Int J Heart Fail. 2024 Jan;6(1):34-35
https://doi.org/10.36628/ijhf.2023.0063
pISSN 2636-154X·eISSN 2636-1558

International Journal of Heart Failure
IJHF

Editorial

Check for updates

The Relationship Between C-reactive Protein and Takotsubo Syndrome: An Old Riddle

Sunki Lee, MD

Cardiovascular Center, Division of Cardiology, Korea University Guro Hospital, Seoul, Korea

See the article "C-Reactive Protein Can Predict Outcomes in Patients With Takotsubo Syndrome" in volume 6 on page 28.

OPEN ACCESS

Received: Nov 30, 2023
Revised: Dec 14, 2023
Accepted: Dec 16, 2023
Published online: Jan 3, 2024

Correspondence to
Sunki Lee, MD
Cardiovascular Center, Division of Cardiology, Korea University Guro Hospital, 148 Guro-dong-ro, Guro-gu, Seoul 08308, Korea.
Email: galiard@naver.com

In the realm of cardiovascular medicine, Takotsubo syndrome represents a clinical entity both mysterious and distinct. Characterized by transient left ventricular dysfunction, this syndrome often mimics acute coronary syndrome but occurs predominantly in the absence of significant coronary artery obstruction.[1] Its predilection for post-menopausal women, particularly following episodes of acute stress, adds to its unique clinical profile.[2,3] As we investigate for the pathophysiology of this condition, a question of notable clinical importance arises: what is the role of C-reactive protein (CRP), a biomarker of inflammation, in the context of Takotsubo syndrome?

CRP, established as an indicator of systemic inflammation, holds a significant place in the diagnosis and management of various cardiovascular diseases.[4] Its elevation is often interpreted as a marker of increased cardiovascular risk.[5] However, the interpretation of elevated CRP levels in Takotsubo syndrome presents a complex diagnostic dilemma.[6] Is the elevation of CRP in these patients a secondary phenomenon, reflecting a systemic inflammatory response to cardiac stress, or does it play a contributory role in the pathogenesis of the syndrome?

The stress-induced catecholamine surge, a central feature in the pathophysiology of Takotsubo syndrome, may trigger a cascade of inflammatory responses, potentially reflected in increased CRP levels.[7,8] However, the exact mechanistic pathways linking stress, catecholamine surge, and CRP elevation remain speculative and warrant further investigation.

In this respect, Moady et al.[9] demonstrated in this issue of *International Journal of Heart Failure* that could help close this gap in clinical knowledge. The study included 86 patients, predominantly female (93%) with an average age of 69 years. The median CRP level was 17.4 mg/L and the average left ventricular ejection fraction (LVEF) was 41.5%. Higher CRP levels were linked to lower LVEF, longer hospital stays, and recurrence of the condition. Further analysis showed that poorer LVEF increased the likelihood of Takotsubo syndrome recurrence, and CRP was the only factor associated with longer length of stay and lower LVEF. An interesting result of this study was that when the patient group was divided into quartiles according to CRP level, the readmission rate due to Takotsubo syndrome recurrence increased in patients with initially high CRP. It aligns with recent research suggesting that ongoing inflammation might hinder recovery and lead to a worse outcome.[10] These results highlight patients with a high residual inflammatory response as a high-risk group for Takotsubo syndrome. Investigating whether reducing inflammation in these patients can improve their prognosis would be a valuable topic for future research. However, caution is advised in interpreting this study result due to various potential

limitations. This study included relatively a small number of patients and the retrospective design inherently carries limitations related to known and unknown confounding factors. Also, the cohort was based on patients who were in a stable condition, so the findings may not apply to Takotsubo syndrome patients in poor condition. Since CRP levels were only measured once, it is not possible to determine if they remained high during the follow-up period. Finally, the study's evaluation of inflammation markers was restricted to CRP. Other parameters reflecting inflammation parameters (such as cytokines, lactic acid and procalcitonin) and natriuretic peptides could have been assessed, potentially providing more information from this study.[11]

