RESPONSE TO COMMENT ON TYNJÄLÄ ET AL.

Arterial Stiffness Predicts Mortality in Individuals With Type 1 Diabetes. Diabetes Care 2020;43:2266–2271

Diabetes Care 2021;44:e71–e72 | https://doi.org/10.2337/dci20-0074

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We thank González-Clemente et al. (1) for presenting an interesting perspective on arterial stiffness as a potential integrative risk factor for cardiovascular disease (CVD) in type 1 diabetes in the light of their findings in a cross-sectional cohort of 179 individuals (2). They demonstrated a strong correlation between aortic pulse wave velocity (PWV) and a CVD risk prediction score obtained from the Steno Type 1 Risk Engine (ST1RE) (3) and determined cutoff values for PWV as a marker of moderate/high (≥10%) and high (≥20%) risk of CVD in individuals with type 1 diabetes.

In the FinnDiane Study, we recently showed an independent association between augmentation index (AIx), another marker of arterial stiffness, and all-cause mortality as well as a composite cardiovascular and/or diabetes-related cause of death in a prospective analysis of 906 individuals with type 1 diabetes (4). Although the longitudinal data on PWV in our cohort is still underpowered for robust analysis, the Comment by González-Clemente et al. prompted us to further assess AIx as a predictor of CVD risk in our study population by including data on incident CVD events (myocardial infarction, coronary revascularization, stroke, lower extremity revascularization, or nontraumatic amputation) from the Finnish Hospital Discharge Register.

After excluding individuals with end-stage renal disease or previous CVD events at baseline, 720 individuals were included in the analysis, 79 of whom suffered a CVD event during a median follow-up time of 9.9 (interquartile range 7.1–11.3) years. AIx remained a significant predictor (standardized hazard ratio 1.82 [95% CI 1.23–2.70], $P = 0.003$) of a first-ever CVD event in a multivariable Cox regression model adjusted for age, sex, triglycerides, albuminuria, estimated glomerular filtration rate, and smoking. In a time-dependent receiver operating characteristics curve, this model showed an area under the curve of 0.83 (95% CI 0.78–0.87), whereas AIx as a single variable had an area under the curve of 0.72 (95% CI 0.67–0.77). Using the %FINDCUT SAS macro (5), an optimal cutoff value for AIx as a predictor of CVD was identified. This cutoff divided the cohort into a lower-risk group (AIx <20.8) with 5.0% (95% CI 2.8–7.1) and a higher-risk group (AIx ≥20.8) with 22.3% (95% CI 18.6–25.9) 10-year cumulative incidence of CVD, respectively.

González-Clemente et al. further raised an idea of building an AIx-based predictive model for the assessment of future CVD risk in type 1 diabetes. This task is well supported by the findings above and, once our data set grows, can potentially be carried out in the future. In our prospective cohort, we showed that AIx predicts not only mortality but also incident CVD in individuals with type 1 diabetes, whereas González-Clemente et al. showed a cross-sectional association between PWV and the ST1RE risk score, i.e., a surrogate marker of CVD risk. Prospective studies comparing AIx and PWV as predictors of CVD in type 1 diabetes could give valuable information about the pathophysiology of vascular complications, as an increase in one of these markers of arterial stiffness might reflect a different involvement of small versus large arteries.

Acknowledgments. The authors thank the FinnDiane research nurses A. Sandelin, J. Tuomikangas, and M. Korolainen, all affiliated with Folkhälsan Institute of Genetics (Folkhälsan Research Center, Helsinki, Finland), for technical assistance.

Funding. This study was supported by grants from Academy of Finland (316644, UAK10121MRI), Biomedicum Helsinki Foundation, Dorothea Olivia, Karl Walter and Jarl Walter Perklén's Foundation, Finnish Medical Foundation, Finska Läkaresällskapet (Medical Society of Finland), Folkhälsan Research Foundation, Liv

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och Hälsa Society, Novo Nordisk Foundation (NNF OC0013659), Päivikki and Sakari Sohlberg Foundation, Sigrid Juselius Foundation, Svenska Litteratursällskapet i Finland (the Society of Swedish Literature in Finland), Swedish Cultural Foundation in Finland, Wilhelm and Else Stockmann Foundation, and University of Helsinki.

Duality of Interest. P.-H.G. is an advisory board member of AbbVie, AstraZeneca, Bayer, Boehringer Ingelheim, Eli Lilly, Janssen, Medscape, MSD, Mundipharma, Novartis, Novo Nordisk, and Sanofi and has received lecture honoraria from AstraZeneca, Boehringer Ingelheim, Eli Lilly, ELO Water, Genzyme, Medscape, MSD, Mundipharma, Novartis, Novo Nordisk, Sanofi, and SCIARC. D.G. has received lecture or advisory honoraria from AstraZeneca, Boehringer Ingelheim, Delta Medical Communications, Fresenius, GE Healthcare and Novo Nordisk as well as support to attend medical meetings from CVRx and Sanofi. No other potential conflicts of interest relevant to this article were reported.

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