

## Evolution of cardiac function in COVID 19 patients in the intensive care unit: insights from machine learning

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**Background:** Repeated echocardiographic assessment of cardiac function is integral in management of intensive care units (ICU) patients. Machine learning (ML) can assist by integrating whole-cardiac cycle echo data derived from flow assessment and deformation imaging, and grouping patients on the basis of patterns of cardiac dysfunction and its evolution over time. Cardiac involvement has been suggested to be important in COVID-19 outcome and echo evaluation can inform on cardiac status. We use unsupervised ML to investigate and integrate longitudinal data from the COVID-HO study (NCT04371679) to determine the potential of tracking changes in cardiac function during ICU hospitalization.

**Methods:** In a single-centre, COVID-19 patients (n = 38) were prospectively followed with echocardiography as part of ICU management. The endpoint was defined as death or ICU discharge. LV myocardial deformation, as well as aortic, mitral and pulmonary artery blood-pool Doppler velocity profiles were used as input for ML. Clinical data was used to validate the ML derived phenotypes. Echo data from the initial and final echo examination were used to create an output space where participants were positioned based on cardiac function blinded to outcome status. Regression was used to estimate the echo and clinical characteristics of different regions in the space. Patient trajectories in the output space were investigated for each patient.

**Results:** Endpoint was not reached in 24% (n = 9) at the time of analysis. The cohort was 68% male, aged  $65 \pm 12$  years, and with an ICU mortality 21% (n = 8). The median spent in ICU was 10 (IQR 7-18) days. The ML analysis demonstrated a heterogeneous output space (Fig 1A) we could define a gradual change in the shape of the pulmonary outflow velocity profile, from a normal towards pulmonary hypertension (Fig 1A, x axis). Jointly with differences in diastolic function (mitral inflow fusion and A wave accentuation) defined two regions: with signs of pulmonary hypertension (gray); and with normal pulmonary pressures but LV diastolic dysfunction (yellow). Investigation of patient trajectories (Fig 1B) demonstrated the feasibility of tracking changes during ICU hospitalization, showing a shift of a patient that died in the ICU, from initial diastolic dysfunction towards pulmonary hypertension (red), and a patient shifting from a region with normal diastolic function towards pulmonary hypertension, but with a positive outcome (blue). Echo data concurs with observed dynamics (Fig 1C and 1D).

**Conclusion:** ML can integrate complex, whole-cardiac cycle echo data to group heterogeneous patients based on similarity of cardiac function. Patient trajectories across the output space demonstrate the feasibility of ML for echo data-based follow-up of patients during ICU hospitalization. Further echo and clinical data integration can improve characterisation of the output space regions and better define changes in cardiac function during hospitalization.

Abstract Figure 1

