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Advanced glycation end-products in Diabetic Cardiomyopathy- An Alternative Hypothesis

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Keywords

Advanced Glycation End-products; cardiomyopathy diabetes; oxidative stress; myeloperoxidase

Advanced glycation end products (AGEs) are chemically heterogeneous structures and include such specific forms as carboxy (methyl)lysine, pentosidine and others, and were previously measured in heart failure patients as serum AGE, skin AGE, and AGE in cardiomyocytes and vascular cells within the heart. The study by Nozynski et al.¹ adds to this body of knowledge as it examines AGE expression directly in explanted hearts: 22 with cardiomyopathy (CMP) and diabetes (DM), 114 with CMP without DM, 20 healthy heart donors, and 14 with DM without CMP. One of the main findings in this study was equally increased AGE accumulation in intramyocardial veins, arterioles and venules in diabetic subjects with and without CMP. This is an unexpected finding, since it is believed that AGE may contribute to mechanical (stiffness) as well as molecular (inflammation) changes contributing to myocardial dysfunction.

However, we would like to offer a hypothesis for this unexpected result not raised by the authors. The diabetic cohort without CMP consists of patients who died in the first 24 hours after admission to the intensive care unit due to cerebral injury, and therefore represent a very sick cohort. It is well established that trauma is associated with a high burden of systemic inflammation, oxidative stress and for instance serum myeloperoxidase activity is highest in the first 6 hours in non-surviving patients with head trauma². Moreover, inflammation, reactive oxygen species and myeloperoxidase enzymatic activity promotes protein glycation and AGE formation as rapidly as in 60 minutes³. AGE formation in human tissue is a dynamic process as recently demonstrated by the rapid decline of AGEs in myeloperoxidase-positive inflammatory cells in carotid endarterectomy tissue after treatment with simvastatin prior to surgery⁴. We speculate that the increased accumulation of AGE in the heart of diabetic subjects without CMP found in the study by Nozynski et al. may be largely explained by the circumstances of this study. The authors cannot exclude the possibility of rapid AGEs formation as a result of enhanced oxidative stress and myeloperoxidase activity associated with lethal trauma in this diabetic control group without CMP. Further studies examining AGE in cardiac tissue are needed to dissect the role of

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AGE in heart failure. Most importantly, more in-depth analysis of the specific AGEs and their concentrations in these tissues must be performed. Indeed, the concept of the heterogeneous nature of AGEs is underscored in Nyzynski's study population and design.

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