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ORIGINAL RESEARCH

Blood Glucose Fluctuation in Older Adults with Diabetes Mellitus and End-Stage Renal Disease on Maintenance Hemodialysis: An Observational Study

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ABSTRACT

Introduction: Patients with diabetes mellitus and end-stage renal disease are at a high risk of developing coronary, cerebrovascular, and peripheral vascular diseases. This study aimed to characterize hypoglycemia and blood glucose fluctuations associated with maintenance hemodialysis in older adult patients with diabetes mellitus and end-stage renal disease using a continuous glucose monitoring system.

Methods: Seven patients were enrolled in this study, and 13 pairs of continuous glucose monitoring system data were collected. Each pair included data of 1 dialysis-on day and 1 dialysis-off day. Information on basic patient characteristics, including age, diabetes mellitus duration, hemodialysis duration, and proportions of hemoglobin A1c and glycated albumin, were collected. Differences in blood glucose fluctuation were compared between dialysis-on days and dialysis-off days.

Results: The mean blood glucose on dialysis-on days (6.96 ± 2.57 mmol/L) was significantly lower than that on dialysis-off days (7.68 ± 2.31 mmol/L; $P < 0.05$). In contrast, the following parameters had significantly higher values (all $P < 0.05$) on dialysis-on days compared to dialysis-off days: large amplitude of glycemic excursion level (5.82 ± 2.86 mmol/L versus 4.21 ± 1.71 mmol/L), large amplitude of glycemic excursion level from 8 a.m. to 2 p.m. (3.6 ± 1.74 mmol/L versus 2.8 ± 1.33 mmol/L), mean amplitude of glycemic excursion level (4.78 ± 1.68 mmol/L versus 3.89 ± 1.67 mmol/L), mean amplitude of glycemic excursion level from 8 a.m. to 2 p.m. (4.01 ± 1.03 mmol/L versus 3.12. ± 0.97 mmol/L), standard deviation of blood glucose (1.55 ± 0.89 mmol/L versus 1.03 ± 0.4 mmol/L), and time below a target glucose range of less than 3.9 mmol/L (8.27% versus 4.25%).

Conclusion: Fluctuations in blood glucose levels were larger on dialysis-on days, particularly from the start of hemodialysis to 2 h post-hemodialysis, than on dialysis-off days. Hypoglycemia, as indicated by the time below a target glucose range of less than 3.9 mmol/L, occurred more frequently on dialysis-on days than on dialysis-off days.

Jinzhu Li and Ruiqin Zhang contributed equally to this work.

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Graphical Abstract:

Analysis of Blood Glucose Fluctuations Using a Continuous Glucose Monitoring System in Elderly Patients with Diabetes Mellitus and End-Stage Renal Disease on Maintenance Hemodialysis- An Observational Study

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Patients

Age≥65 | With T2DM and ESRD | Undergoing maintain hemodialysis

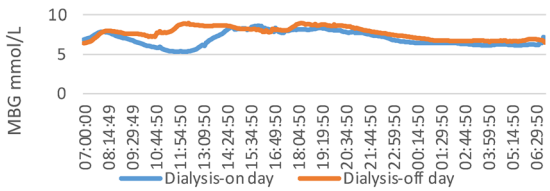
Methods

CGMS was applied, 13 pairs of CGMS data were collected

Dialysis-on day (n=13) **VS** Dialysis-off day (n=13)

Results

An inverted U-shape was observed from the beginning of hemodialysis to 2 hours post-hemodialysis. (8 a.m. to 2 p.m.)



Hyperglycemia happened more on dialysis-on day

	Hypoglycemia frequency				
	Totally	During dialysis	Within post-HD 2h	Afternoon to evening	At night
		8-12	12-14	14-22	22-8
dialysis-on day	12	2	4	3	3
dialysis-off day	3	1	0	0	2

Conclusions: HD not only increased the amplitude of glycemic excursion, but also increased the risk of hypoglycemia. Furthermore, the effect of dialysis on blood glucose levels was usually maintained from the initiation of hemodialysis to 2 hours post-hemodialysis.

PEER-REVIEWED INFOGRAPHIC

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The graphical abstract represents the opinions of the authors. For a full list of declarations, including funding and author disclosure statements, please see the full text online.

Keywords: Continuous glucose monitoring; Diabetes mellitus; Hemodialysis; Older adults; Renal

Key Summary Points

Why carry out this study?

