SUDOSCAN, an effective tool for screening chronic kidney disease in patients with type 2 diabetes

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Abstract. SUDOSCAN is a non-invasive method of measuring peripheral small fiber and autonomic nerve activity by detection of abnormal sweat gland function through electrochemical skin conductance. It has been reported to be an effective screening tool in early detection of microvascular type 2 diabetes mellitus (T2DM) complications including diabetic neuropathy and nephropathy in recent studies. However, previous studies used estimated glomerular filtration rate (eGFR) as the golden standard, which has a 90% chance of being within 30% of the measured GFR at best. No relevant study has been performed in the Chinese population concerning SUDOSCAN in the screening of diabetic nephropathy (DN) in comparison with GFR. In this cross-sectional study, SUDOSCAN was performed in 176 Chinese patients with T2DM between September 2014 and September 2015. It was found that the SUDOSCAN test had a sensitivity of 57.8% and a specificity of 100% to detect chronic kidney disease at a cut-off SUDOSCAN-DN score of 59.5. The area under receiver operating characteristic curve for DN was 0.85 [95% confidence interval (CI), 0.76-0.93] compared with 0.84 for eGFRMDRD (MDRD, modification of diet in renal disease; 95% CI, 0.71-0.98) and 0.77 for eGFRKDOQI (KDOQI, National Kidney Foundation's Kidney Disease Outcomes Quality Initiative; 95% CI, 0.68-0.87). Patients with DN score <59.5 had a significantly lower GFR level (P<0.001) and significantly older age (P<0.001), longer duration of T2DM (P<0.001) and higher risk of diabetic complications, including diabetic neuropathy (P<0.001) and peripheral vascular disease (P<0.05). These results suggested that SUDOSCAN may be useful for detecting patients at risk of impaired renal function as part of a screening program in the Chinese population with T2DM.

Introduction

Diabetic nephropathy (DN) remains the leading cause of end-stage renal disease, indicated by albuminuria and reduced glomerular filtration rate (GFR) as the predictors for prognosis (1,2). The early identification and monitoring of DN is one of the major research areas in diabetes, apart from the control of glycaemia, hypertension and dyslipidemia. The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines (1) recommend using urinary albumin-creatinine ratio (UCAR) and estimated GFR (eGFR) as the screening method for DN during the annual examination for patients with type 2 diabetic mellitus (T2DM), which has facilitated earlier recognition of DN and formed the basis for clinical staging (1,3). Systematic reporting of eGFR using different equations, including modification of diet in renal disease (MDRD) or chronic kidney disease epidemiology collaboration (CKD-EPI) equations, are based on the demographic and laboratory variables, including age and serum creatinine (SCR) level. However, the testing of SCR in an everyday clinical setting may be invasive and costly (3-7).

SUDOSCAN (Impeto Medical SAS, Paris, France) is a non-invasive device for the assessment of sudomotor function through evaluation of sweat gland secretory function as an early reflection of sympathetic nerve impairment (8-10). An electrical current (typically ≤4 V) is applied to the patients automatically by the device, which allows the electrochemical skin conductance (ESC) of the hands and feet to be evaluated. The device may be used to predict diabetic kidney...
disease with built-in algorithms, by evaluating early deficits in sudomotor function. In a previous cross-sectional study, after adjusting for age, sex, BMI and HbA1c, hands and feet ESC have been demonstrated to be associated with eGFR [<60 ml/min/1.73 m² (P<0.01)], UACR (>30 mg/g (P<0.01) ) and UACR (>300 mg/g (P<0.01)) in populations of European Americans and African Americans with T2DM (11). In a recent study, Luk et al (12) evaluated the clinical utility of SUDOSCAN in detecting CKD and determined the cut-off point for DN score at 53 for detecting patients at risk of CKD by using eGFR as the golden standard. Furthermore, the area under the receiver operating characteristic curve of SUDOSCAN for CKD was 0.75 (95% confidence interval: 0.72-0.79). However, it has been indicated in other studies that eGFR has ~90% chance of being within 30% of the measured GFR at best (4,5,13).

Based on all previously performed studies on SUDOSCAN and its diagnostic value in kidney dysfunction by using eGFR as the golden standard for comparison, the present study decided to use a more direct method to determine kidney function in T2DM patients by using 99mTc-pentetic acid (DTPA) renal dynamic imaging method as the confirmatory golden standard (14,15).

