Characteristics of Nephropathy in Severely Obese Japanese Patients Complicated with Type 2 Diabetes Mellitus: A Cross-sectional Cohort Study

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[Abstract]

purpose: We aimed to investigate the characteristics of kidney disease in severely obese Japanese patients with type 2 diabetes mellitus (T2DM).

Methods: This was a cross-sectional study of severely obese patients (body mass index ≥35 kg/m^2) with T2DM treated at Jinnouchi Hospital, Kumamoto, Japan.

Results: A total of 3128 T2DM patients visited the hospital during the survey period, of whom 55 patients (1.7%) were severely obese and 50 patients were enrolled. In terms of diabetic nephropathy (DN), twenty-five patients were stage 1 (non-DN, 50.0%), sixteen were stage 2 (32.0%), five were stage 3 (10.0%), and four were stage 4 (8.0%). There were significant differences in the presence of urinary occult blood (P=0.01) and history of cardiovascular disease (CVD) (P=0.04) between patients with DN (stages 2–4) and those without DN (stage 1). The presence of urinary occult blood (odds ratio, 4.96; 95% confidence interval, 1.32–18.6; P=0.02) was significantly associated with the presence of DN according to multivariate logistic regression analysis with forced inclusion of age, sex, and CVD history.

Conclusions: Urinary occult blood may be a significant independent factor associated with the presence of nephropathy in severely obese Japanese patients with T2DM. The presence of urinary occult blood could thus be an important pathogenic factor in obesity-related nephropathy in patients with T2DM.

Keywords: obesity, nephropathy, type 2 diabetes mellitus, urinary occult blood

1. Introduction

Obesity and type 2 diabetes mellitus (T2DM) are closely related, and both are risk factors for the onset of chronic kidney disease. Diabetes is the leading cause of dialysis in Japan, while obesity is a well recognized risk factor for both T2DM and hypertension, both of which are leading causes of chronic kidney disease (CKD) and end-stage renal disease (ESRD) [1]. It has been disclosed by the kidney biopsies for obesity patients complicated with proteinuria or renal insufficiency that obesity-related glomerulopathy (ORG) and diabetic nephropathy (DN) were present in 40% and 22% of specimens, respectively [2]. The earliest clinical manifestation of DN is microalbuminuria that, over time, can progress to overt proteinuria [3-5], but ORG has also been suggested to have a higher rate of decline of glomerular filtration rate (GFR) and progress faster to ESRD [6]. Obesity also increases the risk of end-stage renal failure, even after accounting for smoking, hypertension, and diabetes [7], and thus has attracted attention via ORG and obesity-related kidney disease [8, 9]. Previous reports also suggested a relationship between visceral fat obesity and the onset of chronic kidney disease [10, 11]. Because obesity and T2DM frequently occur together, nephropathy may be accelerated in obese patients with T2DM.

To the best of our knowledge, there have been no prior reports of the effect of obesity on kidney disorders in Japanese patients with T2DM. We therefore investigated the clinical factors associated with the presence of nephropathy in obese patients with T2DM in a cross-sectional study of kidney disorders in severely obese patients treated for diabetes at Jinnouchi Hospital, Kumamoto, Japan.

2. Subjects and Methods

2.1. Subjects and protocol

This was a cross-sectional study of severely obese patients (body mass index [BMI] ≥35 kg/m^2) with T2DM recruited at Jinnouchi Hospital, Kumamoto, Japan, from August to November 2018. The inclusion criteria were T2DM and BMI ≥35 kg/m^2. Patients receiving artificial hemodialysis therapy were excluded. Because autoimmune or malignant diseases, heart and hepatic failure, have been known to be associated with kidney damage, we also excluded patients with these diseases. This study was conducted in accordance with the Declaration of Helsinki and the study protocol was approved by the Human Ethics Review Committee of Jinnouchi Hospital. This study was registered under the UMIN protocol registration system (ID: UMIN000038305).

2.2. Assessment of nephropathy

Urinary albumin and creatinine (Cr) concentrations were measured using spot urine, and the urinary albumin-to-creatinine ratio (UACR) was calculated. According to the Japan Diabetes Society criteria, diabetic nephropathy (DN) stage was determined based on the estimated GFR (eGFR) and the UACR as follows [12]: stage 1, non-DN, normoalbuminuria (UACR <30 mg/gCr and eGFR ≥30 mL/min/1.73 m^2); stage 2, microalbuminuria (UACR 30–299 mg/gCr and eGFR ≥30 mL/min/1.73 m^2); stage 3,

macroalbuminuria (UACR ≥300 mg/gCr and eGFR ≥30 mL/min/1.73 m^2); and stage 4, kidney failure (eGFR <30 mL/min/1.73 m^2). Patients with stage 5 DN (dialysis therapy) were excluded in advance. Participants with UACR ≥30 mg/gCr and/or eGFR <30 mL/min/1.73 m^2 were categorized as the DN group in the present study [13].

