Applying EASIX in Osteoarthritis. The Link between Inflammation and Cardiovascular Risk

Marcio Roberto Moraes de Carvalho[1]

Universidade Federal Fluminense,[1] Niterói, RJ – Brazil

Short Editorial related to the article: Association of Endothelial Activation and Stress Index with Risk of Cardiovascular Disease and All-cause Mortality in Patients with Osteoarthritis

Osteoarthritis (OA), long regarded as a mechanical wear-and-tear disease of the joints, is increasingly being reinterpreted in light of evidence identifying it as a chronic low-grade inflammatory disease. This shift is more than semantic; it fundamentally reshapes how we assess the systemic risks faced by these patients, particularly their cardiovascular risk (CVR). Given the growing recognition of endothelial dysfunction as a key manifestation of the inflammatory process involved in vascular event development, the pursuit of tools capable of detecting indicators of these underlying mechanisms is of substantial importance.[1]

In this issue,[2] we present a new application of the Endothelial Activation and Stress Index (EASIX) to predict CVR in OA patients. Originally developed for hematological conditions, particularly graft-versus-host disease (GVHD), EASIX integrates three widely available markers - LDH, serum creatinine, and platelet count - into a single index that reflects endothelial stress.[3,4]

Validated in diverse contexts marked by endothelial dysfunction, including acute GVHD, transplant-associated thrombotic microangiopathy, sepsis, and acute pancreatitis, the value measured by EASIX is associated with greater morbidity and mortality.[5,6] Its new application offers a practical and physiologically sound tool for monitoring cardiovascular complications in OA patients.[6,7]

The study[2] applied the EASIX score to a cohort of patients with OA aged 40 to 79 years, excluding those with a known diagnosis of cardiovascular disease (CVD). The results demonstrated that a higher EASIX score was significantly associated with an increased risk of atherosclerotic CVD (OR: 1.94; 95% CI: 1.57–2.41) and all-cause mortality (HR: 1.59; 95% CI: 1.14–2.23). Specifically, individuals with log (EASIX) > -0.78 exhibited a higher risk of death from any cause compared to those with log (EASIX) < -1.29. Subgroup analyses revealed that these associations were particularly pronounced among patients aged ≥65 years, women, and Black individuals, highlighting potential demographic variations in the prognostic utility of the EASIX score within the OA population.

The parallel between inflammation and tissue regeneration in OA is complex, as it involves local and systemic factors.[8] Endothelial dysfunction, central to atherosclerosis and CVD, may partly explain the elevated CVR in OA. Chronic inflammation in OA promotes the systemic release of inflammatory mediators, accelerating endothelial damage and atherosclerosis progression.[9] Low-grade inflammation, mainly mediated by the innate immune system, drives cartilage degradation, bone remodeling, and synovial changes. Cytokines and chemokines not only promote structural damage but also impair tissue regeneration, a well-documented dual role in rheumatoid arthritis [10] and OA.

This editorial raises a main question: Is inflammation the link between degenerative and acquired diseases? Emerging evidence suggests that chronic low-grade inflammation underlies some conditions, such as atherosclerosis, OA, and type 2 diabetes,[11] acting as both a driver of degeneration and a frustrated trigger of regeneration. Recognizing inflammation as a central physiological vertex opens up new therapeutic and diagnostic opportunities.

Naturally, limitations remain. The EASIX has not yet been prospectively validated in this population. Questions about specific cut-off values, interlaboratory reproducibility, and the impact of comorbidities need to be addressed. However, these open questions do not diminish the strength of the underlying physiopathological reasoning.

This editorial sees in this study a fertile conceptual seed, envisioning a future in which CVR is assessed through inflammation, microangiopathy, and endothelial stress, offering new foundations for traditional cardiology. In this context, EASIX can transcend its numerical role to bridge the gap between degenerative rheumatology and preventive cardiology. Medicine will increasingly be cross-sectional, inflammatory, and endothelial, and the use of EASIX could be an opportunity for this understanding.

Keywords

Endothelium; Cardiovascular Diseases; Osteoarthritis.