While it is well established that dialysis can affect blood glucose fluctuations, few studies have evaluated this relationship in older adult patients with diabetes mellitus (DM) and end-stage renal disease (ESRD) on maintenance hemodialysis

This study characterized hypoglycemia and blood glucose fluctuations in older adult patients with DM and ESRD on maintenance hemodialysis, with the aim of highlighting the need for clinicians to closely monitor blood glucose status in patients undergoing dialysis

What was learned from the study?

We observed that fluctuations in blood glucose levels were larger on dialysis-on days, particularly from the start of hemodialysis to 2 h post-hemodialysis, than on dialysis-off days; hypoglycemia occurred more frequently on dialysis-on days than on dialysis-off days

Our results emphasize the importance of monitoring blood glucose in older adult patients with DM and ESRD on maintenance hemodialysis and provide an evidence base that will facilitate the development of future intervention studies

DIGITAL FEATURES

This article is published with digital features, including a graphical abstract, to facilitate understanding of the article. To view digital features for this article go to https://doi.org/10.6084/m9.figshare.20014982.

INTRODUCTION

Patients with diabetes mellitus (DM) and end-stage renal disease (ESRD) are at a high risk of developing coronary, cerebrovascular, and peripheral vascular diseases. These complications are the leading causes of death among patients with ESRD [1, 2]. Hypoglycemia, hyperglycemia, and blood glucose fluctuations can accelerate the occurrence and development of these complications. Patients with DM and ESRD are not only insulin resistant but are also prone to hypoglycemia due to impaired renal gluconeogenesis, malnutrition, altered insulin pharmacokinetics, and hypoglycemic agent therapy [3, 4].

While the risk of hypoglycemia can be reduced by using a glucose-added dialysis fluid [5, 6], the prediction of glycemic patterns remains challenging. Therefore, it is difficult to control blood glucose levels without increasing the risk of hypoglycemia and large variations in blood glucose levels. The degree of blood glucose fluctuations in patients with DM and ESRD on maintenance hemodialysis is controversial. Some studies have reported fluctuations during dialysis-on days [7–13], while other studies have not observed significant fluctuations [14, 15].

A continuous glucose monitoring system (CGMS) enables the direct tracking of short-term (intra- and interday) glucose variability and hyper- and hypoglycemia [16, 17]. In 2019, the Advanced Technologies & Treatments for Diabetes Conference [18] released an updated consensus statement that aimed to refine core metrics for the assessment of glycemic control. It included three key CGMS-derived measurements: (i) the percentage of readings and time per day within a target glucose range of 3.9–-10 mmol/L (time in range $[TIR]_{3.9–10}$); (ii) the percentage of readings and time above a target glucose range of 13.8 mmol/L (time above range $[TAR]_{>13.8}$); and (iii) the percentage of readings and time below a target glucose range of 3.9 mmol/L (time below range $[TBR]_{<3.9}$). The 2020 Kidney Disease Improving Global Outcomes (KDIGO) guidelines state that the CGMS may be advantageous for the self-management of diabetes in individuals with chronic kidney

disease [19]. As the CGMS measures blood glucose levels 288 times daily for up to 7 days, it provides a comprehensive assessment of blood glucose fluctuations on both dialysis-on days and dialysis-off days.

There is currently a lack of data on blood glucose fluctuations in advanced aging patients with DM and ESRD on maintenance hemodialysis. Therefore, in this study, we used the CGMS to compare glycemic variability and hypoglycemia incidence between dialysis-on and dialysis-off days in older adult patients with DM and ESRD on maintenance hemodialysis.

