The Association of Postprandial Triglyceride Variability with Renal Dysfunction and Microalbuminuria in Patients with Type 2 Diabetic Mellitus A Retrospective and Observational Study.

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Original investigation

Keywords: renal dysfunction, albuminuria, triglyceride variability, diabetic mellitus, diabetic kidney disease, postprandial triglyceride

Posted Date: June 30th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-651699/v1

Abstract

Objective: We aim to examine whether day-to-day variation of lipid profile, especially triglyceride (TG) variability, is associated with exacerbation of diabetic kidney disease.

Methods: We conducted a retrospective and observational study. First, 527 patients with type 2 diabetes mellitus (DM) who checked estimated glomerular filtration rate (eGFR) every 6 month since 2012 for longer than 5 years, were registered. Variability in postprandial TG was determined using standard deviation (SD), SD adjusted (Adj-SD) for the number of measurements, and maximum minus minimum difference (MMD) during the first 3-year follow up, respectively. The endpoint was 40% and more decline from baseline in eGFR, initiation of dialysis or death. Next, 181 patients who had no micro- nor macro-albuminuria in February 2013, were selected out of the 527 patients. The endpoint was the incidence of micro-albuminuria, initiation of dialysis or death.

Results: Among 527 participants, 110 participants reached 40% and more decline from baseline in eGFR, or death. Renal survival was lower in the higher SD, higher Adj-SD and higher MMD groups than in the lower SD, lower Adj-SD and lower MMD groups, respectively (Log-rank test p=0.0073, 0.0059 and 0.0195, respectively). Lower SD, lower Adj-SD, lower MMD were significantly associated with renal survival rate in the adjusted model (hazard ratio, 1.62, 1.66, 1.59; 95% confidence intervals, 1.05-2.53, 1.08-2.58, 1.04-2.47, respectively). Next, among 181 participants, 108 participants developed micro-albuminuria or death. The non-incidence of micro-albuminuria was lower in the higher SD, higher Adj-SD and higher MMD groups than in the lower SD, lower Adj-SD and lower MMD groups, respectively (Log-rank test p=0.0241, 0.0352, and 0.0474, respectively).

Conclusions: Postprandial TG variability is a novel risk factor for eGFR decline and incidence of micro-albuminuria in patients with type 2 DM.

Background

Diabetic mellitus (DM) is the most common cause of end-stage renal disease (ESRD) worldwide, and is closely associated with increased cardiovascular risk and mortality (1) (2). The data from United States Renal Data System showed that after a year-by-year rise in the number of incident ESRD cases from 1980 through 2000, the count plateaued between 2007 and 2011 but rose again from 2012 to 2017 due to the aging population and the increasing prevalence of obesity and DM (3). Thus, DM still presents a big problem which should be dealt with.

Recent epidemiological studies suggest that diabetic kidney disease (DKD) patients have a variety of clinical presentations and progression rates to ESRD although typical clinical manifestations of DKD are characterized by slow progression from micro-albuminuria to macro-albuminuria and by hyperfiltration at the early stage and progressive decline of glomerular filtration rate (GFR) at the advanced stage. Some DKD patients lose their renal functions without albuminuria (4). This population is presumably related to atherosclerosis by aging, hypertension, and dyslipidemia. Furthermore, components of metabolic

syndrome, like abdominal obesity, hypertension, hyperglycemia and dyslipidemia, are highly interrelated and contribute to development and progression of DKD (5).

In recent years, increasing evidences suggest that not only the average of blood pressure and blood glucose level, but also glycemic and blood pressure variability can be independent risk factors for development of albuminuria and for decreased GFR in type 2 DM (6). Epidemiological data confirmed that a tight control of glucose and blood pressure level are the pivotal and modifiable key factors in preventing the incidence and progression of DKD (7) (8) (9).

Dyslipidemia, one of the elements for metabolic syndrome, is linked to reduction in GFR and development of albuminuria in patients with type 2 DM (10) (11) (12) (13). Especially, both fasting and postprandial hypertriglyceridemia has already been reported to be associated with reduction in estimated GFR (eGFR) and the development of albuminuria (14) (15) (16). Numerous clinical trials have revealed the importance of lipid control in preserving GFR in patients with DM (17). However, it is still unclear whether lipid variability exacerbates DKD or not, while several observational studies suggest a possible impact of high-density lipoprotein cholesterol (HDL-C) variability and fasting triglyceride (TG) variability on the appearance of albuminuria (18) (19).

