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Jingcheng Ding
the Second Affiliated Hospital of Anhui Medical University

Qian Shi
the Second Affiliated Hospital of Anhui Medical University

Qian Tao
the Second Affiliated Hospital of Anhui Medical University

Hong Su
Anhui Medical University

Yijun Du
the Second Affiliated Hospital of Anhui Medical University

Tianrong Pan
the Second Affiliated Hospital of Anhui Medical University

Xing Zhong (✉ zhongxing761@163.com)
the Second Affiliated Hospital of Anhui Medical University

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Correlation between long-term glycemic variability and cognitive function in middle-aged and elderly patients with type 2 diabetes mellitus

Jingcheng Ding¹, Qian Shi¹, Qian Tao¹, Hong Su², Yijun Du¹, Tianrong Pan¹, and Xing Zhong¹*

Corresponding author: Xing Zhong, Email: zhongxing761@163.com

【Abstract】Objective To investigate the correlation associated with long-term glycemic variability on cognitive function in middle-aged and elderly patients with T2DM. Methods This study was a single-institution, retrospective analysis of data. A total of 138 patients who were hospitalized in the Department of Endocrinology, the Second Affiliated Hospital of Anhui Medical University from June 2021 to November 2022 were recruited. The Montreal Cognitive Assessment (MoCA) was applied to assess the cognitive function of the patients, which were divided into MCI and non-MCI. Glycated hemoglobin A1c standard deviation (HbA1c-SD) and fasting plasma glucose standard deviation (FPG-SD) were used to measure long-term blood glucose fluctuations. General clinical data, blood biochemical indicators, and glycemic variability indicators were compared between the two groups of patients. The differences between the groups were compared using t-test, x² test, or nonparametric test. Correlation and diagnostic power were further analyzed using multiple logistic regression analysis and ROC curve analysis. Results The differences in age, BMI, HbA1c-M, HbA1c-SD, FPG-M, FPG-SD, GFR, 24h urinary protein, and UACR were statistically significant between the two groups (P<0.05). In a multiple
logistic regression analysis, HbA1c-SD and FPG-SD were found to be risk factors for
cognitive dysfunction and eGFR to be a protective factor. The area under the curve
(AUC) of HbA1c-SD for predicting MCI prevalence was 0.828 (95% CI 0.754 ~ 0.887,
P<0.001), with a sensitivity of 62.69%, a specificity of 94.29%, and an optimal
diagnostic value 1.01. The area under the curve (AUC) of FPG-SD for predicting
MCI prevalence was 0.737 (95% CI 0.655 ~ 0.808, P<0.001), with a sensitivity of
76.12%, a specificity of 61.43%, and an best diagnostic value 0.94. The area under the
curve (AUC) of eGFR for prediction of MCI prevalence was 0.712 (95% CI 0.628 ~
0.786, P<0.01), with a sensitivity of 70.15 %, a specificity of 64.29 %, and an optimal
diagnostic value 79.82 ml/min/1.73m². Conclusions Long-term blood glucose
variability affects cognitive function in middle-aged and elderly T2DM patients, and
cognitive function is poorer in those with high blood glucose variability, for whom
renal function is a protective factor.

【Key words】 Diabetes mellitus, type 2; Blood glucose variability; Cognitive
function

Diabetes mellitus is a metabolic disease characterized by hyperglycemia, and
epidemiological surveys show that[1] the prevalence of Type 2 Diabetes Mellitus
(T2DM) among adults in China is as high as 12.8%. The main hazard of diabetes is
the damage it causes to several target organs (e.g. Heart, Brain, Kidney, etc.), which
can be life-threatening in severe cases. Diabetes cognitive dysfunction is one of the
complications of hyperglycemia involving the central nervous system, and T2DM is
also thought to be an independent risk factor for cognitive dysfunction[2].
There are two forms of diabetic hyperglycemia such as persistent hyperglycemia and fluctuating hyperglycemia. The 2014 International Diabetes Federation guideline for the management of postmeal glucose in diabetes\cite{3} highlighted that acute fluctuating hyperglycaemia is more harmful than chronic persistent hyperglycemia, and the greater the fluctuation of blood glucose, the higher the incidence of chronic complications. Patients with T2DM who achieved standard glycemic fluctuation control performed significantly better on tests such as the cognitive assessment, Trail Making Test-B, and verbal fluency test than those with greater glycemic fluctuations\cite{4}.

