

Significant Abnormal Glycemic Variability Increased the Risk for Arrhythmias in Middle-Aged and Elderly Type 2 Diabetic Patients

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Abstract

Background: Little is known about whether the influence of glycemic variability on arrhythmia is related to age in type 2 diabetes mellitus (T2DM). Therefore, we aimed to compare the association between glycemic variability and arrhythmia in middle-aged and elderly T2DM patients.

Methods: A total of 107 patients were divided into two groups: elderly diabetes mellitus group (EDM, n=73) and middle-aged diabetes mellitus group (MDM, n=34). The main clinical data, continuous glucose monitoring (CGM) and dynamic ECG reports were collected. The parameters including standard deviation (SDBG), largest amplitude of glycemic excursions (LAGE), mean amplitude of glycemic excursions (MAGE), absolute means of daily differences (MODD) were tested for glycemic variability evaluation.

Results: In terms of blood glucose fluctuations, MAGE (5.77 ± 2.16 mmol/L vs 4.63 ± 1.89 mmol/L, $P=0.026$), SDBG (2.39 ± 1.00 mmol/L vs 2.00 ± 0.82 mmol/L, $P=0.048$), LAGE (9.53 ± 3.37 mmol/L vs 7.84 ± 2.64 mmol/L, $P=0.011$) was significantly higher in EDM group than those of MDM group. The incidences of atrial premature beat, couplets of atrial premature beat, atrial tachycardia and ventricular premature beat were significantly higher in EDM group compared with the MDM group (all $P < 0.05$). Among patients with hypoglycemia events, the incidences of atrial premature beat, couplets of atrial premature beat, atrial tachycardia and ventricular premature beat (all $P < 0.05$) were significantly higher in the EDM group than those in the MDM group.

Conclusions: The study demonstrated the elderly patients had greater glycemic variability and were more prone to arrhythmias. Therefore, active control of blood glucose fluctuation in elderly patients will help to reduce the risk of severe arrhythmia.

Background

Diabetes mellitus (DM) is a major risk factor for the development of vascular complications. Recently, a series of studies showed that glycemic variability had more deleterious effects than sustained hyperglycemia in the pathogenesis of diabetic cardiovascular complications¹. In patients of acute myocardial infarction with poor blood glucose control, glycemic variability is associated with severity of coronary artery disease beyond chronic hyperglycemia². Another study demonstrated that glycemic variability predicted rapid progression of non-culprit lesions in patients with acute coronary syndrome³. Lu J et al. reported that glycemic variability was associated with the severity of diabetic retinopathy⁴. More recently, the ALLHAT study showed that greater visit-to-visit variability of fasting blood glucose was associated with increased risk of cardiovascular events and all-cause mortality⁵. Up to now, the mechanism by which glycemic variability aggravates the progression of cardiovascular disease is not fully understood, although several researches demonstrated that non-enzymatic glycation, oxidative stress, activation of inflammation and endothelial dysfunction might play a critical role^{6,7}.

It is well known that patients with T2DM have a high risk of arrhythmias. Lately, the impact of glycemic variability on arrhythmia has attracted researchers' attention. Stahn A et al. reported that severe episodes of hypoglycemia increased the risk of severe ventricular arrhythmias⁸. In another study, silent hypoglycemia increased silent cardiac ischemia and the frequency of ventricular extrasystoles or nonsustained ventricular tachycardias⁹. Prolonged QT interval is a potential risk factor for malignant ventricular arrhythmias. Sertbas Y et al. found that increased glycemic variability was associated with prolonged QTc duration and QTc dispersion, suggesting that optimal glycemic control with glycemic variability should be considered as an additional goal point along with the traditional following parameters¹⁰.

However, little is known about whether the influence of glycemic variability on arrhythmia is different between middle-aged and elderly T2DM patients with chronic cardiovascular disease. Therefore, in our current study, we used a retrospective study including middle-aged diabetes mellitus (DM) and elderly diabetes mellitus (DM) patients with chronic cardiovascular disease performed simultaneous 72-hour continuous dynamic blood glucose monitoring and continuous 24-hour Holter monitoring to reveal the potential relationship.

