

RESEARCH

Open Access



Visit-to-visit HbA_{1c} variability is associated with poor prognosis in peritoneal dialysis patients with type 2 diabetes mellitus

Fengping Zhang^{1,2†}, Taotao Shi^{1,2†}, Xiaoran Feng², Yunying Shi¹, Guilin Zhang³, Yu Liu⁴ and Ping Fu^{1*}

Abstract

Background The prognosis of diabetic peritoneal dialysis patients is poor. HbA_{1c} serves as a crucial indicator for monitoring blood glucose control in patients with diabetes. Nevertheless, the relationship between visit-to-visit HbA_{1c} variability and prognosis in peritoneal dialysis with diabetes remains unclear.

Methods All participants were categorized into 3 groups based on the HbA_{1c} variability score (HVS), which is the frequency of 0.5% (5.5 mmol/mol) alter in visit-to-visit HbA_{1c} values. Then, the hazard ratio to HVS with all-cause mortality was analyzed using the Cox hazard model, followed by the Fine-Gray competing risk model for major adverse cardiovascular events. Subgroup and sensitivity analysis were conducted to ascertain the robustness of the findings.

Results Eight hundred twenty patients with type 2 diabetes were finally enrolled in this study from 2,855 participants with a mean age of 56.9 ± 14.6 years and a median follow-up time of 44 months [IQR: 27–70], death occurred in 496 (60.2%) individuals. Compared with the lowest category (HVS < 1/3) after being adjusted by potential confounding factors, the hazard ratio for all-cause mortality was 4.59 (3.74–5.64) and the sub-distribution hazard ratio for major adverse cardiovascular events was 1.91 (1.46–2.51) of the highest category (HVS ≥ 2/3). Subgroup interaction and sensitivity analysis, including the adjustment for variables such as time-weighted average HbA_{1c}, HbA_{1c} measurement times and expansion, confirmed the reliability of the results.

Conclusion The HVS is related to the risk of poor prognosis in peritoneal dialysis with type 2 diabetes mellitus, independently of clinical multiple variables, and is a novel indicator with clinical guidance.

Keywords HbA_{1c}, Variability, Diabetes, Peritoneal dialysis, Prognosis

Introduction

Diabetes mellitus is one of the most prevalent causes of end-stage renal disease worldwide, and peritoneal dialysis is an essential form of renal replacement therapy. In China, diabetes (the vast majority are type 2) accounts for 19% to 22.9% of peritoneal dialysis [1]. The use of glucose dialysate since the unpopularity of icodextrin dialysate and volume overload has led to the vulnerability of patients with diabetes to severe challenges such as blood glucose fluctuations, cardiovascular events and microvascular complications [2]. Despite gradual improvements in dialysis technology and care in recent

[†]Fengping Zhang and Taotao Shi authors contributed equally to this work.

*Correspondence:

Ping Fu

fupinghx@scu.edu.cn

¹ Department of Nephrology, Kidney Research Institute, West China Hospital of Sichuan University, Chengdu, China

² Department of Nephrology, Jiujiang NO.1 People's Hospital, Jiujiang, China

³ Department of Nephrology, The NO.1 Affiliated Hospital of Nanchang University, Nanchang, China

⁴ Department of Nephrology, Pingxiang People's Hospital, Pingxiang, China



years, diabetes individuals still have the highest mortality rate in the dialysis subgroup [3]. Previous studies have demonstrated that control of blood glucose and normalization of HbA_{1c} reduce the risk of cardiovascular events and microvascular complications in general diabetes characters [4], and have similar benefits in dialysis population [5]. However, fasting glucose and HbA_{1c} are somewhat inaccurate in dialysis due to uremic toxin, continuous exposure to glucose peritoneal dialysate and anemia [6, 7]. HbA_{1c} variability is a practical indicator for diabetes management and connected with ill consequences [8]. Interestingly, a study has identified that HbA_{1c} variability is also related to the progression of chronic kidney diseases (CKD) [9], but the role in peritoneal dialysis is unclear. Standard deviation (SD) and coefficient of variation (CV) are commonly used to indicate HbA_{1c} variability [10]. However, in recent years, the HbA_{1c} variability score (HVS), which calculates the frequency of HbA_{1c} rise or fall by 0.5% (5.5 mmol/mol) by visit-to-visit information, has been reported to be associated with cardiovascular disease (CVD) and microvascular complications in diabetes mellitus and is more readable in clinical practice than purely statistical descriptions such as SD and CV [11]. Therefore, we sought to ascertain the correlation between the novel index and overall mortality and major adverse cardiovascular events (MACE) in peritoneal dialysis patients with diabetes by using a multicenter, large-sample database.

Research design and methods

Study design and participants

The study was an observational retrospective cohort study to investigate the relationship between HVS (A new indicator of HbA_{1c} variability) and prognosis in peritoneal dialysis patients with type 2 diabetes mellitus. ALL participants were selected from a multi-center peritoneal dialysis data alliance, which is a multi-designed and continuously updated database designed to investigate various clinical dreadful events, prognosis and other risk information of Chinese peritoneal dialysis individuals. Data are recorded by each sub-center based on uniformly defined criteria and managed by dedicated personnel. The criteria were met for enrollment in our study: (1) Over 18 years old; (2) the dialysate was glucose dialysate; (3) diagnosis of type 2 diabetes at the time of starting peritoneal dialysis; (4) the first HbA_{1c} measurement was performed at 4 weeks of stable peritoneal dialysis (baseline period), otherwise there were at least 3 subsequent HbA_{1c} retests data; (5) exclusion of missing data on regression and loss of follow-up. This protocol was reviewed and authorized by the ethics committee of the local institution. The written informed consent was

approved to be waived, as participant information was anonymous and did not involve any privacy.

