Endogenous catecholamine and inflammatory cascade: a close link with COVID-19 outcome?

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A subset of patients with COVID-19 develop cytokine storm syndrome. Catecholamines may cause dysregulation of physiological cascades, including inflammatory hyperactivation, linked to adverse outcomes in COVID-19. Despite catecholamines detrimental effects, their action over ventilation, vascular tone, and cardiac function could have compensatory influences(1). Higher endogenous cortisol levels have been associated with reduced median survival and increased mortality(2). Catecholamines influence over hypothalamic–pituitary–adrenal axis and glucocorticoid-mediated immune signals, might mitigate some effects of catecholamine excess, such as excess cytokine production, and inflammation. This may be the physiopathologic explanation of RECOVERYtrial(3).

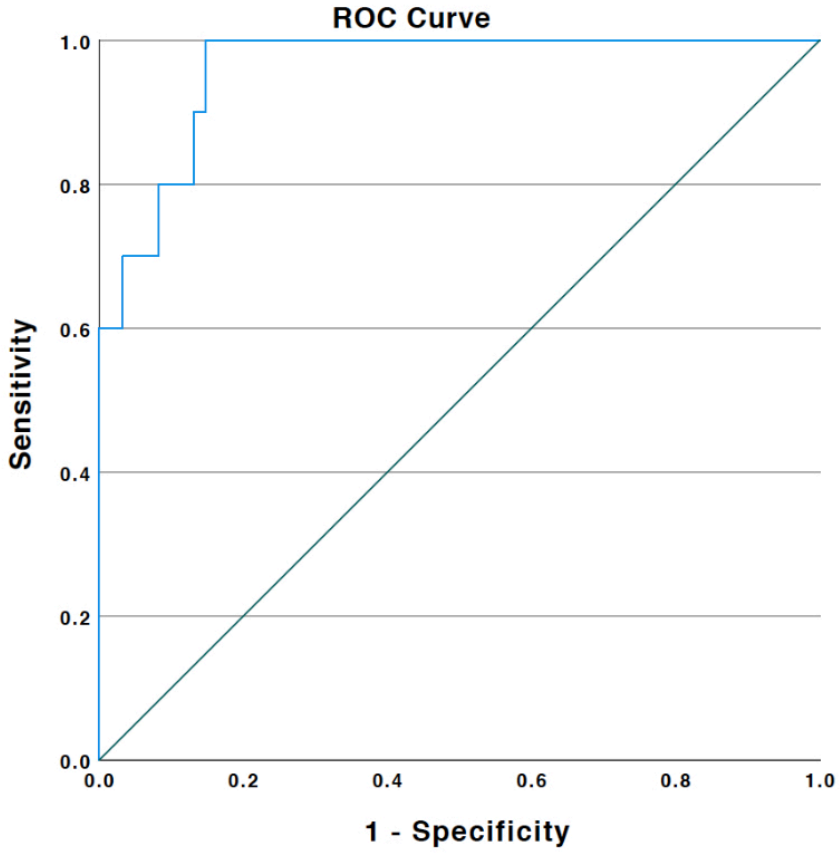
We investigate the possible correlation between high levels of catecholamines with a hyperinflammatory state and mortality in COVID-19.

72 patients(62 ± 11 yo;22% female) underwent catecholamine analysis on top of standard biochemistry and echocardiography at admission in ICU for ARDS related to COVID-19, diagnosed with both nasal swab and PCR analysis on bronchoalveolar lavage.

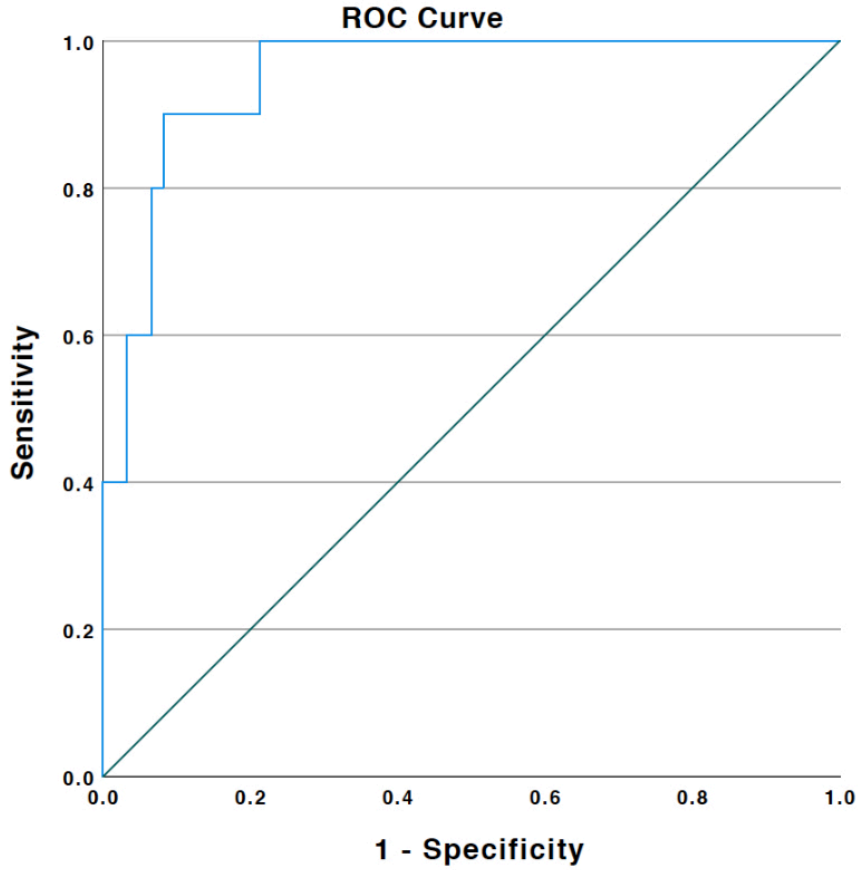
Common comorbidities were hypertension(53·4%), diabetes(39·7%), cardiovascular disease(21·3%). Mortality rate was 16% . Median adrenaline, noradrenaline and dopamine concentration were respectively 468(±351,2 upper limit 84ng/mL), 3020(±5019; upper limit 420ng/mL) and 739,5(±820,2; upper limit 94ng/mL).

Univariable analysis by Cox showed that PCR(OR 2.30 [95% CI 0.88 – 3.38]), IL-6(OR 1.85 [95% CI 1.01 – 3.40]), noradrenaline(OR 3.25 [95% CI 2.01 – 4.40])and D-dimer(OR 1.75 [95% CI 0,86 – 3.10]) were associated with a increased relative risk of mortality($p < 0.01$ for all). In multivariable regression model only noradrenaline levels(p 0.001) and PCR(p 0.01) retained for mortality association (ROC curve in figure A-B). Noradrenaline levels inversely correlated with LVEF(0.03; r –0,55) and TAPSE(p 0.02; r -0,42), interleukin-6(p 0.001; r 0,75), Interleukin-2(p 0.001; r 0,64) and D-dimer(p 0.01; r 0,76).

Higher levels of endogenous noradrenaline correlate with higher inflammatory state and worse outcome. Further insights on endocrine-systemic interaction will be explored in future analysis and might reveal strategies and targets in COVID-19 therapy.



Noradrenaline



PCR