Crit Care Shock (2022) 25:129-134

Correlation between galectin-3 and troponin I in COVID-19 ICU patients: A pilot study on galectin-3

Marilaeta Cindryani[1,2], IMG Widnyana[2], Ni Made Ayu Wulansari[3], IB Rangga Wibhuti[3], Made Wiryana[2], Rudyanto Sedono[1], Aldy Heriwardito[1]

Abstract

Due to its expression by macrophages, galectin-3 is among the most recently studied biomarkers. It is likely involved in the inflammatory process that leads to remodeling and eventually fibrosis of organs such as the heart, brain, and kidneys. Coronavirus disease 19 (COVID-19) infection causes excessive inflammatory reactions in the whole body, playing a role in the development of fibrosis due to the activation of the galectin-3-macrophage-fibroblast axis. Heart failure or cardiac dysfunction occurred not only due to pro-inflammatory activation but also due to the overactivation of sympathetic nerves and failure of the respiratory system. The latter increases the possibility of direct infection or necrosis of the heart due to the heart-lung interaction observed in our pilot study. Forty-five intensive care unit (ICU) patients were recruited consecutively in this study to be observed their galectin-3 and troponin I levels.

This pilot study demonstrates the correlation between galectin-3 as a proinflammatory biomarker and troponin I as a definitive biomarker for direct heart injury and highlights its potential use in COVID-19 patients. With the assessment of appropriate biomarkers such as cardiac fibrosis markers, possible worsening of cardiac conditions in COVID-19 patients treated in the ICU can be detected in its early stages.

Key words: Galectin-3, troponin I, correlation, ICU, COVID-19, pilot.

Introduction

The high morbidity and mortality reported in patients with coronavirus disease 19 (COVID-19) are presumed to be caused only by lung disorders; however, they may result from damage to other vital organs, such as the heart. According to a 2020 study conducted by Guo et al in China, of 187 patients with COVID-19 treated, 52 (27.8%) had myocardial injuries with elevated troponin T levels. Additionally, the mortality was extremely high in such patients (59.6%) compared to those with normal levels of troponin T (8.9%). (1)

Galectin-3 is often expressed by inflammatory cells like macrophages. It is presumably involved in an inflammatory process that results in remodeling and fibrosis of organs like the heart, brain, and kidneys. (2) The galectin-3-monocyte-macrophage axis-mediated inflammatory processes manifest as organ dysfunctions, including a decrease in heart contractility. The reduced ability of the heart muscle to contract and pump blood leads to an increased end-diastolic volume in the left ventricle.

In addition to proinflammatory activation, heart failure or cardiac dysfunction can also occur due to overactivation of the sympathetic nerves and failure of the respiratory system. Moreover, due to heart-lung interaction, there is a possibility of direct in-

[1.] Department of Anesthesiology and Intensive Care, Universitas Indonesia-Cipto Mangunkusumo Hospital, Jakarta, Indonesia
[2.] Anesthesiology and Intensive Care Department, Udayana University/Sanglah Hospital, Denpasar, Indonesia
[3.] Cardiology and Vascular Department, Udayana University/Sanglah Hospital, Denpasar, Indonesia

Address for correspondence:
Marilaeta Cindryani
Department of Anesthesiology and Intensive Care, Universitas Indonesia, Jakarta
Anesthesiology and Intensive Care Department, Sanglah Hospital, Denpasar, Bali, Indonesia
Tel: +6285237019933
Email: onkhenk@yahoo.com