The current study aimed to evaluate the diagnostic value of SUDOSCAN in detecting renal dysfunction of patients with T2DM in comparison with eGFR results calculated by MDRD and EPI by using 99mTc-pentetic acid (DTPA) renal dynamic imaging method as the confirmatory golden standard to provide a more comprehensive view into the use of SUDOSCAN in screening CKD in patients with T2DM.

Patients and methods

Subjects. The present study was conducted in Huashan Hospital, Fudan University (Shanghai, China) from September 2014 to September 2015. The Ethics Committee of Huashan Hospital approved the study. A total of 176 patients (Male: Female 113:63) diagnosed with T2DM, aged 18-80 years, with or without symptoms of nephropathy were continuously enrolled. Written consent was obtained from all patients enrolled in the study. Exclusion criteria were as follows: Undiagnosed hyperglycemia, T1DM diagnosis, treatment with drugs that may have an effect on the sympathetic system such as beta-blockers and antineoplastic drugs, implantation of electrical implantable devices, history of seizures or epilepsy, lumbar sciatic nerve lesion, severe varices of the lower limbs, and other metabolic diseases including thyroid disease or vitamin B12 deficiency.

Physical examination. One trained nurse examined all patients and recorded the results. Basic physical characteristics (height, weight, waist and hip circumference) were measured using standard methods and body mass index (BMI) and waist-hip ratio (WHR) were calculated. Blood pressure was recorded in the supine position following 5 min of rest. Medical history (diabetes, hypertension, dyslipidemia, cardiovascular disease, cerebrovascular disease and other diseases) was recorded for each patient. Cardiovascular disease was defined as history of coronary heart disease. Cerebrovascular disease was defined as history of stroke.

Laboratory examination. Patients underwent comprehensive metabolic assessments. Blood and urine samples were collected for fasting plasma glucose (FPG), glycated hemoglobin (HbA1c) (1-3), glycated albumin, total cholesterol, low density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), triglyceride (1-3) (16,17), renal function test including serum creatinine, blood urea nitrogen and uric acid and UACR, after ≥8 h of fasting (16). HbA1c and glycated albumin were determined by high-pressure liquid chromatography and liquid enzymatic assay, respectively (14). FPG, total cholesterol, triglyceride, LDL-C, HDL-C and SCR were analyzed using an automatic analyzer (AU640; Olympus Corporation, Tokyo, Japan) (18). Urinary creatinine levels were determined using the alkaline picrate method according to previous studies (12). UACR was calculated as a mean average of albumin (mg)/creatinine (g) from three repeats. Microalbuminuria was defined as urine ACR 2.5-25.0 mg/mmol in males and 3.5-25 in females, and macroalbuminuria defined as urine ACR 25.0 mg/mmol in both, as previously described (12) GFR was measured using the 99mTc-DTPA renal dynamic imaging method (4). eGFR was calculated using two different equations: MDRD recalibrated for Chinese patients and CKD-EPI (4,19,20). MDRD equation was as follows: eGFR (ml/min/1.73 m²)=186x(SCR x 0.011)−1.154x(age)−0.203x(0.742 if female/1.0 if male)x1.233, where SCR was in μmol/l and 1.233 was the adjusting coefficient for Chinese patients (12). CKD-EPI equation was as follows: eGFR (ml/min/1.73 m²)=141 x min(SCR/k, 1) x max(SCR/k, (1−0.209)x(0.993⁰²⁸)x(1.018 if female/1 if male), where k is 0.7 for females and 0.9 for males, a is -0.329 for females and -0.411 for males (19,20).

Peripheral neuropathy and vascular examination. Peripheral sensory polyneuropathy was diagnosed by MNSI B score, which consists of two parts: The appearance of the feet (deformity, dry skin, callus, infection or fissures) and examination of foot ulceration, ankle reflex and vibration perception with a 128 Hz tuning fork. Evaluation of each parameter was made at both sides with a maximum score of 8 points. The diagnostic criterion of DPN was a MNSI examination score of ≥2, as previously described (21). All assessments were performed by trained nurses and the analysis of results was undertaken by specialists. The ankle-brachial index was detected by ultrasonic Pocket Doppler-Edan-Sonotrax-Basic (Edan-Instruments Inc., Shenzhen, China) Doppler technique, with an 8 MHz probe and mercury sphygomanometer Riester diplomat-presameter (Rudolf Riester GmbH, Jungingen, Germany) with an adult cuff (arm circumference 24-32 cm). ABI measurements were performed according to previous studies (22,23).