Method

Subjects

This study groups consisted of 107 enrolled patients with known T2DM and chronic cardiovascular disease from February 2002 to September 2017 at Shandong University Qilu Hospital. This study was approved by the ethics committee of Shandong University Qilu hospital and all patients provided written informed consent pt before participation. All research was performed in accordance with the relevant guidelines and regulations.

Patients included in this study met all the following conditions: (1) Patients admitted to Qilu Hospital of Shandong University who met the 1998 World Health Organization (WHO) T2DM diagnostic criteria¹¹; (2) Age \geq 45 years; (3) clinically diagnosed chronic cardiovascular disease, including coronary heart disease, stroke, peripheral arterial disease or cerebrovascular disease³. Patients who met any of the followings were excluded from the study: (1) acute hyperbilirubinemia, ketoacidosis, lactic acidosis and other acute complications; (2) acute and chronic moderate and severe liver dysfunction, advanced tumor, anemia; (3) stress state caused by acute stroke, acute coronary syndrome, acute infection, trauma and perioperative period; (3) congenital heart disease, myocarditis; (4) permanent atrial fibrillation or atrioventricular block, baseline ECG ST segment depression greater than 1 mv; (5) pre-excitation syndrome; (6) installation of artificial cardiac pacing device; (7) taking antiarrhythmic drugs, such as propafenone, amiodarone, digitalis-like cardiac glycosides and other drugs that affect heart rate variability; (8) pregnant and lactating women; (9) mental illness such as epilepsy or neurosis; (10) electrolyte metabolism disorders; (11) thyroid dysfunction.

Clinical baseline data, such as age, gender, height, body weight, blood pressure and medical history, were obtained retrospectively from medical charts. The fasting blood samples were taken after an overnight fast of at least 12 h and sent to the biochemistry laboratory for estimation for glucose, hemoglobin A1c (HbA1C), lipid profiles, urea acid, and creatinine tests. Patients underwent 72-hour continuous glucose monitoring (CGM) and 24-hour Holter examination during hospitalization. The patients were in normal activity during the monitoring period, and the mealtime and exercise time were recorded. In the process of CGM and dynamic ECG monitoring, the professional nurses guided the patients to make relevant clinical records. The dynamic blood glucose monitoring record was interpreted by an endocrinologist, and the Holter record was interpreted by a cardiologist.

Hypoglycemic events (HE) was Graded by peripheral random blood glucose: Grade 1 (3.1 mmol/L-3.9 mmol/L) and Grade 2 (< 3.1 mmol/L or suffering from severe symptoms requiring external intervention). The following blood glucose fluctuation index were calculated and collected: standard deviations of blood glucose (SDBG), large amplitude of glycemic excursion (LAGE), mean amplitude of glycemic excursion (MAGE) and absolute means of daily differences (MODD), were calculated. The MAGE tertiles were layered as MAGE1(1.24–4.37 mmol/l), MAGE2 (4.38–6.36 mmol/l) and MAGE3 (6.37–13.66 mmol/l) as previously reported².

The following arrhythmias were recorded: atrial premature beat (APB), Couplets of atrial premature beat (Couplets of A), atrial tachycardia (AT), ventricular premature beat (VPB), Couplets of ventricular premature beat (Couplets of V) and ventricular tachycardia (VT).

Statistical Analyses

Statistical analyses were performed using SPSS 19.0 (Chicago, IL, USA). Descriptive characteristics were presented as mean \pm standard deviation ($X \pm SD$). The Shapiro-Wilk normality test and the Levene variance homogeneity test are performed. For the variance in accordance with the normal distribution, the difference was compared using the independent sample t test. When the variance was not uniform, the difference between the two groups was compared by rank sum test. The χ^2 test and Fisher exact test were used to determine differences in the proportion of categorical variables. $P < 0.05$ was considered as significantly different.