The baseline parameters and follow-up

The baseline period was defined as about 4 weeks of stable peritoneal dialysis. Basic parameters included: age, sex, smoking history, diabetes history, CVD history, mean arterial pressure, body mass index, etc. Laboratory data: fasting blood glucose, hemoglobin, serum albumin, alanine aminotransferase, high-density lipoprotein low-density lipoprotein, intact parathyroid hormone, C-reactive protein (CRP), residual renal function; dialysis-related data: normalized protein nitrogen appearance (nPNA), urea clearance index (Kt/V_{urea}), dialysate to plasma creatinine concentration ratio (D/P_{cr}) and so on. The study defined the follow-up time in terms of the first outcome event from the start of peritoneal dialysis to its occurrence, with an endpoint of February 2023 in event-free cases.

Evaluation of visit-to-visit HbA_{1c} variability

To minimize the role of the HbA_{1c} variability parameter concerning measurement frequency and to better conform to clinical practice, we adopted HVS to assess the visit-to-visit HbA_{1c} variability. HVS is defined as the proportion of the total number of individual measurements in which the HbA_{1c} has changed by 0.5% (5.5 mmol/mol) compared with the previous measurement [11]. The first HbA_{1c} reference value was the data obtained during the baseline period. To avoid the influence of multiple HbA_{1c} measurements in a short period, we stipulate that the HbA_{1c} obtained repeatedly within 3 months can only be averaged once. HVS was divided into three categories (cut value: 1/3 and 2/3) to compare the relationship with prognosis. Furthermore, we also calculated the time-weighted average HbA_{1c} for subgroup analysis by area under the of HbA_{1c} curve/time.

Outcomes

We reviewed two endpoints of clinical interest: all-cause death and MACE. MACE was defined to include myocardial infarction, unstable angina pectoris, stroke, heart failure, vascular intervention events and other fatal cardiovascular outcomes. MACE was used for research at the time of its first appearance.

Statistical analyses

The data were analyzed by SPSS28.0 (IBM Corporation, NY, USA) and RStudio for Windows (R version 4.0.2). Categorical variables were expressed as frequencies and percentages. The continuous variables of normal distribution were described by means and standard deviation, while the skewed distribution was

described by the median quartile range (IQR). Analysis of variance, Kruskal–Wallis H test or chi-square test were selected to examine the differences between various categories. The overall survival rate was calculated by the Kaplan–Meier survival curve and Log-rank test. The Cox regression model was applied to analyze the relative hazard ratio (HR) of HVS to all-cause death. The sub-distribution hazard ratio (sHR) between HVS and MACE was performed using Fine-Gray competing risk model, and non-CVD deaths before MACE were considered as competitive risk events. Subgroup interaction tests and sensitivity analysis were used to verify the robustness of the conclusions. The *p*-value for linear trend across multiple groups was expressed as the *p* for trend, and the *p*-value less than 0.05 was regarded as statistically significant.

Results

Baseline characteristics

As shown in Fig. 1, 820 patients with type 2 diabetes were finally enrolled in this study from 2,855 participants in four peritoneal dialysis centers in China. The mean age at baseline was 56.9 ± 14.6 (range: 18–85), and 424 (51.7%) were male, the average HbA_{1c} at baseline was $7.0 \pm 2.3\%$ (53.0 ± 24.6 mmol/mol). The median number of measurements was 5.5 (IQR: 4.6, 7.0), and the mean HbA_{1c} follow-up was $7.4 \pm 2.5\%$ (57.7 ± 26.8 mmol/mol). For the details of HbA_{1c} as shown in [Supplementary data](#). According to the classification of HVS values, 428 (52.2%) were found with $HVS < 1/3$, 254 (31.0%) with $1/3 \leq HVS < 2/3$, and 138 (16.8%) with $HVS \geq 2/3$. The baseline characteristics of different HVS categories as shown in Table 1. The results indicated that the increase in HVS was associated with older age, larger body mass index, higher baseline HbA_{1c} levels, increased hemoglobin levels and