SUDOSCAN test procedure. The SUDOSCAN device is composed of two sets of electrodes for the feet and hands, both of which are connected to a computer for recording and data analysis. The test is non-invasive and no special preparation is required. Patients place the palms of their hands and the soles of their feet on the electrodes for 2-3 min and a low-voltage (<4 V) electrical current stimulus will be applied by the device automatically. The device is able to measure ESC values expressed in micro-Siemens (μS) for the hands and the feet (both right and left sides). The mean of left and right ESC
values was used for statistical analysis. The machine also has built-in algorithms which integrate ESC with age height, weight and HbA1c level to produce a score that estimates current risk of kidney dysfunction (SUDOSCAN-DN score). The SUDOSCAN procedure was completed by all subjects without any complaints of discomfort and no adverse effects were reported.

**Diagnostic criteria.** CKD was defined as eGFR <60 ml/min/1.73 m². Microalbuminuria was defined as UACR >30 and <300 and macroalbuminuria was defined as UACR >300, according to the criteria of the National Kidney Foundation (24). In the diagnosis of diabetic peripheral sensory polyneuropathy, a cut-off point of ≥2 was used as the diagnosis standard of MNSI B score, based on previous studies (18,25,26). Peripheral vascular disease was defined as non-traumatic lower extremity amputation and/or ankle-brachial ratio <0.9 by Doppler ultrasound scan (27).

**Statistical analysis.** All data are expressed as the mean±standard deviation, median (inter-quartile range) or percentages according to different data types. Analysis of variance was used to compare mean differences of clinical factors between two groups and χ² analyses were used to assess differences between categorical variables. Correlation was determined using Spearman's rho rank tests. Association between ESC value and biological determinants (such as age, gender, BMI, WHR and duration of T2DM) was tested using multiple linear regression analysis. Receiver-operator characteristic (ROC) curves were constructed to evaluate the sensitivity and specificity of SUDOSCAN-DN score in detecting CKD in T2DM patients. The GFR result was used as the gold standard measurement of the degree of neuropathy, based on the cutoff value of 60 ml/min/1.73 m². The area under the ROC curve was calculated and the optimal cut-off point was the peak of the curve where the sum of sensitivity and specificity was greatest. SPSS 16.0 software (SPSS, Inc., Chicago, IL, USA) was used for all statistical analyses. P<0.05 was considered to indicate a statistically significant difference.

**Results**

**Enrolled patients.** A total of 176 patients with T2DM (113 males and 63 females) were eligible for the present study. Amongst these patients (mean age, 56.0±10.2 years; median duration of T2DM, 7 years, interquartile range 3-12 years), 15.3±1.0% of the subjects had CKD, 19.3±2.5% had microalbuminuria and 5.0±0.7% had macroalbuminuria.

**Clinical and biochemical characteristics.** Clinical and biochemical characteristics of the 176 subjects are presented in Table I. Patients with CKD had significantly higher age (P<0.01), longer duration of T2DM (P<0.01), higher serum creatinine level (P<0.01), higher BUN (P<0.05) and higher UCAR level (P<0.05) compared with patients without CKD. The mean GFR value was significantly lower in the CKD group compared with the non-CKD group (48.13±7.91 vs. 53.8±15.4 ml/min/1.73 m²; P<0.001). Mean SUDOSCAN-DN score was significantly lower in the CKD group compared with the non-CKD group (44.69±11.9 vs. 63.16±16.5; P<0.001).

**Correlation analysis.** Spearman correlation analysis (Table II) demonstrated a significant negative correlation between GFR and age (r=−0.48; P<0.01), duration of diabetes (r=−0.22; P<0.05), WHR (r=−0.25; P<0.01), SCR (r=−0.47; P<0.01), BUN level (r=−0.306; P<0.01) and uric acid (r=−0.307; P<0.01). A significant positive correlation was demonstrated between GFR and SUDOSCAN-DN score (r=0.52; P<0.001), as well as with older age (β-coefficient=-0.368; P<0.001), longer disease duration (β-coefficient=-0.227; P<0.01) and higher WHR (β-coefficient=-0.24; P<0.01).