METHODS

This study included patients with type 2 DM and ESRD who were hospitalized and undergoing maintenance hemodialysis in the Geriatric Nephrology Department of the People's Liberation Army General Hospital (PLAGH). Patients were included if they were at least 65 years of age and underwent stable and regular hemodialysis (three times a week, hemodialysis duration of at least 3 months). The exclusion criteria comprised hormone administration in the previous 6 months, acute complications of diabetes, and acute infection. Data on the following patient demographic and clinical characteristics were collected: age, DM duration, hemodialysis duration, and proportions of hemoglobin A1c (HbA1c) and glycated albumin. The CGMS (iPro 2, Medtronic Inc. Minneapolis, Minnesota, USA) was applied on the afternoon before the day of dialysis. It provided 288 blood glucose level measurements daily and remained in place for 1–2 complete dialysis-on days and dialysis-off days. Trained nurses calibrated the CGMS by measuring capillary blood glucose four times a day (before three meals and bedtime) and recorded the time and number of meals, snacks, medications, and exercise. The three meals were provided at approximately 7:15 a.m., 11:15 a.m., and 5:15 p.m.; however, lunch on a dialysis day was provided at approximately 12:30 p.m. The standard amount of calories provided was 25–30 kcal/kg. Carbohydrates accounted for 55–60% of the calories and were divided among the three meals according to the following ratios: breakfast (1/5), lunch (2/5), and dinner (2/5). During dialysis (from 10 to 11:30 a.m.), extra meals (e.g., two pieces of chocolate and 150 mL of nutrient solution) were consumed according to the patient's habits and preferences. All data were downloaded using CARELINK PRO (Medtronic Inc. Minneapolis, Minnesota, USA). Hypoglycemia referred to blood glucose concentrations below 2.8 mmol/L. Individuals with diabetes were diagnosed with hypoglycemia when the blood glucose level was below 3.9 mmol/L.

The dialysate was a bicarbonate concentrate that contained glucose (5 mmol/L), as well as sodium (138 mmol/L), potassium (2 mmol/L), calcium (1.5 mmol/L), magnesium (0.5 mmol/L), chloride (109 mmol/L), acetate (3 mmol/L), and bicarbonate (32 mmol/L) ions. The dialysis mode was hemodialysis. Each hemodialysis session started at 8 a.m. and lasted for 4 h.

The study protocol was approved by the Ethics Committee of the PLAGH (S2021-424-01). All patients provided written informed consent. Double encryption was used, and all data were stored on a secure computer that was not connected to a network to protect patient data.

Calculation of Glucose Profiles

A single dialysis-on day extended from 8 a.m. on the day of dialysis to 8 a.m. on the following day; the subsequent 24 h were defined as a dialysis-off day. The following variables were calculated from the CGMS for each patient: (1) mean blood glucose (MBG) level (the mean of 288 measured values during the 24-h CGMS monitoring period; (2) standard deviation of blood glucose (SDBG) (standard deviation values during the 24-h CGMS or observation period [normal reference value of less than 1.4 mmol/L]); (3) large amplitude of glycemic excursion (LAGE) (the difference between maximum and minimum blood glucose levels during blood glucose monitoring [normal reference value of less than 5.7 mmol/L]); (4) mean amplitude of glycemic excursion (MAGE) (mean value of effective fluctuation blood glucose

fluctuation range, effective fluctuation means amplitude is greater than one standard deviation [normal reference value of less than 3.4 mmol/L]); (5) $TBR_{<3.9}$; (6) $TIR_{3.9–10}$; and (7) $TAR_{>13.8}$.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics 23.0 (IBM Corporation, Armonk, NY, USA). Tests for normality were conducted using the Shapiro–Wilk test. All normally distributed data are expressed as mean ± standard deviation, and non-normally distributed data are expressed as median (range). Comparisons of normally distributed variables between dialysis-on and dialysis-off days were made with the *t* test; the Wilcoxon test was used for non-normally distributed variables. The level of statistical significance was set at $P < 0.05$.

RESULTS

Patient Demographic and Clinical Characteristics

All patients had type 2 DM. The mean patient age was 82.58 ± 8.97 years. The mean duration of DM was 13.29 ± 11.34 years, and the mean duration of hemodialysis was 2.97 ± 2.16 years. The proportions of HbA1c and glycated albumin were 6.23 ± 0.89% and 19 ± 5.58%, respectively (Table 1).

Table 1 Basic characteristics of participants

Characteristics	No. of patients	Value
Age (years)	7	82.58 ± 8.97
BMI (kg/m^2)	7	22.01 ± 1.95
HD duration (years)	7	2.97 ± 2.16
DM duration (years)	7	13.29 ± 11.34
Urea before HD (mg/dL)	7	16 ± 6.83
Urea after HD (mg/dL)	7	4 ± 1.70
Creatinine before HD(mg/dL)	7	613 ± 143.8
Creatinine after HD (mg/dL)	7	186.67 ± 48.18
HbA1c (%)	7	6.23 ± 0.89
GA (%)	7	19 ± 5.58
History of hypertension (*n*, %)	7	100%
History of diabetic eye disease (*n*, %)	1	14.28%
History of cardiovascular disease (*n*, %)	5	71.43%
Type 2 DM (*n*, %)	7	100%
Oral antidiabetic medication use (*n*, %)	2	28.58%
Insulin therapy (*n*, %)	2	28.58%