Mailing Address: Marcio Roberto Moraes de Carvalho •
Universidade Federal Fluminense - Av. Marquês do Paraná, 303. Postal Code 24220-900, Centro, Niterói, RJ - Brazil
E-mail: carvalhobm@uol.com.br
Manuscript received April 27, 2025, revised manuscript May 02, 2025, accepted May 02, 2025

DOI: https://doi.org/10.36660/abc.20250314i

References

1. De Roover A, Escribano-Núñez A, Monteagudo S, Lories R. Fundamentals of Osteoarthritis: Inflammatory Mediators in Osteoarthritis. Osteoarthritis Cartilage. 2023;31(10):1303-11. doi: 10.1016/j.joca.2023.06.005.
2. Li R, Feng C, Lin K, Wang N, Fan X. Associação da Ativação Endotelial e do Índice de Estresse com Risco de Doença Cardiovascular e Mortalidade por Todas as Causas em Pacientes com Osteoartrite. Arq Bras Cardiol. 2025; 122(7):e20250012. DOI: https://doi.org/10.36660/abc.20250012.
3. Luft T, Brenner A, Jodele S, Dandoy CE, Storb R, Gooley T, et al. EASIX-GVHD Score in Patients with Acute GVHD after Allogenic Stem-Cell Transplantation [Internet]. Haaksbergen: Evidencio; 2025 [cited 2025 Apr 25]. Available from: https://www.evidencio.com/models/show/936.
4. Sanchez-Escamilla M, Flynn J, Devlin S, Maloy M, Fatmi SA, Tomas AA, Escribano-Serrat S, Ponce D, Sauter CS, Giralt SA, Scordo M, Perales MA. EASIX score predicts inferior survival after allogeneic hematopoietic cell transplantation. Bone Marrow Transplant. 2023 May;58(5):498-505. doi: 10.1038/s41409-023-01922-8. Epub 2023 Jan 31. PMID: 36721042; PMCID: PMC10513445.
5. Sang M, Ma X, Zhu F, Zhu C, Ying Z. Association between endothelial activation and stress index and 30-day mortality risk in acute myocardial infarction patients: a study based on the medical information mart for intensive care-IV database. BMC Cardiovasc Disord. 2024 Dec 4;24(1):699. doi: 10.1186/s12872-024-04353-5. PMID: 39633266; PMCID: PMC11619625.
6. Wang J, Chen X, Qin C, Zeng X, Du X, Wang D. The endothelial activation and stress index is a potential prognostic indicator for patients with acute pancreatitis managed in the intensive care unit: a retrospective study. Front Med (Lausanne). 2024 Dec 11;11:1498148. doi: 10.3389/fmed.2024.1498148. PMID: 39722816; PMCID: PMC11668595.
7. Luft T, Benner A, Jodele S, Dandoy CE, Storb R, Gooley T, et al. EASIX in Patients with Acute Graft-versus-Host Disease: A Retrospective Cohort Analysis. Lancet Haematol. 2017;4(9):e414-23. doi: 10.1016/S2352-3026(17)30108-4.
8. Park D, Park YM, Ko SH, Choi YH, Min DU, Ahn JH, et al. Association between Knee Osteoarthritis and the Risk of Cardiovascular Disease and the Synergistic Adverse Effects of Lack of Exercise. Sci Rep. 2023;13(1):2777. doi: 10.1038/s41598-023-29581-1.
9. Hébert JJ, Saritas S, Niloofar P, Lazarova-Molnar S, Houlind KC, Wedderkopp N. Knee and Hip Osteoarthritis Increase the Risk of Cardiovascular Disease: A National Registry-Based Longitudinal Cohort Study. PLoS One. 2025;20(4):e0321290. doi: 10.1371/journal.pone.0321290.
10. van Zonneveld AJ, de Boer HC, van der Veer EP, Rabelink TJ. Inflammation, Vascular Injury and Repair in Rheumatoid Arthritis. Ann Rheum Dis. 2010;69(Suppl 1):i57-60. doi: 10.1136/ard.2009.119495.
11. Rezuş E, Cardoneanu A, Burlui A, Luca A, Codreanu C, Tamba BI, et al. The Link between Inflammaging and Degenerative Joint Diseases. Int J Mol Sci. 2019;20(3):614. doi: 10.3390/ijms20030614.