**ROC curve.** The area under the ROC curve of SUDOSCAN-DN score to predict CKD was 0.85 [95% confidence interval (CI), 0.76-0.93; Fig. 1] compared with 0.84 for GFR MDRD (95% CI, 0.71-0.98) and 0.77 for GFR EPI (95% CI, 0.68-0.87). The sensitivity and specificity to detect CKD with SUDOSCAN-DN score was 57.6 and 100%, at a cut-off of 59.5.

**Patient comparison.** The clinical characteristics of the subjects were further analyzed when patients were divided into two groups by SUDOSCAN-DN score at the cut-off point of 59.5 (Table IV). Patients with DN score <59.5 had a significantly higher age, longer duration of T2DM, lower blood hemoglobin...
Table I. Clinical characteristics of patients with T2DM classified by the presence of CKD with normal reference values.

| Variable                                      | Patients with CKD \(^a\) (n=27) | Patients without CKD \(^b\) (n=149) | P-value |
|-----------------------------------------------|---------------------------------|-------------------------------------|---------|
| Sex, n (M/F)                                  | 14/13                           | 79/70                               | 0.62    |
| Age, years                                    | 67.75±9.48 \(^c\)              | 53.01±11.87                         | <0.001  |
| Duration of T2DM, years                       | 14 (8, 23) \(^y\)             | 7 (3, 11)                           | 0.001   |
| Smoking, %                                     | 15.8                            | 31.4                                | 0.17    |
| Family history of T2DM, %                     | 26.3                            | 46.2                                | 0.11    |
| Body mass index, kg/m\(^2\)                   |                                 |                                     |         |
| Male                                          | 24.42±3.55                      | 24.52±4.96                          | 0.87    |
| Female                                        | 25.6±3.1                        | 24.3±4.5                            | 0.38    |
| Waist-hip ratio                               |                                 |                                     |         |
| Male                                          | 1.03±0.18                       | 0.95±0.06                           | 0.14    |
| Female                                        | 0.95±0.01                       | 0.93±0.08                           | 0.59    |
| Systolic BP, mmHg                             | 135.25±15.8                     | 128.5±15.2                          | 0.091   |
| Diastolic BP, mmHg                            | 79.63±11.96                     | 80.57±9.65                          | 0.79    |
| Glycated hemoglobin, % (normal range, ≤6.5)   | 8.8±2.3                         | 8.7±2.1                             | 0.93    |
| Glycated albumin, % (normal range, 5-9)       | 20.3±7.1                        | 21.0±7.8                            | 0.91    |
| Fasting blood glucose, mmol/l                 | 8.6±2.8                         | 8.0±2.6                             | 0.16    |
| (normal range: 3.9-6.1)                       |                                 |                                     |         |
| Low-density lipoprotein cholesterol, mmol/l   | 2.21 (1.81, 2.66)               | 2.47 (1.88, 2.96)                   | 0.18    |
| High-density lipoprotein cholesterol, mmol/l  |                                 |                                     |         |
| (normal range, 0.9-2.1)                       | 1 (0.91, 1.23)                  | 0.97 (0.83, 1.2)                    | 0.54    |
| Triglyceride, mmol/l (normal range, 0.6-1.5)  | 1.15 (0.99, 2.2)                | 1.5 (0.96, 2.28)                    | 0.62    |
| Cholesterol, mmol/l                           | 4.22 (3.36, 4.78)               | 4.3 (3.5, 4.92)                     | 0.66    |
| Serum creatinine, µmol/l                      | 89.3±34.6\(^c\)               | 59.6±14.7                           | <0.001  |
| (normal range, 35-71)                         |                                 |                                     |         |
| Blood urea nitrogen, mmol/l                   | 8 (4.2, 10.3)\(^d\)            | 5.4 (4.8, 6.6)                      | 0.03    |
| Uric acid, mg/dl                              | 0.36 (0.27, 0.47)               | 0.29 (0.25, 0.36)                   | 0.17    |
| Mean urinary albumin-creatinine ratio         | 221.5 (10.6, 441.9)\(^y\)      | 12.6 (6.0, 24.9)                    | 0.012   |
| Glomerular filtration rate, ml/min/1.73 m\(^2\) | 48.13±7.91\(^c\)          | 85.83±15.4                          | <0.001  |
| Diabetic complications, %                     |                                 |                                     |         |
| Microalbuminuria                              | 16.7                            | 19.4                                | 0.26    |
| Macroalbuminuria                              | 27.8\(^c\)                     | 1.0                                 | <0.001  |
| Coronary heart disease                        | 2.1                             | 1.6                                 | 0.58    |
| Stroke                                        | 7.1                             | 13.1                                | 0.1     |
| Diabetic peripheral neuropathy                | 57.9\(^c\)                     | 24.3                                | 0.003   |
| Peripheral vascular disease                   | 10.5\(^d\)                     | 1.0                                 | 0.01    |
| SUDOSCAN results, µS                         |                                 |                                     |         |
| Hands ESC value                               | 56.74±20.5                      | 59.34±18.65                         | 0.06    |
| Feet ESC value                                | 49.11±23.13                     | 59.58±21.84                         | 0.66    |
| Diabetic nephropathy value                    | 44.69±11.9\(^d\)               | 63.16±16.5                          | <0.001  |
| Medication use, %                             |                                 |                                     |         |
| Metformin                                     | 10.5                            | 24.8                                | 0.172   |
| Insulin                                       | 42.1                            | 41.9                                | 0.98    |
| Statins                                       | 8.3                             | 39.4                                | 0.83    |
| Angiotensin converting enzyme inhibitor       | 68.4                            | 44.8                                | 0.06    |