Here, we aimed to investigate the association of intraindividual variability in postprandial TG with eGFR decline and the incidence of micro-albuminuria in type 2 DM in order to figure out whether postprandial visit-to-visit TG variability is correlated to the exacerbation of DKD.

Patients And Methods

Study Design and Participants

A longitudinal, retrospective and observational cohort study was conducted to examine the association of visit-to-visit postprandial TG variability with eGFR decline in patients, aged >20 years, with type 2 DM who checked eGFR every 6 month since February 2012 for longer than 5 years at a single hospital. Patients who regularly checked their renal function every February and August, were registered. The patients who checked postprandial (non-fasting) TG between February 2012 and February 2015 less than three times, were excluded. Data were collected up to the last observation at February 2020. A total number of participants accounted for 527 patients, including 42 patients who dropped out from 5.5 to 7.5 years follow-up (Figure 1).

Three indices of postprandial TG variability were calculated, including standard deviation (SD), SD adjusted (Adj-SD) for the number of measurements, and maximum minus minimum difference (MMD) of postprandial TG during the first 3-year follow up (19) (20) (21) (22) (23) (24). To minimize any effect of different numbers of TG measurements on the calculated values, an Adj-SD was defined according to the formula: $\text{Adj-SD} = \text{SD}/\sqrt{[n/(n-1)]}$. The participants were separated to two groups by the median value of SD, Adj-SD and MMD. The primary endpoint was 40% and more decline from baseline in eGFR, initiation of dialysis or death.

We also extracted the participants who checked urine albumin-to-creatinine ratio (UACR) every year between February 2013 and February 2020, over 7 years from the 527 participants to analyze the association between postprandial TG variability and incidence of microalbuminuria in patients with type 2 DM. The patients who already had micro- or macroalbuminuria in 2013 were excluded. Total participants accounted for 181 patients (Figure 1). The participants were also divided into two groups by the median value of SD, Adj-SD and MMD. The secondary endpoint was the incidence of microalbuminuria (UACR ≥30 mg/gCr), initiation of dialysis or death.

Anthropometric Measurement

Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared.

Laboratory Measurements

eGFR was calculated using formula modified for Japanese subjects: eGFR (mL/min/1.73 m^2) = 194 x serum creatinine (mg/dL)$^{-1.094}$ x Age$^{-0.287}$ (x 0.739 for females) (25). Blood samples were collected 2 to 6 hours after breakfast or lunch as postprandial (non-fasting) samples. Mean TG is the average of postprandial TG between February 2012 and February 2015. Serum TG was tested by using an enzyme method (TG-EX, Denka®). Assay was performed within 24 hours with an automated clinical chemistry analyzer. Urinary albumin excretion was tested by using an immuno-nephelometric technique (TIA Micro Alb, Nittobo®).

Definition of the risk factors and the covariates

DM was defined as glycated hemoglobin (HbA1c) ≥6.5% and fasting plasma glucose ≥126 mg/dL and/or postprandial plasma glucose ≥200 mg/dL, self-reported history of DM, or use of any anti-diabetes medication. Patients with type 1 DM or gestational diabetes were excluded. Regarding smoking status, current smokers were defined as the participants who had regular cigarette smoking habit in 2012, past smokers as the participants who had had regular cigarette smoking habit and stopped smoking before 2012, and never smokers as the participants who had never smoked. Proteinuria was defined by urine dipstick tests by semi-quantitative measure ≥±. Statin, fibrates, and cholesterol transport inhibitor intake was defined by having regular drug intake in 2012.

The definition of risk factors for the multivariate Cox's proportional hazard regression model was as follows: 1) age, BMI, baseline eGFR, mean TG and HbA1c as continuous variables, 2) proteinuria: urine dipstick tests by semi-quantitative measure ≥±, 3) smoking habit: current smoker, 4) hypertension: systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥80 mmHg, 5) fibrates intake: taking fibrates in 2012. All the data was collected from the medical charts.

