



Biomarkers of Endothelial Glycocalyx Integrity for Cardiovascular Events in Individuals Without Cardiovascular Disease

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Ikonomidis et al. investigated the association between disturbance of glycocalyx integrity and incident cardiovascular events [1]. They measured perfused boundary region (PBR5-25), which was a marker of glycocalyx integrity, in sublingual microvessels with a diameter ranging 5–25 μm . Increased PBR indicates reduced glycocalyx thickness, and cardiovascular events, which were defined as death by major adverse cardiovascular events, myocardial infarction, and stroke, were monitored during a 6-year follow-up. The adjusted hazard ratio (HR) of PBR5-25 for cardiovascular events significantly increased in any statistical models. The authors concluded that glycocalyx integrity was a significant predictor for cardiovascular events in individuals without cardiovascular disease. I have some comments about the study.

First, the number of events was 57 during the follow-up period, and stable estimation may be conducted as follows. Peduzzi et al. reported that more than 10 events per independent variable (EPV) in Cox proportional hazards regression analysis is needed for stable estimate [2]. The authors used 9 adjusting variables and PBR5-25 as independent variables, which at least require 100 events. If the association between PBR5-25, and cardiovascular events was checked, EPV value of less than 10 can be acceptable [3]. But the authors intended to know the ability of prediction, strict criteria should be applied. Anyway, additional data are needed to complete the risk assessment.

Second, Kim et al. measured serum biomarkers of endothelial glycocalyx, which were elevated in acute decompensated heart failure patients with reduced ejection fraction (HFrEF) of <40% [4]. The adjusted HR (95% confidence interval) of a doubling of serum heparan sulfate concentration for all-cause mortality was 1.315 (1.012–1.709). The cardiovascular events were not checked for the analysis, and the target populations had presented overt cardiovascular disorder. There are different types of biological markers for endothelial glycocalyx disturbance, and established biomarkers for cardiovascular disease should also be included for the analysis.

On this point, Kim et al. clarified a strong positive relationship between serum N-terminal pro-B-type natriuretic peptide and all-cause mortality [4]. Kitagawa et al. observed that the serum syndecan-1 concentration was significantly associated with readmission-free survival in patients with heart failure, and the administration of human atrial natriuretic peptide and antibiotics modified the relationship [5]. There may be an interaction between serum N-terminal pro-B-type natriuretic peptide and serum syndecan-1 concentration for predicting mortality risk in patients with heart failure. When conducting multi-variate analysis, some biological markers should be inserted for adjusting the mortality risk. Anyway, additional number of events is required for the analysis.

Editor-in-Chief Enrique Lara-Pezzi oversaw the review of this article.

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Declarations

Conflict of Interest The author declares no competing interests.

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