: p-value (gray values are >0.05)

Fig. 1. Correlation (and its significance) between dynamic change of image-features and dynamic change of inflammatory parameters; lung improving/worsening and state transition in percentage of common lung, lung/cons/ggo/healthy Δ in percentage of initial lung volume and plef Δ in ml (left to right: both waves, 1st wave, 2nd wave).