

Systemic Biomarkers in Heart Failure: To Measure or Not to Measure?

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Editorial referring to the article: *Procalcitonin and D-dimer in Predicting the Severity of Congestive Heart Failure*

Heart failure (HF) is an aggressive disease with unfavorable prognosis if not treated properly. Even after optimal medical treatment, some patients may remain at high risk for clinical events.¹ As such, it is important to identify patients at risk of death or hospitalization. Biomarkers have been used to establish prognosis in HF, and natriuretic peptides (NP) are considered the gold standard biomarker in HF, not only for diagnosis but also for prognosis.¹

NP are cardiac biomarkers, produced by the heart ventricles in response to wall stretch.² However, several systemic biomarkers, reflecting different pathways, have been shown to be elevated in HF with the potential to add information on top of NP (Figure 1).³⁻⁵ Nevertheless, these biomarkers have not been strongly recommended in HF guidelines because their utility in aiding decision-making is unclear.

Procalcitonin is a protein that is produced by the body in response to bacterial infections and is often measured to aid diagnose and manage sepsis and other inflammatory conditions.⁶ It is a precursor of the hormone calcitonin and is typically present at low levels in healthy individuals. However, during bacterial infections, procalcitonin levels can rise significantly, making it a useful biomarker for distinguishing between bacterial and viral infections.⁶ This helps clinicians make informed decisions regarding antibiotic therapy and can guide the treatment of patients with suspected septic conditions. Procalcitonin is elevated in some patients with HF, especially when they have associated infection, and may confer prognostic information.^{7,8}

D-dimer is a fibrin degradation product that is formed when a blood clot dissolves in the body. It is typically present at low levels in the bloodstream, but elevated levels can indicate the presence of abnormal clotting and are often associated with conditions such as deep vein thrombosis, pulmonary embolism, and disseminated intravascular

coagulation.⁹ Clinically, the D-dimer test is commonly used as a diagnostic tool to rule out thromboembolic disorders, especially in patients presenting with symptoms related to clot formation. While a negative D-dimer test can be reassuring and suggest that significant clotting is unlikely, a positive result does not provide a definitive diagnosis, necessitating further investigation to determine the underlying cause. HF is one of these causes.¹⁰

In this issue of *International Journal of Cardiovascular Sciences*, Liyis BG et al. report an original investigation about the association of procalcitonin and D-dimer with HF severity in patients hospitalized with acute HF.¹¹ They found that both biomarkers were correlated with the severity of HF, as assessed by New York Heart Association functional class. After adjusting for confounders (multivariate analysis), only D-dimer maintained statistical significance.

Their study has some strengths. Prognostic markers are welcome, and the authors used adequate methodology and robust statistical analysis. Some limitations have already been pointed out by the authors, for example, the retrospective single-center design of the study. Unfortunately, the authors did not provide any prognostic information. The relationship of such biomarkers with hospital mortality would have strengthened the manuscript. A major limitation is the fact that NP, such as BNP or NT-proBNP, were not measured. NP are the gold standard biomarker in HF, and any new biomarker that is a candidate for the management of HF should be compared to them.

In conclusion, many systemic biomarkers may be elevated and correlated with the severity of HF. However, to be useful in clinical practice, they need to add new information that might aid decision-making. Until new data emerge, procalcitonin and D-dimer should not be routinely measured in acute HF, unless bacterial infection or thromboembolic disorders are suspected.

Keywords

Heart Failure; Biomarkers; Infections; Thrombosis; Prognosis

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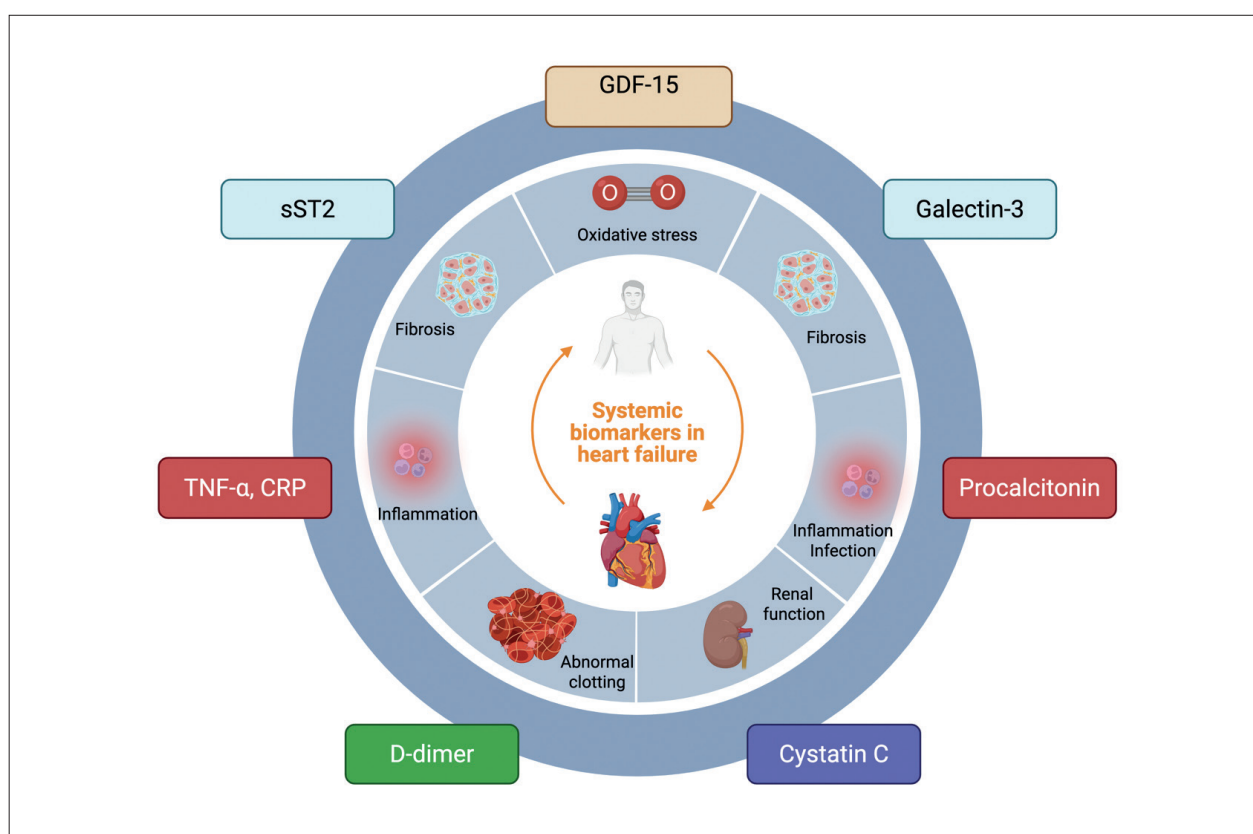