BMI body mass index, *DM* diabetes mellitus, *HD* hemodialysis, *HbA1c* hemoglobin A1c, *GA* glycated albumin

Blood Glucose Levels on Dialysis-on Days and Dialysis-off Days

The MBG level was significantly lower on dialysis-on days (6.96 ± 2.57 mmol/L) than on dialysis-off days (7.68 ± 2.31 mmol/L, $P = 0.03$). LAGE (5.82 ± 2.86 mmol/L versus 4.21 ± 1.71 mmol/L, $P = 0.04$), MAGE (4.78 ± 1.68 mmol/L versus 3.89 ± 1.67 mmol/L, $P = 0.04$), SDBG (1.55 ± 0.89 mmol/L versus 1.03 ± 0.4 mmol/L, $P = 0.04$), and the percentage of hypoglycemia time (8.27% versus 4.25%, $P = 0.02$) were significantly greater on dialysis-on days than on dialysis-off days (all $P < 0.05$) (Table 2). Blood glucose fluctuations for each patient were the same as the overall trend (Table 3).

Blood Glucose Drift, LAGE, and MAGE of Different Periods on Dialysis-on Days and Dialysis-off Days

The blood glucose curves on dialysis-on and dialysis-off days differed from the beginning of

Table 2 Blood glucose monitoring on dialysis-on days and dialysis-off days

Parameter	Dialysis-on day	Dialysis-off day	*P*
MBG (mmol/L)	6.96 ± 2.57 (95% CI 6.86–7.06)	7.68 ± 2.31 (95% CI 7.6–7.76)	0.03
LAGE (mmol/L)	5.82 ± 2.86 (95% CI 4.44–7.22)	4.21 ± 1.71 (95% CI 3.27–5.05)	0.04
MAGB (mmol/L)	4.78 ± 1.68 (95% CI 3.87–5.21)	3.89 ± 1.67 (95% CI 2.57–5.13)	0.04
SDBG (mmol/L	1.55 ± 0.89 (95% CI 1.14–2.12)	1.03 ± 0.40 (95% CI 0.81–1.25)	0.04
CV (%)	0.23 ± 0.09	0.16 ± 0.09	0.02
24 h CGM-derived $TBR_{<3.9}$ (% of readings)	8.27	4.25	0.02
24 h CGM-derived $TIR_{3.9–10}$ (% of readings)	77.27	80.39	0.62
24 h CGM-derived $TAR_{>13.8}$ (% of readings)	1.87	1.31	0.51

CI confident interval, *CV* coefficient of variation, *TBR* time below range, *TAR* time above range, *TIR* time in range, *MAGE* mean amplitude of glycemic excursion

hemodialysis to 2 h post-hemodialysis (8 a.m. to 2 p.m.); an inverted U-shape was observed. In other periods, the blood glucose curves were not different (Fig. 1).

LAGE from the beginning of hemodialysis to 2 h post-hemodialysis (8 a.m. to 2 p.m.) was significantly greater on dialysis-on days (3.6 ± 1.74 mmol/L) compared to that on dialysis-off days (2.8 ± 1.33 mmol/L; $P < 0.05$). In the other two periods, the difference was not significant ($P > 0.05$). MAGE from the beginning of hemodialysis to 2 h post-hemodialysis (8 a.m. to 2 p.m.) was significantly greater on dialysis-on days (4.01 ± 1.03 mmol/L) compared to that on dialysis-off days (3.12 ± 0.97 mmol/L; $P < 0.05$). In the other two periods, the difference was not significant ($P > 0.05$) (Table 4).

MBG Level from 8 a.m. to 2 p.m. on Dialysis-on Days and Dialysis-off Days

The MBG level did not change significantly from 1 h pre-hemodialysis to 1–3 h post-hemodialysis between dialysis-on days and dialysis-off days ($P > 0.05$); the changes were significant from the 2nd hour of hemodialysis to 2 h post-hemodialysis ($P < 0.05$). The most significant changes were observed from the 4th hour of hemodialysis to 1 h post-hemodialysis (Fig. 2).

Hypoglycemia

Hypoglycemia occurred 12 times on dialysis-on days and three times on dialysis-off days. None of the hypoglycemic episodes were associated with any symptoms (Table 5).

