Impact of COVID-19 on critically ill patients

- Mortality Prediction models based on Serum FTIR-spectra

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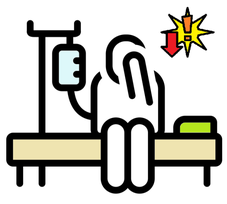
(SOME OF) THE PROBLEM(S)



Due to the **relevance of mortality prediction in critically ill patients**, it is common practice at intensive care units (ICU) to use physiological scores, *e.g.*, APACHE II. However, these type of scorings don't enable to predict individual patients' outcome, being mostly used for comparing groups of patients and ICUs [1]. They can also be overly complex and time-consuming.

- It is paramount to discover robust, rapid and economic biomarkers of mortality prediction at ICU.
- FTIR spectroscopy can capture the whole molecular fingerprint of a system in a very specific and sensitive mode [2,3].
- In this work, diverse mortality predictive models of support vector machines (SVM), based on FTIR-spectra of serum of critically ill patients, were developed.

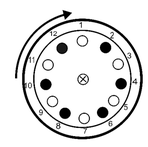
AIMS

Evaluate if FTIR spectroscopic analysis of serum would enable to discriminate and predict COVID-19 related mortality in critically ill patients in an ICU environment.

MATERIALS AND METHODS

A. BIOLOGICAL ASSAY: 200 ICU patients

136 — *Age avg. = 55 years*; 64 — *Age avg. = 62 years* → Taking of blood samples → All patients were submitted to Real-Time PCR analysis for COVID-19 detection → Waiting for blood to clot → Serum was obtained by **centrifugation** of fresh blood samples - **3000 rpm for 10 min**



B. MIR SPECTRA ACQUISITION:

Triplicates of 25µl of serum (DF 10) → Transferred to a **96-wells Si plate** → Dehydrated for 2.5h, in a desiccator under vacuum → Spectral data collected with a FTIR spectrometer (Vertex 70, Bruker), equipped with a HTS-XT (Bruker) accessory

C. SPECTRA PRE-PROCESSING AND PROCESSING:

- **Atmospheric** compensation
- **Baseline** correction
- **Unit vector** normalization
- **Second derivative** (2nd order polynomial - 15 point window)

OPUS → **t-SNE** (t-distributed stochastic neighbour embedding), performed with: → Orange 3.19.0 *(University of Ljubjana, Slovenia)* → **Support Vector Machine (SVM)** learner models were used and a feature selection algorithm (FCBF – Fast Correlation Based Filter), was applied to all models, to identify and select the most relevant features (wavenumbers)

RESULTS

- **A total of 200 patients, all hospitalised at an ICU, were considered. Patients between the two groups (with and without COVID-19) did not present significant differences concerning gender or age ($p > 0.05$).**

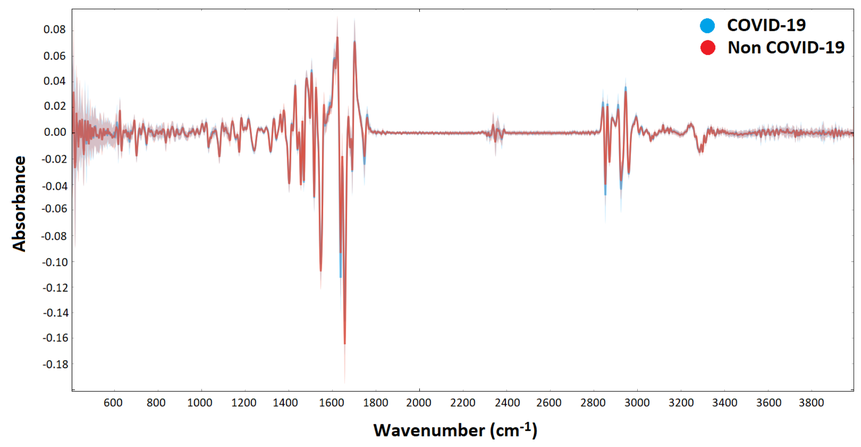


Fig.1. FTIR pre-processed spectra with atmospheric compensation and a normalised second derivative spectra. In blue, the spectra of the COVID-19 group and in red the spectra of non-COVID-19, with colour shading representing minimum and maximum values, and solid lines representing their averaged values.