2.3. Measurement of body fat and muscle masses by bioelectrical impedance

We measured body composition, including body fat mass and body fat percentage, as described previously [14, 15]. Elemental body composition was measured using an InBody770 direct segmental multi-frequency bioelectrical impedance analyzer (InBody770; Biospace, Seoul, Korea), and total muscle mass, skeletal muscle mass, total fat mass, and body fat percentage were assessed. The analyzer processed 30 impedance measurements using six different frequencies (1, 5, 50, 250, 500, 1000 kHz) on each of five body segments (right arm, left arm, trunk, right leg, left leg), and 15 reactance measurements using tetrapolar 8-point tactile electrodes using three different frequencies (5, 50, 250 kHz) on each of the five above-mentioned body segments [16, 17].

2.4. Blood and urine sampling and measurement of clinical parameters

Blood and urine samples were collected and analyzed at hospital visits. Blood samples were collected from the antecubital vein. Blood and urine analyses were conducted in the hospital laboratory to

determine hemoglobin (Hb) A1c, fasting plasma glucose (FPG), total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, non-HDL cholesterol, triglycerides, eGFR, blood urea nitrogen (BUN), Cr, urinary albumin, urinary Cr, and urine occult blood.

2.5. Statistical analysis

The normality of distribution for continuous data was assessed by the Shapiro–Wilk test. Normally distributed data were expressed as mean ± standard deviation, and data with skewed distributions as median (interquartile range). Categorical data were presented as frequencies and percentages. Differences in categorical variables between two groups were tested by Fisher's exact test, and differences in continuous variables were analyzed by unpaired *t*-test or Mann–Whitney U test, as appropriate. Significant factors for the presence of DN were initially identified by simple logistic regression. For multivariate logistic regression analysis, we created a forced-inclusion model adjusted by age, sex, CVD history, and urinary occult blood. A P value <0.05 indicated statistical significance. All statistical analyses were performed using SPSS version 23 (SPSS Inc., Tokyo, Japan).

3. Results

3.1. Subjects

A total of 3128 T2DM patients visited the hospital during the survey period, of whom 55 patients (1.7%) were severely obese and five patients (three patients with a history of mammary cancer,1 patient with endometrial cancer, and 1 patient with heart failure) were excluded. The clinical backgrounds of the patients are shown in Table 1. Details of the respective DN stages are shown in Figure 1. Twenty-five patients (50.0%) were stage 1 (non-DN), sixteen were stage 2 (32.0%), five were stage 3 (10.0%), and four were stage 4 (8.0%). A previous large nationwide study of Japanese patients with T2DM found that 58% had no DN and 42% had DN [18], which was similar to the prevalence of DN in the current study. Among the included patients, 43 (86.0%) had hypertension and were treated with calcium channel antagonists (n=28, 56.0%) and/or angiotensin II receptor blockers (ARBs) (n=27, 54.0%).

3.2. Comparison of patients with and without DN

We compared patients with and without DN. Significantly more patients in the DN group had urinary occult blood (P=0.01) (Fig.2) and a history of CVD (P=0.04) (Table 2). Although there was no statistical difference, HbA1c levels tended to be higher in the DN group (Table 2).

3.3. Logistic regression analysis for presence of DN

Simple logistic regression analysis for the presence of DN identified urinary occult blood (odds ratio [OR], 5.63; 95% confidence interval [CI], 1.65–19.2; P<0.01) and CVD history (OR, 6.47; 95%CI, 1.23–34.0; P=0.03) were factors significantly associated with the presence of DN (Table 3). The presence of urinary occult blood (OR,4.96; 95%CI, 1.32–18.6; P=0.02) was also a significant factor for the presence of DN in multivariate logistic regression analysis with forced inclusion of age, sex, and CVD history (Table 3). The OR of hematuria for end-stage renal failure has previously been reported as 1.2, and the incidence of hematuria increases in patients with advanced renal dysfunction [19]. We therefore performed simple logistic regression analysis for the presence of DN in a subgroup of patients without kidney failure (eGFR ≥30 ml/min/1.73 m^2), and showed that the presence of urinary occult blood was still a significant factor predicting DN (n=46, OR,4.22; 95%CI, 1.20–14.7; P=0.03).