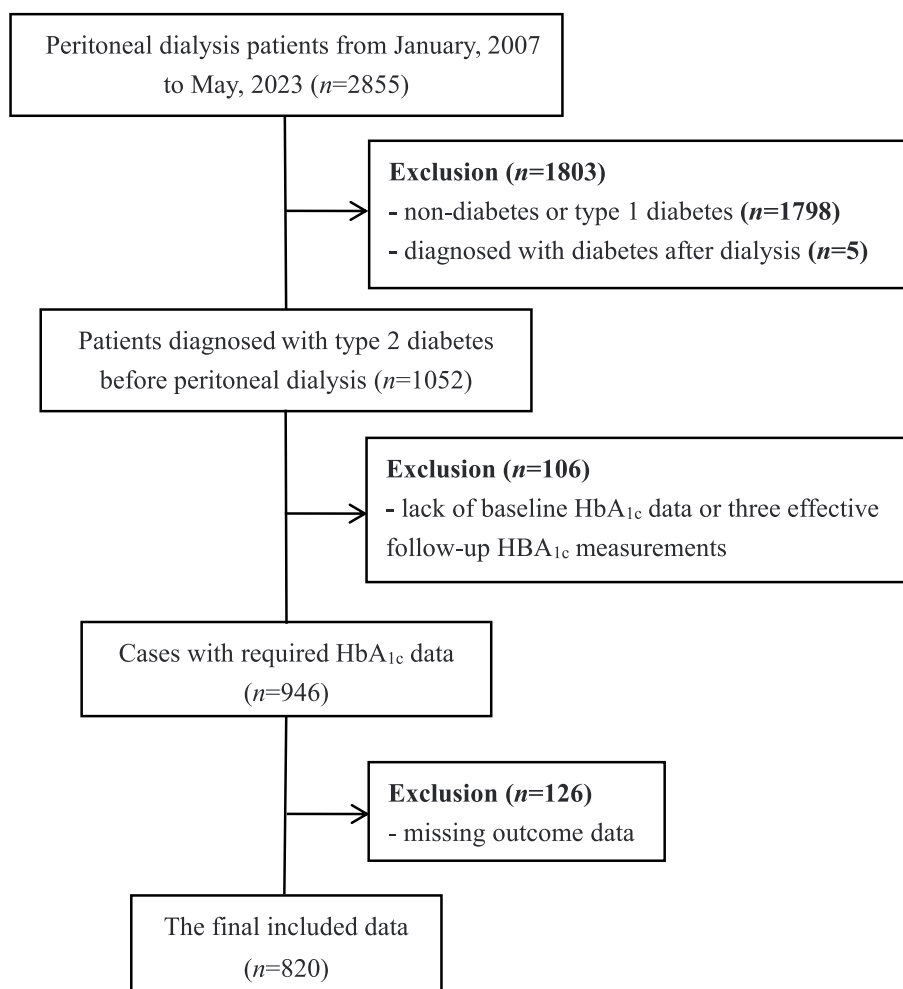


Fig. 1 Flow-chart of the participant's election

Table 1 Baseline characteristics of different categories HVS in peritoneal dialysis patients with diabetes

	All patients (n = 820)	HVS < 1/3 (n = 428)	1/3 ≤ HVS < 2/3 (n = 254)	HVS ≥ 2/3 (n = 138)	p for trend
Age (years)	56.9 ± 14.6	55.8 ± 14.9	58.2 ± 14.2	60.1 ± 13.7	< 0.001
Sex, Male, n (%)	424 (51.7)	224 (52.3)	130 (51.2)	70 (50.2)	0.706
Smoking, n (%)	204 (24.6)	102 (23.8)	64 (25.2)	38 (27.5)	0.381
Drinking, n (%)	112 (13.7)	54 (12.6)	36 (14.2)	22 (15.9)	0.328
Cardiovascular disease history, n (%)	266 (32.4)	136 (31.8)	90 (35.4)	40 (28.9)	0.848
Hypertension, n (%)	670 (81.7)	354 (82.7)	202 (79.5)	114 (82.6)	0.714
Drugs					
Insulin, n (%)	686 (83.7)	362 (84.6)	212 (83.5)	112 (81.2)	0.353
Statins, n (%)	178 (21.7)	98 (22.9)	52 (20.5)	28 (20.3)	0.427
Antiplatelet, n (%)	250 (30.5)	112 (29.0)	92 (36.2)	34 (24.6)	0.527
Hypertensive agent, n (%)	666 (81.2)	340 (79.4)	214 (84.3)	112 (81.2)	0.370
Mean arterial pressure (mmHg)	97.2 ± 12.1	96.6 ± 11.8	97.3 ± 12.0	97.8 ± 12.9	0.547
Body mass index (kg/m ²)	21.9 ± 3.5	21.6 ± 3.3	22.2 ± 3.6	22.8 ± 4.1	0.010
Mean time of diabetes history (years)	15.5 ± 6.7	15.2 ± 5.1	15.6 ± 5.8	16.0 ± 7.1	0.153
Frequencies of HbA _{1c} measurement (per patient)	5.5 (4.6, 7.0)	5.6 (4.3, 7.2)	5.3 (4.2, 7.1)	5.2 (4.0, 6.4)	0.109
HbA _{1c} at baseline (%)	7.0 ± 2.3	6.8 ± 2.1	7.4 ± 2.8	8.0 ± 3.2	< 0.001
HbA _{1c} at baseline (mmol/mol)	53.0 ± 24.6	51.1 ± 23.0	57.7 ± 30.2	64.3 ± 35.1	< 0.001
Fasting blood-glucose (mmol/L)	8.1 ± 2.7	7.8 ± 2.5	8.0 ± 2.8	8.2 ± 3.1	0.146
Hemoglobin (g/L)	90.6 ± 10.4	88.8 ± 10.1	90.1 ± 10.5	92.3 ± 9.8	< 0.001
Alanine aminotransferase (U/L)	23.2 ± 8.0	22.9 ± 8.1	23.5 ± 7.8	24.1 ± 8.6	0.072
Serum albumin (g/L)	35.0 ± 5.3	34.9 ± 5.1	35.0 ± 5.4	34.8 ± 5.2	0.807
High-density lipoprotein (mmol/L)	1.4 ± 0.4	1.4 ± 0.4	1.4 ± 0.5	1.4 ± 0.5	0.143
Low-density lipoprotein (mmol/L)	3.1 ± 1.2	3.0 ± 0.9	3.1 ± 1.1	3.2 ± 1.4	0.072
Intact parathyroid hormone (pg/ml)	250 ± 110	254 ± 109	246 ± 127	259 ± 104	0.953
Residual renal function (ml/min)	3.8 (1.2, 9.2)	3.7 (1.1, 7.1)	3.8 (1.6, 9.9)	3.9 (1.8, 10.4)	0.095
C-reactive protein (mg/L)	5.9 (4.3, 8.0)	5.8 (4.2, 7.5)	6.1 (4.6, 7.8)	6.4 (4.5, 8.3)	< 0.001
nPNA (g/kg/day)	1.1 ± 0.2	1.1 ± 0.3	1.0 ± 0.2	1.1 ± 0.2	0.460
D/P _{cr}	0.7 ± 0.2	0.7 ± 0.3	0.7 ± 0.1	0.7 ± 0.2	0.389
Total Kt/V _{urea}	1.8 ± 0.5	1.8 ± 0.5	1.8 ± 0.4	1.8 ± 0.4	0.246

