

## Inflammation and Prognosis in Acute Heart Failure: Is There a Role for Pan-Immune-Inflammation Value?

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Short Editorial related to the article: Association of Pan Immune-Inflammation Value with Long Term Outcomes of Acute Decompensated Heart Failure

Heart failure (HF) is a major health problem, with high morbidity and mortality rates.<sup>1</sup> Patients with HF are frequently hospitalized. Inflammation plays a role in the pathophysiology of HF and several cytokines, such as tumor necrosis factor (TNF), transforming growth factor- $\beta$  (TGF- $\beta$ ), and interleukins 6 and 1, are elevated in HF.<sup>2</sup> In acute decompensated HF (ADHF) the triggers of this inflammatory cascade are secondary to neurohormonal activation and oxidative stress, but in addition, there is evidence for elevated bacterial or endotoxin translocation, due to gut edema or relative hypoperfusion.<sup>2,3</sup> The measurement of cytokines is not appropriate for day-to-day clinical practice and C-reactive protein (CRP),<sup>4,5</sup> another biomarker of inflammation, is usually chosen to assess inflammation. However, a more robust and convenient marker is warranted.

A new marker of inflammation has been recently introduced. Pan-immune-inflammation value (PIV) is calculated from peripheral blood immune-inflammatory components, including neutrophil, platelet, monocyte, and lymphocyte counts, as shown in Figure 1. PIV has been shown to be prognostic in some cardiovascular disorders and also in non-cardiovascular diseases, such as cancer and advanced renal disease.<sup>6-10</sup>

In this issue of *Arquivos Brasileiros de Cardiologia*, an original study presents an investigation into the prognostic value of PIV in patients with ADHF.<sup>11</sup> The study's findings suggest that higher PIV levels at admission are associated with increased short and long-term all-cause mortality in patients with ADHF. One notable strength of the study is its focus on a novel biomarker, PIV, which offers a comprehensive assessment of inflammation by incorporating multiple immune-inflammatory components. This approach provides

a more nuanced understanding of the inflammatory status in HF patients compared to single-component markers. By considering various aspects of the immune response, PIV may offer improved prognostic accuracy and predictive value. Of note, the prognostic value of PIV in this study was independent of N-terminal pro-B-type natriuretic peptide (NT-proBNP) and CRP.

Some limitations of the study<sup>11</sup> have already been addressed by the authors and should be considered when interpreting the study findings. Firstly, the study's retrospective design and single-center setting may introduce selection bias and limit the generalizability of the results. Additionally, the relatively small sample size of 409 patients raises concerns about statistical power and the robustness of the findings. Larger, multicenter studies are needed to validate the prognostic utility of PIV in diverse patient populations.

Furthermore, while the study<sup>11</sup> demonstrates an association between PIV and mortality outcomes, the underlying mechanisms driving this relationship remain unclear. The study does not provide insights into the specific pathways through which immune-inflammatory dysregulation contributes to adverse outcomes in HF patients. Future research should aim to elucidate the pathophysiological mechanisms linking PIV to HF prognosis, potentially through mechanistic studies or biomarker validation in animal models.

Despite these limitations, this study<sup>11</sup> brings new and relevant information. To the best of our knowledge, only one previous study evaluated PIV in ADHF, and, therefore, the present study adds information in this scenario, where data is scarce.<sup>12</sup> We look forward to future studies with this new biomarker in larger populations.

### Keywords

Heart Failure; Inflammation; Biomarkers; Prognosis; Hospitalization; Endotoxins.