Statistical Analysis

Data was expressed as n (%) for categorical variables and mean ± SD for continuous variables. The following patient characteristics were collected in 2012: age, sex, duration of DM, BMI, systolic and

diastolic blood pressure, eGFR, serum creatinine, HDL-C, low-density lipoprotein cholesterol (LDL-C), HbA1c, smoking habit (current, past, never), proteinuria, and medication (Statins, Fibrates, and Cholesterol transport inhibitor). Kaplan–Meier analysis and Cox's proportional hazard regression model were adopted to calculate the cumulative probability to reach the endpoint and hazard ratio (HR) of eGFR decline and incidence of albuminuria. The estimated standard error of the confidence estimate was used to establish confidence intervals (CI) of the estimated HR. The statistical analyses were performed by JMP version 14.0.0 (SAS Institute, Inc, Cary, NC), and all P-values were calculated as two-sided. The association was considered significant with p-values less than 0.05.

Results

Primary Analysis: eGFR decline

Characteristics

Baseline characteristics of the study participants for the primary analysis, divided by the median of SD, Adj-SD and MMD are listed in Table 1. The median value of SD, Adj-SD and MMD were 37, 34 and 95, respectively. The average number of measuring times of postprandial TG between 2012 and 2015 was 5.5. Compared with the lower SD, lower Adj-SD and lower MMD groups, the patients in the higher SD, higher Adj-SD and higher MMD groups were significantly younger, and had shorter duration of DM, higher BMI, higher diastolic blood pressure, lower HDL-C, a higher prevalence of proteinuria (≥±) and more patients who received fibrates or cholesterol transport inhibitor (Table 1).

Clinical Outcomes

Among 527 participants, during a median follow-up of 8.0 years, 110 (21%) participants reached to the primary endpoint. Ninety-two participants encountered eGFR decline ≥40%, and 18 participants died.

The patients with SD ≥37 demonstrated 73.7% of 8-year renal survival, while the patients with SD <37 83.1%. Renal survival was lower in the group with SD ≥37 than in the group with SD <37 (Log-rank test p=0.0073) (Figure 2). We performed a Cox's proportional hazard regression analysis of the baseline factors for a possible association with renal survival. In this analysis, higher SD was significantly associated with the primary endpoint in the adjusted model (HR, 1.62; 95% CI, 1.05 to 2.53) (Table 2).

Next, regarding Adj-SD, 8-year renal survival was 73.5% in the group with Adj-SD ≥34 and 83.1% in the group with Adj-SD <34. Renal survival was lower in the group with Adj-SD ≥34 than in the group with Adj-SD <34 (Log-rank test p=0.0059) (Figure 2). In a Cox's proportional hazard regression analysis, higher Adj-SD was significantly associated with the primary endpoint in the adjusted model (HR, 1.66; 95% CI, 1.08 to 2.58) (Table 2).

Third, regarding MMD, 8-year renal survival was 74.3% in the group with MMD ≥95 and 82.4% in the group with MMD <95. Renal survival was lower in the group with MMD ≥95 than in the group with MMD <95 (Log-rank test p=0.0195) (Figure 2). In a Cox's proportional hazard regression analysis, higher MMD

was significantly associated with the primary endpoint in the adjusted model (HR, 1.59; 95% CI, 1.04 to 2.47) (Table 2).

Secondary Analysis: incidence of microalbuminuria

Characteristics

Baseline characteristics of the study participants for the secondary analysis, divided by the median of SD, Adj-SD and MMD are listed in Table 3. The median value of SD, Adj-SD and MMD were 37, 34 and 93, respectively. Compared with the lower SD, lower Adj-SD and lower MMD groups, the patients in the higher SD, higher Adj-SD and higher MMD groups had significantly shorter duration of DM, lower HDL-C, and more patients who received fibrates and cholesterol transport inhibitor (Table 3).

Clinical Outcomes

Among 181 participants, 108 (60%) participants reached to the secondary endpoint. One hundred and four participants encountered microalbuminuria, and 4 participants died.

As for SD, 7-year non-incidence of microalbuminuria was 33.0% in the group with SD ≥37 and 47.8% in the group with SD <37. The non-incidence of microalbuminuria was lower in the group with SD ≥37 than in the group with SD <37 (Log-rank test p=0.0241) (Figure 3). We performed a Cox's proportional hazard regression analysis of the baseline factors for a possible association with incidence of microalbuminuria. In this analysis, higher SD was significantly associated with the secondary endpoint in the adjusted model (HR, 1.77; 95% CI, 1.08 to 2.88) (Table 4).