fection or necrosis of the heart (**Figure 1**). (3)
Troponin I is associated with troponin T and C, creating a 3-unit complex on actin filaments. It plays a vital role in regulating calcium-mediated muscle contraction in the skeletal and cardiac muscles, thereby serving as an important biomarker for cardiac muscle injury.
A study conducted by Fayed et al in 2013 compared galectin-3 and troponin I levels in healthy individuals and patients with heart failure. Levels of troponin I and galectin-3 were found to be significantly higher in patients with heart failure (18.40±11.5 and 0.429±0.630 ng/ml, respectively) compared to the healthy group (5.75±1.427 and 0.019±0.0544 ng/ml, respectively). Consequently, relevant biomarkers in combination with troponin I and galectin-3 indicated an improved sensitivity (84%), specificity (80%), positive predictive value (PPV) (87.5%), and negative predictive value (NPV) (75%) for the diagnosis of heart failure. (4)
Another 2020 study by Manocha et al reported elevated levels of biomarkers such as troponin, B-type natriuretic peptide, C-reactive protein, ferritin, and D-dimer in COVID-19 patients. When compared to other biomarkers, increased troponin I had the highest predictive value for assessing mortality in COVID-19 patients (adjusted odds ratio 4.38, $p<0.001$). (5)
The possible worsening of heart conditions in COVID-19 patients treated in the intensive care unit (ICU), which may later lead to heart failure, can be monitored through the assessment of galectin-3. (6) We also demonstrate the correlation between troponin I as a definitive biomarker with galectin-3 as an early inflammatory biomarker for direct cardiac injuries in COVID-19 patients.

Method

This was a prospective analytical observational study. Analysis was conducted on primary data obtained from COVID-19 patients treated in the COVID-19 ICU of Sanglah Hospital, Bali, Indonesia, between June and October 2021. The study has been approved by the Research Ethics Committee of Sanglah Hospital and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Research subjects were identified based on inclusion and exclusion criteria. Individuals aged 18-65 years who confirmed positive for COVID-19 using reverse transcription-polymerase chain reaction (RT-PCR) were included in this study. Samples were taken consecutively from COVID-19 patients who received treatment in the ICU of Sanglah Hospital from June to October 2021. All participants gave their informed consent prior to their inclusion in the study.
Blood samples were collected from 45 research subjects to be tested for galectin-3 and troponin I levels after 72 hours of hospitalization in the COVID-19 ICU. Data were processed and analyzed using Stata software.

Discussion

The median values for galectin-3 and troponin I levels were 78.79 ng/ml and 79 ng/l, respectively. There was a tendency for direct myocardial injury due to COVID-19 infection as indicated by high troponin I level in most of the subjects (75.5%) (**Table 1**). This was in accordance with the pathophysiological theory of injury and decreased cardiac function in COVID-19 patients.
Spearman's rank coefficient was used to determine the correlation between galectin-3 and troponin I due to non-normal data distribution. A significant correlation ($p<0.0001$) between galectin-3 and troponin I levels was observed (correlation coefficient 0.6595) (**Figure 2**).
D-dimer is one of the strongest inflammatory markers that increase markedly in COVID-19 and is a significant mortality predictor. We further explored the correlation between galectin-3 and D-dimer levels in subjects; however, no correlation was found between these two parameters ($r=0.0988$, $p>0.05$).

Conclusion

A linear correlation existed between galectin-3 and troponin I level in 45 patients treated in the COVID-19 ICU. This finding was supported by the pathophysiological theory of direct cardiac injury and decreased cardiac function in COVID-19 patients; however, further investigation of galectin-3 as a biomarker would extend its novelty in clinical pathways and management of COVID-19.

