Study links small pancreas size to faster progression to stage 3 type 1 diabetes

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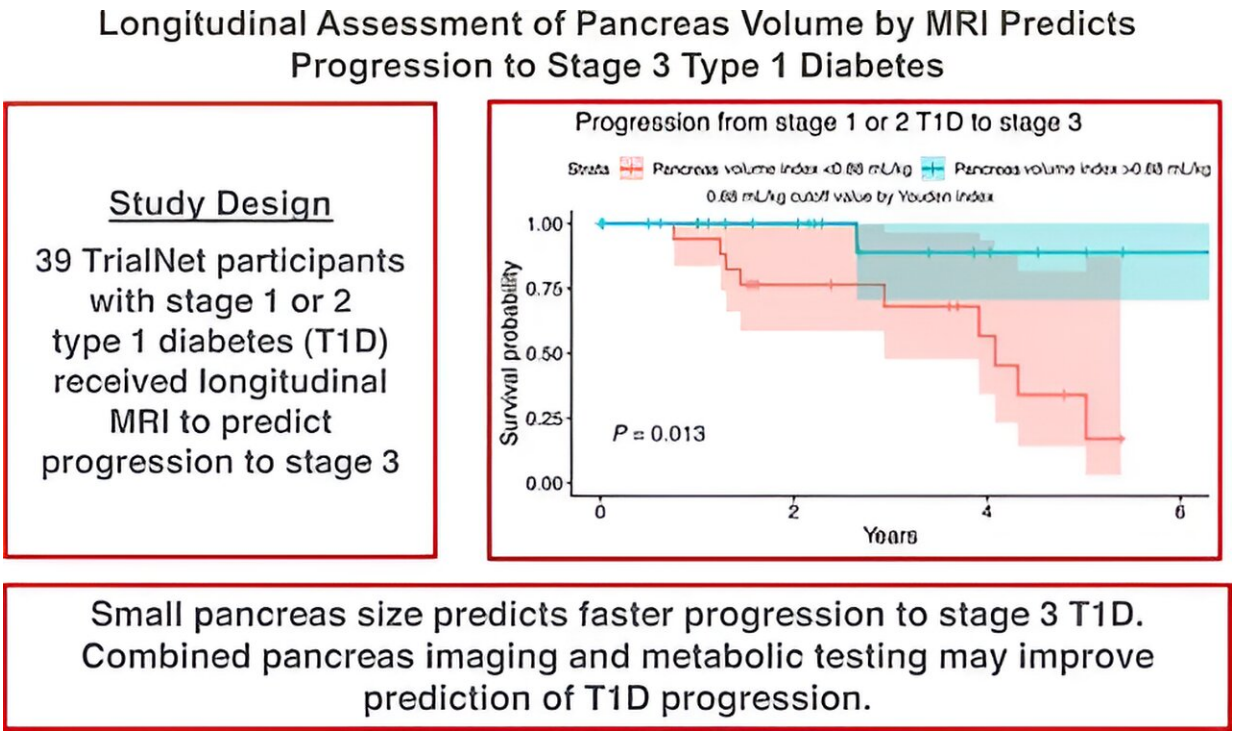

Graphical Abstract. Credit: *Diabetes Care* (2023). DOI: 10.2337/dc23-1681

A multicenter, longitudinal study, co-led by investigators at the Vanderbilt Diabetes Research and Training Center (DRTC), has discovered that a small pancreas size predicts a faster progression to stage 3 type 1 diabetes (T1D), the point at which clinical diagnosis occurs.

The team also found that using pancreas volume measurement combined with validated metabolic T1D risk measures can more accurately predict disease development than either method alone.

These findings demonstrate that pancreas size is an early marker of risk for T1D progression and that pancreas imaging can have a benefit in tracking disease development and recruitment for preventive and therapeutic trials.

"By the time a person has developed stage 3 type 1 diabetes, there is significant beta cell loss, and symptoms are usually present," said lead author Jack Virostko, Ph.D., assistant professor of Diagnostic Medicine in the Dell Medical School at the University of Texas at Austin, formerly with the Vanderbilt University Institute of Imaging Science.

"If we can better predict the progression to stage 3, our hope is that we can better identify and apply therapies to slow or even stop the advance of the disease, even before diagnosis."

The study team collaborated with TrialNet, a research network that investigates how T1D can be prevented in people at high risk for disease. TrialNet screening looks for diabetes-related autoantibodies that signal an increased risk of developing T1D.

The screening can detect these autoantibodies years to decades before diagnosis. The presence of two or more of the autoantibodies indicates a high risk of future disease development, but the risk factors that determine when diabetes will develop have remained elusive.

For this study, the pancreas volume of 65 TrialNet participants was determined by using non-contrast magnetic resonance imaging (MRI), metabolic scores from oral glucose tolerance testing (OGTT), and a combination of pancreas volume and metabolic scores to predict

progression to stage 3 T1D in individuals with multiple diabetes-related autoantibodies.

The MRI scans, performed at six- or 12-month intervals, followed a standardized protocol validated for quantitative pancreas evaluation across imaging centers and hardware. The protocol was previously developed by members of this research team through the Multicenter Assessment of the Pancreas in Type 1 Diabetes (MAP-T1D) consortium, which is led by VUMC.

"We investigated whether MRI measurement of pancreas volume in individuals identified as being at risk of type 1 diabetes could predict progression to stage 3 disease and how these imaging measures correlated with metabolic testing," said Vanderbilt University Medical Center (VUMC) site investigator Daniel Moore, Ph.D., MD, associate professor of Pediatrics and of Pathology, Microbiology, and Immunology.

"Our results suggest small pancreas volume can predict progression to stage 3 type 1 diabetes, with discrimination similar to that of measurements derived from oral glucose tolerance testing and the Diabetes Prevention Trial–Type 1 Risk Score (DPTRS), a prediction tool validated by TrialNet.

"Of note, pancreas volume and metabolic measures were not correlated, suggesting that they reflect different aspects of the disease process underlying T1D and provide different information regarding disease risk. Our prediction model, using both pancreas volume and metabolic measures, outperformed imaging or metabolic testing alone for predicting progression to stage 3 type 1 diabetes."

Limitations of the study include a small sample size with limited progression events. A larger data set of pancreas MRI is needed to assess

the generalizability of combined pancreas volume and OGTT for diabetes risk progression. Study participants were also overwhelmingly non-Hispanic white, so future studies are needed to see whether the results are reproducible in diverse populations.

"It's vital that we better understand the progressive changes that occur in the pancreas and what they mean for the development of type 1 diabetes and for all populations," said Moore. "The findings of this study are the result of a years-long collaboration between dedicated teams who first developed a better way to evaluate pancreas volume. We will continue to use this foundation to make discoveries which will lead to improved patient care."

The findings are published in the journal *Diabetes Care*.

More information: John Virostko et al, Longitudinal Assessment of Pancreas Volume by MRI Predicts Progression to Stage 3 Type 1 Diabetes, *Diabetes Care* (2023). DOI: 10.2337/dc23-1681

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