·全军老年医学会议专栏·

糖尿病肾病和血糖控制的关系及相关危险因素分析

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【摘 要】 **目的** 探讨糖尿病肾病(DKD)与血糖控制指标关系以及相关危险因素。**方法** 回顾性分析2010年3月至2016年12月在西京医院老年病科住院且使用持续血糖监测系统(CGMS)的2型糖尿病(T2DM)患者142例,根据是否伴有DKD分为DKD组($n=54$)和非DKD组($n=88$)。收集患者一般临床资料、实验室指标及CGMS结果,分析DKD与血糖控制指标关系并对其危险因素进行综合分析。采用SPSS 19.0统计软件对数据进行分析,组间比较采用t检验、非参数检验或χ^2检验。Spearman秩相关分析两变量相关性,多因素分析采用逐步二元logistic回归分析。**结果** 相比非DKD组,DKD组患者年龄偏大、病程长、高血压病史比例较高、高密度脂蛋白胆固醇(HDL-C)水平偏低、双胍类降糖药物使用率明显降低,糖化血红蛋白A1c(HbA1c)水平、完整24 h高血糖时间波动百分比、高血糖曲线下面积(AUC)、餐后2 h血糖(2h-PBG)和24 h平均血糖水平(MBG)显著升高,差异有统计学意义($P<0.05$);胱抑素C(CysC)、尿素氮(BUN)、血肌酐(SCr)水平显著高于非DKD组,估算肾小球滤过率(eGFR)显著低于非DKD组,差异有统计学意义($P<0.001$)。Spearman相关分析结果显示,DKD与年龄、病程、高血压史、HbA1c、24 h高血糖时间波动百分比、高血糖AUC、24 h MBG、2h-PBG均呈正相关,与HDL-C呈负相关($r=-0.205$,$P=0.014$)。逐步二元logistic回归分析结果显示年龄($OR=1.048$,95% CI 1.022~1.074;$P=0.000$)和HbA1c($OR=1.569$,95% CI 1.212~2.031;$P=0.001$)与DKD呈正相关。**结论** HbA1c是T2DM患者发生DKD的主要危险因素,DKD的发生与血糖波动并无显著相关。

【关键词】 2型糖尿病;糖尿病肾病;血糖;血糖控制
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Relationship between diabetic kidney disease and glucose control in type 2 diabetes mellitus patients and analysis of relative risk factors

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【Abstract】 **Objective** To investigate the relationship of diabetic kidney disease (DKD) with glucose control in the patients with type 2 diabetes mellitus (T2DM) and to analyze the related risk factors. **Methods** A total of 142 T2DM patients who received continuous glucose monitoring (CGM) in the Geriatric Department of Xijing Hospital from March 2010 to December 2016 were recruited in the study. The patients were divided into DKD group ($n=54$) and non-DKD group ($n=88$). The general clinical data, and laboratory indices and CGM data of the subjects were collected. The relationship between DKD and glucose control and the effect of risk factors were analyzed. SPSS statistics 19.0 was used to analyze the data. Student's t test, non-parametric test or Chi-square test was employed for the comparison between groups. Spearman rank correlation analysis was adopted for the correlation of 2 variables, and stepwise binary logistic regression was used for multivariate analysis. **Results** Compared with the patients of the non-DKD group, those in DKD group were older, and had longer duration of DM, higher ratio of hypertension, lower level of high-density lipoprotein cholesterol (HDL-C), lower utilization ratio of guanidine, higher glycosylated hemoglobin (HbA1c) level, larger percentage of 24-hour hyperglycemia fluctuation time, larger area under hyperglycemic curve (AUC), higher postprandial 2-hour blood glucose (2h-PBG) and 24-hour mean blood glucose (24h-MBG) (all $P<0.05$). They also had higher levels of cystatin C (CysC), blood urea nitrogen (BUN), and serum creatinine (SCr), but obviously lower estimated glomerular filtration rate (eGFR) than the patients of the non-DKD group ($P<0.001$). Spearman's correlation analysis showed that DKD was positively correlated with age, duration of

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the disease, hypertension history, HbA1c level, percentage of hyperglycemia fluctuation time, AUC of hyperglycemia, 24h-MBG and 2h-PBG, while negatively correlated with HDL-C ($r = -0.205$, $P = 0.014$). Logistic regression analysis indicated that age ($OR = 1.048$, 95% CI 1.022 – 1.074, $P = 0.000$) and HbA1c ($OR = 1.569$, 95% CI 1.212 – 2.031, $P = 0.001$) had positive correlation with DKD. **Conclusion** HbA1c is a major risk factor of DKD in T2DM patients, and the occurrence of DKD is not associated with glucose fluctuation.

