

## Cardiac biomarkers as prognosticators among SARS-CoV-19 patients in a tertiary hospital in Philippines

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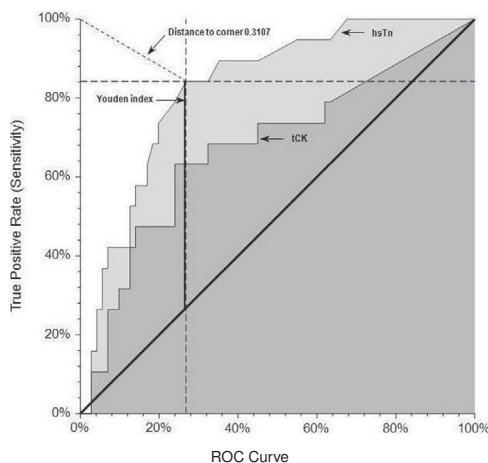
**Background:** There is overwhelming volume of confirmed cases of COVID-19, despite this numerous knowledge gaps remain in the diagnosis, management, and prognostication of this novel coronavirus infection, making prevention and control a challenge.

**Methods:** This retrospective cohort study included patients with real-time reverse transcriptase polymerase chain reaction (rRT-PCR)-confirmed COVID-19. Binary logistic regression was used to determine the association between the cardiac biomarkers and in-hospital mortality. ROC, AUC, and cutoff analyses were used to determine optimal cutoff values for the cardiac biomarkers.

**Results:** A total of 90 subjects with a complete panel of cardiac biomarkers out of the 224 rRT-PCR confirmed cases were included. The median age was 57 years (IQR, 47–67 years), majority were males. Sixty-six (77.6%) subjects survived while 19 (22.4%) expired. The most common presenting symptom was fever (75.6%), and the most common comorbidity was hypertension (67.8%). Spearman rho correlation analysis showed moderate positive association of high sensitivity troponin I (hsTnI) with in-hospital mortal-

ity (R, 0.434,  $p = <0.001$ ). Multivariate binary logistic regression analysis showed that creatine kinase and hsTnI were independently associated with in-hospital mortality (OR, 4.103 [95% CI, 1.241–13.563],  $p=0.021$ ; and OR, 7.899 [95% CI, 2.430–25.675],  $p=0.001$ , respectively). ROC curve analysis showed that hsTnI was a good predictor for in-hospital mortality (AUC, 0.829 [95% CI, 0.735–0.923],  $p = <0.001$ ) and that creatine kinase was a poor predictor (AUC, 0.677 [95% CI, 0.531–0.823],  $p=0.018$ ). Optimal cut-off point derived from the ROC curve for hsTnI was 0.010 ng/ml (J, 0.574) with a sensitivity of 84% (TPR, 0.842 [95% CI, 0.604–0.966]), specificity of 73% (TNR, 0.732 [95% CI, 0.614–0.386]), and an adjusted negative predictive value of 99% (Known prevalence\*adjusted NPV, 0.989), a positive likelihood ratio of 20% (LR+, 3.147 [95% CI, 2.044–4.844]) and a negative likelihood ratio of 30% (LR-, 0.216 [95% CI, 0.076–0.615]).

**Conclusion:** High sensitivity troponin I level was a good tool with a very high negative predictive value in significantly predicting in-hospital mortality among rRT-PCR positive COVID-19 patients.



ROC Curve, Cutoff and Area Under the Curve Analysis for Elevated Cardiac Biomarkers with In-hospital Mortality Among COVID-19 Patients.

	hs Troponin I	Creatine kinase
Reference value used	0.015 ng/ml	168 U/liter
Area under the Curve (AUC)	0.829 (0.735-0.923)	0.677 (0.531-0.823)
Sig. <sup>a</sup>	< 0.001	0.018
Distance to corner (d)	0.311	0.439
Youden index (J)	0.574	0.392
Derived optimal cutoff value	0.010 ng/ml	173 U/liter
Sensitivity (TPR)	0.842 (0.604-0.966)	0.632 (0.384-0.837)
Specificity (TNR)	0.732 (0.614-0.831)	0.761 (0.645-0.854)
False positive rate	0.268 (0.169-0.386)	0.239 (0.146-0.355)
False negative rate	0.158 (0.034-0.396)	0.368 (0.163-0.616)
Positive predictive value (PPV)	0.457 (0.288-0.633)	0.414 (0.235-0.611)
Known prevalence*Adjusted PPV <sup>b</sup>	0.142	0.122
Negative predictive value (NPV)	0.945 (0.849-0.989)	0.885 (0.778-0.953)
Known prevalence*Adjusted NPV <sup>b</sup>	0.989	0.975
Prevalence	0.211 (0.132-0.310)	0.211 (0.132-0.310)
Accuracy	0.756 (0.654-0.840)	0.733 (0.630-0.821)
Positive likelihood ratio (LR+)	3.147 (2.044-4.844)	2.638 (1.540-4.519)
Negative likelihood ratio (LR-)	0.216 (0.076-0.615)	0.484 (0.265-0.885)
Diagnostics odds ratio	14.596 (3.821-55.786)	5.445 (1.850-16.032)

<sup>a</sup> P value less than 0.05 is considered significant.

<sup>b</sup> ROC curve analysis was not done for CK-MB isoenzyme since it was not associated with in-hospital mortality.

<sup>c</sup> Adjusted predictive values based on known prevalence of the disease (5%).

<sup>d</sup> Definitions adopted from NCSS 2020 Statistical Software (2020). NCSS, LLC, Kaysville, Utah, USA, [ncss.com/software/ncss](http://ncss.com/software/ncss). <sup>e</sup> Cutoff Value indicates the criterion value range that predicts a positive condition. TPR is the true positive rate or sensitivity is the proportion of the units with a known positive condition for which the predicted condition is positive. TNR is the true negative rate or specificity is the proportion of the units with a known negative condition for which the predicted condition is negative. PPV is the positive predictive value or precision is the proportion of the units with a predicted positive condition for which the true condition is positive. NPV is the negative predictive value is the proportion of the units with a predicted negative condition for which the true condition is negative. Youden Index is the Sensitivity + Specificity - 1. PPV is Distance to Corner is the distance from the top left corner of the ROC curve to the point on the ROC curve. LR+ is the positive likelihood ratio is the ratio of the true positive rate (sensitivity) to the false positive rate (1 - specificity). LR- is the negative likelihood ratio is the ratio of the false negative rate to the true negative rate (specificity). The diagnostic odds ratio is the ratio of the positive likelihood ratio to the negative likelihood ratio. The distance to the top-left corner of the ROC curve for each cutoff value is given by  $d = \sqrt{(1 - \text{sensitivity})^2 + (1 - \text{specificity})^2}$ . The accuracy reflects the total proportion of units that are correctly predicted or classified.