Abbreviation: nPNA normalized protein nitrogen appearance, D/P_{cr} dialysate to plasma creatinine concentration ratio, Kt/V_{urea} urea clearance index

more baseline CRP levels. It is worth pointing out that the duration of diabetes history, the difference in the frequency of HbA_{1c} measurement and the proportion of insulin therapy was not statistically significant.

HVS and outcome

The median duration was 44 (12–198) [IQR: 27, 70] months, when all participants were followed up to the end. Deaths from all causes occurred in 494 (60.2%) patients, including 340 (41.5%) deaths from CVD disease, accounting for 68.8% of all-cause deaths. MACE occurred in 390 (47.6%) of all participants. The Kaplan–Meier survival curve by Log-rank test showed that the overall survival rate decreased significantly with the rise of HVS ($p < 0.001$) (Fig. 2). Fine-Gray competing risk model test displayed that the MACE cumulative incidence of HVS ≥ 2/3 category was significantly higher than that of the other two categories ($p < 0.001$) (Fig. 3).

For further analysis, set the lowest category (HVS < 1/3) as the reference, unadjusted Cox regression analysis suggested that the HR of all-cause mortality and the sHR of MACE with HVS ≥ 2/3 category were 4.87 [95% confidence intervals (CIs): 4.02–5.89, $p < 0.001$] and 2.13 (95% CI: 1.67–2.71, $p < 0.001$), respectively. Adjusted for a multivariate model, the HR was 4.59 (95% CI: 3.74–5.64, $p < 0.001$), and the sHR was 1.91 (95% CI: 1.46–2.51, $p < 0.001$), (Tables 2 and 3). These findings implied that the increase in HVS was distinctly related to the inferior outcomes of peritoneal dialysis individuals.

Subgroup and sensitivity analysis

For the sake of verifying the robustness of the correlation between HVS and outcomes, we performed a subgroup analysis. After multivariate adjusted, the results showed that for the age subgroup, the risk association between HVS and all-cause death was enhanced in

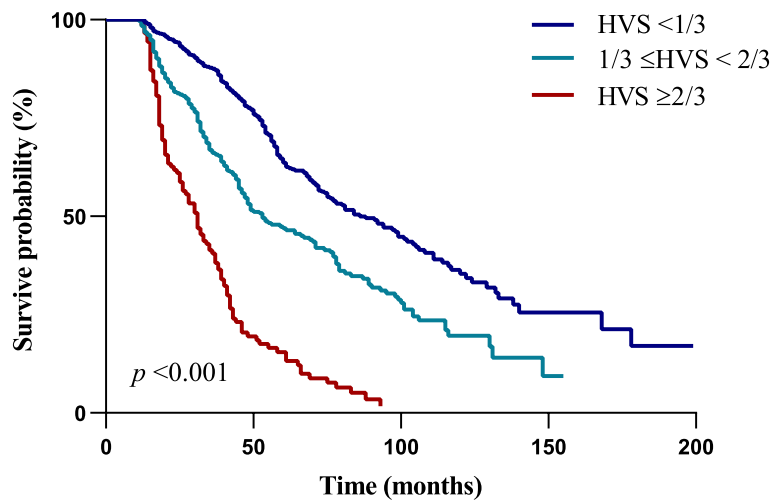


Fig. 2 Survive curve of all-cause mortality in different HVS categories

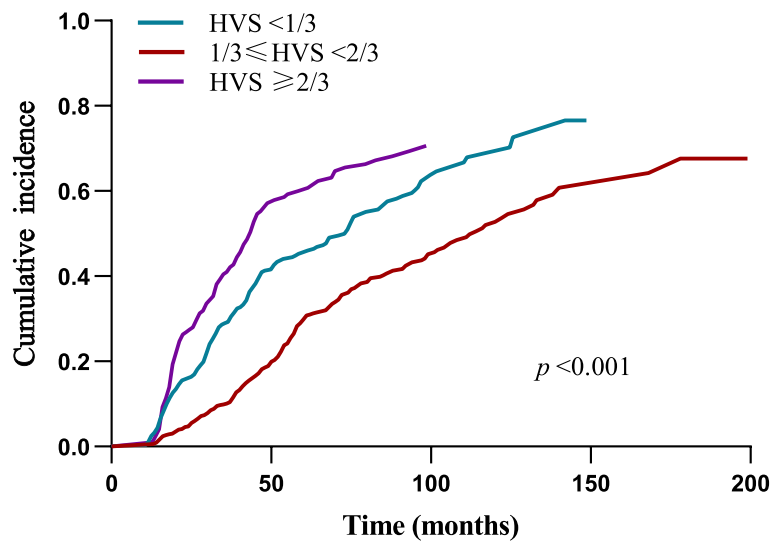


Fig. 3 Association between HVS and MACE (Fine-Gray competing risk model)

