



## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Cardiology*

**Manuscript NO:** 85096

**Title:** Remdesivir, dexamethasone and angiotensin-converting enzyme inhibitors use and mortality outcomes in COVID-19 patients with concomitant troponin elevation

**Provenance and peer review:** Invited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05229914

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Chairman, Chief Doctor, Director

**Reviewer's Country/Territory:** Thailand

**Author's Country/Territory:** United States

**Manuscript submission date:** 2023-04-21

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2023-04-25 01:14

**Reviewer performed review:** 2023-04-26 04:42

**Review time:** 1 Day and 3 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Novelty of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
<b>Creativity or innovation of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation



<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<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
<b>Conclusion</b>	<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
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	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**

The MAIN issue with the current study is that it is unclear what Elevated Troponin represents, in general and in the present study? The present study relies on an inferred diagnosis of myocarditis, or CHF or increased myocardial load, manifesting as elevated troponin and looks at the effect of dexamethasone, remdesivir, and ACEI on the mortality of those patients, a very dissimilar group. You suggest that viral load could result in Troponin increase. I wonder if it is the same type of shedding as elevated serum-ACE2 observed in COVID-19. I wonder if you looked into any association with CK-MB, LDH, ASAT and troponin, not as a group as you do in Table 3, but on same patient basis? I mean how many of the 205 patients with elevated troponin had concurrent elevation in LDH, CPK? I see 148 had LDH and 116 had CPK elevations; how many of those were concurrent, meaning: how many had cTn+LDH+ CPK, cTn+LDH, or cTn+CPK (do not see ASAT measurements). Patients with myocarditis should have elevations in all 3, as would any other patients with a real cardiac muscle involvement. On the other side, I see HTN, CKD, Bradycardia, and remdesivir use had almost 50% elevated troponin. The CKD group (and HTN) tells me that this could be a troponin



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renal clearance issue? Those are questions to be resolved before having any meaningful discussion on mortality and troponin. Finally, you mention that “Troponin elevation (HR 1.25, p=0.1) was not independently associated with mortality after adjusting for age, comorbidities like CHF, ICU admission, and inflammatory markers”. How do you reconcile this with an inferred myocarditis diagnosis? I feel that the current results are not strong enough to make recommendations on the use of dexamethasone, remdesivir or ACEI use on an inferred diagnosis of myocardial involvement. Moreover, were Dexamethasone, remdesivir or ACEI initiated due to elevated cTn? Did cTn have any impact in deciding the treatment that was given or ICU admission, or was it just a part of a general algorithm deciding treatment options? Those are some of my thoughts and questions.



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**Reviewer's code:** 05426937

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor, Professor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** United States

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**Reviewer chosen by:** Geng-Long Liu

**Reviewer accepted review:** 2023-06-13 04:14

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<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Novelty of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
<b>Creativity or innovation of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation



<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<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
<b>Conclusion</b>	<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
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	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**

Myocarditis from direct viral injury or related to angiotensin-converting enzyme 2 (ACE2) downregulation with subsequent hyperactivity of the renin-angiotensin-aldosterone (RAAS) system plays an essential role in troponin elevation in COVID-19 patients. However, the effect of antiviral medications and steroids used to treat viral myocarditis has not been well-studied in patients with elevated troponins. This 1788 samples multicenter retrospective study aims to evaluate the effect of dexamethasone, remdesivir, and ACEI on mortality in COVID-19 patients with elevated troponin. And found no significant difference in survival rates in COVID-19 patients with elevated troponin that received remdesivir, dexamethasone, or ACEI versus those that did not. The implication for practice is that treatment with various medications that could be beneficial in viral myocarditis did not show any mortality benefit in this study for COVID-19 patients with troponin elevation. The content of this manuscript is interesting. We believe this manuscript is valuable for all the researchers who are interested in viral myocarditis in COVID-19 patients. This study focuses on current research hot spots and frontiers, which is very important for



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subsequent research. The article also puts forward the current problems and future research directions. But some sample sizes are in doubt, for example, in Table 2 Remdesivir, no 853, yes 883, total 1736 not 1788; CKD, no 1355, yes 427, total 1782 not 1788; in Table 4 Use of Remdesivir, total 1715 not 1788...Please check. Therefore, I recommend accepting and publishing this manuscript after being revised. Some sample sizes are in doubt, for example, in Table 2 Remdesivir, no 853, yes 883, total 1736 not 1788; CKD, no 1355, yes 427, total 1782 not 1788; in Table 4 Use of Remdesivir, total 1715 not 1788...Please check.