【Key words】 type 2 diabetes mellitus; diabetic kidney disease; blood glucose; glucose control

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大规模流行病学调查研究结果显示,糖尿病目前已成为我国三大慢性非传染性疾病之一[1,2]。糖尿病肾病(diabetic kidney disease,DKD)是常见的糖尿病微血管并发症,其发病率高,危害严重,是导致终末期肾病(end-stage renal disease, ESRD)和心血管死亡的主要原因[3]。因此,筛选其危险因素并早期预防DKD的发生,已成为一个重要的临床问题。以往研究显示,DKD与糖尿病病程、高血压、高血脂等众多因素相关,而血糖是DKD重要的决定因素,疾病发生发展与糖化血红蛋白(glycosylated hemoglobin A1c, HbA1c)水平呈正相关。然而HbA1c反映的是过去3个月的平均血糖水平,完整血糖谱还应包括短期内血糖平均水平、空腹血糖(fasting blood glucose,FBG)水平、餐后血糖水平、低血糖反应以及血糖波动,许多研究人员发现血糖波动是除血糖水平外反映血糖控制状况的重要指标,并且血糖波动与糖尿病大血管及微血管并发症密切相关[4,5]。因此,本研究通过持续血糖监测系统(continuous glucose monitoring system, CGMS)采集患者动态血糖数据后,分析DKD与血糖控制指标关系以及相关危险因素。

1 对象与方法

1.1 研究对象

回顾性分析2010年3月至2016年12月在西京医院老年病科住院且使用CGMS的2型糖尿病(type 2 diabetes mellitus,T2DM)患者142例,根据是否伴有DKD分为DKD组($n = 54$)和非DKD组($n = 88$)。纳入标准:(1)糖尿病病程至少半年以上;(2)入院前3个月内未更换降糖药物。排除标准:(1)伴有糖尿病急性并发症,如糖尿病酮症酸中毒、高血糖昏迷等;(2)严重感染及重度心、肝、肾功能不全者;(3)急性肾损伤、肾病综合征、狼疮性肾炎等其他肾脏疾病患者;(4)恶性肿瘤晚期患者。DKD诊断标准参考《中国2型糖尿病防治指南(2013年版)》[2]。微量白蛋白尿是DKD早期的临床表现,也是诊断DKD的主要依据。微量白蛋白尿的评价标准为尿白蛋白排泄率≥30 mg/24 h,或尿白蛋白/肌酐增高(男性≥2.5 mg/mmol,女性≥3.5 mg/mmol),排除感染等其他因素后3次检测结果中有2次升高即诊断为DKD。

1.2 方法

1.2.1 一般临床资料和实验室检查 收集患者入院时的一般临床资料,包括年龄、性别、病程、吸烟史、高血压史、降糖药物使用情况。FBG、甘油三脂(triglycerides, TG)、总胆固醇(total cholesterol, TC)、低密度脂蛋白胆固醇(low-density lipoprotein cholesterol, LDL-C)、高密度脂蛋白胆固醇(high-density lipoprotein cholesterol, HDL-C)、丙氨酸氨基转移酶(alanine amino transferase,ALT)、天门冬氨酸氨基转移酶(aspartate amino transferase,AST)、胱抑素C(cystatin C, Cys C)、尿素氮(blood urea nitrogen, BUN)、血肌酐(serum creatinine,SCr)等采用酶法检测,HbA1c采用离子交换高效液相色谱法测定。根据慢性肾脏疾病流行病学协作组(chronic kidney disease-epidemiology collaboration, CKD-EPI)公式[6]计算估算肾小球滤过率(estimated glomerular filtration rate,eGFR)。