Data are presented as the mean ± standard deviation, median (interquartile range) values or number of patients (%). \(^a\) CKD was defined as GFR of <60 ml/min/1.73 m\(^2\). \(^b\) Non-CKD was defined as GFR of ≥60 ml/min/1.73 m\(^2\). \(^c\) P<0.01 vs. patients without CKD and \(^d\) P<0.05. CKD, chronic kidney disease; T2DM, type 2 diabetes mellitus; BP, blood pressure; ESC, electrochemical skin conductance.
and lower GFR level compared patients with score ≥59.5 (all P<0.001). A significantly increased rate of stroke (13.2 vs. 3.1%; P<0.01), diabetic peripheral neuropathy (41.9 vs. 15.4%; P<0.001) and peripheral vascular disease (4.9 vs. 1.0%; P<0.05) was observed in the group of T2DM patients with DN level <59.5. A significant decrease in the ESC level of hands and feet (P<0.001) in the group of T2DM patients with DN level <59.5 was also detected in the study, as presented in Table IV. ESC values of hands in DN the ≥59.5 group was 65.1±17.1 vs. 56.7±20.5 in the DN<59.5 group and ESC of feet in DN ≥59.5 was 66.4±19.5 vs. 51.2±21.7 in the DN <59.5 group. Both of these differences are significant (P<0.001).

### Discussion

Sudomotor function is a subtype of autonomic function reflecting the integrity of sympathetic C fibers innervating the sweat glands, which can be highly susceptible to damage by metabolic processes, including longstanding diabetes (9,28-31). Processes downstream to sustained hyperglycemia, including activation of protein kinase C, activation of the polyol pathway and formation of advanced glycosylation end products, which are known to drive diabetic renal changes, have been implicated in causing reduction of endoneurial blood flow as well as causing direct nerve injury (1,3,32). Therefore, a previous study proposed that sudomotor dysfunction may have similar pathogenic mechanisms to diabetic kidney disease and SUDOSCAN may be used to perform early detection of CKD in diabetic patients (33). This proposal has been supported by previous studies that used SUDOSCAN to detect CKD in diabetic patients based on the premise that patients with CKD are likely to have vascular and nerve dysfunction (9). In a previous study, SUDOSCAN, as the modified and improved generation of EZSCAN with different built in algorithms, was reported to be effective in detecting CKD in a large cross-sectional sample of Chinese patients with T2DM (5). Statistics in that study showed the area under ROC curve of SUDOSCAN-DN score for CKD was 0.75 (95% CI, 0.72-0.79), which indicated SUDOSCAN may be useful in detecting patients at risk of having CKD. In 2011, Gin et al (30) first reported EZSCAN as the new screening tool for kidney disease in Chinese patients with T2DM. Freedman et al (11) studied 390 African and European American patients with T2DM and 166 controls, and found an independent association between ESC and GFR in African Americans.