Next, regarding Adj-SD, 7-year non-incidence of microalbuminuria was 33.7% in the group with Adj-SD ≥34 and 46.7% in the group with Adj-SD <34. The non-incidence of microalbuminuria was lower in the group with Adj-SD ≥34 than in the group with Adj-SD <34 (Log-rank test p=0.0352) (Figure 3). In a Cox's proportional hazard regression analysis, higher Adj-SD was significantly associated with the secondary endpoint in the adjusted model (HR, 1.72; 95% CI, 1.05 to 2.81) (Table 4).

Third, regarding MMD, 7-year non-incidence of microalbuminuria was 34.1% in the group with MMD ≥93 and 46.7% in the group with MMD <93. The non-incidence of microalbuminuria was lower in the group with MMD ≥93 than in the group with MMD <93 (Log-rank test p=0.0474) (Figure 3). In a Cox's proportional hazard regression analysis adjusted for age, sex and BMI (Model 1), higher MMD was significantly associated with the secondary endpoint in the adjusted model (HR, 1.49; 95% CI, 1.02 to 2.20), however, the significant association was diminished when further adjusted by mean TG, and/or baseline eGFR (Model 2 and 3) (Table 4).

Discussion

In this study, the association of visit-to-visit TG variability with eGFR decline and incidence of albuminuria in patients with type 2 DM were examined, respectively. The visit-to-visit variability of postprandial TG

was a significant predictor of eGFR decline in patients with type 2 DM during long-term follow-up, even when adjusting for confounding factors. In addition, the visit-to-visit variability of postprandial TG was also significantly associated with incidence of microalbuminuria. Thus, we found that the visit-to-visit variability of postprandial TG is associated with DKD progression.

When considering “variability”, experimental models in vitro have shown that intermittent hyperglycemia is more detrimental for endothelial cells than continuous hyperglycemia (26). Glycemic variability is associated with the occurrence of various microvascular and macrovascular complications in DM because of excessive protein glycation end products and activation of oxidative stress in the causation of vascular complication (27) (28). In addition, blood pressure variability is also a significant prognostic factor in ESRD (29) (30) (31). Both plasma glucose level and blood pressure originally fluctuate to a certain extent and are components of metabolic syndrome, which are highly interrelated to the development and progression of DKD (5). Given these observation, it is likely that a similar association may be found for variability of TG, which is another factor of metabolic syndrome and fluctuates to a certain extent because it has already reported that both fasting and postprandial hypertriglyceridemia are associated with eGFR decline and incidence of albuminuria (14) (15) (16), variability of fasting TG is predictive of coronary events (20), and is also linked to incident microalbuminuria in patients with type 2 DM (19).

An appropriate device to measure the trend for 24-hour blood pressure and plasma glucose level is available, however, not for serum TG concentration. Therefore, we analyzed postprandial TG variability by SD, Adj-SD and MMD. Many previous papers about “variability” used various indices to evaluate their variability. SD has been used for evaluating glycemic, blood pressure and fasting TG variability (19) (20) (32) (33) (34) (35). Adj-SD has also been used for evaluating glycemic and fasting TG variability to adjust for the number of measurements (19) (21) (36) (22). MMD has been used for evaluating glycemic and blood pressure variability (37) (23) (24) (38). Our study suggested that SD and Adj-SD might be more reliable than MMD. However, MMD is calculated more easily. In this sense, this method could be suitable for clinical situations. In any method, postprandial TG variability is a significant risk factor for eGFR decline and incidence of microalbuminuria in patients with type 2 DM.

It is important to take the best timing for measurement of TG for consideration for the clinical setting. The lipid profile is conventionally measured in plasma or serum obtained after fasting for at least 8 hours, and therefore may not reflect the daily average plasma lipid (39). In patients with DM, remnant lipoprotein cholesterol levels remain high throughout the day except for a few hours before breakfast (40). There is no evidence that fasting is superior to postprandial when evaluating the lipid profile (41). The Danish Society for Clinical Biochemistry recommended that all laboratories in Denmark use random postprandial lipid profile measurements rather than fasting profiles (42). Traditionally, the Friedewald equation has been applied to a fasting lipid profile; however, calculated LDL-C which is determined with this equation at TG concentrations of 400 mg/dL or less, is similar to LDL-C measured directly on both fasting and postprandial lipid profiles (43) (44). In addition, numerous population-based studies and at least three major statin trials used random, postprandial blood sampling, providing a robust evidence

base for a change in the conventional practice of using fasting samples (45) (46) (47). Thus, there are both advantages and disadvantages in taking postprandial lipid profile. Especially, in DM patients, both fasting and postprandial plasma glucose level are important information in controlling DM in clinical practice, but fasting test has a hypoglycemic risk, and HbA1c can be accurately evaluated in either fasting or non-fasting.