Results

Patient baseline characteristics

EDM group (n = 73): 43 patients received insulin, 13 patients used insulin secretagogues and 17 patients used other oral hypoglycemic agents. 41 patients with coronary heart disease, 15 patients with cerebrovascular disease, 10 patients combined with coronary heart disease and peripheral arterial disease, and 7 patients with peripheral arterial disease.

MDM group (n = 34): 19 cases used insulin, 6 cases treated with insulin secretagogue and 15 cases used other oral hypoglycemic agents. 8 cases with coronary heart disease, 2 cases with cerebrovascular disease, 8 patients combined with coronary heart disease and peripheral arterial disease, and 16 cases with peripheral arterial disease.

Comparison of the clinical characteristics between patients in EDM and MDM groups

The BMI ($25.68 \pm 3.23 \text{ kg/m}^2$ vs $27.29 \pm 3.50 \text{ kg/m}^2$, $P = 0.021$) and DBP levels ($68.25 \pm 9.21 \text{ mmHg}$ vs $77.47 \pm 14.41 \text{ mmHg}$, $P = 0.001$) of the EDM group were significantly lower, while the prevalence of hypertension (HP) (79.5% vs 52.9% , $P = 0.005$) were significantly higher than those of the MDM group. There was no significant difference in fasting blood glucose, hemoglobin A1c, uric acid, creatinine and blood lipid levels between the two groups. (Table 1)

Table 1
Comparison of general clinical data of EDM and MDM patients

| Variables | EDM | MDM | P |
|--|----------------|----------------|---------|
| n | 73 | 34 | |
| Male [n,(%)] | 56 (76.7) | 22 (64.7) | 0.536 |
| Age(yrs) | 81.08 ± 5.36 | 56.68 ± 5.24 | < 0.001 |
| BMI(kg/m) | 25.68 ± 3.23 | 27.29 ± 3.50 | 0.021 |
| SBP(mmHg) | 142.03 ± 18.20 | 135.26 ± 23.12 | 0.139 |
| DBP(mmHg) | 68.25 ± 9.21 | 77.47 ± 14.41 | 0.001 |
| Anti-diabetes drugs | | | |
| sulfonylurea[n,(%)] | 13(17.8) | 6(17.6) | 0.507 |
| Insulin[n,(%)] | 43(58.9) | 19(55.9) | 0.528 |
| Others[n,(%)] | 17 (35.6) | 9 (26.5) | 0.223 |
| HP [n,(%)] | 58 (79.5) | 18 (52.9) | 0.005 |
| FBG(mmol/L) | 7.21 ± 3.30 | 7.33 ± 3.05 | 0.649 |
| HbA _{1c} (%) | 7.47 ± 1.70 | 7.69 ± 2.16 | 0.456 |
| TC(mmol/L) | 4.38 ± 1.16 | 4.69 ± 1.05 | 0.375 |
| TG(mmol/L) | 1.45 ± 0.94 | 2.01 ± 1.07 | 0.012 |
| HDL-C(mmol/L) | 1.23 ± 0.28 | 1.21 ± 0.41 | 0.830 |
| LDL-C(mmol/L) | 2.53 ± 0.89 | 2.57 ± 0.79 | 0.284 |
| UA(umol/L) | 335.16 ± 99.02 | 321.13 ± 91.65 | 0.501 |
| Cr(umol/L) | 80.07 ± 17.71 | 74.29 ± 25.65 | 0.655 |
| BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HP, hypertension; FBG, fast blood glucose; HbA _{1c} , hemoglobin A1c; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; UA, uric acid; Cr, Creatinine. | | | |

Comparison Of Hypoglycemia Between Edm And Mdm Groups

The incidences of grade 1 hypoglycemia (55.9% vs 64.7%, P = 0.403) and grade 2 hypoglycemia (15.1% vs 20.6%, P = 0.477) in EDM group were lower than those of the MDM group, but the differences were not

statistically significant. For the occurrence time of hypoglycemia, 20 case-times occurred during the day and 23 case-times occurred at night in the EDM group, and in the MDM group, 13 case-times occurred during the day and 11 case-times occurred at night. (6am-10 pm during the day; 10 pm-6am at night).