Blood glucose variability\cite{5} refers to the unstable state of blood glucose levels between maximum and minimum values. The harms of glucose variability on cognitive function can be monitored in several ways, but are mainly limited to short-term continuous glucose monitoring systems of one or two weeks duration, and the effects of long-term fluctuations in glucose levels on cognitive function have rarely been reported in middle-aged and older patients. This study investigated the effects of long-term glycaemic variability on cognitive function and other related factors in middle-aged and older patients with T2DM through a retrospective survey study, in order to provide a reference for future clinical treatment.

Methods

Subjects

This was a retrospective study. One hundred and thirty-eight middle-aged and elderly patients with T2DM who attended the outpatient and inpatient departments of
the Second Affiliated Hospital of Anhui Medical University from June 2021 to
November 2022 were selected for the study. Inclusion criteria were the following: (1)
All participants was diagnosed with T2DM and met the 1999 WHO diagnostic criteria
for diabetes; (2) they were between 50 and 75 years old; (3) they were no clear
cerebral infarction and extensive cerebral white matter demyelination on head
magnetic resonance examination. Exclusion criteria were the following: (1) previous
clear diagnosis of dementia, stroke, Parkinson's, and other diseases affecting cognitive
function; (2) acute and chronic severe diabetic complications (DKA, HHS, diabetic
foot); (3) major medical illness, such as severe heart disease, and damaged liver or
kidney function, tumors and chronic infections, blood and immune system diseases,
psychiatric Patients, especially those who need to take hormones. (5) Severe hearing,
visual impairment or physical disability.

Demographic and Clinical information

Demographic and Clinical data were collected from all patients, such as age,
gender, duration of diabetes, educational background, height, weight, SBP and DBP,
etc. Body Mass Index (BMI) was calculated; After an overnight fast, the patients’
fasting venous blood was drawn at 5:00 a.m. the next day to measure fasting plasma
glucose (FPG), Glycated hemoglobin A1c (HbA1c), AST, ALT, TC, TG, creatinine, 24h
urine protein, UACR, and thyroid stimulating hormone (TSH), etc. Based on the
recorded Glycated hemoglobin A1c (HbA1c), fasting plasma glucose (FPG) at each
visit, Mean Glycated hemoglobin A1c (HbA1c-M) and standard deviation (HbA1c-SD),
mean fasting plasma glucose (FPG-M) and standard deviation (FPG-SD) were
calculated, respectively. And the standard deviation (SD) of HbA1c and FPG were used as indicators of glucose variability in the present study. Calculation of patient surface area (BSA) based on the DuBois formula\(^6\): \(0.007184 \times \text{weight (kg)}^{0.425} \times \text{height (cm)}^{0.725}\). Calculation of glomerular filtration rate (GFR) using Cockcroft-Gauh (CG) formula\(^7\): eCcr for men= \((140-\text{age}) \times \text{weight} / (72 \times \text{Scr})\); eCcr for women = \(0.85 \times (140-\text{age}) \times \text{weight} / (72 \times \text{Scr})\); according to gender, GFR calculated by the Cockcroft-Gauh (CG) formula was normalized by BSA: GFR[ml/min/1.73m\(^2\)]\(=0.84\times\text{eCcr}\times(1.73/\text{BSA})\). The unit of blood creatinine in the above formula is mg/dl, and 1umol/l=0.0113mg/dl.

Cognitive function assessment

Evaluators are rigorously trained and a uniform survey scale is used. All enrolled patients were evaluated on the Montreal Cognitive Assessment Scale (MoCA). This cognitive test covers many cognitive skills, and scores range from 0 to 30. Criteria for cognitive impairment\(^8\): Illiterate education ≤ 13 points, elementary school education ≤ 19 points, junior high school education and above ≤ 24 points.

Statistical Methods

All statistical analyzes using SPSS Ver. 22.0 software. Comparisons between groups were made using \(t\)-test for normally distributed variables, the Mann-Whitney \(U\) test for asymmetrically distributed variables, and \(\chi^2\) test for categorical variables. For all participants, Spearman’ correlation analysis was used to assess the relationship between scores obtained from MOCA tests and glucose variability parameters. Indicator variables with statistical differences in the single-factor analysis were
included in the multiple logistic regression analysis as independent variables, and whether cognitive dysfunction occurred was included as dependent Variable. Odds ratio (OR) and corresponding 95% confidence intervals (CI) were calculated. Using (1-specificity) as transverse coordinates and sensitivity as longitudinal coordinates, the subjects' working characteristic curves (ROCs) were mapped and the area under the ROC curve was calculated (AUC) using MedCalc Software version 20.100 (https://www.medcalc.org/). A two-sided P-value < 0.05 was considered to indicate statistical significance.

