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Microvascular function is an independent predictor for albuminuria progression among Asians with type 2 diabetes - A prospective cohort study

Dr Xiao Zhang[1], A/Prof Su Chi Lim[1], Dr Serena Low[1], Dr Keven Ang[1], A/Prof Subramaniam Tavintharan[1], A/Prof Chee Fang Sum[1]
[1]*Khoo Teck Puat Hospital , Singapore, Singapore*

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Objective. Microvascular endothelial dysfunction has been associated with albuminuria in cross-sectional studies. We aim to investigate whether it is an independent predictor for future albuminuria progression in in type 2 diabetes (T2DM) cohort in Singapore.
Materials and Methods. In a prospective cohort, 1,106 T2DM patients were clinically assessed at baseline and after a median follow-up of 3.2 years. Patients were divided into progression and non-progression according to changes of urinary-albumin-to-creatinine ratio (ACR). Progression was defined as transition from normo- (ACR<30mg/g) to microalbuminuria (ACR=30-299mg/g) or macroalbuminuria (ACR>300mg/g), or micro- to macroalbuminuria. Microvascular endothelial vasodilation at baseline was quantified using 2-dimensional laser Doppler flowmetry. The increase in perfusion in response to acetylcholine (Ach, endothelium-dependent vasodilation) and sodium nitroprusside (NaNP, endothelium-independent vasodilatation) was calculated. Logistic regression model was used to estimate the odds ratio (OR) for albuminuria progression.
Results. Albuminuria progression occurred in 232 (21.0%) patients. The median baseline Ach was significantly higher in non-progression (72.5 (40.9-108.7)%) than progression group (59.9 (36.1-99.6)%, p=0.033). There is no significant difference in NaNP between the two groups (109.9 (50.4-181.2)% vs. 97.0 (42.9-167.8)%, p=0.203). After multivariable-adjustment, one-unit increase in natural logarithm (ln) Ach was not associated with progression (OR=0.768, [95%CI, 0.534-1.106], p=0.156) in all patients. When stratified by baseline albuminuria, one-unit increase in lnAch was associated with progression in normoalbuminuria (OR=0.581, [0.347-0.972], p=0.039, n=874), but not in microalbuminuria patients (OR=1.113, [0.520-2.384], p=0.782, n=370).
Conclusion. Impaired endothelial dependent micro-vascular reactivity predicts albuminuria progression in normoalbuminuria patients, suggesting that it may drive the onset of albuminuria in T2DM.