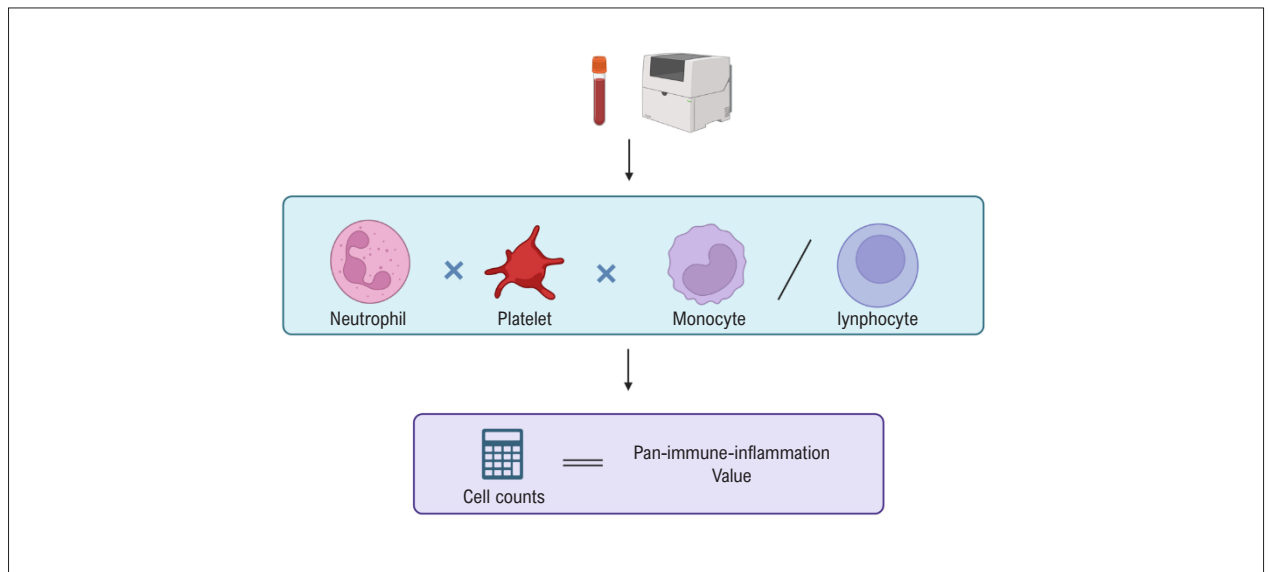
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**Figure 1** – The pan-immune-inflammation value is a new biomarker, associated with systemic inflammation, calculated by multiplying neutrophil, platelet, and monocyte counts, divided by the lymphocyte count.

## References

1. 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
2. Njoroje JN, Teerlink JR. Pathophysiology and therapeutic approaches to acute decompensated heart failure. *Circ Res.* 2021;128(10):1468-86. doi: 10.1161/CIRCRESAHA.121.318186
3. Peschel T, Schönauer M, Thiele H, Anker SD, Schuler G, Niebauer J. Invasive assessment of bacterial endotoxin and inflammatory cytokines in patients with acute heart failure. *Eur J Heart Fail.* 2003;5(5):609-14. doi: 10.1016/s1388-9842(03)00104-1
4. Villacorta H, Masetto AC, Mesquita ET. C-reactive protein: an inflammatory marker with prognostic value in patients with decompensated heart failure. *Arq Bras Cardiol.* 2007;88(5):585-9. doi: 10.1590/s0066-782x2007000500014
5. Mueller C, Laule-Killian K, Christ A, Bruner-La Rocca HP, Perruchoud AP. Inflammation and long-term mortality in acute congestive heart failure. *Am Heart J.* 2006;151(4):845-50. doi: 10.1016/j.ahj.2005.06.046
6. Murat B, Murat S, Ozgeyik M, Bilgin M. Comparison of pan-immune-inflammation value with other inflammation markers of long-term survival after ST-segment elevation myocardial infarction. *Eur J Clin Invest.* 2023;53(1):e13872. Doi 10.1111/eci.13872.
7. Wang S, Zhang L, Qi H, Zhang FL, Fang Q, Qiu L. Pan-immune-inflammation value predicts the 3 months outcomes in acute ischemic stroke patients after intravenous thrombolysis. *Curr Neurovasc Res.* 2023;20(4):464-71. doi: 10.2174/0115672026276427231024045957
8. Yang XC, Liu H, Liu DC, Tong C, Liang XW, Chen RH. Prognostic value of pan-immune-inflammation value in colorectal cancer patients: a systematic review and meta-analysis. *Front Oncol.* 2022;12:1036890. doi 10.3389/fonc.2022.1036890.
9. Baba Y, Nakagawa S, Toihata T, Harada K, Iwatsuki M, Hayashi H, et al. Pan-immune-inflammation value and prognosis in patients with esophageal cancer. *Ann Surg Open.* 2021;3(1):e113. doi: 10.1097/AS9.000000000000113.
10. Zhang F, Li L, Wu X, Wen Y, Zhan X, Peng F, et al. Pan-immune-inflammation value is associated with poor prognosis in patients undergoing peritoneal dialysis. *Ren Fail.* 2023;45(1):2158103. Doi 10.1080/0886022X.2022.2158103.
11. Murat B, Murat S, Altınbas ME, Yalvac HE, Durmaz FE, Mert KU, Cavusoglu Y. Associação do Valor Pan-Imune-Inflamatório com Desfechos de Longo Prazo na Insuficiência Cardíaca Agudamente Descompensada. *Arq Bras Cardiol.* 2024; 121(6):e20230817. DOI: <https://doi.org/10.36660/abc.20230817>.
12. Inan D, Erdogan A, Pay L, Genc D, Demirtola AI, Yıldız U, et al. The prognostic impact of inflammation in patients with decompensated acute heart failure, as assessed using the pan-immune inflammation value (PIV). *Scand J Clin Lab Invest.* 2023;86(6):371-8. doi: 10.1080/00365513.2023.2233890