4. Discussion

Among 3128 Japanese patients with T2DM who visited our hospital, 55 (1.7%) were severely obese (BMI ≥35 kg/m^2). Furthermore 10 (0.3%) had a BMI of ≥40 kg/m^2, meeting the globally proposed the candidates for ORG. The incidence of obesity-related kidney disease was thus low among Japanese patients with T2DM.

The prevalence of DN among severely obese Japanese patients with T2DM in the current study was not significantly different from that in Japanese T2DM patients as a whole [18]. This may have been due to the low number of patients with a BMI ≥40 kg/m^2 who would meet the criteria for ORG, and the high proportion of cases already treated with sodium glucose co-transporter 2 (SGLT2) inhibitors [20] or glucagon-like peptide-1 (GLP-1) receptor agonists [21], both of which have renoprotective effects.

This cross-sectional study provided the first evidence for urinary occult blood as a significant factor related to the presence of nephropathy in severely obese Japanese patients with complicating T2DM. The frequency of hematuria reportedly increases with age in women [22] and we therefore adjusted for age and sex, but the results remained the same. The results were also similar in a sub-group analysis excluding patients with kidney failure (stage 4). Urinary occult blood/hematuria are generally not considered to be common features and are thus not recognized as important findings in DN. It has the histological diagnostic feature of diabetic glomerulosclerosis [23], and ORG is reportedly characterized histologically by glomerular hypertrophy and secondary focal segmental glomerulosclerosis (FSGS) [24].

The high frequency of microscopic hematuria in FSGS suggests that occult blood in the urine may also occur in ORG, and our results were pathologically consistent with these observations.

HbA1c levels tended to be high in the DN group in the current study. This suggests that strict control of blood glucose levels in obese patients with T2DM may help to prevent the progressive worsening of renal function in obesity-related kidney disease. Renal dysfunction may progress in patients without DN but positive for urinary occult blood, and future prospective studies of renal function changes in these patients may reveal a clinical significance of urinary occult blood in obese patients with complicating T2DM.

The present study had several limitations. No renal biopsies were performed and there was no detailed differentiation between the various forms of nephritis. Furthermore, therapeutic effects were not assessed. This was a single-center study with a small sample size, and further larger, multicenter studies are needed to confirm the current findings. Because this study design is hypothesis exploratory research, we didn't pre-calculate a hypothetical sample size in this study. All the patients in this study were already receiving several medications with renoprotective effects, such as SGLT2 inhibitors, GLP-1 receptor agonists, or ARBs, and there was therefore no clinical information for untreated patients.

In conclusion, this study revealed that urinary occult blood was a significant independent factor associated with the presence of DN in severely obese Japanese patients complicated with T2DM. eGFR, proteinuria, and albuminuria are already recognized as important factors in the daily clinical management

of patients with diabetic kidney disease, and we propose that the presence of urinary occult blood may also be an important and useful pathogenic factor of nephropathy in severely obese patients with T2DM.

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Compliance with ethical standards Conflict of interest

HJ has received honoraria from Novo Nordisk, Sanofi, AstraZeneca Pharmaceuticals, Astellas Pharma, Boehringer Ingelheim, Daiichi-Sankyo, Eli Lilly, Takeda, and Novartis Pharmaceuticals. SS has received honoraria from MSD, AstraZeneca Pharmaceuticals, Ono Pharmaceutical, Bayer Yakuhin, Ltd., and Novo Nordisk. There are no other potential conflicts of interest relevant to this article.