The potential relationship between CRP and Takotsubo syndrome presents clinically relevant query. Unraveling this relationship could significantly enhance our understanding of the syndrome's pathophysiology. However, the current state of research on this subject is limited by certain constraints, including small study cohorts and a paucity of longitudinal data. Such studies should aim to elucidate the long-term impact of CRP levels on the prognosis of Takotsubo syndrome and determine whether CRP acts merely as a marker of stress-induced cardiac injury or plays a more active role in the pathophysiology of the syndrome. Should future research establish a direct involvement of CRP in the pathogenesis of Takotsubo syndrome, it could not only facilitate more accurate diagnosis but also open avenues for targeted therapeutic interventions. Presently, management strategies for Takotsubo syndrome are predominantly supportive, with beta-blockers frequently utilized to manage symptomatic relief. A direct implication of CRP in the disease process could pave the way for the implementation of anti-inflammatory strategies, potentially altering the clinical course of this clinically important "riddle-like" syndrome.

ORCID iDs
Sunki Lee
https://orcid.org/0000-0002-5247-7981

Conflict of Interest
The author has no financial conflicts of interest.

REFERENCES

1. Sato H, Tateishi H, Dote K, Uchida T, Ishihara M. Tako-tsubo-like left ventricular dysfunction due to multivessel coronary spasm. In: Kodama K, Haze K, Hori M, editors. Clinical Aspect of Myocardial Injury: From Ischemia to Heart Failure. Tokyo: Kagakuhyoronsha Publishing Co.; 1990. p.56-64.
2. Akashi YJ, Nef HM, Lyon AR. Epidemiology and pathophysiology of Takotsubo syndrome. Nat Rev Cardiol 2015;12:387-97. PUBMED | CROSSREF
3. Patel SM, Chokka RG, Prasad K, Prasad A. Distinctive clinical characteristics according to age and gender in apical ballooning syndrome (Takotsubo/stress cardiomyopathy): an analysis focusing on men and young women. J Card Fail 2013;19:306-10. PUBMED | CROSSREF
4. Lagrand WK, Visser CA, Hermens WT, et al. C-reactive protein as a cardiovascular risk factor: more than an epiphenomenon? Circulation 1999;100:96-102. PUBMED | CROSSREF
5. Burger PM, Pradhan AD, Dorresteijn JA, et al. C-reactive protein and risk of cardiovascular events and mortality in patients with various cardiovascular disease locations. Am J Cardiol 2023;197:13-23. PUBMED | CROSSREF
6. Singh T, Khan H, Gamble DT, Scally C, Newby DE, Dawson D. Takotsubo syndrome: pathophysiology, emerging concepts, and clinical implications. Circulation 2022;145:1002-19. PUBMED | CROSSREF
7. Scally C, Abbas H, Ahearn T, et al. Myocardial and systemic inflammation in acute stress-induced (Takotsubo) cardiomyopathy. Circulation 2019;139:1581-92. PUBMED | CROSSREF
8. Morel O, Sauer F, Imperiale A, et al. Importance of inflammation and neurohumoral activation in Takotsubo cardiomyopathy. J Card Fail 2009;15:206-13. PUBMED | CROSSREF
9. Moady G, Yelin B, Sweid R, Atar S. C-reactive protein can predict outcomes in patients with Takotsubo syndrome. Int J Heart Fail 2024;6:28-33. CROSSREF
10. Lachmet-Thebaud L, Marchandot B, Matsushita K, et al. Impact of residual inflammation on myocardial recovery and cardiovascular outcome in Takotsubo patients. ESC Heart Fail 2021;8:259-69. PUBMED | CROSSREF
11. Wettersten N. Biomarkers in acute heart failure: diagnosis, prognosis, and treatment. Int J Heart Fail 2021;3:81-105. PUBMED | CROSSREF