Conflict of interest

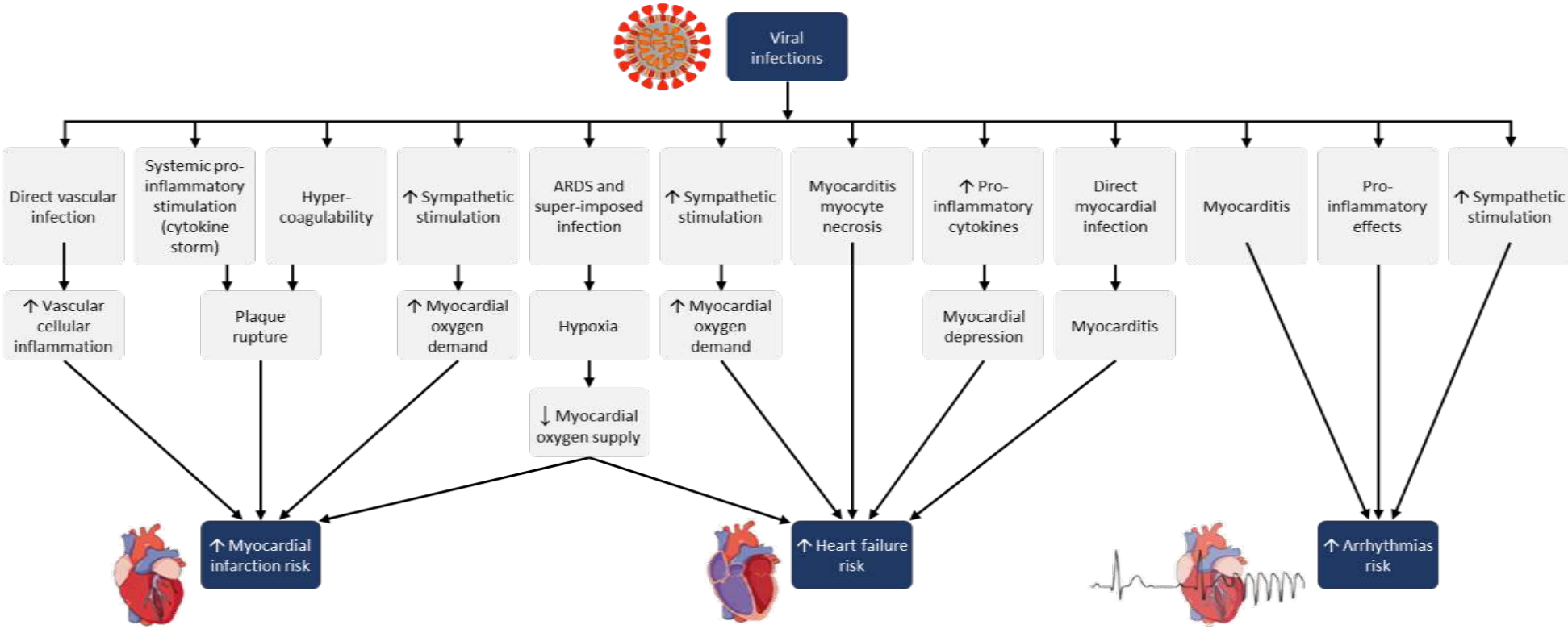
None

Table 1. Troponin I level in COVID-19 patients after 72 hours of treatment in the ICU

Troponin I level (ng/l)	n (%)
<10	11 (24.5%)
>10	34 (75.5%)
Total subjects	45 (100%)