Results

Participant characteristics

The clinical characteristics of the participants are presented in Table 1. Among 138 middle-aged and elderly patients with T2DM, there were 30 males and 37 females in the MCI group, age (64.60±5.76) years, diabetic duration (13.34±6.24) years; 33 males and 38 females in the control group, age (61.39±5.70) years, diabetic duration (13.83±6.96) years; There were no statistically significant differences between the two groups in terms of gender, education levels, duration of diabetes, SBP, DBP, BSA, TC, TG, ALT, AST, and TSH (P>0.05). The differences were statistically significant when comparing age, BMI, HbA1c -M, HbA1c -SD, FPG-M, FPG-SD, eGFR, 24h urinary protein, and UACR between the two groups (P < 0.05).

(Table 1)

Associations of blood glucose variability with cognitive dysfunction
For all participants, Spearman’ correlation analysis indicated a negative correlation between the HbA1c-SD and the FPG-SD and MOCA scores ($r = -0.389$, $p <0.001$; $r = -0.233$, $p=0.006$, respectively), whereas renal function was positively correlated with the MOCA scores ($r=0.175$, $p=0.041$). Univariate logistic regression analysis showed a statistically significant difference in age, BMI, HbA1c-M, HbA1c-SD, FPG-M, FPG-SD, eGFR, 24h urine protein, and UACR alterations between the MCI and control groups. (Table 2) Further Multiple logistic regression analysis displayed that HbA1c-SD, FPG-SD, and eGFR were independently associated with MCI after adjusting for relevant factors such as age, BMI, and HbA1c-M, etc. (Table 3)

ROC curve analysis of the predictive value of HbA1c-SD, FPG-SD, and eGFR for MCI prevalence.

Multiple logistic regression analysis showed that HbA1c-SD and FPG-SD were risk factors for cognitive function and the eGFR was a protective factor for cognitive function. The area under the curve (AUC) of HbA1c-SD for predicting MCI prevalence was 0.828 (95% CI 0.754~0.887, $P<0.001$), with a sensitivity of 62.69%, a specificity of 94.29%, and an optimal diagnostic value 1.01. The area under the curve (AUC) of FPG-SD for predicting MCI prevalence was 0.737 (95% CI 0.655~0.808, $P<0.001$), with a sensitivity of 76.12%, a specificity of 61.43%, and an best diagnostic value 0.94. The area under the curve (AUC) of eGFR for prediction of MCI prevalence was 0.712 (95% CI 0.628~0.786, $P<0.001$), with a sensitivity of
70.15%, a specificity of 64.29% and an optimal diagnostic value 79.82 ml/min/1.73m². (Fig.1)

Discussion

Glycemic variability[^1], also known as blood glucose fluctuations, consists mainly of short-term blood glucose fluctuations and long-term blood glucose fluctuations. Short-term glycemic fluctuations reflect the intra-and inter-day blood glucose levels using the continuous glucose monitoring system (CGMS) and the self-monitoring of blood glucose (SMBG), while long-term blood glucose fluctuations are typically calculated on the basis of multiple measures of the HbA1c or other glycemic indicators over a longer period of time, reflecting glycemic fluctuations over a period of months to years. The gold standard for glycemic control is glycosylated haemoglobin (HbA1c).

Recent studies[^9] have shown that even in those T2DM patients with well-controlled HbA1c (<7%), greater variability in HbA1c was associated with worse kidney function and more serious microvascular complications. HbA1c variability[^10] was defined as changes in HbA1c from one clinic visit to the next over a longer period of time than intra-day blood glucose, inter-day blood glucose, and weekly blood glucose fluctuations, which can better reflect blood glucose fluctuations. HbA1c-SD can be viewed as an indicator for assessing HbA1c variability, and FPG-SD is also closely associated with microvascular complications[^11,12]. In the current study, HbA1c-SD and FPG-SD were used to indicate the variability of glucose over the long term for patients with T2DM.
In addition to HbA$_1c$, FPG, and PPG, daily acute glucose fluctuations are also closely related to impaired cognitive function in older patients with type 2 diabetes\textsuperscript{[13]}. One study\textsuperscript{[14]} evaluated glucose variability in the short term using continuous dynamic glucose monitoring, suggesting that greater glucose variability was associated with brain atrophy and worse cognitive function in T2DM patients. HbA$_1c$-SD and FPG-SD were in this study used to evaluate long-term glucose variability. In a multiple logistic regression analysis, HbA$_1c$-SD and FPG-SD were found to be risk factors for cognitive function, with (95\% CI 7.312 $\sim$ 153.705, $P$<0.01) for HbA$_1c$-SD and (95\% CI 2.279 $\sim$ 22.709, $P$<0.01) for FPG-SD, respectively. Animal studies\textsuperscript{[15]} have shown that glycemic fluctuations were more likely to impair cognitive function than persistent hyperglycemia in T2DM model rats, and the mechanism could be related to oxidative stress and inflammatory damage. Therefore, it is suggested that long-term glucose variability (HbA$_1c$-SD and FPG-SD) was significantly associated with impaired cognitive function.