Ethical approval

The article does not contain any studies with animals performed by any of the authors. The study was conducted in accordance with the Declaration of Helsinki and the study protocol was approved by the Human Ethics Review Committee of Jinnouchi Hospital.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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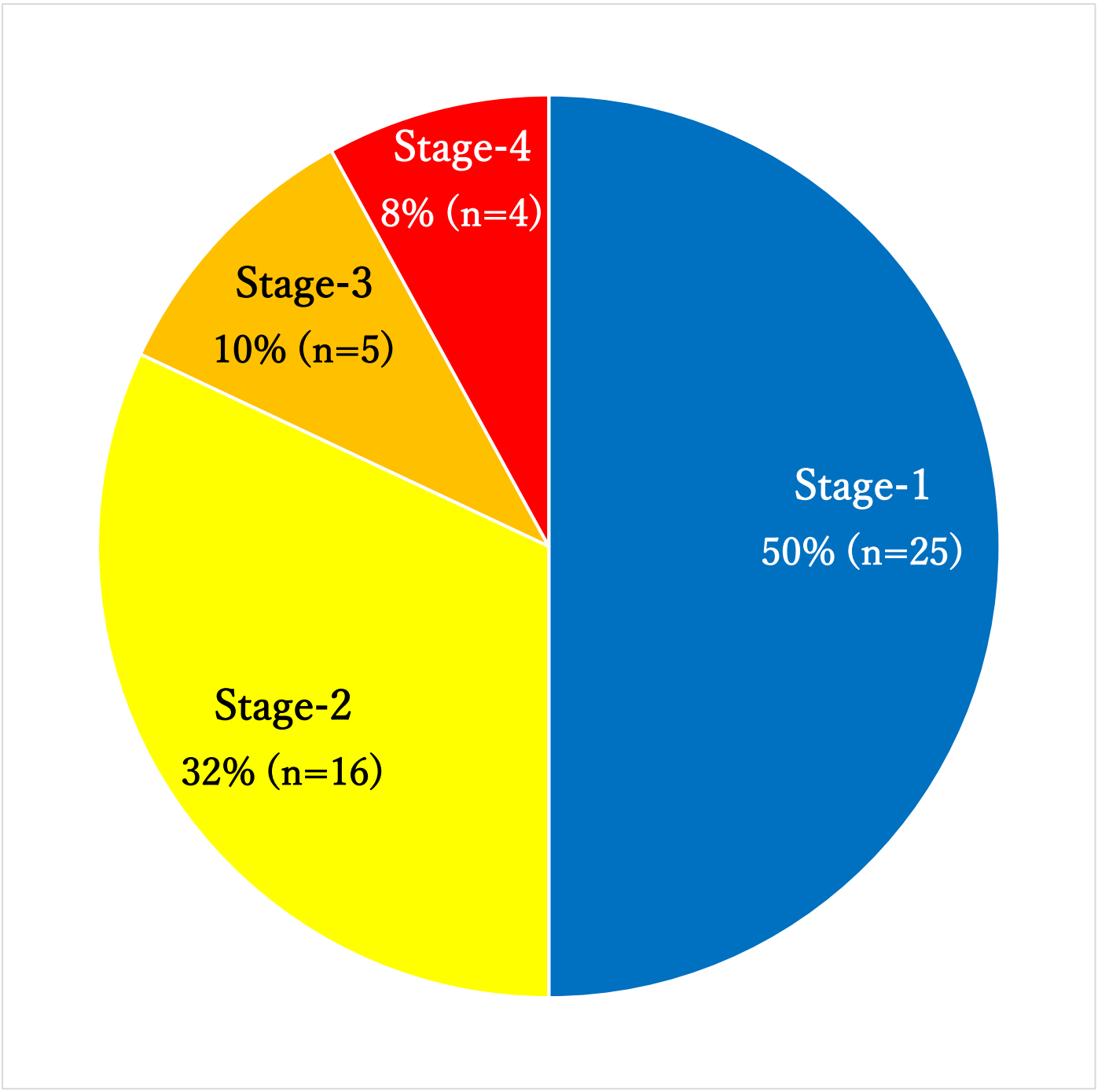
Fig. 1 Proportions patients with different stages of nephropathy based on eGFR and UACR. eGFR: estimated glomerular filtration rate; UACR: urine albumin-to-creatinine ratio