Comparison of blood glucose fluctuation indicators between EDM and MDM groups

The SDBG (2.39 ± 1.00 mmol/L vs 2.00 ± 0.82 mmol/L, $P = 0.048$), LAGE (9.53 ± 3.37 mmol/L vs 7.84 ± 2.64 mmol/L, $P = 0.011$) and MAGE (5.77 ± 2.16 mmol/L vs 4.63 ± 1.89 mmol/L, $P = 0.026$) in EDM group were significantly higher than those of the MDM group. These results suggested that patients of EDM have greater blood glucose fluctuations. (Table 2)

Table 2

Comparison of the blood glucose variability index between the groups of EDM and MDM (mean \pm SD)

| Variables | EDM | MDM | <i>P</i> |
|--|-----------------|-----------------|----------|
| n | 73 | 31 | |
| SDBG(mmol/L) | 2.39 ± 1.00 | 2.00 ± 0.82 | 0.048 |
| LAGE(mmol/L) | 9.53 ± 3.37 | 7.84 ± 2.64 | 0.011 |
| MAGE(mmol/L) | 5.77 ± 2.16 | 4.63 ± 1.89 | 0.026 |
| MODD(mmol/L) | 2.13 ± 1.09 | 1.72 ± 1.03 | 0.063 |
| SDBG, Standard Deviations of Blood Glucose; LAGE = Large Amplitude of Glycemic Excursion; MAGE, Mean Amplitude of Glycemic Excursion; MODD, Absolute Means of Daily Differences. | | | |

Comparison of heart rate and arrhythmia between EDM and MDM groups

The maximum heart rate (100.26 ± 13.73 vs 112.27 ± 20.75 , $P = 0.017$) and average heart rate (67.93 ± 9.82 vs 73.22 ± 9.03 , $P = 0.026$) in the EDM group were significantly lower than those in the MDM group. There was no significant difference of the minimum heart rate between the two groups. The incidences of atrial premature beat, couplets of atrial premature beat, atrial tachycardia, ventricular premature beat and couples of ventricular premature beat in the EDM group were significantly higher than those in the MDM group (all $P < 0.05$). The mean QTc interval (0.47 ± 0.01 vs 0.45 ± 0.00 , $P = 0.029$) in the EDM group was significantly longer than that of the MDM group. (Table 3)

Table 3 Comparison of arrhythmia indicators between the groups of EDM and MDM

| | n | Maximal heart rate (mean±SD) | Minimal heart rate (mean±SD) | Mean heart rate (mean±SD) | APB [M(Q1, Q3)] | Couplets of A [M(Q1, Q3)] | AT [M(Q1, Q3)] |
|----------|----|------------------------------|------------------------------|---------------------------|-----------------|---------------------------|----------------|
| EDM | 73 | 100.26±13.73 | 51.84±9.99 | 67.93±9.82 | 135(35,382) | 2(1,8) | 1(0,3) |
| MDM | 34 | 112.27±20.75 | 56.82±17.84 | 73.22±9.03 | 7(2,18) | 0(0,0) | 0(0,0) |
| <i>P</i> | | 0.017 | 0.222 | 0.026 | ∞0.001 | ∞0.001 | ∞0.001 |

| | n | VPB [M(Q1, Q3)] | Couplets of V [M(Q1, Q3)] | VT [M(Q1, Q3)] | Mean QTc (s) (mean±SD) |
|----------|----|-----------------|---------------------------|----------------|------------------------|
| EDM | 73 | 25(3,303) | 0(0,0) | 0(0,0) | 0.47±0.01 |
| MDM | 34 | 1(0,3) | 0(0,0) | 0(0,0) | 0.45±0.00 |
| <i>P</i> | | ∞0.001 | 0.034 | 0.122 | 0.029 |

APB, atrial premature beats∞Couplets of A, Couplets of atrial premature beats∞ AT, atrial tachycardia∞ VPB, ventricular premature beats∞ Couplets of V, Couplets of ventricular premature beats∞ VT, ventricular tachycardia.