1.2.2 动态血糖监测 由专业技师将CGMS(Medtronic MiniMed公司,美国)置于受试者腹部皮下,每天至少输入4次指尖血糖进行校正,并输入进餐、运动、降糖药物、低血糖反应等事件,连续佩戴72 h后取下感应器,每天收集288个血糖值,采用CGMS报告管理系统V 3.0进行数据分析,统计完整血糖谱,包括FBG、餐后2 h血糖(postprandial 2-hour blood glucose,2h-PBG)。计算24 h平均血糖水平(mean blood glucose,MBG)、完整24 h高血糖波动时间百分比和高血糖曲线下面积(area under curve,AUC)。血糖波动指标包括血糖标准差(standard deviation of blood glucose,SDBG)、平均血糖波动幅度(mean amplitude of glycemic excursions, MAGE)、最大血糖波动幅度(largest amplitude of glycemic excursions,LAGE)以及低血糖发生率。

1.3 统计学处理

采用SPSS 19.0统计软件对数据进行分析。计量资料呈正态分布者用均数±标准差($\bar{x} \pm s$)表示,

方差齐时两组比较采用 t 检验，方差不齐时比较采用 t' 检验。呈偏态分布者用四分位数间距表示，组间比较采用非参数检验。计数资料用百分率表示，组间比较用 χ^2 检验。采用 Spearman 秩相关分析两变量相关性，多因素分析采用逐步二元 logistic 回归分析。$P<0.05$ 为差异有统计学意义。

2 结 果

2.1 两组患者基线资料比较

两组患者性别、吸烟者比例、TG、TC、LDL-C、ALT、AST 水平差异无统计学意义（$P>0.05$）。相比非 DKD 组，DKD 组患者年龄偏大、病程长、高血压病史比例较高、HDL-C 水平偏低，双胍类降糖药物使用率明显降低，差异有统计学意义（$P<0.05$）；Cys C、BUN、SCr 水平显著高于非 DKD 组，eGFR 显著低于非 DKD 组，差异有统计学意义（$P<0.001$；表 1）。

2.2 两组患者血糖控制指标比较

两组患者 FBG、低血糖发生率及 SDBG、MAGE、LAGE 等指标差异无统计学意义（$P>0.05$）。相比非 DKD 组患者，DKD 组患者的糖化 HbA1c 水平、完整 24 h 高血糖时间波动百分比、高血糖 AUC、2h-PBG 和 24 h MBG 显著升高，差异有统计学意义（$P<0.05$；表 2）。

2.3 DKD 影响因素的分析

DKD 影响因素 Spearman 相关分析结果显示，DKD 与年龄、病程、高血压史、糖化 HbA1c、24 h 高血糖时间波动百分比、高血糖 AUC、24 h MBG、2h-PBG 均呈正相关，与 HDL-C 呈负相关（表 3）。以有无 DKD 为因变量，以上述因素为自变量进行逐步二元 logistic 回归分析，结果显示年龄（$OR=1.048$，95% CI 1.022 ~ 1.074；$P=0.000$）和 HbA1c（$OR=1.569$，95% CI 1.212 ~ 2.031；$P=0.001$）与 DKD 呈正相关。

3 讨 论

本研究结果表明 T2DM 患者 DKD 的发生与糖化 HbA1c、24 h MBG、2h-PBG、24 h 高血糖时间波动百分比及高血糖 AUC 呈正相关，而与血糖波动指标无关。患者的年龄和糖化 HbA1c 是 DKD 风险增加的主要危险因素。