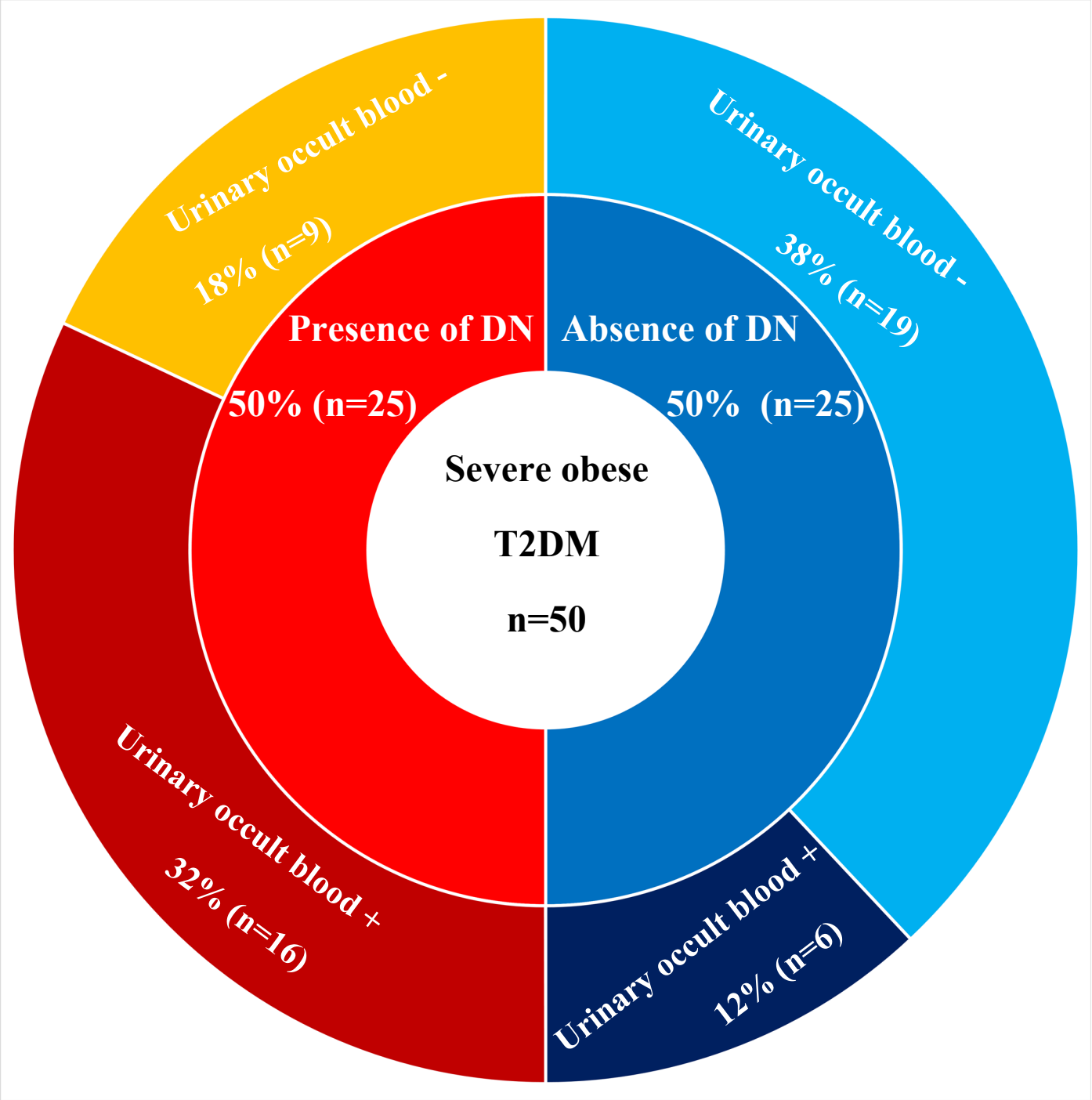
Fig. 2 Prevalence of DN and urinary occult blood. DN: diabetic nephropathy; T2DM: type 2 diabetes mellitus

Figure 1



Proportions patients with different stages of nephropathy based on eGFR and UACR. eGFR: estimated glomerular filtration rate; UACR: urine albumin-to-creatinine ratio.

Figure2



Prevalence of DN and urinary occult blood. DN: diabetic nephropathy; T2DM: type 2 diabetes mellitus

