

LACK OF EFFECT ON IN-HOSPITAL MORTALITY OF DRUGS USED DURING COVID-19 PANDEMIC: FINDINGS OF THE RETROSPECTIVE MULTICENTER COVOCA STUDY.

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Introduction & Aims

During COVID-19 pandemic, the use of several drugs has represented the worldwide clinical practice. However, though the current increase of knowledge about the disease, there is still no effective treatment and information about a proper timeline for the usage of drugs [1]. On these bases, **we aimed to retrospectively assess the frequency of use of drugs**, both as a single class and in association with each other, and the effects of therapeutic regimens started in hospitalized patients on in-hospital mortality. We also **evaluated whether an early or delayed use of these drugs could determine different outcomes**.

Methods

COVOCA (COVID-19 population hospitalized in Campania Region) is a retrospective observational cohort study, which involved 18 COVID centres throughout Hospitals of Campania Region [2]. Demographic, anthropometric, and clinical data, such as pre-existing chronic diseases, and the need for respiratory support were collected at admission.

Data on drug therapies introduced during hospitalization, were widely collected. Particularly for most reported treatment and of interest in COVID-19 literature, in parallel to the description of whether they were used, a time-lag variable was created to identify patients undergoing either to an early or late treatment. This was done to avoid survivorship bias, considering that patients who live longer are more likely to receive a certain treatment/combination.

Specifically, the time-lags variable (early/late) was categorized using a cut-off time (day-2). Day-2 represents treatments performed within the first two days since admission, considering day-0 as the time of hospitalization. Under this pattern, treatments were classified as: No treatment, early treatment (until day 2) and late treatment (from day 3 onwards). Multivariable logistic regression models were performed to evaluate association between in-hospital mortality and specific COVID-19 treatments. Moreover, each model was fitted both on the whole population and on a subpopulation excluding patients under invasive ventilation/OTI on admission, to test the effect of drugs in a less compromised population.

Parameter	
Hydroxychloroquine, n (%)	
No	189 (30.6%)
early treatment	349 (56.5%)
late treatment	80 (12.9%)
Anticoagulants, n (%)	
No	202 (32.7%)
early treatment	325 (52.6%)
late treatment	91 (14.7%)
Antibiotics, n (%)	
No	153 (24.8%)
early treatment	402 (65.0%)
late treatment	63 (10.2%)
Monoclonal Antibodies, n (%)	
No	514 (83.2%)
early treatment	41 (6.6%)
late treatment	63 (10.2%)
Antivirals, n (%)	
No	107 (17.3%)
early treatment	445 (72.0%)
late treatment	66 (10.7%)
Corticosteroids, n (%)	
No	391 (63.3%)
early treatment	129 (20.9%)
late treatment	98 (15.8%)

Results 2

During the observation period, 143 in-hospital mortality events were recorded, with a cumulative incidence of 23.1%. We fitted different multivariable models (Table 2) to test for the association between in-hospital mortality and each COVID-19 specific therapy, according to the time of administration and, furthermore, stratified on the whole population as well as on a subpopulation excluding (data not shown) patients who were already under OTI on admission. All models did not disclose any significant association.

[1] WHO. "Clinical management of COVID-19 disease". <https://www.who.int/publications/item/WHO-2019-nCoV-clinical-2021-1>

[2] Galiero R, Pafundi PC, Simeon V, et al. Impact of chronic liver disease upon admission on COVID-19 in-hospital mortality: Findings from COVOCA study. *PLoS One.*;15(12):e0243700

Results

618 patients were included in the study. Patients were differentiated based on either an early (within the first two days since admission) and late administration (from day 3 in after). As reported in Table 1, 72% of patients underwent to an early treatment with antivirals. Antibiotics were administered at beginning of hospitalization in the 65% of patients, whilst hydroxychloroquine and anticoagulants in almost half of the study cohort. Corticosteroid therapy administration was almost similar both early and late during hospitalization (20.9% and 15.8%, respectively), whilst mAbs were larger prescribed late during hospitalization.

Table 2. Association between in-hospital mortality and each COVID-19 specific therapy: multivariable analysis* (n=618). – Whole sample

	OR	95% CI	p
Corticosteroids			
No (ref.)			
early treatment	1.14	0.64-2.02	0.654
late treatment	1.38	0.76-2.51	0.291
Hydroxychloroquine			
No (ref.)			
early treatment	1.07	0.64-1.81	0.792
late treatment	1.19	0.58-2.46	0.633
Anticoagulants			
No (ref.)			
early treatment	1.44	0.83-2.48	0.190
late treatment	1.42	0.69-2.95	0.341
Antibiotics			
No (ref.)			
early treatment	1.08	0.63-1.83	0.784
late treatment	0.73	0.31-1.73	0.478
Monoclonal Antibodies			
No (ref.)			
early treatment	1.23	0.51-2.96	0.651
late treatment	1.51	0.74-3.06	0.254
Antivirals			
No (ref.)			
early treatment	1.36	0.73-2.54	0.331
late treatment	1.77	0.71-4.26	0.228

*adjusted by age, sex, GCS/15 (mild/moderate/severe), Respiratory Severity Scale, Chronic Liver Disease, Malignancies