The association between renal dysfunction and dyslipidemia had been reported as a lipid nephrotoxicity hypothesis (48). There are pieces of evidence that renal lipid accumulation can cause structural and functional changes in mesangial cells, podocytes and proximal tubule cells, which all contribute to the nephron function. Thus, it is widely recognized that ectopic deposition of lipids causes harm to target cells and organs; ectopic lipid accumulation in the kidney promotes maladaptive responses of renal cells to the mechanical forces of hyperfiltration, leading to podocyte depletion, proteinuria, focal segmental glomerulosclerosis and interstitial fibrosis (49). Regarding lipid nephrotoxicity, our study adds a new significance of better lipid management to optimal DKD treatment, namely, only casual plasma TG concentration but also TG variability should be controlled.

In our study, no significant difference in baseline eGFR was found between the higher group and the lower group, divided by the median value of SD, Adj-SD and MMD, respectively. Although more patients with hyperfiltration might be included in the group with higher SD, higher Adj-SD and higher MMD, it is still important to note that the patients with shorter renal survival demonstrated higher variability of postprandial TG. It is also suggested that the patients with a higher peak of TG presented a higher risk of DKD progression. Furthermore, the possibility that pathophysiological mechanisms underlying postprandial TG variability also induce DKD progression, independent of TG levels, should be considered.

Several studies demonstrated that postprandial hypertriglyceridemia is involved in the production of proinflammatory cytokines, recruitment of neutrophils and generation of oxidative stress, resulting in endothelial dysfunction which is an initial process of atherogenesis and it might contribute to develop albuminuria in healthy subjects as well as hypertriglyceridemic patients and type 2 DM patients (50) (51) (52) (53). Our study showed that the patients with higher variability of postprandial TG developed microalbuminuria significantly earlier, although no significant differences were found in HbA1c, baseline UACR and baseline eGFR between the higher group and the lower group in SD, Adj-SD or MMD, respectively. Hence, it is important to consider deeply that microalbuminuria may be developed earlier in the type 2 DM patients with higher variability of postprandial TG.

Our study was not an interventional study, but an observational study. Therefore, further study is needed to clarify that lowering postprandial TG variability might be helpful for treating early stage of DKD to prevent its progression. So far, a clinical study, the Fenofibrate Intervention and Event Lowering in Diabetes study, showed that fenofibrate prevented progression from normo-albuminuria to micro-albuminuria in patients with type 2 DM (54) (55) (56). Fenofibrate in diabetic mice normalizes endothelial function by balancing vascular reactivity via increasing nitric oxide production and suppressing the vasoconstrictor prostaglandin, suggesting a mechanism of action of fenofibrate (57). It has also been

reported that ezetimibe, alogliptin, bezafibrate, vildagliptin and omega-3 fatty acids improve postprandial hypertriglyceridemia and endothelial dysfunction, therefore, these medications have potential to be a treatment option for preventing DKD progression (58) (59) (60) (61) (62). Moreover, a higher variability of postprandial TG could be a marker of incomplete or intermittent compliance to lifestyle measures. In patients with type 2 DM, the risk of kidney events tended to decrease by multifactorial intensive treatment, including lipid control in addition to control of glucose level and blood pressure (63). Given these observations, it may be better to include care for visit-to-visit postprandial TG variability in the lipid control. Thus, further follow-up interventional study is required to clarify the efficacy of lowering postprandial TG variability on delaying progression of DKD to ESRD.

Study Limitations

Several limitations of this study should be considered when interpreting its results. First, the sample size is relatively small, and this cohort was entirely enrolled in a single hospital by eight doctors. Second, this is a retrospective and observational study. Therefore, this study cannot mention lowering visit-to-visit postprandial TG variability prevents progression of DKD. Third, most of the participants were at an early stage of DKD. Fourthly, what the participants ate was not restricted by the protocol. Fifthly, the effect of the medications during the observational period was not considered. Lastly, the influence of alcohol intake of daily or the day before visiting was not included.

