A deep-learning-based retinal cardiovascular disease biomarker and risk of stroke, myocardial infarction, atrial fibrillation, and heart failure in the UK Biobank

C.J. Lee¹, T.H. Rim², H.G. Kang³, G. Lee³, M. Yu², Y.-C. Tham², T.Y. Wong², C.-Y. Cheng², S.S. Kim³, S.-M. Kang¹, S. Park¹

¹Yonsei University College of Medicine, Department of Internal Medicine, Division of Cardiology, Seoul, Korea (Republic of)
²Singapore National Eye Centre, Singapore Eye Research Institute, Singapore, Singapore
³Yonsei University College of Medicine, Division of Retina, Severance Eye Hospital, Seoul, Korea (Republic of)
⁴Mediwhale, Seoul, Korea (Republic of)

Funding Acknowledgements: Type of funding sources: Private company. Main funding source(s): Mediwhale

Background: Retinal photographs allow a non-invasive way to see the human vasculature and provide insights into cardiovascular disease (CVD). In our previous study, we developed the Reti-CVD, a deep-learning algorithm to predict the future CVD events from retinal photographs.

Purpose: In this study, we extend the application of Reti-CVD by investigating the association between the Reti-CVD score and the occurrence of individual cardiovascular events, including stroke, myocardial infarction (MI), atrial fibrillation (AF), and heart failure (HF).

Methods: The Reti-CVD scores were calculated and stratified into three risk groups based on optimized cut-off values from the UK Biobank. The cumulative incidence of cardiovascular events (stroke, MI, AF, and all-cause HF each) rate was evaluated across the three groups (low, moderate, and high risk) defined by the Reti-CVD score. Cox proportional hazards model was used to estimate the adjusted hazard ratios (aHRs), trends in HRs, and respective p-values were examined by fitting a linear model for the three categories after adjustment of age, gender, diabetes, hypertension, hyperlipidemia, and smoking. C-statistics was used to assess the prognostic value of the Reti-CVD score.

Results: A total of 44,677 participants were included at baseline and tracked for up to 7 years. There were 277 (0.62%) strokes, 506 (1.13%) MIs, 1053 (2.32%) AFs, and 431 (0.94%) HFs. An increase in Reti-CVD score was significantly associated with increased risk of stroke (adjusted hazard ratio [aHR] trends, 1.40; 95% confidence interval [CI], 1.09-1.80, p=0.008), MI (aHR trends, 1.22; 95% CI, 1.01-1.08, p<0.001), and AF (aHR trends, 1.33; 95% CI, 1.17-1.52, p<0.001). However, the association of Reti-CVD score-based three-risk groups and the occurrence of HF showed a trend for increased risk without statistical significance (aHR trends, 1.17; 95% CI, 0.96-1.43, p=0.123). C-statistics based on Reti-CVD alone were 0.65 (0.63-0.68) for stroke, 0.64 (0.62-0.66) for MI, 0.66 (0.65-0.67) for AF, and 0.65 (0.60-0.70) for HF.

Conclusion: A deep-learning-based retinal CVD biomarker, the Reti-CVD has the potential to identify individuals with a risk of stroke, MI, and AF, who are likely to benefit from earlier preventative CVD interventions. For the relationship between the Reti-CVD and HF, it seems necessary to analyze by HF subtypes.