CARDIOLOGICAL FACTORS ASSOCIATED WITH IN-HOSPITAL MORTALITY IN A COHORT OF PATIENTS WITH COVID-19. RESULTS OF A MULTICENTER STUDY.

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Introduction

During COVID-19 a major reorganization of the healthcare system took place in the most affected areas: cardiology units began to deal almost exclusively with COVID-19 patients, mostly those with associated cardiac disorders.

Aims

- To investigate several hypotheses on the cardiological risk factors associated with in-hospital mortality focusing on markers of myocardial injury (MI) (i.e., troponin) and of cardiac disease (i.e., natriuretic peptides), as well as on cardiac comorbidities.
- To evaluate the role of sex on the risk of death and its interaction with other variables at admission.

Methods

- Data on COVID-19 patients hospitalized in 13 italian cardiology units from March 1 to April 9, 2020 were retrieved (patients' demographics, medical history, and in-hospital clinical course including laboratory findings and therapy).
- Main clinical markers of interest were standardized as "normal" or "elevated" because the type of troponin (either I or T) and of natriuretic peptide (either BNP or NT-proBNP) were heterogeneous between centers, which also used different assays.
- Survival analyses were conducted building different models according to clinical hypotheses. Cumulative incidence function (CIF) of death was computed taking into account hospital discharge as a competing event. Variables clinically relevant and significantly associated with the risk of death at the univariable analysis were tested via selection methods in a multiple Cox regression model to identify independent risk factors.

Results

- 701 patients were enrolled (mean age 67.2±13.2 years, 69.5% males) of whom 165 (23.5%) died during a median hospitalization of 15 (IQR, 9-24) days.
- Patients with preexisting cardiac disease had a higher risk of death and having a history of heart failure (HF) was an independent predictor of in-hospital mortality even after adjusting for clinical variables related to COVID-19, age, and HF severity[1].
- Elevated troponin (Tn) at admission was found to be associated with an increased in-hospital mortality (adjusted HR 1.71, 95%CI 1.13-2.59, p=0.01) and was independent from concomitant cardiac comorbidities[2].
- Among patients who had a second Tn evaluation on day 2 of hospitalization, those with at least one elevated assay had a higher risk of death compared to those with normal Tn at both evaluations (Fig.1). Besides, patients with elevation on day 2 had the highest mortality risk (HR 3.78, 95%CI 1.10-13.09, p=0.035)[3].
- Natriuretic peptides (NPs) were also found to provide an additional risk stratification in patients with normal Tn values at admission (Fig.2). Elevated levels of both biomarkers were associated with a 3-fold increase of in-hospital mortality as compared with normal values of both biomarkers.
- Despite sex was not found to be an independent predictor for mortality, a sex-based heterogeneity in the association between variables at admission and the patients' risk of death was detected. For example (Fig 3), the risk was more than double in men with low vs high lymphocytes count, whereas there was no effect in women (p for heterogeneity=0.03), and platelets count was associated with better outcome in men but not in women (p=0.03).

Conclusions

- Patients with an history of HF have an extremely poor outcome.
- Tn evaluation is highly recommended both at admission and within on day 2 of hospitalization as it accurately identifies patients at higher risk of death.
- NPs can further improve the prognostic stratification as they detect high-risk patients also among those with normal Tn.
- Sex is a relevant variable that should be taken into account when evaluating risk of death from COVID-19.

Fig 1. CIF for intra-hospital mortality stratifying patients according to the trend of Tn level during the first two days of hospitalization.

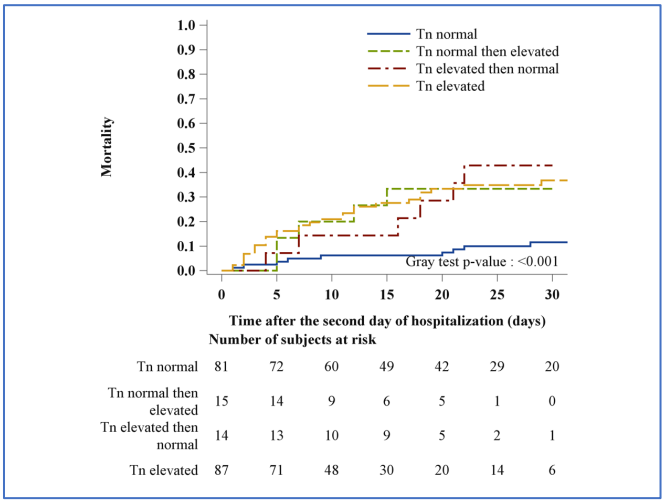


Fig 2. CIF for intra-hospital mortality stratifying patients according to NPs and Tn level at admission.

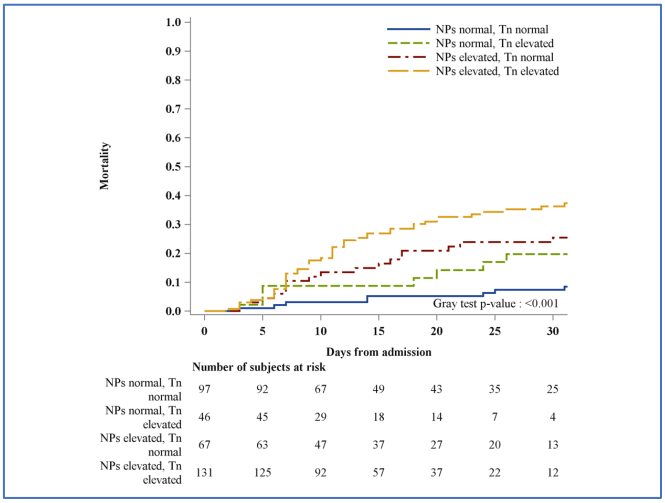
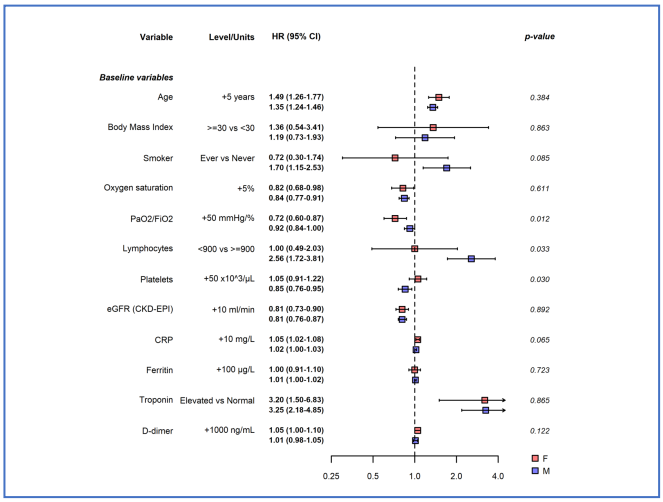


Fig 3. Forest plot comparing association of variables at admission with risk of death between females and males.



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