

PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Oncology*

Manuscript NO: 72022

Title: Co-relation of SARS-CoV-2 related 30 days mortality with HRCT score and RT-PCR Ct value-based viral load in patients with solid malignancy: A tertiary cancer Centre based study

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05824934

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Singapore

Author's Country/Territory: India

Manuscript submission date: 2021-10-03

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-17 15:18

Reviewer performed review: 2021-10-23 02:06

Review time: 5 Days and 10 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection

Re-review	[<input checked="" type="checkbox"/>] Yes [<input type="checkbox"/>] No
Peer-reviewer statements	Peer-Review: [<input type="checkbox"/>] Anonymous [<input checked="" type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No

SPECIFIC COMMENTS TO AUTHORS

In this manuscript, the authors investigated the co-relation of SARS-CoV-2 related 30-day mortality with HRCT score and RT-PCR Ct value based viral load in cancer patients. The results show that the mortality rate is high for patients with high value of baseline HRCT values at presentation and required ICU stay. Yet, RT PCR based different viral load levels have no significant effect on mortality. The results reported in this study is interesting, and should be published if the authors can make the following minor revisions: 1) The authors may discussion further why there is no correlation between RT-PCR based different viral load levels and the severity or motility of COVID-19 disease. Similar results are also reported by Shah et al. [1]. When we talk about infectious diseases, we need to distinguish between Infection (the presence of a pathogen) and disease (signs, symptoms and pathology) [2]. Disease severity is the function of pathogen virulence, host tolerance and pathogen load [2]. Pathogenicity or disease is often the consequence of an overactive immune or inflammatory response [2,3]. 2) Cancer patients normally have a compromised immunity due to their existing cancer and associated treatment [4]. So cancer patients may have persistent SARS-CoV-2 viral infection which cannot be cleared by their compromised immune system in short time, but their COVID-19 disease is not severe, and some of them may still recover from the COVID-19 disease. On the contrary, patients with obesity or other metabolic syndromes like diabetes mellitus still have a competent immunity which may be malfunctioning due to overnutrition. When these patients are infected by SARS-CoV-2 virus, the infection may trigger hyperinflammation which makes a lot of collateral damage to all

organs (that are not infected by the virus) in the body. So the COVID-19 disease can be very severe or even the quick demise of the patient, even if their competent immune system is able to clear the SARS-CoV-2 viruses effectively. The following typos in the manuscript should be corrected: 1. In the manuscript title, "SARS-CoV" should be "SARS-CoV-2"; "sold malignancy" should be "solid malignancy" 2. On page 3, in "Abstract" –"Background", line 4, "SARS-CoV-19" should be "SARS-CoV-2" 3. On page 3, in "Abstract" –"Results": "Out of 131,123 patients met" should be "Out of 131 patients, 123 met" 4. On page 4, line 6, "with a history of or active malignancy" should be "with a history of active malignancy" 5. On page 4, in "Materials and methods", line 4, "confirmed COVID-19 infection" should be "confirmed SARS-CoV-2 infection". Basically, when talking about infection, one should refer to the SARS-CoV-2 virus; when talking about the disease caused by the virus, one should refer to the COVID-19 disease. The following references may be included in the revision: 1. Shah S, Singhal T, Davar N, Thakkar P. No correlation between Ct values and severity of disease or mortality in patients with COVID 19 disease. Indian J Med Microbiol. 2021; 39(1): 116- 117.DOI: 10.1016/j.ijmmb.2020.10.021 2. Humphries DL, Scott ME, Vermund SH. Pathways linking nutritional status and infectious disease. In: Humphries D, Scott ME, Vermund SH, editors. Nutrition and infectious disease: shifting the clinical paradigm: Humana Press; 2020, pp4-5. https://doi.org/10.1007/978-3-030-56913-6_1 3. Levin BR, Antia R (2001) Why we don't get sick: The within-host population dynamics of bacterial infections. Science, 292:1112-1115. DOI: 10.1126/science.1058879 4. Jennifer Couzin-Frankel (2021) A cancer survivor had the longest documented COVID-19 infection. Here's what scientists learned. Science. Published online on 19 OCT 2021. DOI: 10.1126/science.acx9383