表 1 两组患者基线资料比较

Table 1 Comparison of baseline data between two groups

Item	Non-DKD group ($n=88$)	DKD group ($n=54$)	t/χ^2	P value
Male/female (n/n)	72/16	50/4	3.210	0.073
Age [years, $M(Q_1, Q_3)$]	58(49,79)	75(56,82)	3.176	0.001
Duration of disease [year, $M(Q_1, Q_3)$]	8(5,13)	12(5,20)	2.742	0.006
Smoking [n(%)]	26(29.55)	17(31.48)	0.059	0.807
Hypertension [n(%)]	59(67.05)	45(83.33)	4.530	0.033
Antidiabetic [n(%)]				
Sulfonylureas	8(9.09)	4(7.41)	0.123	0.726
Glinides	11(12.50)	7(12.96)	0.006	0.936
Biguanides	36(40.91)	8(14.81)	10.656	0.001
Thiazolidinediones	1(1.14)	2(3.70)	1.067	0.302
α-glucosidase inhibitors	20(22.73)	8(14.81)	1.324	0.250
DPP-4 inhibitors	5(5.68)	2(3.70)	0.279	0.597
Insulin	48(54.55)	38(70.37)	3.509	0.061
TG [mmol/L, $M(Q_1, Q_3)$]	1.36(0.98,1.87)	1.48(0.95,2.50)	0.832	0.405
TC [mmol/L, $M(Q_1, Q_3)$]	3.91(3.30,4.49)	4.00(3.38,4.48)	0.435	0.664
LDL-C (mmol/L, $\bar{x}\pm s$)	2.36 ± 0.92	2.33 ± 0.63	−0.233	0.816
HDL-C (mmol/L, $\bar{x}\pm s$)	1.06 ± 0.26	0.96 ± 0.26	−2.250	0.026
ALT [U/L, $M(Q_1, Q_3)$]	24(16,38)	17(12,27)	−1.771	0.079
AST [U/L, $M(Q_1, Q3)$]	19(16,25)	16(13,20)	−0.912	0.364
CysC [mg/L, $M(Q_1, Q_3)$]	0.99(0.87,1.14)	1.27(1.06,1.69)	5.321	0.000
BUN (mmol/L, $\bar{x}\pm s$)	4.98 ± 1.29	6.68 ± 1.89	5.809	0.000
SCr (μmol/L, $\bar{x}\pm s$)	94.73 ± 13.33	120.61 ± 27.01	6.568	0.000
eGFR [ml/(min · 1.73 m^2), $M(Q_1, Q_3)$]	70.87(63.12,80.46)	51.98(41.20,68.92)	5.654	0.000

DKD: diabetic kidney disease; DPP-4: dipeptidyl peptidase-4; TG: triglycerides; TC: total cholesterol; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; ALT: alanine amino transferase; AST: aspartate amino transferase; Cys C: cystatin C; BUN: blood urea nitrogen; SCr: serum creatinine; eGFR: estimated glomerular filtration rate

表2 两组患者血糖控制指标比较

Table 2 Comparison of glycemic indices between two groups

Item	Non-DKD group ($n=88$)	DKD group ($n=54$)	t/χ^2	P
FBG[mmol/L, $M(Q_1, Q_3)$]	6.97(5.60,8.59)	7.16(5.38,10.53)	0.700	0.484
HbA1c(%, $\bar{x}\pm s$)	7.53±1.51	8.39±1.72	3.128	0.002
Percentage of hyperglycemia fluctuation time[%, $M(Q_1, Q_3)$]	10.00(0.00, 24.75)	27.50(8.00,50.75)	3.359	0.001
Area under hyperglycemic curve[$M(Q_1, Q_3)$]	0.10(0.00,0.55)	0.40(0.10,1.65)	3.176	0.001
Hypoglycemia[n(%)]	5(5.68)	5(9.26)	0.654	0.419
MBG[mmol/L, $M(Q_1, Q_3)$]	8.25(7.40,9.68)	9.55(7.88,11.78)	2.888	0.004
2h-PBG[mmol/L, $M(Q_1, Q_3)$]	9.48(8.28,11.40)	11.62(8.37,13.39)	2.423	0.015
SDBG[mmol/L, $M(Q_1, Q_3)$]	2.00(1.50,2.70)	2.15(1.80,2.90)	1.684	0.092
MAGE[mmol/L, $M(Q_1, Q_3)$]	4.69(3.22,6.81)	4.94(3.97,6.89)	1.122	0.262
LAGE[mmol/L, $M(Q_1, Q_3)$]	8.64±3.58	9.80±3.38	1.981	0.058

DKD: diabetic kidney disease; FBG: fasting blood glucose; HbA1c: glycosylated hemoglobin A1c; MBG: mean blood glucose; 2h-PBG: postprandial 2-hour blood glucose; SDBG: standard deviation of blood glucose; MAGE: mean amplitude of glycemic excursions; LAGE: largest amplitude of glycemic excursions

表3 DKD影响因素的Spearman相关分析

Table 3 Spearman correlation analysis of influencing factors of DKD

Factor	r	P value
Age	0.267	0.001
Duration of disease	0.231	0.006
Hypertension	0.179	0.033
HDL-C	−0.205	0.014
HbA1c	0.259	0.002
Percentage of hyperglycemia fluctuation time	0.283	0.001
Area under hyperglycemic curve	0.267	0.001
MBG	0.243	0.004
2h-PBG	0.204	0.015

