

Red blood cells cause cardiovascular injury in type 2 diabetes

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Harmful effects of substances secreted from red blood cells could explain the increased risk of cardiovascular diseases in patients with type 2 diabetes, the results of two new studies conducted at Karolinska Institutet in Sweden indicate. The studies are published in the *Journal of the American College of Cardiology* and *JACC: Basic to Translational Science*.

It is a known fact that patients with diabetes are at considerable risk of developing cardiovascular diseases caused by organ-vessel damage that leads to heart attack, stroke, kidney disease, eye damage etc. Patients with diabetes also have a worse prognosis following a heart attack. However, the underlying causes of cardiovascular injury in diabetes are largely unknown, and there is no specific treatment to prevent it.

Red blood cells change in type 2 diabetes

Research suggests that the red blood cells that transport oxygen to the body's tissues are more inclined to adhere to the vessel wall in diabetes. Researchers at Karolinska Institutet have now studied how red blood cells change in type 2

diabetes and if they contribute to the cardiovascular injury occurring. Their results are presented in The *Journal of the American College of Cardiology* and *JACC: Basic to Translational Science*.

"We found that healthy blood vessels exposed to red blood cells from patients with type 2 diabetes suffer damage to their innermost cell layers, the endothelial cells," says Professor John Pernow at Karolinska Institutet's Department of Medicine in Solna who led both the studies. "This phenomenon, which is called endothelial dysfunction, appears early on in the development of diabetes-related vessel injury and greatly reduces the ability of the vessels to dilate while aggravating the inflammation."

Harmful effects caused by the enzyme arginase

Using an experimental model, the team was also able to show that red blood cells from diabetic patients or diabetic mice impair heart function and cause greater myocardial injury in the event of a heart attack than red blood cells from healthy individuals. Their detailed analyses of rat and human blood vessels also demonstrate that the harmful effects are caused by elevated activity of the enzyme arginase, reduced production of the vasodilating molecule nitric oxide and increased formation of harmful oxygen-derived free radicals in the red blood cells.

"We also found that treatment that targeted arginase or oxygen-derived free radicals normalised red blood cell function, which meant that their harmful effect on cardiovascular function could be prevented," explains Professor Pernow. "Our hope is that this knowledge will give rise to new treatments, specifically targeted at red blood cells, that prevent vascular injury and protect the heart in the event of heart attack in patients with type 2 diabetes."

More information: Zhichao Zhou et al.



Erythrocytes From Patients With Type 2 Diabetes Induce Endothelial Dysfunction Via Arginase I, *Journal of the American College of Cardiology* (2018). DOI: 10.1016/j.jacc.2018.05.052

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