Table 1 Baseline clinical characteristics

	all (N=50)	Stage 1 (N=25, 50%)	Stage 2 (N=16, 32%)	Stage 3 (N=5, 10%)	Stage 4 (N=4, 8%)
Male (%)	21 (42.0%)	10 (40.0%)	8 (50.0%)	3 (60.0%)	0 (0.0%)
Age (years)	50.0 ± 12.3	50.0 ± 12.3	59.9 ± 11.6	44.4 ± 15.92	58 ± 10.3
Height (cm)	162.1 ± 10.2	163.3 ± 9.1	161.3 ± 9.2	166.08 ± 18.59	153.45 ± 3.91
Weight (kg)	100.4 ± 13.7	101.8 ± 12.9	97.9 ± 11.9	107.34 ± 22.66	92.65 ± 11.19
Muscle quantity (kg)	49.0 (43.9–61.0)	49.0 (44.9–62.6)	50.2 (42.4–60.9)	60.8 (49.8–69.3)	42.7 (41.33–45.13)
Body fat quantity (kg)	44.7 ± 6.7	45.5 ± 6.7	43.5 ± 5.3	42.9 ± 10.03	46.53 ± 8.99
Waist circumference (cm)	116.6 ± 7.8	115.8 ± 8.0	114.8 ± 5.7	121.4 ± 7.23	122.83 ± 11.57
BMI (kg/m^2)	37.7 (36.1–39.3)	37.7 (36.4–39.4)	37.5 (35.7–38.6)	39.27 (35.48–41.47)	38.47 (36.8–40.92)
Body fat percentage (%)	46.3 (39.4–50.3)	46.3 (40.4–49.7)	44.5 (39.7–50.4)	35.0 (33.4–51.3)	0.45.0 (41.0–50.5)
BMFR	1.10 (0.94–1.46)	1.10 (0.96–1.39)	1.18 (0.93–1.44)	1.75 (0.9–1.88)	1 (0.93–1.03)
Urinary albumin (mg/gCr)	30.3 (11.2–98.6)	11.2 (6.7–16.5)	59.1 (45.0–116.6)	556.8 (500.62–2539.8)	1245.13 (664.28–3392.07)
Serum BUN (mg/dL)	11.8 (10.0–14.4)	11.3 (9.9–13.3)	12.0 (10.3–13.0)	10.9 (9.8–19.4)	27.15 (25.13–28.93)
Serum creatinine (mg/dL)	0.73 (0.61–0.89)	0.74 (0.62–0.81)	0.60 (0.58–0.80)	0.64 (0.6–0.85)	2.24 (2.11–2.46)
eGFR (ml/min/1.73 m^2)	74.8 ± 24.8	78.1 ± 17.1	81.9 ± 20.0	80.7 ± 28.32	18.73 ± 5.19
Diabetes duration (year)	9.0 (4.3–15.8)	6.0 (2.0–11.0)	8.5 (4.8–13.5)	10.0 (6.0–13.0)	19.5 (18.0–13.0)
Hemoglobin A1c (%)	7.5 (6.5–8.5)	6.9 (6.5–7.6)	7.6 (6.4–8.2)	8 (6.6–10.1)	8.6 (8.45–9.5)
Total cholesterol (mg/dL)	165 (150.3–182.5)	156 (150–177)	171 (151–197)	181 (156–183)	157 (147.25–170.25)
Triglyceride (mg/dL)	155 (110.5–228.8)	132 (110–177)	146 (116.5–177)	236 (176–236)	276.5 (243.75–381.75)
HDL cholesterol (mg/dL)	44.9 ± 10.8	46.8 ± 11.9	43.9 ± 8.6	46.4 ± 12.5	35.75 ± 6.55
LDL cholesterol (mg/dL)	89.6 ± 27.5	85.8 ± 26.1	99.0 ± 24.8	96.6 ± 39.56	67 ± 20.46
Non-HDL cholesterol (mg/dL)	115 (103.3–138.3)	110 (101–127)	129 (19.8–142.5)	130 (99 - 151)	124 (108.5–39.5)
Systolic BP (mm Hg)	130.6 ± 13.5	129.3 ± 12.4	132.8 ± 10.3	142.2 ± 19.7	114 ± 8.3
Diastolic BP (mm Hg)	78.0 ± 9.8	76.7 ± 8.3	81.0 ± 11.9	82.8 ± 6.8	68.5 ± 5.3
Urine occult blood (%)	22 (44.0%)	6 (24.0%)	9 (56.3%)	3 (60.0%)	2 (50.0%)
Leukocyturia (%)	6 (12.0%)	2 (8.0%)	2 (12.5%)	0 (0.0%)	2 (50.0%)
Current smoking (%)	15 (30.0%)	6 (24.0%)	5 (31.3%)	2 (40.0%)	2 (50.0%)

CVD history (%)	11 (22.0%)	2 (8.0%)	3 (18.8%)	3 (60.0%)	3 (75.0%)
Retinopathy (%)	14 (28.0%)	5 (20.0%)	5 (31.3%)	0 (0.0%)	4 (100.0%)
Neuropathy (%)	2 (4.0%)	1 (4.0%)	0 (0.0%)	1 (20.0%)	0 (0.0%)
ARB (%)	27 (54.0%)	14 (56.0%)	8 (50.0%)	3 (60.0%)	2 (50.0%)
CCB (%)	28 (56.0%)	11 (44.0%)	10 (62.5%)	3 (60.0%)	4 (100.0%)
Statin (%)	37 (74.0%)	18 (72.0%)	12 (75.0%)	3 (60.0%)	4 (100.0%)
Anti-diabetic medicines (%)					
SGLT2 inhibitor (%)	37 (74.0%)	19 (76.0%)	10 (62.5%)	4 (80.0%)	4 (100.0%)
GLP-1 receptor agonist (%)	19 (38.0%)	12 (48.0%)	4 (25.0%)	1 (20.0%)	2 (50.0%)
DPP-4 inhibitor (%)	12 (24.0%)	7 (28.0%)	2 (12.5%)	3 (60.0%)	0 (0.0%)
Metformin (%)	29 (58.0%)	12 (48.0%)	11 (68.8%)	3 (60.0%)	3 (75.0%)
Thiazolidinedione (%)	3 (6.0%)	2 (8.0%)	1 (6.3%)	0 (0.0%)	0 (0.0%)
Sulfonylureas (%)	8 (16.0%)	6 (24.0%)	1 (6.3%)	1 (20.0%)	0 (0.0%)
Glinide (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Alpha-glucosidase inhibitor (%)	3 (6.0%)	3 (12.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Insulin (%)	19 (38.0%)	11 (44.0%)	5 (31.3%)	1 (20.0%)	2 (50.0%)