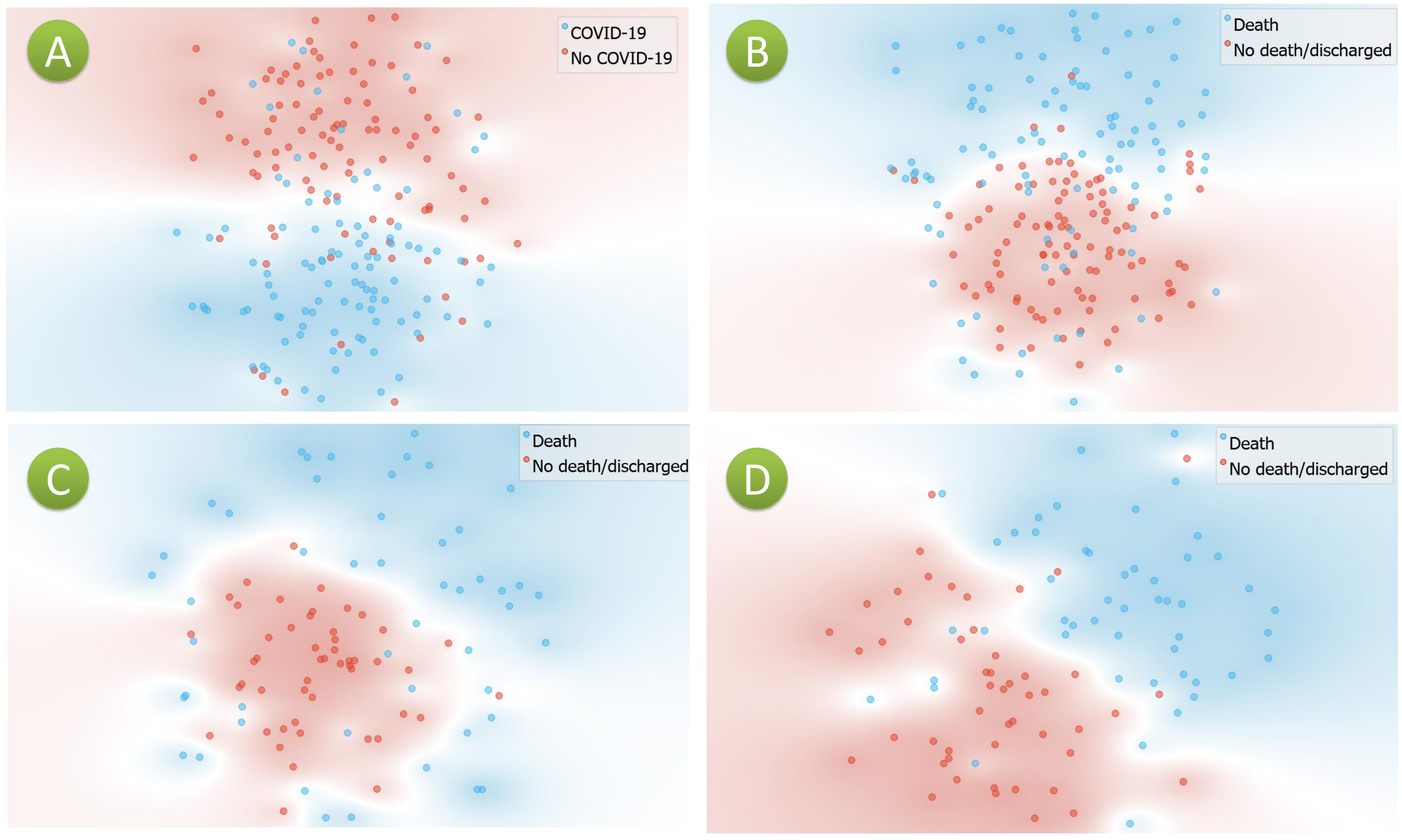


Fig.2. t-SNE representative of the 200 total ICU patients with COVID-19 (blue) and non-COVID-19 (red) patients, based on serum spectra after atmospheric compensation and normalized second derivative (A) and mortality prediction for the entire population of the study (B). The t-SNE represented on (C) and (D), pertain to the mortality models for a COVID-19 only population and non-COVID-19 (100 patients per model), respectively.

	AUC	Accuracy	Precision	Sensitivity	Specificity
A	0.842	0.762	0.765	0.762	0.762
B	0.916	0.865	0.867	0.865	0.865
C	0.951	0.880	0.880	0.880	0.880
D	0.889	0.875	0.877	0.875	0.875

Table 1. SVM models' performance, with atmospheric compensation and normalized second derivative to predict COVID-19 based on spectra from serum of 200 patients (A) or mortality (B). The variable mortality was also discriminated for a COVID-19 population only (C), consisting of 100 ICU patients (23 Female and 77 male) and non-COVID-19 population (D), consisting of the remainder 100 patients (41 Female and 59 male). Model performance results from 10 random iterations (for each model), each based on the random selection of 80% of data for model training and 20% as an independent data set for model validation.

CONCLUSIONS

The present work points to an alternative mode to discriminate, predict and evaluate the impact of COVID-19 (and associated mortality) among ICU admitted patients. It was possible to develop very good SVM models to predict mortality based only on patients without COVID-19 (AUC=0.89), with a better model having been achieved for patients with COVID-19 (AUC=0.95). This difference can result from COVID-19 patients presenting a different metabolic status in relation to non-COVID-19 patients. Indeed, a very good SVM model enabled to discriminate these two populations (AUC=0.84). When considering the mixed population (*i.e.*, with and without COVID-19), a very good SVM model was obtained when predicting mortality (AUC=0.92). Furthermore, the technique can be implemented based on a simple workflow, is rapid, economic and easily scalable.

ACKNOWLEDGEMENTS:

This work was supported by the project grant DSAIPA/DS/0117/2020 supported by *Fundação para a Ciência e a Tecnologia*, Portugal and by the project grant NeproMD/ISEL/2020 financed by *Instituto Politécnico de Lisboa*.

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