Figure 1 – Systemic biomarkers and their specific pathways in patients with HF. CRP: C-reactive protein; GDF-15: growth differentiation factor 15; sST2: soluble suppression of tumorigenicity 2; TNF- α : tumor necrosis factor alpha.

References

- Marcondes-Braga FG, Moura LAZ, Issa VS, Vieira JL, Rohde LE, Simões MV, et al. Emerging Topics Update of the Brazilian Heart Failure Guideline - 2021. *Arq Bras Cardiol.* 2021;116(6):1174-212. doi: 10.36660/abc.20210367.
- Yasue H, Yoshimura M, Sumida H, Kikuta K, Kugiyama K, Jougasaki M, et al. Localization and Mechanism of Secretion of B-Type Natriuretic Peptide in Comparison with those of A-Type Natriuretic Peptide in Normal Subjects and Patients with Heart Failure. *Circulation.* 1994;90(1):195-203. doi: 10.1161/01.cir.90.1.195.
- Meijers WC, Bayes-Genis A, Mebazaa A, Bauersachs J, Cleland JGF, Coats AJS, et al. Circulating Heart Failure Biomarkers Beyond Natriuretic Peptides: Review from the Biomarker Study Group of the Heart Failure Association (HFA), European Society of Cardiology (ESC). *Eur J Heart Fail.* 2021;23(10):1610-32. doi: 10.1002/ehf.2346.
- Villacorta H, Maisel AS. Soluble ST2 Testing: A Promising Biomarker in the Management of Heart Failure. *Arq Bras Cardiol.* 2016;106(2):145-52. doi: 10.5935/abc.20150151.
- Ávila DX, Candia AMD, Moreira GR, Scaramussa VD, Lopes RD, Villacorta H. Growth Differentiation Factor-15 and Clinical Outcomes in Patients with Chronic Heart Failure. *J Card Fail.* 2024;30(5):734-6. doi: 10.1016/j.cardfail.2024.02.026.
- Velissaris D, Zareifopoulos N, Lagadinou M, Platanaki C, Tsiotsios K, Stavridis EL, et al. Procalcitonin and Sepsis in the Emergency Department: An Update. *Eur Rev Med Pharmacol Sci.* 2021;25(1):466-79. doi: 10.26355/eurrev_202101_24416.
- Villanueva MP, Mollar A, Palau P, Carratalá A, Núñez E, Santos E, et al. Procalcitonin and Long-Term Prognosis after an Admission for Acute Heart Failure. *Eur J Intern Med.* 2015;26(1):42-8. doi: 10.1016/j.ejim.2014.12.009.
- Aïssou L, Sorbets E, Lallmahomed E, Goudot FX, Pop N, Es-Sebbani S, et al. Prognostic and Diagnostic Value of Elevated Serum Concentration of Procalcitonin in Patients with Suspected Heart Failure. A Review and Meta-Analysis. *Biomarkers.* 2018;23(5):407-13. doi: 10.1080/1354750X.2018.1443511.
- Olson JD. D-Dimer: An Overview of Hemostasis and Fibrinolysis, Assays, and Clinical Applications. *Adv Clin Chem.* 2015;69:1-46. doi: 10.1016/bbs.2014.12.001.
- Huang L, Liang L, Tian P, Zhao L, Chen Y, Huang Y, et al. D-Dimer and Outcomes in Hospitalized Heart Failure Patients Across the Ejection Fraction Phenotypes. *ESC Heart Fail.* 2022;9(5):3060-70. doi: 10.1002/ehf2.14049.
- Liyis BG, Sutedja JC, Sadeva IGKA, Mareska V, Salim A, David G, et al. Procalcitonin and D-Dimer in Predicting the Severity of Congestive Heart Failure. *Int J Cardiovasc Sci.* 2025;38:e20230144. doi: 10.36660/ijcs.20230144.



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