BMI: body mass index; BMFR: body muscle to fat ratio; BUN: B-type natriuretic peptide; eGFR: estimated glomerular filtration rate; HDL: high-density lipoprotein; LDL: low-density lipoprotein; BP: blood pressure; CVD: cardiovascular disease; ARB: angiotensin II receptor blocker; CCB: calcium channel blocker; SGLT2: sodium glucose co-transporter 2; GLP-1: glucagon-like peptide-1; DPP-4: dipeptidyl peptidase-4.

Table 2 Comparison between patients with and without diabetic nephropathy

	all (N=50)	Non-DN group (N=25, 50%)	DN group (N=25, 50%)	P value
Male (%)	21 (42.0%)	10 (40.0%)	11 (44.0%)	1.0000
Age (years)	50.0 ± 12.3	50.0 ± 12.3	50.1 ± 12.5	0.9639
Height (cm)	162.1 ± 10.2	163.3 ± 9.1	161.0 ± 11.3	0.4309
Weight (kg)	100.4 ± 13.7	101.8 ± 12.9	98.9 ± 14.5	0.4658
Muscle quantity (kg)	49.0 (43.9–61.0)	49.0 (44.9–62.6)	48.5 (41.6–60.8)	0.7237
Body fat quantity (kg)	44.7 ± 6.7	45.5 ± 6.7	43.9 ± 6.8	0.3956
Waist circumference (cm)	116.6 ± 7.8	115.8 ± 8.0	117.4 ± 7.6	0.4844
BMI (kg/m^2)	37.7 (36.1–39.3)	37.7 (36.4–39.4)	37.6 (35.7–39.3)	0.9951
Body fat percentage (%)	46.3 (39.4–50.3)	46.3 (40.4–49.7)	46.6 (39.3–50.9)	0.9327
BMFR	1.10 (0.94–1.46)	1.10 (0.96–1.39)	1.09 (0.92–1.47)	0.8206
Diabetes duration (year)	9.0 (4.3–15.8)	6.0 (2.0–11.0)	12.0 (6.0–16.0)	0.1452
Hemoglobin A1c (%)	7.5 (6.5–8.5)	6.9 (6.5–7.6)	8.0 (6.6–8.7)	0.0943
Total cholesterol (mg/dL)	165 (150.3–182.5)	156 (150–177)	168 (151–187)	0.2813
Triglyceride (mg/dL)	155 (110.5–228.8)	132 (110–177)	174 (122–236)	0.1575
HDL cholesterol (mg/dL)	44.9 ± 10.8	46.8 ± 11.9	43.12 ± 9.4	0.2372
LDL cholesterol (mg/dL)	89.6 ± 27.5	85.8 ± 26.1	93.4 ± 28.9	0.3338
Non-HDL cholesterol (mg/dL)	115 (103.3–138.3)	110 (101–127)	129 (109–150)	0.1703
Systolic BP (mm Hg)	130.6 ± 13.5	129.3 ± 12.4	131.8 ± 14.7	0.5366
Diastolic BP (mm Hg)	78.0 ± 9.8	76.7 ± 8.3	79.4 ± 11.2	0.3461
Urine occult blood (%)	22 (44.0%)	6 (24.0%)	16 (64.0%)	0.0096
Leukocyturia (%)	6 (12.0%)	2 (8.0%)	4 (16.0%)	0.6671
ARB (%)	27 (54.0%)	14 (56.0%)	13 (52.0%)	1.0000
CCB (%)	28 (56.0%)	11 (44.0%)	17 (68.0%)	0.1536
Statin (%)	37 (74.0%)	18 (72.0%)	19 (76.0%)	1.0000
Current smoking (%)	15 (30.0%)	6 (24.0%)	9 (36.0%)	0.5380
CVD History (%)	11 (22.0%)	2 (8.0%)	9 (36.0%)	0.0374
Retinopathy (%)	14 (28.0%)	5 (20.0%)	9 (36.0%)	0.3451
Neuropathy (%)	2 (4.0%)	1 (4.0%)	1 (4.0%)	1.0000
SGLT2 inhibitor (%)	37 (74.0%)	19 (76.0%)	18 (72.0%)	1.0000
GLP-1 analog (%)	19 (38.0%)	12 (48.0%)	7 (28.0%)	0.2436
DPP-4 inhibitor (%)	12 (24.0%)	7 (28.0%)	5 (20.0%)	0.7416
Metformin (%)	29 (58.0%)	12 (48.0%)	17 (68.0%)	0.2516
Thiazolidinedione (%)	3 (6.0%)	2 (8.0%)	1 (4.0%)	1.0000
Sulfonylureas (%)	8 (16.0%)	6 (24.0%)	2 (8.0%)	0.2467
Glinide (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Alpha-glucosidase inhibitor (%)	3 (6.0%)	3 (12.0%)	0 (0.0%)	0.2347
Insulin (%)	19 (38.0%)	11 (44.0%)	8 (32.0%)	0.5607