Based on UKPDS, ACCORD, and VADT clinical trials, Zhou\textsuperscript{[15]} found an association between FPG variability and increased risk of moderate-to-severe diabetic nephropathy. The study\textsuperscript{[16]} showed that higher HbA$_1c$ variability is more likely to progress to macro-albuminuria in T2DM patients in especially those patients under a micro-albuminuria state. The glomerular filtration rate is the amount of fluid produced by two kidneys per unit of time and is thought to be an important indicator of kidney function. The Brain in Kidney Disease (BRINK) Cohort Study\textsuperscript{[17]} showed that kidney function was associated with cognitive performance, especially when participants had
an eGFR \(<30\) ml/min/1.73m². In a prospective study\(^{[18]}\) on renal function and cognitive
function in an elderly population in China, involving 284 participants with an average
follow-up of 3.3 years, participants with mild to moderate eGFR had a higher relative
risk of cognitive decline compared to those with normal kidney function. We also
found that eGFR upregulation is a protective factor for cognitive function
in the present study. Therefore, it is suggested that renal function is closely related to
cognitive function.

Blood glucose fluctuations are reflected in glycemic variability. And
increasing the range of glycemic fluctuations and the duration of the
fluctuation can increase the risk of diabetic macrovascular and microvascular
complications. These studies have demonstrated that glycemic variability is strongly
associated with adverse events such as cardiovascular disease\(^{[20]}\), peripheral
neuropathy\(^{[21]}\) and high mortality\(^{[22]}\) in T2DM patients. The mechanism of adverse
effects of glycemic fluctuations on cognitive function may include: (1) Effects of
blood glucose fluctuations on cognitive function are associated with oxidative stress
and inflammatory damage. Using an in vitro model of murine microglia, Hsieh\(^{[23]}\)
demonstrated that abnormal fluctuations in blood glucose could mediate oxidative
stress in murine microglial cells, resulting in ongoing neurodegenerative lesions. The
study\(^{[24]}\) showed that acute glycemic fluctuations can lead to the over-expression of
inflammatory factors such as TNF-a and IL-1a, which in turn induced neuronal
apoptosis in hippocampal tissue, impairing the integrity of the blood-brain barrier, and
aggravating central neurodegeneration. (2) Abnormal glycemic fluctuations were also
associated with renal insufficiency, retinopathy, islet function, and insulin resistance\cite{12,25,26}. All of which may impact cognitive function in diabetic patients.

Our study has several limitations. First, the present study employed a single-center retrospective design. We did not include a large number of participants. Due to the small sample size, the statistical power of the analyses was limited. Secondly, the age of the population included in this study was only 50-75 years. Therefore, it is not sufficient to explain the relationship between other age groups and blood glucose fluctuations. We will continue to improve on these deficiencies in future work.

Conclusion

Overall, our findings provide further support that long-term glucose variability is strongly associated with cognitive function in middle-aged and older individuals with T2DM, and the greater the fluctuation in blood glucose, the more severe the cognitive decline. For this reason, we should consider glycemic variability as one of the therapeutic targets for reducing the risk of cognitive impairment and other associated complications in middle-aged and older T2DM patients.

Abbreviations

MoCA = The Montreal Cognitive Assessment; BMI is body mass index; BSA is body surface area. HbA1c-M is mean glycated hemoglobin A1c; HbA1c -SD is standard deviation of glycated hemoglobin A1c; FPG-M is mean fasting plasma glucose; FPG-SD is standard deviation of fasting glucose; TC is total cholesterol; TG is
triglycerides; ALT is alanine aminotransferase; AST is aspartate aminotransferase; eGFR is expected glomerular filtration rate; UACR is urinary micro-albumin/creatinine ratio; TSH is thyroid stimulating hormone. 1 mmHg = 0.133 kPa.