Table 2 Cox regression analysis of HVS and all-cause mortality

	Unadjusted Model		Model 1		Model 2	
	HR (95%CI)	p-value	HR (95%CI)	p-value	HR (95%CI)	p-value
HVS < 1/3	1.0 (reference)		1.0 (reference)		1.0 (reference)	
1/3 ≤ HVS < 2/3	1.73 (1.46—2.04)	< 0.001	1.59 (1.33—1.91)	< 0.001	1.62 (1.35—1.94)	0.002
HVS ≥ 2/3	4.87 (4.02—5.89)	< 0.001	4.48 (3.66—5.49)	< 0.001	4.59 (3.74—5.64)	< 0.001
p for trend	< 0.001		< 0.001		< 0.001	

Model 1: adjusted for time-weighted average HbA_{1c}

Model 2: adjusted for time-weighted average HbA_{1c} and other factors (age, sex, cardiovascular disease history, body mass index, hemoglobin, albumin and C-reactive protein)

Table 3 Association between HVS and MACE (Fine-Gray competing risk model)

	Unadjusted Model		Model 1		Model 2	
	sHR (95%CI)	p-value	sHR (95%CI)	p-value	sHR (95%CI)	p-value
HVS < 1/3	1.0 (reference)		1.0 (reference)		1.0 (reference)	
1/3 ≤ HVS < 2/3	1.58 (1.29—1.94)	< 0.001	1.51 (1.22—1.86)	< 0.001	1.44 (1.14—1.81)	0.002
HVS ≥ 2/3	2.13 (1.67—2.71)	< 0.001	2.04 (1.58—2.62)	< 0.001	1.91 (1.46—2.51)	< 0.001

Model 1: adjusted for time-weighted average HbA_{1c}

Model 2: adjusted for time-weighted average HbA_{1c} and other factors (age, sex, cardiovascular disease history, body mass index, hemoglobin, albumin and C-reactive protein)

patients less than 45 years old, while it was weakened in the subgroup based on time-weighted average HbA_{1c} ≥ 7.0% (53 mmol/mol). However, the overall trend remained largely consistent. When stratified analyses were performed for gender, baseline hemoglobin,

baseline albumin and baseline CRP, the interaction test showed that all the p-value for interaction of each subgroup were over 0.05, indicating that the results were not significantly dependent on these variables (Figs. 4 and 5).