DN: diabetic nephropathy; BMI: body mass index; BMFR: body muscle to fat ratio; BUN: B-type natriuretic peptide; eGFR: estimated glomerular filtration rate; HDL: high-density lipoprotein; LDL: low-density lipoprotein; BP: blood pressure; CVD: cardiovascular disease; ARB: angiotensin

II receptor blocker; CCB: calcium channel blocker; SGLT2: sodium glucose co-transporter 2; GLP-1: glucagon-like peptide-1; DPP-4: dipeptidyl peptidase-4.

Table 3 Logistic regression analysis for presence of diabetic nephropathy

	Simple logistic regression analysis			Multivariate logistic regression analysis		
	OR	95% CI	P value	OR	95% CI	P value
Male	0.85	0.28–2.61	0.77	0.85	0.22–3.22	0.81
Age	1.00	0.96–1.05	0.96	0.99	0.94–1.05	0.79
Height	0.98	0.92–1.03	0.42			
Weight	0.98	0.94–1.03	0.49			
Muscle quantity	0.99	0.94–1.04	0.72			
Body fat quantity	0.96	0.88–1.05	0.39			
Waist circumference	1.03	0.95–1.10	0.48			
BMI	1.00	0.79–1.27	1.00			
Body fat percentage	1.00	0.91–1.09	0.93			
BMFR	1.22	0.23–6.56	0.82			
Diabetes duration	1.05	0.98–1.13	0.15			
Hemoglobin A1c	1.40	0.94–2.10	0.10			
Total cholesterol	1.01	0.99–1.03	0.28			
Triglyceride	1.00	1.00–1.01	0.18			
HDL cholesterol	0.97	0.92–1.02	0.23			
LDL cholesterol	1.01	0.99–1.03	0.33			
non-HDL cholesterol	1.01	0.99–1.03	0.15			
Systolic BP	1.01	0.97–1.06	0.53			
Diastolic BP	1.03	0.97–1.09	0.34			
Urine occult blood	5.63	1.65–19.2	<0.01	4.96	1.32–18.6	0.02
Leukocyturia	2.20	0.35–4.37	0.39			
ARB	0.85	0.28–2.59	0.78			
CCB	2.70	0.85–8.57	0.09			
Statin	1.23	0.35–4.37	0.75			
Current smoking	1.78	0.52–6.09	0.36			
CVD history	6.47	1.23–34.0	0.03	5.69	0.86–37.8	0.07
Retinopathy	2.25	0.63–8.06	0.22			
Neuropathy	1.00	0.06–16.9	1.00			
SGLT2 inhibitor	0.81	0.23–2.88	0.75			
GLP-1 analog	0.42	0.13–1.36	0.15			
DPP-4 inhibitor	0.64	0.17–2.39	0.51			
Metformin	2.30	0.73–7.27	0.16			
Thiazolidinedione	0.48	0.04–5.65	0.56			
Sulfonylureas	0.28	0.05–1.53	0.14			
Glinide	-	-	-			
Alpha-glucosidase inhibitor	-	-	-			
Insulin	0.60	0.19–1.90	0.38			

BMI: body mass index; BMFR: body muscle to fat ratio; BUN: B-type natriuretic peptide; eGFR: estimated glomerular filtration rate; HDL: high-density lipoprotein; LDL: low-density lipoprotein; BP: blood pressure; CVD: cardiovascular disease; ARB: angiotensin II receptor blocker; CCB: calcium channel blocker; SGLT2: sodium glucose co-transporter 2; GLP-1: glucagon-like peptide-1; DPP-4: dipeptidyl peptidase-4. Hosmer–Lemeshow goodness-of-fit χ^2 4.577, P=0.711.