DKD: diabetic kidney disease; HDL-C: high-density lipoprotein cholesterol; HbA1c: glycosylated hemoglobin A1c; MBG: mean blood glucose; 2h-PBG: postprandial 2-hour blood glucose

DKD是糖尿病主要微血管并发症之一,是欧美国家ESRD的最主要原因[3]。其发病机理与多种因素密切相关,包括糖代谢紊乱、糖基化终末产物的生成和积聚、多元醇通路活化、蛋白激酶C激活、血流动力学异常、氧化应激、细胞因子(血管内皮生长因子、肿瘤坏死因子-α)等。本研究表明DKD组患者年龄偏大、病程长、高血压病史比例较高、HDL-C水平偏低,Cys C、BUN、SCr水平显著高于非DKD组,eGFR显著低于非DKD组,差异具有统计学意义($P<0.001$)与以往研究结果相似[7]。近期国外一项大型临床研究结果提示较低水平的HDL-C是T2DM患者DKD发生发展的独立危险因素[8],本研究也表明DKD与HDL-C呈负相关。

DCCT研究组结果表明,强化降糖可使T1DM患者微血管并发症的发生降低50%~60%[9]。UKPDS研究组同样发现对于新诊断的T2DM患者,强化降糖可显著改善微血管并发症[10]。因此,HbA1c被认为是糖尿病微血管并发症最重要的危险因素[11,12],可作为预测微血管并发症的"金标准"。本研究结果也表明HbA1c与DKD呈正相关。相关研究表明,HbA1c与死亡率的相关呈U型曲线,严格地控制血糖会引发低血糖,从而增加心血管死亡的发生。ADVANCE、ACCRDS以及Duckworth等[13-15]的研究均表明强化降糖(HbA1c<6.5%)虽可显著降低微血管并发症的发生,延缓蛋白尿进展,但却会显著增加心血管事件及患者的死亡风险。因此,改善全球肾脏病预后组织推荐HbA1c水平控制在7%则能有效降低糖尿病微血管并发症,同时应个体化调整HbA1c水平。

血糖波动与DKD是否相关,目前尚无定论。周健等[16]通过对HbA1c<6.5%的T2DM患者进行动态血糖监测,发现血糖波动是患者发生微量白蛋白尿的危险因素。也有研究表明血糖波动与氧化应激指标丙二醛是导致T2DM肾病患者蛋白尿严重程度的危险因素,而超氧化物歧化酶是其保护因素,表明血糖波动促进氧化应激,从而参与DKD的发生与发展[17]。本研究结果未表明DKD与低血糖发生、SDBG、MAGE、LAGE等血糖波动指标存在相关性,考虑与研究样本的数量及采集有关,需在以后的研究中扩大样本量继续探讨。

综上所述,血糖控制是DKD发生发展的决定性因素,HbA1c是预测"金标准",应根据患者年龄、病程、低血糖反应、是否合并心血管疾病等因素,制定个体化的降糖目标值,从而更好地减少糖尿病微血管并发症和大血管并发症的发生。

【参考文献】

[1] Xu Y, Wang L, He J, *et al*. Prevalence and control of diabetes in Chinese adults[J]. JAMA, 2013, 310(9): 948-959. DOI: 10.1001/jama.2013.168118.

[2] 中华医学会糖尿病学分会. 中国2型糖尿病防治指南(2013年版)[J]. 中华糖尿病杂志, 2014, 6(7): 447-497.
Chinese Diabetes Society. Guidelines for prevention and treatment of type 2 diabetes in China (2013 Ed)[J]. Chin J Diabetes Mellitus, 2014, 6(7): 447-497.

[3] Tuttle KR, Bakris GL, Bilous RW, *et al*. Diabetic kidney disease: a report from an ADA consensus conference[J]. Am J Kidney Dis, 2014, 64(4): 510-533. DOI: 10.1053/j.ajkd.2014.08.001.

[4] Mi SH, Su G, Li Z, *et al*. Comparison of glycemic variability and glycated hemoglobin as risk factors of coronary artery disease in patients with undiagnosed diabetes[J]. Chin Med J (Engl), 2012, 125(1): 38-43.