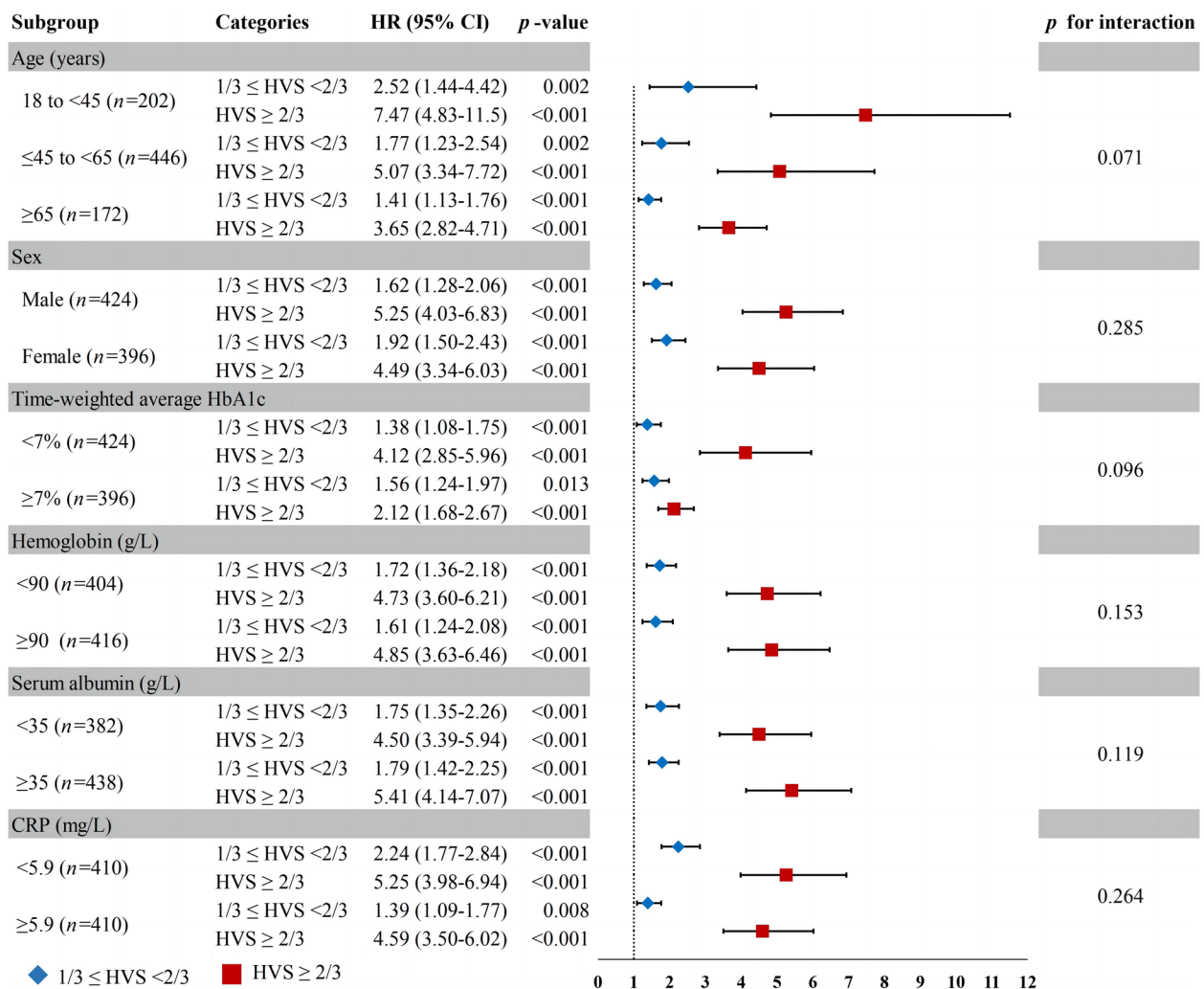


Fig. 4 Forest plot for subgroup analysis of HVS and all-cause mortality (refer to HVS < 1/3)

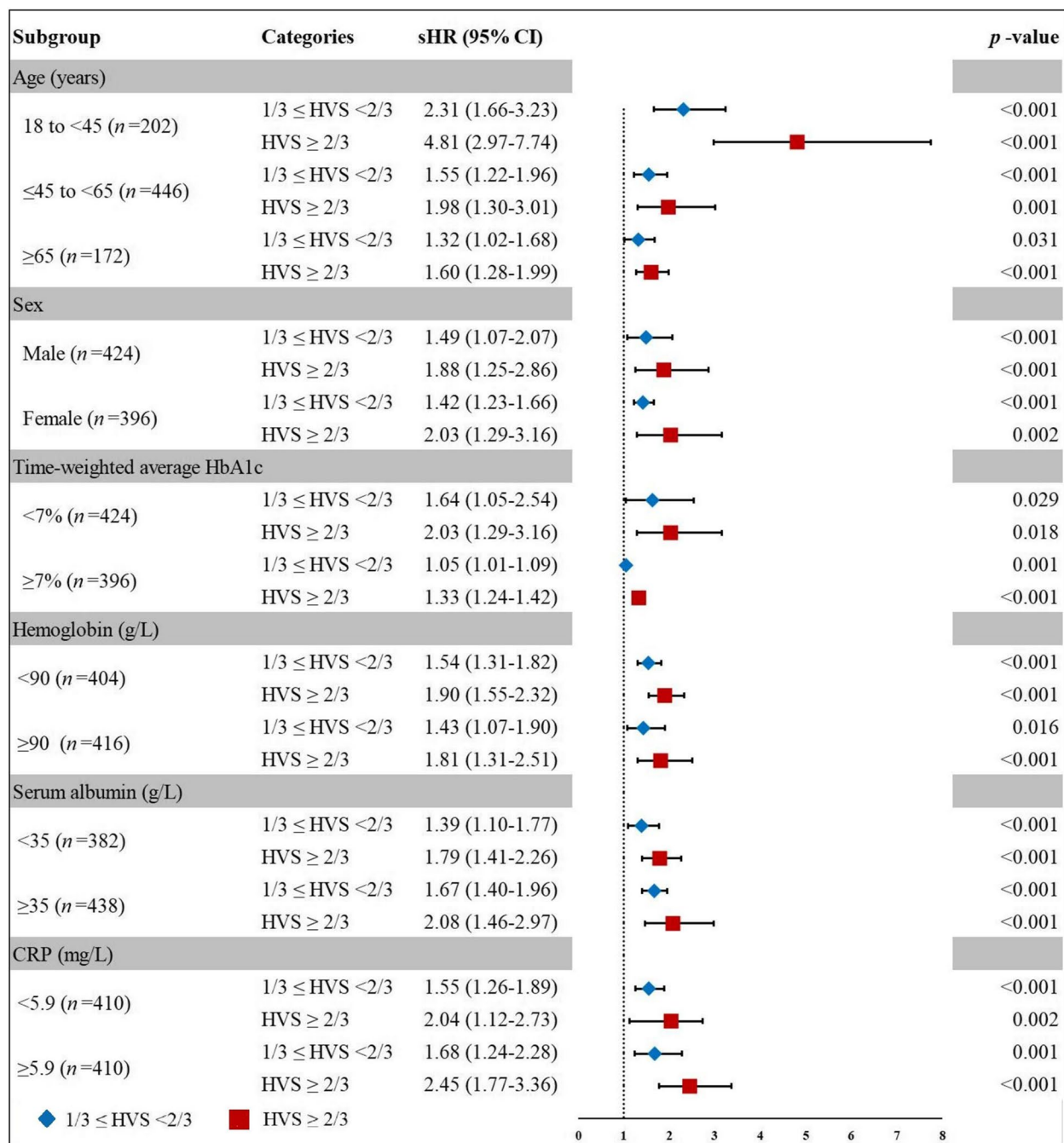


Fig. 5 Forest plot for subgroup analysis of HVS and MACE (refer to HVS < 1/3)

Time-dependent ROC curve

By analyzing time-dependent receiver operator characteristic curves, we examined the ability of HVS, SD and CV to predict all-cause mortality. As shown in Fig. 6, regardless of the predicted value of 3 years or 5 years, the performance of HVS is superior to that of SD and CV.