In the present cross-sectional study, GFR was used instead of eGFR as the diagnostic standard for patients with or without CKD. The diagnostic value of SUDOSCAN in the detection of CKD in T2DM patients was evaluated using ROC curve analysis. The area under ROC curve was 0.85 (95% CI, 0.76-0.93) with a cut-off point of 59.5 for DN score. This cut-off point had 57.6% sensitivity and 100% specificity in detecting CKD. Compared with those without CKD, patients with CKD were older, had longer duration of disease, lower blood hemoglobin and more diabetic complications including peripheral neuropathy and peripheral vascular disease. By multiple linear regression analysis, the associated risk factors with GFR were found to be SUDOSCAN-DN score, disease duration, age, waist-hip ratio and hemoglobin level. Clinical characteristics were also compared in two groups divided by cut-off point of DN drawn from ROC analysis, and a lower GFR level was observed in patients with DN score <59.5.

The natural progression of kidney dysfunction in T2DM involves the gradual progress from albuminuria to declined GFR. Microalbuminuria is traditionally viewed as an early indicator of diabetic renal involvement, but its predictive value for renal dysfunction is challenged by poor sensitivity and specificity as well as many impact factors including pathological or physiological processes unrelated to diabetes such as

### Table II. Spearman correlation analysis between glomerular filtration rate and clinical characteristics.

| Variable                          | R     | P-value |
|-----------------------------------|-------|---------|
| Age                               | -0.48a| <0.001  |
| Duration of diabetes              | -0.22b| 0.015   |
| Body mass index                   | -0.11 | 0.24    |
| Waist-hip ratio                   | -0.25a| 0.006   |
| Systolic BP                       | -0.18 | 0.052   |
| Diastolic BP                      | 0.013 | 0.89    |
| Glycated hemoglobin               | 0.15  | 0.11    |
| Glycated albumin                  | 0.07  | 0.47    |
| Fasting blood glucose             | 0.15  | 0.16    |
| Total cholesterol                 | 0.15  | 0.1     |
| Triglycerides                     | 0.08  | 0.37    |
| High-density lipoprotein cholesterol | 0.01 | 0.9     |
| Low-density lipoprotein cholesterol | 0.2a | 0.03    |
| Serum creatinine                  | -0.47a| <0.001  |
| Blood urea nitrogen               | -0.31a| 0.001   |
| Uric acid                         | -0.31a| 0.001   |
| Mean urinary albumin-creatinine ratio | -0.16 | 0.08    |
| Hands ESC value                   | 0.13  | 0.14    |
| Feet ESC value                    | 0.23b | 0.01    |
| SUDOSCAN-DN value                 | 0.52a | <0.001  |

*P<0.01 and *P<0.05. BP, blood pressure; ESC, electrochemical skin conductivity; DN, diabetic nephropathy.

### Table III. Multiple linear regression analysis between glomerular filtration rate and clinical characteristics in Chinese patients with type 2 diabetes.

| Clinical factors     | Standard β-coefficient | P-value |
|----------------------|------------------------|---------|
| Age                  | -0.368a                | <0.001  |
| Duration of diabetes | -0.227a                | 0.008   |
| Glycated hemoglobin  | 0.11                   | 0.21    |
| Body mass index      | -0.48                  | 0.24    |
| Waist-hip ratio      | -0.24a                 | 0.007   |
| Low-density lipoprotein cholesterol | 0.016 | 0.85 |
| SUDOSCAN-DN score    | 0.42a                  | <0.001  |

*P<0.01; *P<0.008. DN, diabetic nephropathy.
posture, exercise, obesity and infection (2). This may explain the insignificant correlation between UCAR and DN score that was observed in the current study.

The current study had some limitations. The sample size of this cross-sectional cohort was not large enough to analyze the correlation between kidney function with all associated clinical characteristics. The possibility of selection bias could not be excluded in drawing the conclusion of high specificity of SUDOSCAN-DN score in detecting CKD. Further studies with larger sample sizes are needed to confirm the clinical use of SUDOSCAN for diagnosing risk of CKD.

The majority of guidelines recommend regular screening for complications and risk factors in patients with diabetes, including eye, foot, blood and urine examinations (1,3,28,34,35).