DISCUSSION

According to data from the 10th edition of the International Diabetes Federation Diabetes Atlas, 537 million adults lived with diabetes worldwide in 2021, and the age-adjusted comparative prevalence of diabetes is estimated to be 9.8%. The proportion of diabetes-related deaths is as high as 32.6% [20]. Hypoglycemia and blood glucose fluctuation can result in serious complications, such as diabetes-related macrovascular and microvascular disorders. Acute hypoglycemia can result in coma and subsequent mortality. Patients with both diabetes and ESRD are at a high risk of developing acute cardiovascular and cerebrovascular events; therefore, good glycemic control is necessary to improve their long-term prognosis [21] and quality of life. Previous studies identified CGMS as an appropriate and reliable tool for the detection of glycemic variations and

Table 3 Bood glucose fluctuation indicators of individuals

Subject no.	Dialysis-on day	Dialysis-off day	*P*
1	MAG 7.33 ± 1.38 (95% CI 6.48–8.44)	MAG 8.17 ± 1.01 (95%CI 7.56–8.97)	0.04
	MAGE 4.00 ± 0.00 (95% CI 4.00–4.00)	MAGE 1.98 ± 0.66 (95% CI 1.33–2.61)	0.02
	$TBR_{<3.9}$ 0	$TBR_{<3.9}$ 0	
2	MAG 7.97 ± 1.84 (95% CI 7.06–9.45)	MAG 9.29 ± 1.37 (95% CI 8.31–10.27)	0.03
	MAGE 4.40 ± 1.69 (95% CI 3.23–5.97)	MAGE2.18 ± 0.46 (95% CI 1.84–2.51)	0.02
	$TBR_{<3.9}$ 0	$TBR_{<3.9}$ 0	
3	MAG 9.25 ± 1.57 (95% CI 8.55–10.39)	MAG11.24 ± 1.51 (95% CI 9.97–12.01)	0.03
	MAGE 3.65 ± 1.06 (95% CI 2.89–4.12)	MAGE3.03 ± 0.90 (95% CI 2.42–3.65)	0.03
	$TBR_{<3.9}$ 0	$TBR_{<3.9}$ 0	
4	MAG 9.58 ± 4.05 (95% CI 6.52–12.81)	MAG 8.28 ± 2.35 (95% CI 8.06–8.50)	0.03
	MAGE 5.47 ± 1.85 (95% CI 4.01–7.05)	MAGE 5.07 ± 2.98 (95% CI 2.69–7.44)	0.04
	$TBR_{<3.9}$ 8.09%	$TBR_{<3.9}$ 0	
5	MAG 4.57 ± 1.77 (95% CI 3.12–6.89)	MAG 5.18 ± 1.83 (95% CI 5.04–5.32)	0.04
	MAGE 3.66 ± 1.68 (95% CI 2.19–5.13)	MAGE3.43 ± .0.61 (95% CI 2.89–3.96)	0.05
	$TBR_{<3.9}$ 28.70%	$TBR_{<3.9}$ 14.50%	
6	MAG 5.89 ± 0.86 (95% CI 5.75–6.53)	MAG 6.43 ± 0.61 (95% CI 6.37–6.49)	0.04
	MAGE 1.87 ± 1.33 (95% CI 0.89–2.86)	MAGE1.73 ± .0.46 (95% CI 1.49–1.96)	0.05
	$TBR_{<3.9}$ 0.36%	$TBR_{<3.9}$ 0	
7	MAG 6.66 ± 1.24 (95% CI 5.42–7.88)	MAG 6.61 ± 0.86 (95% CI 6.55–6.67)	0.05
	MAGE 2.60 ± 0.99 (95% CI 1.87–3.33)	MAGE 2.08 ± 1.31 (95% CI 1.01–3.09)	0.04
	$TBR_{<3.9}$ 0	$TBR_{<3.9}$ 0	

hypoglycemic episodes in individuals with diabetes, particularly on the day of hemodialysis [22].

A previous study showed that HbA1c was weakly correlated with MBG level in patients with type 2 DM undergoing hemodialysis compared to those not undergoing hemodialysis [15]. The continuous monitoring of blood glucose facilitates the detection of hyperglycemia and hypoglycemia, especially in patients with diabetes and advanced chronic kidney disease—such monitoring was recommended by the 2020 KDIGO guideline—because of the drawbacks of currently established glycemic biomarkers, such as HbA1c [19]. In the present study, we determined the influence of hemodialysis on blood glucose by using the CGMS to evaluate blood glucose parameters and compare them between dialysis-on days and dialysis-off days in older adult patients. We found that fluctuations in blood glucose levels were larger on dialysis-on days, particularly from the start of hemodialysis to 2 h post-hemodialysis, than on dialysis-off days. Hypoglycemia, as indicated by the time below a target glucose range of less than 3.9 mmol/L, occurred more frequently on dialysis-on days than on dialysis-off days.