Acknowledgments

We would like to express our heartfelt gratitude to all the staff of the Department of Endocrinology, the Second Affiliated Hospital of Anhui Medical University and Department of Epidemiology and Health Statistics, Anhui Medical University for their selfless help and valuable assistance.

Authors’ contributions

Jingcheng Ding, Yijun Du, Tianrong Pan, and Xing Zhong contributed to the planning and design of the study. Jingcheng Ding, Qian Shi, Qian Tao collected the clinical data. Jingcheng Ding, Hong Su, and Xing Zhong performed the statistical analysis. Jingcheng Ding and Xing Zhong contributed to the writing of the manuscript.

All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The protocol and informed consent document were approved by the research ethics committees of the Second Affiliated Hospital of Anhui Medical University (Approved No. of ethic committee: YX2022-043). For illiterate participants, we obtained informed consent from their legally authorized representatives. All individuals gave written informed consent before their participated in the study protocol. All the procedures were followed in accordance with the relevant guidelines (eg. Declaration of Helsinki).

Consent for publication

Not Applicable in the declaration section.

Competing interests

The authors report no conflicts of interest in this work.

Author details

1Department of Endocrinology, the Second Affiliated Hospital of Anhui Medical University, Hefei 230601, China

2Department of Epidemiology and Health Statistics, Anhui Medical University, Hefei 230601, China

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https://doi.org/10.1002/jcb.29523.


https://doi.org/10.1038/s41598-021-84150-8.


Table 1. Characteristics of the study cohort.

<table>
<thead>
<tr>
<th>Projects</th>
<th>MCI group (n=67)</th>
<th>Non-MCI group (n=70)</th>
<th>t/z² /Z</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years, mean ±SD)</td>
<td>64.60±5.76</td>
<td>61.49±5.69</td>
<td>3.179</td>
<td>0.002</td>
</tr>
<tr>
<td>Gender (n, male/female)</td>
<td>37/30</td>
<td>38/32</td>
<td>0.012</td>
<td>0.912</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Illiteracy (n, %)</td>
<td>6 (9.0%)</td>
<td>6 (8.5%)</td>
<td>1.513</td>
<td>0.469</td>
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<tr>
<td>Primary School (n, %)</td>
<td>14 (20.9%)</td>
<td>21 (30.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Junior high school and above (n, %)</td>
<td>47 (70.1%)</td>
<td>43 (61.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MOCA (minutes, mean ±SD)</td>
<td>19.84±3.62</td>
<td>24.36±3.70</td>
<td>-7.226</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of diabetes mellitus (years,mean ±SD)</td>
<td>13.45±6.33</td>
<td>13.89±6.96</td>
<td>-0.385</td>
<td>0.701</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg, mean ±SD)</td>
<td>128.64±13.16</td>
<td>127.40±12.17</td>
<td>0.574</td>
<td>0.567</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg, mean ±SD)</td>
<td>74.90±9.03</td>
<td>75.49±9.38</td>
<td>-0.375</td>
<td>0.708</td>
</tr>
<tr>
<td>BMI (kg/m² , mean ±SD)</td>
<td>24.02±2.80</td>
<td>25.54±3.03</td>
<td>-3.043</td>
<td>0.003</td>
</tr>
<tr>
<td>BSA(m² , mean ±SD)</td>
<td>1.71±0.17</td>
<td>1.76±0.17</td>
<td>-1.948</td>
<td>0.053</td>
</tr>
<tr>
<td>HbA1c -M(%, mean ±SD)</td>
<td>8.29±1.47</td>
<td>7.42±1.21</td>
<td>3.761</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HbA1c -SD(%, mean ±SD)</td>
<td>1.26±0.67</td>
<td>0.55±0.41</td>
<td>7.393</td>
<td>&lt;0.001</td>
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<tr>
<td>FPG-M (mmol/L, mean ±SD)</td>
<td>7.82±1.57</td>
<td>6.92±1.25</td>
<td>3.716</td>
<td>&lt;0.001</td>
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<td>FPG-SD (% mean ±SD)</td>
<td>1.52±0.75</td>
<td>0.92±0.44</td>
<td>5.735</td>
<td>&lt;0.001</td>
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<tr>
<td>TC (mmol/L, mean ±SD)</td>
<td>4.40±1.01</td>
<td>4.39±0.88</td>
<td>0.095</td>
<td>0.924</td>
</tr>
<tr>
<td>TG (mmol/L, mean ±SD)</td>
<td>1.40±0.70</td>
<td>1.47±0.70</td>
<td>-0.568</td>
<td>0.571</td>
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</tbody>
</table>
Table 2. Univariate Logistic Regression Analysis of Factors Influencing Cognitive Dysfunction in T2DM Patients

