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Euro Diabetes 2019: Aortic stiffness in type 2 diabetes is contributed by endothelial-to-mesenchymal transition- Melanie S. Hulshoff- University Medical Center Göttingen

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Background/Introduction - In the past decades, the prevalence of diabetes mellitus has risen considerably and is currently affecting more than 422 million people worldwide. Cardiovascular diseases including myocardial infarction and heart failure represent the major cause of death in type 2 diabetes. Diabetes patients exhibit accelerated aortic stiffening which is associated with myocardial infarction and heart failure. Importantly, aortic stiffening is an independent predictor of cardiovascular disease and mortality in diabetes mellitus patients. We recently showed that aortic stiffness precedes hypertension in a mouse model of diabetes (db/db mice), making aortic stiffness an early contributor to cardiovascular disease development. Endothelial-to-mesenchymal transition (EndMT) is a process in which endothelial cells lose their characteristics and gain a myofibroblast-like phenotype. EndMT was originally identified in heart development, but we now know that it contributes to several pathologies such as organ fibrosis, cardiovascular disease and cancer.
Purpose - We hypothesized that EndMT contributes to aortic stiffness in the context of type 2 diabetes. Aortic stiffness is an early contributor and independent predictor of cardiovascular disease and mortality in type 2 diabetes patients.

Type 2 diabetes is very common syndrome now-a-days. Initially, highblood glucose level is where the body's cells fail to respond fully to insulin. insulin resistance, high aldohexose and relative absence of insulin. Simple aspect effects incorporate expanded thirst, incessant pee, and unexplained weight reduction. Signs could likewise incorporate swollen desire, feeling tired, and bruises that don't recuperate. Regularly indications go ahead gradually. Complications from high like strokes, diabetic retinopathy which can cause visual impairment, kidney problems, and low blood stream which may cause removals. Type 2 diabetes is mostly preventable by continuing a typical weight, practicing consistently, and eating legitimately. Treatment includes activity and dietary alterations. Diabetes mellitus may be a upsetting and metabolic disorder, expected to affect over 500 million people worldwide by the year 2030; up from 350 million in 2010. Approximately 96% of patients suffer from type 2 diabetes, and its prevalence is expected to increase in the future. Cardiovascular diseases are the one that cause for, from one-third, to half diabetes-related deaths. Diabetes and high blood glucose levels are associated with an estimated doubling of cardiovascular diseases risk.

Methods - To confirm the presence of EndMT, aortic sections of db/db mice (a murine model for diabetes) were co-immunofluorescent stained with the endothelial marker CD31 and the mesenchymal markers α-SMA or S100A4. Moreover, mRNA expression of the EndMT transcription factors SNAIL, SLUG and TWIST was analyzed in aortic tissue from db/db mice as well as in aortic tissue from diabetic patients. To identify how EndMT is initiated, we performed co-immunofluorescent staining of the endothelial marker CD31 in combination with the macrophage marker F4/80 in aortic sections from db/db mice. We also performed co-culture of mouse endothelial cells with macrophages and assessed EndMT.

Results - We demonstrated a robust co-localization of CD31 with either α-SMA or S100A4 in aortas of db/db mice which was almost absent in control mice. We also showed that the mRNA levels of the EndMT transcription factors were significantly upregulated in aortic tissue of both db/db mice and diabetic patients when compared to controls. We demonstrated that the macrophage staining was in close proximity with endothelial cells undergoing EndMT. In line with this, we showed in vitro that macrophaghes induce EndMT in a contact-dependent manner.

Conclusion - We demonstrated that EndMT contributes to aortic stiffness in the context of type 2 diabetes.

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