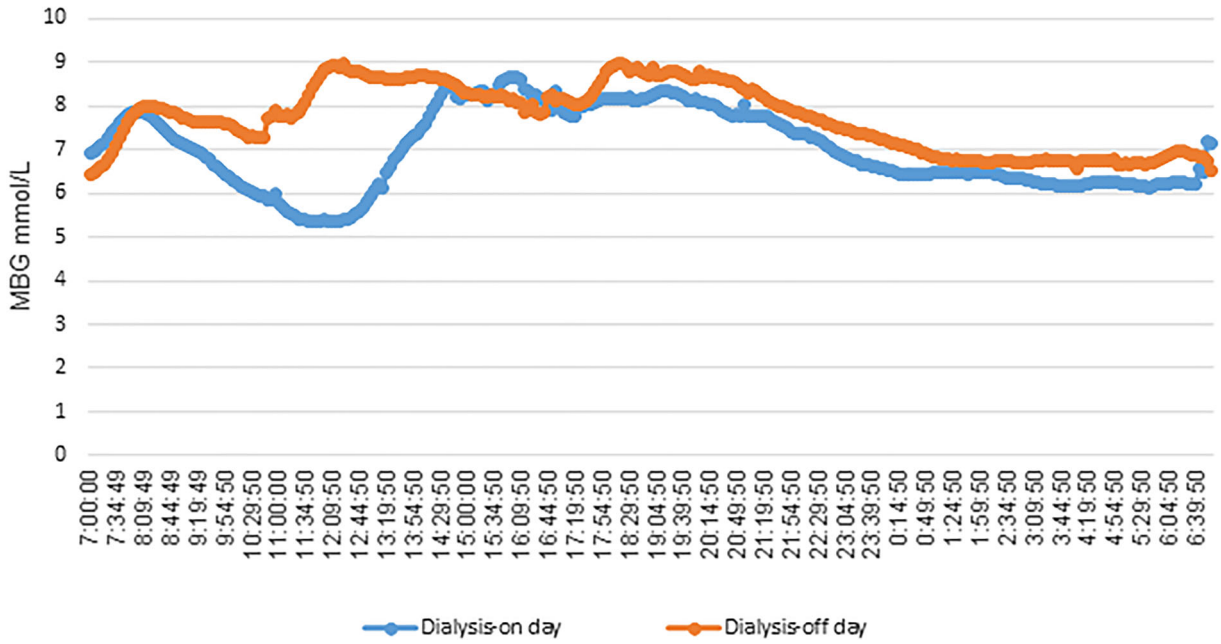

Fig. 1 Blood glucose fluctuation trend on dialysis-on and dialysis-off days (blue, on dialysis-on day; orange, on dialysis-off day)