| Variable                                          | DN score <59.5 (n=79) | DN score ≥59.5 (n=97) | P-value |
|---------------------------------------------------|-----------------------|------------------------|---------|
| Sex, n (M/F)                                      | 45/34                 | 48/49                  | 0.052   |
| Age, years                                        | 64.7±9.9             | 46.7±9.9               | <0.001  |
| Duration of T2DM, years                           | 10 (5, 15)            | 6.5 (1, 9.5)           | <0.001  |
| Smoking, %                                        | 20.9                  | 36.7                   | 0.13    |
| Family history of T2DM, %                         | 39.5                  | 49.4                   | 0.20    |
| Body mass index, kg/m²                            |                       |                        |         |
| Male                                              | 24 (21,26)            | 25 (23, 28)            | 0.09    |
| Female                                            | 25 (22,26)            | 22 (20, 26.3)          | 0.24    |
| Waist-hip ratio                                   |                       |                        |         |
| Male                                              | 0.96 (0.91, 1.02)     | 0.96 (0.91, 0.99)      | 0.55    |
| Female                                            | 0.92 (0.86, 0.98)     | 0.93 (0.86, 0.98)      | 0.77    |
| Systolic BP, mmHg                                 | 132.9±14.2            | 126.9±15.2             | 0.006   |
| Diastolic BP, mmHg                                | 80.2±10.2             | 80.4±9.4               | 0.84    |
| Glycated hemoglobin, %                            |                      |                        | 0.06    |
| Low-density lipoprotein cholesterol, mmol/l       | 2.21 (1.81, 2.66)     | 2.47 (1.88, 2.96)      | 0.48    |
| High-density lipoprotein cholesterol, mmol/l      | 1.03 (0.9, 1.3)       | 0.95 (0.82, 1.2)       | 0.07    |
| Triglyceride, mmol/l                              | 1.2 (0.9, 1.9)        | 1.8 (1.2, 2.6)         | 0.003   |
| Cholesterol, mmol/l                               | 4.4 (3.5, 5.2)        | 4.4 (3.7, 4.8)         | 0.39    |
| Serum creatinine, μmol/l                          | 66.9±27.6             | 60.0±13.8              | 0.36    |
| Blood urea nitrogen, mmol/l                       | 5.5 (4.6, 7.3)        | 5.2 (4.5, 6.2)         | 0.054   |
| Uric acid, mg/dl                                  | 0.29 (0.25, 0.40)     | 0.31 (0.26, 0.38)      | 0.70    |
| Mean urinary albumin-creatinine ratio             | 290 (10.6, 441.9)     | 16 (6.0, 24.9)         | 0.16    |
| Glomerular filtration rate, ml/min/1.73 m²        | 72.5±19.7             | 89.9±16                | <0.001  |
| Diabetic complications, %                         |                       |                        |         |
| Microalbuminuria                                  | 14.1                  | 20.5                   | 0.12    |
| Macroalbuminuria                                  | 0.9                   | 1.4                    | 0.08    |
| Coronary heart disease                            | 2.3                   | 1.5                    | 0.32    |
| Stroke                                            | 13.2                  | 3.1                    | 0.005   |
| Diabetic peripheral neuropathy                    | 41.9                  | 15.4                   | <0.001  |
| Peripheral vascular disease                       | 4.9                   | 1.0                    | 0.048   |
| SUDOSCAN results, μS                              |                       |                        |         |
| Hands ESC value                                   | 56.7±20.5             | 65.1±17.1              | <0.001  |
| Feet ESC value                                    | 51.2±21.7             | 66.4±19.5              | <0.001  |
| DN value                                          | 46.8±10.6             | 73.8±11.6              | <0.001  |
| Medication use, %                                 |                       |                        |         |
| Metformin                                         | 23.3                  | 27.8                   | 0.5     |
| Insulin                                           | 38.4                  | 50.6                   | 0.11    |
| Statins                                           | 24.1                  | 24.1                   | 0.57    |
| Angiotensin converting enzyme inhibitor or angiotensin II receptor blocker, % | 52.1                  | 47.9                   | 0.003   |

Data are presented as the mean ± standard deviation, median (interquartile range) values or number of patients (%). *CKD was defined as DN score of <59.5 according to ROC analysis. **Non-CKD was defined as GFR ≥59.5 μS. *P<0.01 and **P<0.05 vs. DN score ≥59.5. CKD, chronic kidney disease; T2DM, type 2 diabetes mellitus; BP, blood pressure; ESC, electrochemical skin conductance; DN, diabetic nephropathy.
The results of the current study suggest that SUDOSCAN may be considered as a useful screening tool in an outpatient service or low resource setting, as part of a CKD screening program, due to its low invasiveness and convenience.

In conclusion, the current results suggested that the assessment of sudomotor function using SUDOSCAN may provide an effective screening method for the detection of kidney dysfunction in Chinese patients with T2DM.

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