Conclusion

In conclusion, three different indices of postprandial visit-to-visit TG variability may be a risk factor for eGFR decline and incidence of microalbuminuria in patients with type 2 DM. The pathophysiological mechanisms underlying these associations and the effect of lowering postprandial TG variability for preventing the progression of DKD remain to be further elucidated.

Abbreviations

eGFR: estimated glomerular filtration rate; DM: diabetes mellitus; TG: triglyceride; SD: standard deviation; Adj-SD: adjusted SD; MMD: maximum and minus minimum difference; HR: hazard ratio; CI: confidence intervals; ESRD: end-stage renal disease, DKD: diabetic kidney disease; GFR: glomerular filtration rate; HDL-C: high-density lipoprotein cholesterol; UACR: urine albumin-to-creatinine ratio; BMI: body mass index; HbA1c: glycated hemoglobin; LDL-C: low-density lipoprotein cholesterol; CKD: chronic kidney disease.

Declarations

Ethics approval and consent to participate

This study followed the Declaration of Helsinki (seventh revision, 2013) on medical protocol and ethics. The ethics committees of Nakashima Hospital Institutional Review Board, Okayama, Japan approved the protocol (approval number: 2020.08.01-1). Opt-out consent was applied to obtain participants' consent for this research.

Consent for publication

Not applicable.

Availability of data

The datasets generated during and/or analyzed during the current study are not publicly available as these have not been anonymized but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

None.

Authors' contributions

NMU participated in the design and planning of the study, acquisition of data and drafted the manuscript. HN participated in acquisition of data. HAU was responsible for the design, planning of the study and took final decision for publication. SO, YO, KK, MTN, RT, YH, NK, JE, and JW were all involved in reviewing/editing the manuscript. All authors read and approved the final manuscript.

Acknowledgements

We would like to thank Yuko Nakae, Chiasto Nishimura, Hiroko Iguchi, Hiroko Haramoto, Mizuho Aoyama, and Yuki Ando for the management of the database.

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Tables

Table 2. Multivariate Cox's proportional hazard regression model for the association between postprandial TG variability and eGFR decline (primary endpoint).

HR [95% CI] p value	SD≥37	Adj-SD≥34	MMD≥95
Model 1	1.69 [1.15-2.52] **0.0076**	1.73 [1.18-2.57] **0.0052**	1.64 [1.12-2.43] **0.0110**
Model 2	1.61 [1.05-2.51] **0.0276**	1.66 [1.09-2.58] **0.0193**	1.56 [1.02-2.41] **0.0388**
Model 3	1.58 [1.03-2.46] **0.0351**	1.63 [1.06-2.52] **0.0251**	1.54 [1.01-2.37] **0.0463**
Model 4	1.62 [1.05-2.53] **0.0284**	1.66 [1.08-2.58] **0.0218**	1.59 [1.04-2.47] **0.0340**

Model 1: Adjusted for age, sex, and BMI

Model 2: Adjusted for age, sex, BMI, and mean TG

Model 3: Adjusted for age, sex, BMI, mean TG, baseline eGFR, and proteinuria

Model 4: Adjusted for age, sex, BMI, mean TG, baseline eGFR, proteinuria, HbA1c, smoking, hypertension, and fibrates intake.

TG, triglyceride; SD, standard deviation; Adj-SD, adjusted SD; MMD, maximum minus minimum difference; HR, hazard ratio; 95% CI, 95% confidence intervals; BMI, body mass index; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin.

Table 4. Multivariate Cox's proportional hazard regression model for the association between postprandial TG variability and the incidence of micro-albuminuria.

HR [95% CI] p value	SD≧37	Adj-SD≧34	MMD≧93
Model 1	1.60 [1.09-2.36] **0.0170**	1.56 [1.06-2.23] **0.0232**	1.49 [1.02-2.20] **0.0399**
Model 2	1.79 [1.09-2.91] **0.0205**	1.73 [1.06-2.83] **0.0295**	1.60 [0.98-2.58] 0.0591
Model 3	1.77 [1.08-2.88] **0.0228**	1.72 [1.05-2.81] **0.0319**	1.58 [0.97-2.56] 0.0657

Model 1: Adjusted for age, sex, and BMI

Model 2: Adjusted for age, sex, BMI, and mean TG

Model 3: Adjusted for age, sex, BMI, mean TG, and baseline eGFR

TG, triglyceride; SD, standard deviation; Adj-SD, adjusted SD; MMD, maximum minus minimum difference; HR, hazard ratio; 95% CI, 95% confidence intervals; BMI, body mass index; eGFR, estimated glomerular filtration rate.

