Insulin resistance in patients suffering from severe AS

L. Freitag¹, P. Leuders¹, M. Kelm¹, T. Zeus¹, C. Quast¹
¹University Hospital Duesseldorf, Duesseldorf, Germany

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Background: There are several cardiovascular risk factors known to promote the development of AS, one of them being type 2 diabetes (T2D). T2D is increasingly recognized as a heterogeneous disease, leading to the latest concept of five diabetes clusters based on clinical parameters. Until now, the impact of the respective clusters, especially insulin resistance in prediabetes, on valvular cells and therefore the development of AS is not clear.

Purpose: We hypothesize that insulin resistance, which is frequently underrated, features a specific pattern of aortic valve calcification characterized by an elevated degree of calcification.

Methods: In order to analyze the impact of diabetes on AS we examined 200 patients with severe AS, scheduled for a transcatheter aortic valve implantation (TAVI). With the exemption of previously diagnosed diabetics, we performed an oral glucose tolerance test (OGTT), identifying patients with prediabetes and T2D. Additionally, blood was drawn from all included patients 2-5 days after TAVI, depicting their metabolic condition and thereby assigning them to a diabetes cluster. These findings were subsequently correlated with data from computer tomography in all patients pertaining the severity of the stenosis, including the Agatston score, which illustrates the aortic valve calcium burden.

Results: Following the hypothesis that the extent of insulin resistance impacts the aortic valve calcification, we correlated the HOMA-IR with the Agatston score, resulting in a weak non-significant linear correlation ($r=-0.129$, $p=0.097$, $n=166$). Therefore, increased insulin resistance has not been shown to be associated with increased aortic valve calcification. Moreover, no differences in the extent of calcification between diabetic, prediabetic and non-diabetic patients could be demonstrated ($F(2,147) = 0.410$, $p=0.665$). However, it was clearly striking that the majority of the patients examined had already developed prediabetes or diabetes (Non-Diabetic = 7.1%, Prediabetic = 34.6%, Diabetic = 58.2%, $n=182$).

Conclusion: Although we were able to observe an increased rate in prediabetic and diabetic patients in our AS cohort, there was no significantly elevated aortic valve calcification in patients with pronounced insulin resistance. This suggests that insulin resistance might not directly impact valvular calcification but upstream processes in valvular cells predisposing for AS since the majority of AS patients in our cohort is (pre)diabetic.