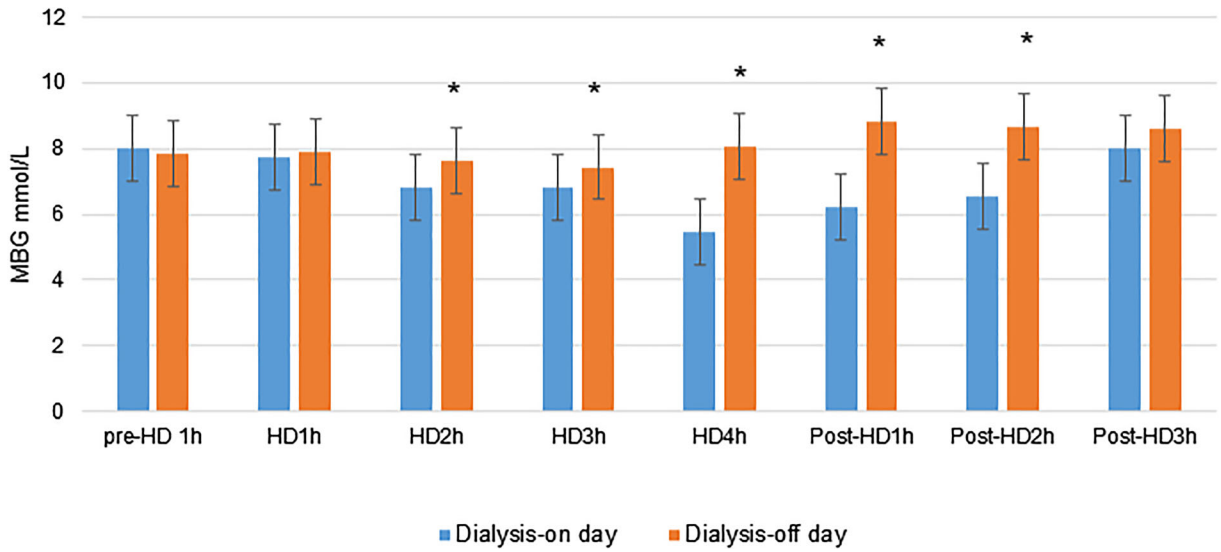

Fig. 2 Mean blood glucose at different periods. * Significant difference compared to dialysis-on day, $P < 0.05$ (blue, on dialysis-on day; orange, on dialysis-off day)

Blood glucose fluctuations contribute to the development of diabetes complications, such as cardiovascular and cerebrovascular events, and have been shown to cause more serious harm than continuous hyperglycemia [23–25]. Our results indicated that MBG level was generally lower on dialysis-on days than on dialysis-off days. Furthermore, coefficient of variation (CV), LAGE, and SDBG were higher on dialysis-on days than on dialysis-off days. This indicates

Table 4 Large and mean amplitude of glycemic excursion of different periods

Time	Dialysis-on day	Dialysis-off day	*P*
LAGE all day	5.82 ± 2.86 (95% CI 4.44–7.22)	4.21 ± 1.71 (95% CI 3.27–5.05)	0.04
LAGE (8:00–14:00)	3.6 ± 1.74 (95% CI 3.43–4.85)	2.8 ± 1.33 (95% CI 2.02–3.58)	0.02
LAGE (14:00–22:00)	3.38 ± 1.99 (95% CI 2.4–4.36)	3.09 ± 1.16 (95% CI 2.7–3.48)	0.06
LAGE (22:00–8:00)	1.97 ± 1.73 (95% CI 0.84–2.8)	2.04 ± 1.23 (95% CI 1.43–2.65)	0.06
MAGE all day	4.78 ± 1.68 (95% CI 3.75–5.89)	3.89 ± 1.67 (95% CI 2.69–4.87)	0.03
MAGE (8:00–14:00)	4.01 ± 1.03 (95% CI 3.45–4.65)	3.12 ± 0.97 (95% CI 2.66–3.63)	0.02
MAGE (14:00–22:00)	2.34 ± 1.14 (95% CI 1.56–3.12)	2.96 ± 1.39 (95% CI 2.01–4.03)	0.06
MAGE (22:00–8:00)	3.12 ± 0.87 (95% CI 2.57–3.36)	2.76 ± 1.13 (95% CI 2.01–3.14)	0.06

LAGE large amplitude of glycemic excursion, *MAGE* mean amplitude of glycemic excursion, *CI* confident interval

Table 5 Hypoglycemia events of different periods

	Hypoglycemia frequency				
	Total	During dialysis 8–12	Within post-HD 2 h 12–14	Afternoon to evening 14–22	At night 22–8
Dialysis-on day	12	2	4	3	3
Dialysis-off day	3	1	0	0	2

that blood glucose levels tend to fluctuate more substantially on dialysis-on days. While prior reports have also documented similar trends for blood glucose fluctuations, not all studies have found consistent differences in MBG levels between dialysis-on days and dialysis-off days [12, 14, 15, 17]. For example, Jung et al. [14] observed fluctuations in blood glucose levels using the CGMS in nine patients with type 2 DM undergoing maintenance hemodialysis; however, there was no difference in the MBG level between dialysis-on days and dialysis-off days. The results of their subgroup analysis showed that glucose levels decreased significantly with hemodialysis initiation in patients who were maintained on antidiabetic agents on dialysis days; this is consistent with our results. The lack of a difference in the MBG level may have been related to the reduction in hypoglycemic treatment in some patients on the day of dialysis. Divani et al. [17] did not find a difference in the mean 24-h CGM-derived glucose level between dialysis-on and dialysis-off days in 37 individuals with diabetes; however, the 24-h CV of glucose readings and the $TBR_{<70}$ were significantly higher during dialysis-on days than dialysis-off days. Mirani et al. [12] assessed 12 patients with DM on hemodialysis for 2 days (1 hemodialysis day and the following non-hemodialysis day) and found that the MBG level and glycemic variability were significantly higher on the day of hemodialysis. The results of this study are consistent with our findings. Riveline et al. [15] compared glucose levels in 19 hemodialyzed and 39 non-hemodialyzed patients with type 2 DM in a double-center study; a CGMS was used for 4-day monitoring (2 days with and without dialysis).