Due to technical limitations, Table 1 and 3 are only available as a download in the Supplemental Files section.

Figures

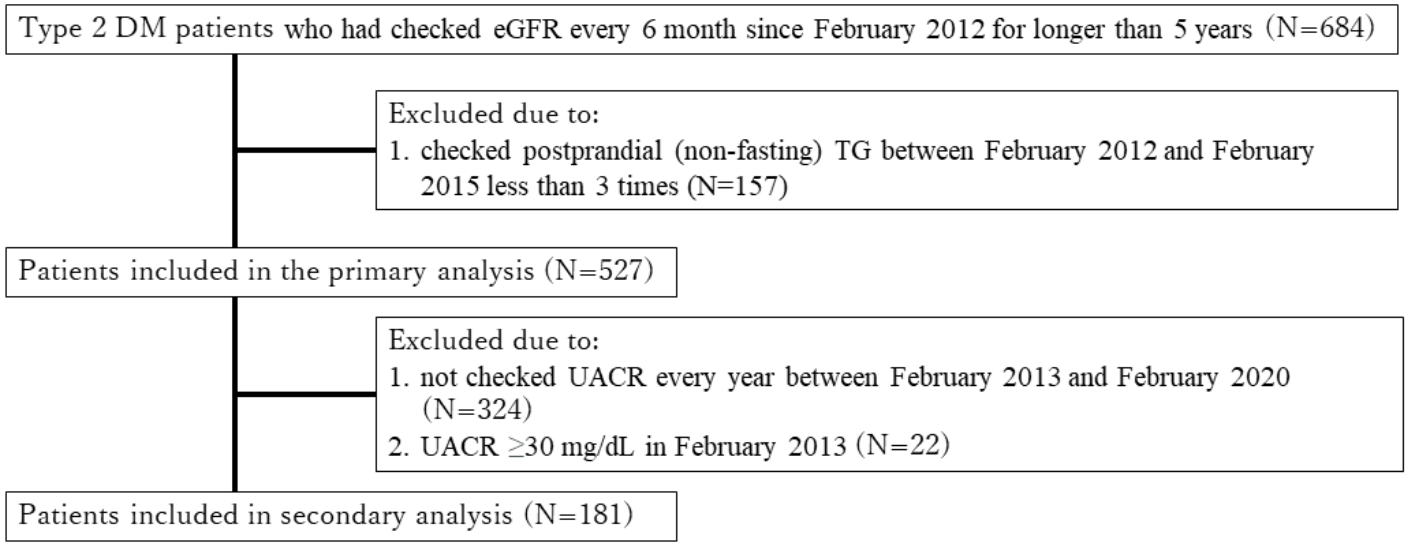

Figure 1

Study flow. After excluding subjects who did not meet our study criteria, a total of 527 participants were included in the primary analysis, and a total of 181 participants were included in the secondary analysis. DM, diabetic mellitus; eGFR, estimated glomerular filtration rate; TG, triglyceride; UACR, urine albumin-to-creatinine ratio.