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Peer-review model: Single blind

Reviewer's code: 05899451

Position: Peer Reviewer

Academic degree: BSc, PhD, RN

Professional title: Academic Fellow, Nurse

Reviewer's Country/Territory: United Kingdom

Author's Country/Territory: India

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection

Re-review	[<input checked="" type="checkbox"/>] Yes [<input type="checkbox"/>] No
Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No

SPECIFIC COMMENTS TO AUTHORS

The study is single-centre, retrospective, conducted at a tertiary cancer care hospital. Patients with active cancer presented to the hospital between April 2020 to April 2021, and with confirmed COVID-19 infection were included. The inclusion criteria was the availability of the database for various study parameters for comparing the 30 days outcomes which includes the initial course of illness while COVID-19 and cancer details. Potential prognostic variables were included: age, sex, obesity, smoking status, HRCT scoring, Baseline laboratory values for D dimer, C-reactive protein (CRP), number of comorbidities, Eastern Cooperative Oncology Group (ECOG) performance status, requiring active treatment, recent surgery (including, but not limited to cancer surgeries, within 4 weeks of COVID-19 diagnosis), type of malignancy, cancer status (remission vs active disease), with active further need as stable versus responding to treatment versus progressing disease), anticancer therapy, and COVID-19 treatment with azithromycin, hydroxychloroquine, Ivermectin or in combination versus various other treatment options used i.e. Steroid alone or in combination with Remdesivir, Tocilizumab, Plasma therapy. The study has been approved by the Institutional Review Board (RGCIRC/Res/SCM/46 2021/95) and was conducted according to the Declaration of Helsinki.

1. The authors need to attend grammatical errors across the manuscript. For instance in the abstract results section the first sentence reads " Out of 131,123 patients met inclusion criteria for our analysis. As you can see, this is missing the actual number that met the inclusion criteria.

2. Methodological design based on the above section and the statistics there on do not seem to align; it seems that the study design

here is a retrospective epidemiological study with a methodological design resembling a quantitative single-centre data based project. 3. This entire section should be revised and written as per the STROBE statement and equator guidelines. This will aide clarity and easy of reading the manuscript. Please refer to the link below: <https://www.equator-network.org/reporting-guidelines/strobe/> 4. The inclusion criteria is not clearly stated. Availability of the data is not an inclusion criteria but the actual eligibility for data to be included into the study. 5. Prognostic variables described here are actually demographic characteristics, therefore this has been written incorrectly and requires revision. 6. The clonic variables (i.e. tests) should be written separately to the demographics. These are fundamental details that should be properly represented by the authors. Statistical analysis 1. Could the authors clarify what is "all cause mortality"? Do they mean mortality ? And then causation? These are two different outcomes and as such should be reflected clearly. 2. Secondary outcomes appear to be comorbidities; can this be written comprehensively as at present, this seems to be unclear. 3. At present the scientific rationale is missing. To depict the outcomes, a section prior describing the overall aims and scientific rationale should be available. This will help the readers to understand and follow the narrative with easy. 4. The statistical components needs to be revised and written clearly to aid readability; continuous datahow can this be the case for this study design? Continuous data require different time points where by data has been gathered and yet the mortality outcome is one that is binary....in its current state, the manuscript would benefit from a complete statistical analysis plan with a clear outline of the descriptive statistics used as in its current form this is not clear. 5. In order to consider and address the above point, the statistics would benefit from a re-run. The use of a multivariate model for example is used to predict outcomes when there are multiple variables; are the authors predicting anything in this case? This is a standard retrospective data analysis; it



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should stipulate as such. I would encourage the authors to consider the following if they would like to use an advanced mathematics method; <https://www.sciencedirect.com/topics/psychology/multivariate-model> 6. A canonical correlation analysis may be a better fit where one set of variables can be set as outcome variables and the second set as predictor variables. 7. The authors could consider an OLS regression where individual coefficients as well as their standard errors would be used where a separate regression analysis would be performed for each variable. 8. Some of these variables explored here by the authors are dichotomous. Therefore a multivariate probability or bi-probability could be used. The discussion section can be amended to reflect the changes above.