[5] Bergenstal RM. Glycemic variability and diabetes complications: does it matter? Simply put, There are better glycemic markers![J]. Diabetes Care, 2015, 38(8): 1615-1621. DOI: 10.2337/dc15-0099.

[6] Levey AS, Stevens LA. Estimating GFR using the CKD Epidemiology Collaboration (CKD-EPI) creatinine equation: more accurate GFR estimates, lower CKD prevalence estimates, and better risk predictions[J]. Am J Kidney Dis, 2010, 55(4): 622-627. DOI: 10.1053/j.ajkd.2010.02.337.

[7] 杨永杰. 尿微量白蛋白在高血压和糖尿病肾病早期诊断的价值分析[J]. 中国实用医刊, 2016, 43(10): 6-7. DOI: 10.3760/cma.j.issn.1674-4756.2016.10.003.
Yang YJ. Value of microalbuminuria in hypertensive and early diagnosis of diabetic nephropathy[J]. Chin J Prac Med, 2016, 43(10): 6-7. DOI: 10.3760/cma.j.issn.1674-4756.2016.10.003.

[8] Russo GT, De Cosmo S, Viazzi F, *et al*. Plasma triglycerides and HDL-C levels predict the development of diabetic kidney disease in subjects with type 2 diabetes: the AMD annals initiative[J]. Diabetes Care, 2016, 39(12): 2278-2287. DOI: 10.2337/dc16-1246.

[9] Diabetes Control and Complications Trial Research Group, Nathan DM, Genuth S, *et al*. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus[J]. N Engl J Med, 1993, 329(14): 977-986. DOI: 10.1056/NEJM199309303291401.

[10] UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33)[J]. Lancet, 1998, 352(9131): 837-853.

[11] Zoppini G, Verlato G, Targher G, *et al*. Is fasting glucose variability a risk factor for retinopathy in people with type 2 diabetes?[J]. Nutr Metab Cardiovasc Dis, 2009, 19(5): 334-339. DOI: 10.1016/j.numecd.2008.02.007.

[12] Hirsch IB, Brownlee M. Beyond hemoglobin A1c-need for additional markers of risk for diabetic microvascular complications[J]. JAMA, 2010, 303(22): 2291-2292. DOI: 10.1001/jama.2010.785.

[13] ADVANCE Collaborative Group, Patel A, MacMahon S, *et al*. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes[J]. N Engl J Med, 2008, 358(24): 2560-2572. DOI: 10.1056/NEJMoa0802987.

[14] The Action to Control Cardiovascular Risk in Diabetes Study Group. Effects of intensive glucose lowering in type 2 diabetes[J]. N Engl J Med, 2008, 358(24): 2545-2559. DOI: 10.1056/NEJMoa0802743.

[15] Duckworth W, Abraira C, Moritz T, *et al*. Glucose control and vascular complications in veterans with type 2 diabetes[J]. N Engl J Med, 2009, 360(2): 129-139. DOI: 10.1056/NEJMoa0808431.

[16] 周健, 贾伟平, 马晓静, 等. 糖化血红蛋白控制理想的2型糖尿病患者血糖波动特征及其与微量白蛋白尿的关系[J]. 中华医学杂志, 2008, 88(42): 2977-2981. DOI: 10.3321/j.issn:0376-2491.2008.42.007.
Zhou J, Jia WP, Ma XJ, *et al*. Relationship between blood glucose variability and microalbuminuria in type 2 diabetic patients with well-controlled glycosylated hemoglobin[J]. Nat Med J Chin, 2008, 88(42): 2977-2981. DOI: 10.3321/j.issn:0376-2491.2008.42.007.

[17] 龙艳, 苏珂, 彭鹰, 等. 血糖波动与氧化应激对2型糖尿病微血管病变的影响[J]. 中华老年心脑血管病杂志, 2014, 16(2): 147-150. DOI: 10.3969/j.issn.1009-0126.2014.02.009.
Long Y, Su K, Peng Y, *et al*. Effect of blood glucose fluctuation and oxidative stress on microangiopathy in type 2 diabetes mellitus patients[J]. Chin J Geriatr Heart Brain Vessel Dis, 2014, 16(2): 147-150. DOI: 10.3969/j.issn.1009-0126.2014.02.009.

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