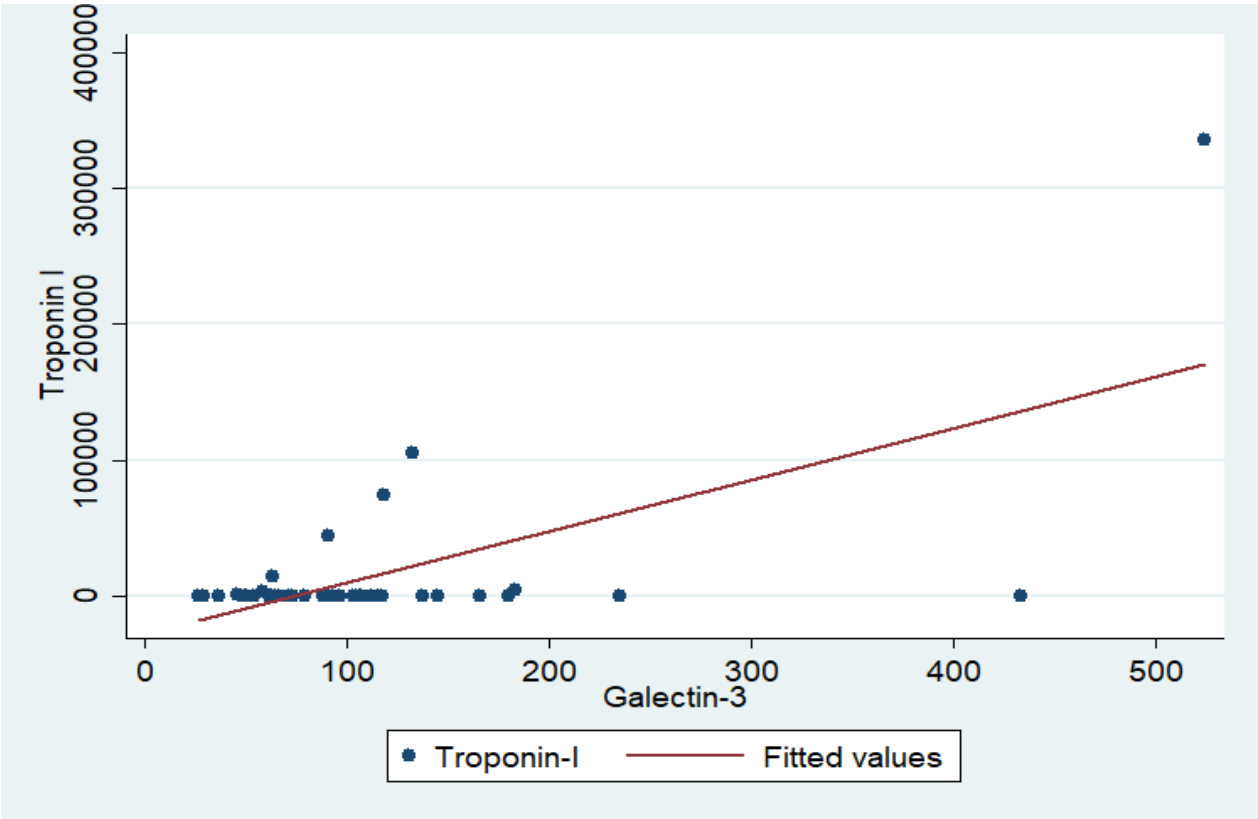
Legend: COVID-19=coronavirus disease 19; ICU=intensive care unit.

Figure 1. Pathophysiology of cardiac dysfunction in COVID-19 infection (3)



Legend: COVID-19=coronavirus disease 19; ARDS=acute respiratory distress syndrome.

Figure 2. Correlation between galectin-3 and troponin I levels



References

1. Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). JAMA Cardiol 2020;5:1-8.
2. World Health Organization. COVID-19 Weekly Epidemiological Update [Internet]. 2020 Oct 18 [cited 2020 Dec 27]. Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20201020-weekly-epi-update-10.pdf
3. Abboud A, Januzzi Jr JL. Heart Failure Biomarkers in COVID-19 [Internet]. 2020 Jul 27 [cited 2020 Dec 27]. Available from: https://www.acc.org/latest-in-cardiology/articles/2020/07/27/09/25/heart-failure-biomarkers-in-covid-19
4. Fayed HM, Alsenbesy MA, Saleem TH, Ahmed MA. Comparative Study of Circulating Cardiac Biomarker Galectin-3 and Troponin I in Heart Failure Patients. Clin Med Diag 2013;3:92-100.
5. Manocha KK, Kirzner J, Ying X, Yeo I, Peltzer B, Ang B, et al. Troponin and Other Biomarker Levels and Outcomes Among Patients Hospitalized With COVID-19: Derivation and Validation of the HA2T2 COVID-19 Mortality Risk Score. J Am Heart Assoc 2021;10:e018477.
6. Caniglia JL, Asuthkar S, Tsung AJ, Guda MR, Velpula KK. Immunopathology of galectin-3: an increasingly promising target in COVID-19. F1000Res 2020;9:1078.