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COVID-19 Related Myocardopathy: Can Dual- Energy Computed Tomography Be a Diagnostic Tool?

Dear Editor,

Thank you for giving us the opportunity to submit a revised draft of the manuscript. We appreciate the time and effort that you and the reviewers dedicated to providing feedback on our manuscript and are grateful for the insightful comments on and valuable improvements to our paper. We have incorporated most of the suggestions made by the reviewers. Those changes are highlighted with track changes function through the manuscript. Please see below for a point-by-point response to the reviewers' comments and concerns.

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The aim is stated clear. The authors stated clearly what study found and how they did it. The title is informative and relevant. The references are relevant and recent. The cited sources are referenced correctly. Appropriate and key studies are included. The introduction reveals what is already known about this topic. The research question is clearly outlined. The research question also justified given what is already known about the topic. The process of selection of the subjects was clear. The variables are well defined and measured appropriately. The study methods are valid and reliable. There are enough details provided in order to replicate the study. The data is presented in an appropriate way. The text in the results add to the data and it is not repetitive. Statistically significant results are clear. It is clear which results are with practical meaning. Results are discussed from different angles and placed into context without being overinterpreted. The conclusions answer the aim of the study. The conclusions are supported by references and own results. Specific comments on weaknesses of the article and what could be improved: Major points - none Minor points 1. Please, state the limitations of the study 2. Could you please discuss the clinical implications of the results

Response:

1. Limitations were added into the discussion section: "There are a few significant limitations in this study. The study's retrospective nature and small sample size are the key restrictions. Coronary arterial findings were not confirmed invasive angiography. CMR scans were not done on any of the individuals included in the study to confirm the identified perfusion anomalies. We are unable to offer patients with clinical follow-up data."

2. The clinical implications were discussed: "In cases of COVID-19, chest pain and thromboembolic cardiovascular complications are extremely common. Particularly in emergency situations, chest pain caused by COVID-19 pneumonia and other cardiovascular complications or diseases can easily coexist. Cardiac CT exams are increasingly utilized in the diagnostic evaluation of chest pain (14). By using DECT to detect COVID-19-associated myocardial damage and distinguish this entity from other cardiovascular causes in a single session, we can provide rapid and effective diagnosis and treatment. In addition, CMR, the alternative diagnostic tool for defining COVID-19-associated myocardial damage, is more difficult to access and considerably more costly than DECT. In addition to more claustrophobic complaints, CMR has longer examination periods, too (26)."

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: In the retrospective study, The authors demonstrate that myocardial perfusion deficits can be found in COVID-19 patients and is positively correlated with D-dimer levels. This theme is very novel. But as a retrospective study, the grouping is not very clear. The time of case collection was not explained clearly. How to select the control group was not explained clearly also. Tables 1 and 2 can be summarized into one table. Most importantly, there is no exactly perfusion data between two groups.

Response:

-Table 1 and 2 were merged.

Table 1: Age, Troponin-I and D-dimer Values

Case Group	Mean \pm Standard Deviation	Median (min-max)
AGE	42.95 \pm 17.53	43.00 (20-73)
TROPONIN-I	103.77 \pm 446.24	3.5 (0.3-2051)
D-DIMER	820.71 \pm 1022.05	390 (105-4000)
Control Group		
AGE	49.68 \pm 10.71	52.00 (28-64)
TROPONIN-I	3.46 \pm 3.49	2.7 (0.01-13)
D-DIMER	273.9 \pm 76.6	267 (105-426)

- The grouping parameters and process were added into the materials and methods section. The time of data collection was also added into the materials and methods section: "Data from this retrospective study include patients from January 2021 to June 2022. Case group included hospitalized individuals with the diagnosis of COVID-19 who had a cardiology consultation due to chest pain and underwent DECT on suspicion of heart abnormalities. COVID-19 was identified using real-time reverse transcriptase-polymerase chain reaction (RT-PCR) tests on nasal and pharyngeal swabs.

As a control group, we included patients who had a DECT scan to evaluate chest pain and a negative RT-PCR assay of nasal and pharyngeal swabs for COVID-19. For both study and control groups,; an exclusion criterion was the existence of any previously known concomitant condition (coronary artery disease, hypertension, hyperlipidemia, diabetes, history of coronary stent or by-pass, arrhythmia, etc.). Furthermore, etiological factors that

may induce D-dimer increase, such as deep venous thrombosis, pulmonary embolism, liver and renal failure, were evaluated, and patients with these conditions were eliminated. Finally, DECT examinations with insufficient qualifications (with poor image quality and numerous artifacts) were barred.”

-The perfusion data for both groups was added into the results section: “Perfusion deficit was identified in 66.6% (n=30) of the case group in the myocardial perfusion imaging data analyzed with the iodine distribution map. On the other hand no perfusion deficit was detected in the control group (Figure 1). Rate of presence of myocardial perfusion deficits was significantly higher in the case group ($p<0.001$).”