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REVOLUTIONISING MEDICINE - THE NEW FRONTIER

Triglyceride-Glucose Index, Mediated by Pigment Epithelium-derived Factor, is an Independent Predictor of Chronic Kidney Disease Progression in Type 2 Diabetes

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Aims

- Triglyceride-glucose (TyG) index is a surrogate measure of insulin resistance. It is a known predictor of incident non-alcoholic fatty liver disease and cardiovascular outcomes in type 2 diabetes (T2D). Its role in the chronic kidney disease (CKD) progression is unknown.
- Pigment epithelium-derived factor (PEDF) has anti-inflammatory, anti-oxidant and anti-angiogenic functions, and its plasma level may be elevated in CKD.
- We investigated the association between TyG index and CKD progression and possible mediation of the association by PEDF.

Methods

- A prospective study on 1,571 patients from Singapore Study of Macro-angiopathy and Microvascular Reactivity in Type 2 Diabetes (SMART2D) cohort recruited from Diabetes Centre in KTPH, Admiralty Medical Centre and NHG polyclinics between Apr 2011 and Jul 2014. Inclusion and exclusion criteria are shown in Figure 1 and patient flowchart in Figure 2.
- The renal function was followed up till Jun 2021. Figure 2 shows the patient flowchart.
- CKD progression defined as ≥ 25% decrease in eGFR together with worsening across eGFR categories (Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group 2012 clinical practice guideline)
- TyG index was calculated as Ln [fasting triglyceride level (mg/dl) x fasting plasma glucose (FPG) (mg/dl)/2]. PEDF and insulin were measured using enzyme-linked immunosorbent assay. HOMA2-IR was calculated using online programme HOMA Calculator v2.2 (http/www.dtu.ox.sc.uk).

Fig 1. Research Workflow

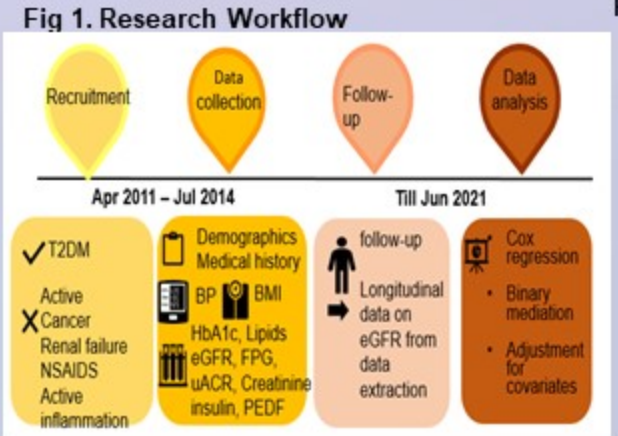
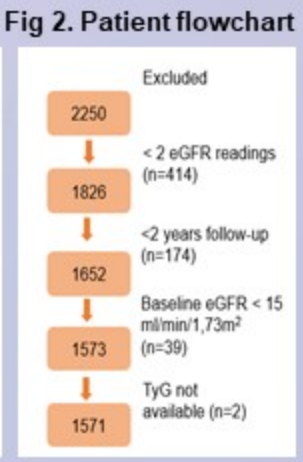


Fig 2. Patient flowchart



Results

- Figure 3 shows the baseline characteristics. The mean TyG index was 9.1±0.7 (Tertile 1,8.5±0.3; Tertile 2, 9.1±0.1; and Tertile 3, 9.9±0.5).
- Over a period of up to 8.6 years, CKD progression occurred in 42.6% of the subjects. The progressors had higher TyG than non-progressors (9.23 ± 0.66 vs. 9.08 ± 0.64; p<0.001).
- Patients with Tertile 3 TyG index had poorer event-free survival than Tertiles 1 and 2. See Figure 4.
- Every 1 unit above baseline TyG index was positively associated with CKD progression. See Figure 5.
- Compared to Tertile 1, Tertiles 2 and 3 TyG index were positively associated with CKD progression in unadjusted and fully adjusted models in Figure 6.

Results (continued)

- Binary mediation analysis in Figure 7 revealed that PEDF accounted for 36.0% of association between TyG index and CKD progression.