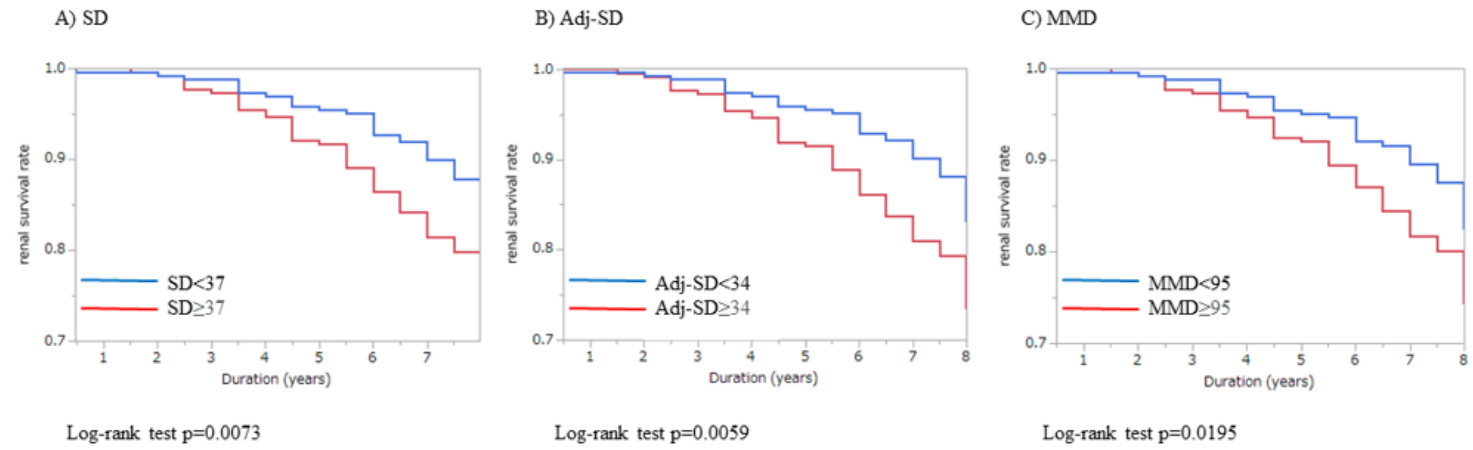

Figure 2

The comparison about renal survival rate for 8 years between two groups divided by the median value of SD, Adj-SD and MMD. TG, triglyceride; SD, standard deviation; Adj-SD, SD adjusted for the number of measurements; MMD, maximum minus minimum difference.

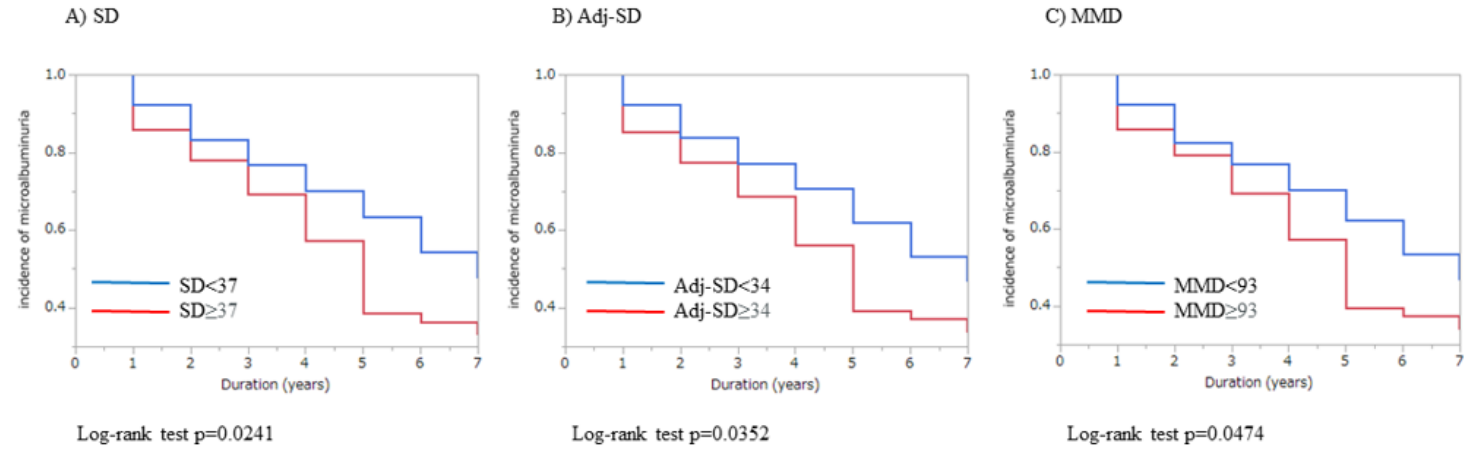

Figure 3

The comparison about non-incidence of microalbuminuria rate for 7 years between two groups divided by the median value of SD, Adj-SD and MMD. TG, triglyceride; SD, standard deviation; Adj-SD, SD adjusted for the number of measurements; MMD, maximum minus minimum difference.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1and3.docx