Comparison of arrhythmias between EDM group and MDM group under different MAGE layers

In patients of MAGE1 (1.24–4.37 mmol/L), the number of atrial premature beat ($P = 0.012$) was significantly higher in the EDM group. In patients of MAGE2 (4.38–6.36 mmol/L), atrial premature beat ($P < 0.001$), couples of atrial premature beat ($P < 0.001$), atrial tachycardia ($P = 0.001$), and ventricular premature beat ($P < 0.001$) occurred significantly more frequent in the EDM group. The QTc interval (0.48 ± 0.01 s vs 0.45 ± 0.01 s, $P = 0.047$) was significantly longer in the EDM group. In patients of MAGE3 (6.37–13.66 mmol/L), we also found significant higher incidences of atrial premature beat ($P < 0.001$), couples of atrial premature beat ($P < 0.001$), atrial tachycardia ($P < 0.001$), and ventricular premature beat ($P = 0.013$) in EDM group. (Table 4)

Table 4

Difference in arrhythmia according to MAGE and the tertiles MAGE between the groups of EDM and MDM

| Variables | | EDM | MDM | P |
|---|---------------------------|---------------|-------------|--------|
| n | | 28 | 8 | |
| MAGE1 | APB [M(Q1, Q3)] | 129(44.5,228) | 18(4,51) | 0.012 |
| | Couplets of A [M(Q1, Q3)] | 2.5(1,7) | 2(0,4.5) | 0.256 |
| | AT [M(Q1, Q3)] | 1(0,4) | 0.5(0,1.5) | 0.127 |
| | VPB [M(Q1, Q3)] | 21(2,237.5) | 0(0,49) | 0.083 |
| | Couplets of V [M(Q1, Q3)] | 0(0,0) | 0(0,0) | 0.279 |
| | VT [M(Q1, Q3)] | 0(0,0) | 0(0,0) | 0.472 |
| | Mean QTc (s)(mean ± SD) | 0.45 ± 0.01 | 0.46 ± 0.01 | 0.362 |
| n | | 24 | 12 | |
| MAGE2 | APB [M(Q1, Q3)] | 108(23.5,450) | 7(2,15.5)) | <0.001 |
| | Couplets of A [M(Q1, Q3)] | 2(0,5) | 0(0,0) | <0.001 |
| | AT [M(Q1, Q3)] | 1(0,3) | 0(0,0) | 0.001 |
| | VPB [M(Q1, Q3)] | 97.5(4,923) | 1.5(0,3) | <0.001 |
| | Couplets of V [M(Q1, Q3)] | 0(0,0) | 0(0,0) | 0.221 |
| | VT [M(Q1, Q3)] | 0(0,0) | 0(0,0) | 0.331 |
| | Mean QTc (s)(mean ± SD) | 0.48 ± 0.01 | 0.45 ± 0.01 | 0.047 |
| n | | 21 | 14 | |
| MAGE3 | APB [M(Q1, Q3)] | 210(46,750) | 5.5(4,9) | <0.001 |
| | Couplets of A [M(Q1, Q3)] | 4(1,28) | 0(0,0) | <0.001 |
| | AT [M(Q1, Q3)] | 2(1,7) | 0(0,0) | <0.001 |
| | VPB [M(Q1, Q3)] | 7(2,196) | 0.5(0,4) | 0.013 |
| | Couplets of V [M(Q1, Q3)] | 0(0,0) | 0(0,0) | 0.259 |
| | VT [M(Q1, Q3)] | 0(0,0) | 0(0,0) | 0.448 |
| | Mean QTc (s)(mean ± SD) | 0.47 ± 0.01 | 0.45 ± 0.01 | 0.234 |
| APB, atrial premature beats;Couplets of A, Couplets of atrial premature beats; AT, atrial tachycardia; VPB, ventricular premature beats; Couplets of V, Couplets of ventricular premature beats; VT, ventricular tachycardia. | | | | |

Comparison of arrhythmias in patients with hypoglycemic events between EDM and MDM groups