Discussion

We analyzed the relationship between visit-to-visit HbA_{1c} Variability and adverse endpoint events in peritoneal dialysis with type 2 diabetes and used HVS as a new index to evaluate HbA_{1c} variability for the first time. It is proved that frequent fluctuations of HbA_{1c} adjacent to measurements are independent risk factors for

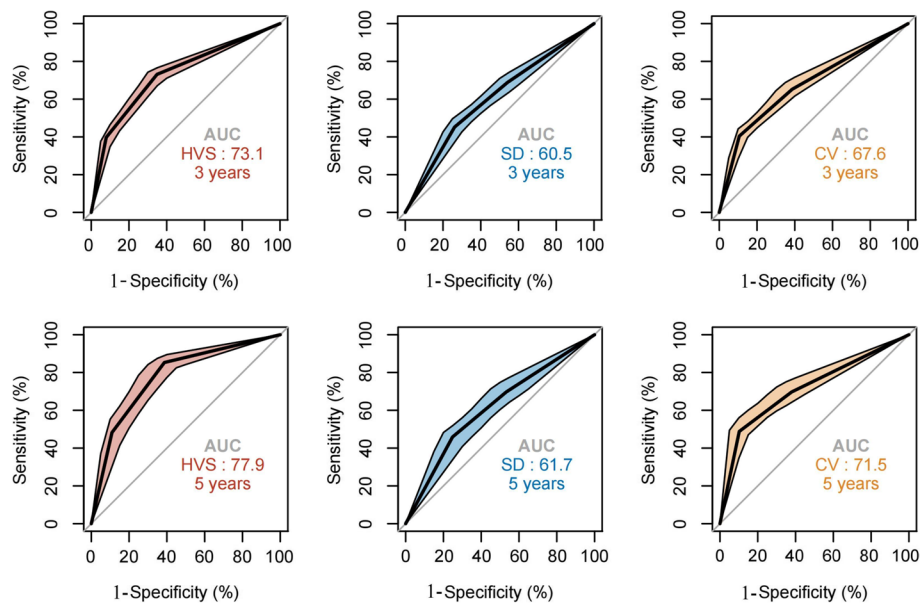


Fig. 6 Time-dependent ROC curve of HVS, SD and CV of HbA_{1c} with all-cause mortality

all-cause mortality and MACE in patients with type 2 diabetes. Our study showed that after adjustment for several parameters, including time-weighted average HbA_{1c}, patients with HVS $\geq 2/3$ had a substantially increased risk of detrimental outcomes. The HR of all-cause mortality and sHR of MACE were 4.59 and 1.91, respectively, compared with patients with HVS $< 1/3$. Additionally, we adjusted several unique confounding factors of peritoneal dialysis, such as residual renal function, normalized protein nitrogen appearance, and dialysis adequacy. Rich subgroup interaction effects confirmed that there was no remarkable alteration in the trend of high HVS classification associated with a high risk of harmful endpoint events among diverse individuals, though the sample size might not have been sufficient to achieve the desired *p*-value in the stratified analyses. Simultaneously, the efficiency in predicting outcomes of HVS was superior to SD and CV.

As is known to all, glucose level, hemoglobin and the interaction time between them will affect the variation of HbA_{1c} [12], and continuous exposure to glucose dialysate, low levels of albumin and hemoglobin and other states are inevitable in peritoneal dialysis, so we focused on correcting the influence of these factors in this study. It is worth noting that for subgroups with a time-weighted average HbA_{1c} $\geq 7.0\%$ (53 mmol/mol), although a positive association was observed between HVS and detrimental foreground, the correlation seemed to be diluted. We deem that higher HbA_{1c} levels often indicate more peritoneal glucose exposure and peritoneal injury, resulting in high peritoneal transport, reduced ultrafiltration

capacity, aggravating volume load and contributing to higher mortality, which diminish the relationship between HVS and prognosis to a certain extent. Interestingly, we found an enhanced association between HVS and the risk of death in peritoneal dialysis patients under 45 years of age. As previously reported, young patients with diabetes have fewer regular visits, and a large proportion of these population are in the HbA_{1c} measurement mode with discrete (SD at measurement intervals in the high quartile), which may miss an appropriate opportunity for readmission [13]. Recently accumulated evidence suggests that compared with the characteristics of the geriatric, such as large blood glucose fluctuations, the occurrence of abnormal blood glucose in young patients may be more indicative of the decline of organ function or unhealthy lifestyle, which leads to a higher mortality risk [14]. In brief, our study indicates that stable HbA_{1c} control still has a substantial benefit in peritoneal dialysis patients as well.