<table>
<thead>
<tr>
<th></th>
<th>β</th>
<th>SE</th>
<th>Wald x²</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.095</td>
<td>0.031</td>
<td>9.035</td>
<td>1.099</td>
<td>1.033-1.169</td>
<td>0.003</td>
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<tr>
<td>BMI</td>
<td>-0.182</td>
<td>0.063</td>
<td>8.222</td>
<td>0.834</td>
<td>0.737-0.944</td>
<td>0.004</td>
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<tr>
<td>HbA1c -M</td>
<td>0.498</td>
<td>0.146</td>
<td>11.609</td>
<td>1.645</td>
<td>1.235-2.191</td>
<td>0.001</td>
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<tr>
<td>HbA1c -SD</td>
<td>2.577</td>
<td>0.492</td>
<td>27.477</td>
<td>13.161</td>
<td>5.021-34.500</td>
<td>&lt;0.001</td>
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<tr>
<td>FPG-M</td>
<td>0.463</td>
<td>0.137</td>
<td>11.377</td>
<td>1.589</td>
<td>1.214-2.080</td>
<td>0.001</td>
</tr>
<tr>
<td>FPG-SD</td>
<td>1.616</td>
<td>0.348</td>
<td>21.508</td>
<td>5.034</td>
<td>2.543-9.966</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>eGFR</td>
<td>-0.044</td>
<td>0.011</td>
<td>16.258</td>
<td>0.957</td>
<td>0.936-0.978</td>
<td>&lt;0.001</td>
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<tr>
<td>24h urinary protein</td>
<td>0.010</td>
<td>0.005</td>
<td>4.907</td>
<td>1.010</td>
<td>1.001-1.019</td>
<td>0.027</td>
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<td>UACR</td>
<td>0.039</td>
<td>0.019</td>
<td>3.994</td>
<td>1.039</td>
<td>1.001-1.080</td>
<td>0.046</td>
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</tbody>
</table>

Table 3. Multi-Factor Logistic Regression Analysis of Factors Influencing Cognitive Dysfunction in T2DM Patients

<table>
<thead>
<tr>
<th></th>
<th>β</th>
<th>SE</th>
<th>Wald x²</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.011</td>
<td>0.050</td>
<td>0.046</td>
<td>1.011</td>
<td>0.917-1.114</td>
<td>0.830</td>
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<tr>
<td>BMI</td>
<td>-0.184</td>
<td>0.120</td>
<td>2.339</td>
<td>0.832</td>
<td>0.658-1.053</td>
<td>0.126</td>
</tr>
<tr>
<td>HbA1c -M</td>
<td>0.014</td>
<td>0.238</td>
<td>0.004</td>
<td>1.014</td>
<td>0.636-1.618</td>
<td>0.952</td>
</tr>
<tr>
<td>HbA1c -SD</td>
<td>3.512</td>
<td>0.777</td>
<td>20.436</td>
<td>33.523</td>
<td>7.312-153.705</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FPG-M</td>
<td>0.015</td>
<td>0.235</td>
<td>0.004</td>
<td>1.015</td>
<td>0.641-1.608</td>
<td>0.949</td>
</tr>
<tr>
<td>FPG-SD</td>
<td>1.973</td>
<td>0.587</td>
<td>11.318</td>
<td>7.194</td>
<td>2.279-22.709</td>
<td>0.001</td>
</tr>
<tr>
<td>eGFR</td>
<td>-0.075</td>
<td>0.021</td>
<td>13.249</td>
<td>0.928</td>
<td>0.891-0.966</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>24h urinary protein</td>
<td>0.009</td>
<td>0.007</td>
<td>1.347</td>
<td>1.009</td>
<td>0.994-1.023</td>
<td>0.246</td>
</tr>
<tr>
<td>UACR</td>
<td>0.020</td>
<td>0.032</td>
<td>0.378</td>
<td>1.020</td>
<td>0.958-1.085</td>
<td>0.538</td>
</tr>
</tbody>
</table>

Fig1. ROC curves for HbA1c -SD, FPG-SD and eGFR
A. The predictive value of HbA1c-SD and FPG-SD in MCI.

B. The predictive value of eGFR in MCI.