The maximum heart rate (99.52 ± 12.47 beat/min vs 111.83 ± 18.08 beat/min, $P = 0.006$) and mean heart rate (67.60 ± 9.28 beat/min vs 74.26 ± 8.93 beat/min, $P = 0.007$) in EDM patients were significantly lower than those of MDM patients, while the minimum heart rate was not significantly different. The incidences of atrial premature beat ($P < 0.001$), couples of atrial premature beat ($P < 0.001$), atrial tachycardia ($P < 0.001$) and ventricular premature beat ($P = 0.002$) in patients with EDM were significantly higher than those in the MDM group. (Table 5)

Table 5 Comparison of arrhythmias in patients with HE in groups of EDM and MDM

| HE | n | Maximal heart rate (mean±SD) | Minimal heart rate (mean±SD) | Mean heart rate (mean±SD) | APB [M(Q1, Q3)] | Couplets of A [M(Q1, Q3)] | AT [M(Q1, Q3)] |
|----------|-------|------------------------------|------------------------------|---------------------------|-----------------|---------------------------|----------------|
| EDM | 42/73 | 99.52±12.47 | 53.14±9.41 | 67.60±9.28 | 120(34,379) | 2(1,6) | 1(0,3) |
| MDM | 23/34 | 111.83±18.08 | 58.09±17.19 | 74.26±8.93 | 7(2,22) | 0(0,2) | 0(0,0) |
| <i>P</i> | | 0.006 | 0.211 | 0.007 | 0.001 | 0.001 | 0.001 |

| HE | n | VPB [M(Q1, Q3)] | Couplets of V [M(Q1, Q3)] | VT [M(Q1, Q3)] | Mean QTc (s) (mean±SD) |
|----------|-------|-----------------|---------------------------|----------------|------------------------|
| EDM | 42/73 | 14.5(2,278) | 0(0,0) | 0(0,0) | 0.45±0.01 |
| MDM | 23/34 | 1(0,14)) | 0(0,0) | 0(0,0) | 0.46±0.01 |
| <i>P</i> | | 0.002 | 0.199 | 0.302 | 0.135 |

HE, hypoglycemic event. APB, atrial premature beats; Couplets of A, Couplets of atrial premature beats; AT, atrial tachycardia; VPB, ventricular premature beats; Couplets of V, Couplets of ventricular premature beats; VT, ventricular tachycardia.

Discussion

Controlling blood glucose fluctuations in diabetic patients has gradually become an emerging therapeutic target for improving diabetes metabolism and preventing related complications¹². Large cohort studies have shown that blood glucose fluctuations are not only an important predictor of mortality in diabetic patients but also in non-diabetic patients¹³. MAGE is the "gold standard" which can best reflect the blood glucose fluctuation¹⁴. However, up to now, there are few reports comparing the effects of glycemic variability on arrhythmias between the middle-aged and the elderly patients. Our current study found that the levels of SDBG, LAGE and MAGE in EDM group were statistically higher than those in MDM group, indicating the greater blood glucose fluctuations in EDM patients. Accordingly, the incidences of

supraventricular and ventricular arrhythmia were higher in EDM groups. Thus, it may be more meaningful to monitor the blood glucose fluctuations and act corresponding treatment to prevent severe arrhythmia in elder T2DM patients.

ADVANCE study found that T2DM patients with severe hypoglycemia had a threefold increased risk of major cardiovascular events and a twofold increased risk of microvascular complications¹⁵. History of episodes of severe hypoglycemia was associated with increased incidence of new atrial fibrillation and all-cause mortality¹⁶. In patients with T2DM complicated with cardiovascular disease, the incidence of bradycardia, atrial premature beat and ventricular premature beat was high, especially when spontaneous hypoglycemia occurs in patients during sleep at night¹⁷. Due to the course of disease, age and other reasons, the decline of β cell function in EDM patients is more obvious than that in young and middle-aged T2DM patients, which may lead to the greater amplitude of blood glucose fluctuation¹⁴. Our research shows that although the incidence of hypoglycemia was not obvious different in patients between EDM and MDM groups, the incidences of atrial premature beat, couples of atrial premature beat, atrial tachycardia and ventricular premature beat were significant higher in EDM patients, suggesting the elderly patients were more prone to supraventricular and ventricular arrhythmia.