While the mean glucose level was not significantly different between dialysis-on and dialysis-off days, it was remarkably lower in the first 3 h of dialysis. In the present study, we also observed a blood glucose drift from the beginning of hemodialysis to 2 h post-hemodialysis. This finding emphasizes the importance of monitoring changes in blood glucose not only during but also after dialysis, especially in older adult patients.

Hypoglycemia is a common and serious complication of diabetes. The clinical manifestations of hypoglycemia in older adult patients may vary due to poor physical fitness and self-consciousness. Quality of life may be severely impacted, and impaired consciousness and coma are associated with a high rate of disability and fatality [26]. Increased susceptibility to hypoglycemia in individuals with diabetes and ESRD is attributed to impairment of renal gluconeogenesis and insulin clearance. Dialysis also has a large influence on blood glucose levels; indeed, our results demonstrated that the frequency and duration of hypoglycemia were greater on dialysis-on days than on dialysis-off days. In individuals with diabetes, hypoglycemia is defined by blood glucose levels of less than 3.9 mmol/L [27]. Thus, we used $TBR_{<3.9}$ as a hypoglycemia assessment index; values were higher on dialysis-on days than on dialysis-off days. We observed two periods during which blood glucose levels were relatively low, and most hypoglycemia events occurred. The first was a blood glucose drift from 10 p.m. to 8 a.m. on the following morning, on both dialysis-on days and dialysis-off days. The second blood glucose drift only occurred on dialysis-on days, from the initiation of hemodialysis to 2 h post-hemodialysis (8 a.m. to 2 p.m.); this was indicated by an inverted U. We identified 15 cases of asymptomatic hypoglycemia in three patients; 12 (80%) of these cases occurred during hemodialysis days. One case of hypoglycemia lasted from the start of hemodialysis to 2 h post-hemodialysis (360 min). Kazempour-Ardebili et al. [11] reported that hemodialysis was associated with a higher risk of hypoglycemia; this was evident within 24 h of dialysis, during which most instances of asymptomatic hypoglycemia and glucose nadir occurred. The association between dialysis and hypoglycemia was also evaluated by Jung et al. [14], who used the CGMS to evaluate nine patients with DM on hemodialysis; five of these patients experienced a total of 10 episodes of hypoglycemia, with 80% occurring on the day of hemodialysis. Most of these episodes were asymptomatic and occurred during the first 12 h on the day of dialysis. Riveline et al. [15] also reported two cases of intradialytic hypoglycemia. Furthermore, Mori et al. [13] documented an acute decline in blood glucose levels during a hemodialysis session in a patient with DM. Therefore, increased vigilance is warranted to detect and prevent asymptomatic hypoglycemia, especially on the day of dialysis, in patients with DM.

The average age of the patients in the present study was 82.52 ± 8.97 years, while that in previous studies has ranged from 61 ± 9 to 65 ± 13 years; participants in this study were the oldest on average among all relevant studies. Our study also has some limitations, including the relatively small sample size and the lack of a long-term follow-up. As a result of the limited number of cases, it is uncertain whether the results can be generalized to all older adult patients; additional studies with larger samples sizes are required. Furthermore, as we did not perform capillary blood glucose monitoring, we were unable to assess CGMS precision.

CONCLUSION

The results of this study indicated that hemodialysis not only increased the amplitude of glycemic excursion but also increased the risk of hypoglycemia in older individuals with diabetes undergoing maintenance hemodialysis. Furthermore, the effect of dialysis on blood glucose levels was usually maintained from the initiation of hemodialysis to 2 h post-hemodialysis. Our results emphasize the importance of monitoring changes in blood glucose levels in older adult patients undergoing dialysis. As a result of the limited sample size, it is uncertain whether the results of this study are applicable to all older adult patients; additional

studies with larger sample sizes are needed. Future interventional studies are required to determine optimal methods for reducing blood glucose fluctuations and the incidence of hypoglycemia.

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Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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