Fig 3. Baseline characteristics

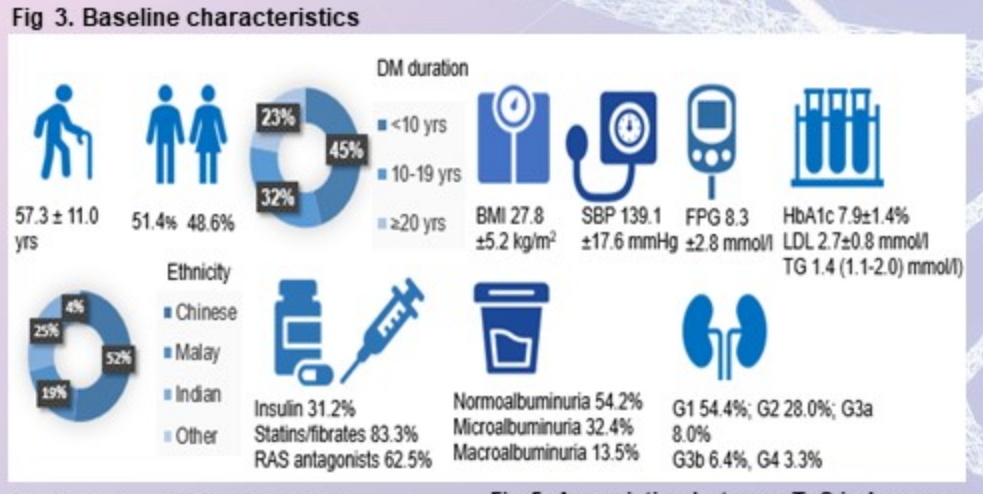


Fig 4. Kaplan Meier Survival Curves

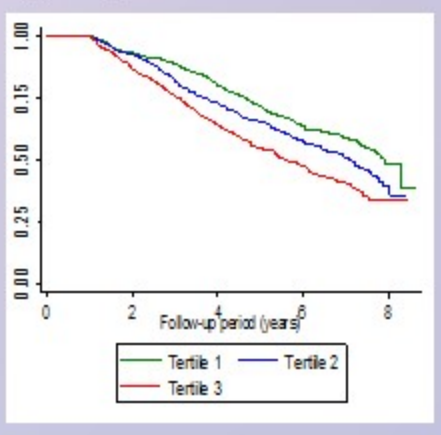


Fig 5. Association between TyG index as a continuous variable and CKD progression

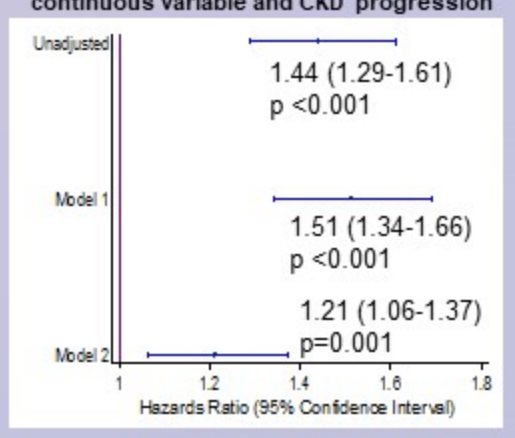


Fig 6. Association between TyG index in tertiles and CKD progression

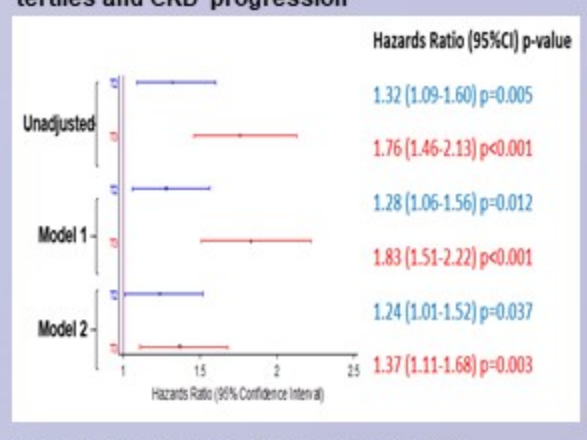
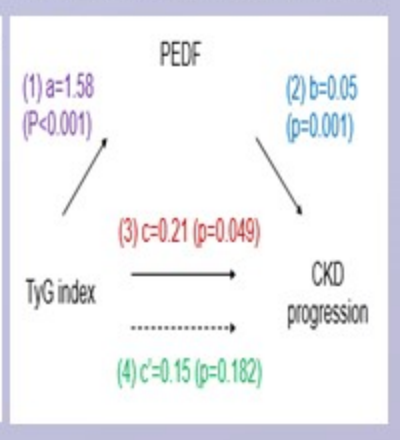


Fig 7. Binary mediation analysis



Model 1 adjusted for age, gender and ethnicity
Model 2 adjusted for Model 1 + diabetes duration, BMI, SBP, LDL-C, eGFR categories, uACR categories, use of hypolipidemic agent, use of insulin and use of RAS antagonist

Conclusions

- Higher TyG index was an independent predictor of CKD progression in T2D.
- PEDF mediated the association between TyG index and CKD progression.
- TyG index is a simple and inexpensive index for predicting CKD progression for potential use in routine clinical practice.

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