Prolonged cardiac repolarization causes fatal cardiac arrhythmias. The prolongation of QTc is a strong risk factor for severe ventricular arrhythmia and sudden death. Studies have shown that experimental hypoglycemia caused acquired long QTc syndrome¹⁸, probably through sympathoadrenal stimulation and catecholamine-mediated hypokalemia. Up to now, few studies showed the association between glycemic variability and QT interval and dispersion. Ninkovic et al. mentioned about the GV as a risk factor of prolonged QT interval and QT dispersion¹⁹. Another study showed that in patients with T2DM, increased glycemic variability is associated with prolonged QTc duration and QTc dispersion¹⁰. Our present study demonstrated that the average QTc interval was significantly longer than that of MDM patients, suggesting that the elderly were prone to arrhythmia than the middle-aged subjects.

Previous studies found that the rapid fluctuation of average blood glucose fluctuation (MAGE > 5 mmol/L) increased the vulnerability of the electrical stability of the heart, leading to higher incidence of arrhythmia, such as atrial fibrillation^{20, 21}. In our study, the incidences of atrial premature beat, couples of atrial premature beat, atrial tachycardia and ventricular premature beat of EDM patients in MAGE2 and MAGE3 groups were significantly higher than those of MDM patients. Our study also analyzed the incidence of arrhythmia between EDM and MDM patients with HE. The incidences of atrial premature beat, couples of atrial premature beat, atrial tachycardia and ventricular premature beat in EDM patients were significantly higher than those in MDM patients. These results suggested that the elderly patients with moderate or high blood glucose fluctuations are more likely to cause arrhythmias.

The limitation of this study should be also considered. The dynamic ECG only collects 24-hour ECG data, thus dynamic blood glucose also only analyses the corresponding 24-hour data. In future studies, we will continue to synchronize dynamic ECG and dynamic blood glucose monitoring for 72 hours in order to more accurately reflect the relationship between blood glucose fluctuation and arrhythmia, and further

explore the correlation between abnormal blood glucose fluctuation and complications such as macrovascular, microvascular and nervous system in elderly patients with T2DM.

Conclusions

The elderly patients with cardiovascular disease had greater fluctuation of blood glucose and the incidences of arrhythmia. Thus, the risk of arrhythmia in elderly patients with cardiovascular disease is significantly greater than that in elderly patients due to fluctuation of blood glucose and hypoglycemia. Therefore, active control of blood glucose fluctuation in elderly patients will help to reduce the risk of severe arrhythmia.

Abbreviations

CGM, continuous blood glucose monitoring; ECG, electrocardiogram; T2DM, type 2 diabetes; EDM, elderly diabetes mellitus group; MDM, middle-aged diabetes mellitus; SDBG, standard deviation; LAGE, largest amplitude of glycemic excursions; MAGE, mean amplitude of glycemic excursions; MODD, absolute means of daily differences; WHO, World Health Organization; HE, Hypoglycemic events; APB, atrial premature beat; Couplets of A, Couplets of atrial premature beat; AT, atrial tachycardia; VPB, ventricular premature beat; Couplets of V, Couplets of ventricular premature beat; VT, ventricular tachycardia; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HP, hypertension; FBG, fast blood glucose; HbA1C, hemoglobin A1c; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; UA, uric acid; Cr, Creatinine.

Declarations

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Conflicts of interests

The authors declare they have no conflicts of interests.

Author contributions:

KXT designed the study. JBZ, JMY and KXT prepared the first draft of the paper. JBZ, LWL and SW were responsible for statistical analysis of the data. KXT, JBZ, LWL and LYL designed the methodology for searching. LWL, JYC, LYL and JBZ performed the data collection. All authors revised the paper critically for intellectual content and approved the final version. All authors agree to be accountable for the work and to ensure that any questions relating to the accuracy and integrity of the paper are investigated and properly resolved.

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