In the general population, HbA_{1c} variability is undoubtedly associated with MACE, microvascular disease and all-cause mortality. Oxidative stress, endothelial cell dysfunction, hypoglycemia events and cumulative epigenetic modification caused by blood glucose fluctuations are considered to be the potential causes of this relevance [15]. In patients with chronic kidney disease and dialysis, there are few studies on blood glucose control and prognosis. Data on hemodialysis from Japan suggests that a high ratio of Glycated Albumin to Glycated Hemoglobin is correlated with a higher mortality rate [16]. Another study of 2,798 peritoneal dialysis cases found that patients

with $\text{HbA}_{1c} \geq 8.0\%$ (63 mmol/mol) had higher all-cause mortality, but the study also noted that HbA_{1c} was vulnerable to albumin, inflammation, and hemoglobin [5]. About the variability of HbA_{1c} and the prognosis of dialysis patients, *Afghahi H*, et al. [17] demonstrated that the inflation risk of all-cause mortality in peritoneal dialysis patients with diabetes was prominently connected with the increase of CV in HbA_{1c} , which is consistent with our conclusion, but 48.9% of the patients included in their study were measured only twice, and it would weaken the accuracy of CV.

Our finding possesses certain advantages. Firstly, We have effectively integrated large-scale multicenter data, long follow-up time and clinically important negative outcomes were recorded, and confirmed by a variety of stratified and robust analyses. And we demonstrated consistent outcomes about two commonly occurring adverse events. Secondly, all subjects were tracked by their first HbA_{1c} measurements from balanced dialysis, so the dialysate glucose exposure was stable and there was no loss of disease progression after dialysis. In addition, the study stems from real-world data of Chinese peritoneal dialysis patients, so the results can be directly translated into clinical practice. Finally, the HVS, rather than SD or CV, is more likely to represent a trend of statistical discretization with no clinical guidance value, but it is more clinically readable when adopting HVS. Nephrologists can examine individual HbA_{1c} fluctuation curves and determine that patients with frequent differences of more than 0.5% (5.5 mmol/mol) in pre- and post-measurement results are at high risk. To put it simply, our study demonstrates from a practical point of view that frequent fluctuations in HbA_{1c} are a hazard factor for worse outcomes. Meanwhile, these findings indicate that HVS can be used as a potential clinical parameter to guide the management of diabetic peritoneal dialysis patients.

This study still has some limitations. First of all, as an observational retrospective cohort study, it is possible that some potential confounders (such as irregular measurement, hypoglycemic events or nursing quality) may limit the use of HVS, and we cannot point out the causal relationship between variability itself and prognosis. Secondly, due to the shortcomings of follow-up data, we failed to fully evaluate the role of changes in peritoneal dialysis prescription and accurate hypoglycemic drug dosage in the correlation between HVS and outcomes. In addition, participants with diabetes in this study were not specifically analyzed according to HbA_{1c} , socio-demographic or non-diabetes medical-related segmentation, which may have broad applications for evaluating clinical prognosis and deserve further investigation [18]. Finally, on account of the limitation of the numbers included in HbA_{1c} , almost every participant in the study was followed up for more than one

year, early deaths and some incomplete data were not taken into account accordingly. To some extent, this limits the value of early mortality forecast, although we know that the death of dialysis patients within one year may be susceptible to age, cardiac function, blood pressure, volume load and other basic states [19]. However, this study is of great significance for the judgment of medium- and long-term outcomes.

Conclusion

In conclusion, our research indicates that a higher visit-to-visit HVS in peritoneal dialysis patients with diabetes is independently related to an increased risk of all-cause mortality and MACE.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12882-023-03348-2>.

Additional file 1: Supplementary data Fig. S1. The HbA_{1c} at the baseline and follow-up.

Acknowledgements

The authors of this article would like to thank the patients who contributed to the data in the article.

Authors' contributions

Fengping Zhang and Taotao Shi wrote the manuscript. Fengping Zhang analysed data. Fengping Zhang and Taotao Shi prepared data for statistical analysis. Taotao Shi, and Yu Liu collected data, revised the manuscript and contributed to the discussion. Fengping Zhang and Ping Fu designed the study. Yunying Shi, Xiaoran Feng, Guilin Zhang and Yu Liu had contributed to the the database in the study. All authors reviewed the manuscript.

Funding

Not applicable.

Availability of data and materials

The data that supports these results of our research are available from the corresponding author on acceptable demand.

Declarations

Ethics approval and consent to participate

This study was conducted in compliance with the ethical standards of the Declaration of Helsinki and authorized by the Medical Research Ethics Committee of the Jiujiang NO.1 people's Hospital (No.jjsdyrmyy-xyyj-2021-107). And the Medical Research Ethics Committee of Jiujiang NO.1 people's Hospital waived the informed consent procedure due to the noninvasive and anonymous.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 6 July 2023 Accepted: 23 September 2023

Published online: 29 September 2023

References

1. Yang X, Yi C, Liu X, et al. Clinical outcome and risk factors for mortality in Chinese patients with diabetes on peritoneal dialysis: a 5-year clinical cohort study. *Diabetes Res Clin Pract.* 2013;100(3):354–61.
2. Chen JH, Johnson DW, Wong G, et al. Associations between diabetes and sex with peritoneal dialysis technique and patient survival: results from the Australia and New Zealand Dialysis and Transplant Registry cohort study. *Perit Dial Int.* 2021;41(1):57–68.
3. Pecoits-Filho R, Okpechi IG, Donner JA, et al. Capturing and monitoring global differences in untreated and treated end-stage kidney disease, kidney replacement therapy modality, and outcomes. *Kidney Int Suppl* (2011). 2020;10(1):e3–9.
4. de Boer IH, Caramori ML, Chan JCN, et al. Executive summary of the 2020 KDIGO Diabetes Management in CKD Guideline: evidence-based advances in monitoring and treatment. *Kidney Int.* 2020;98(4):839–48.
5. Duong U, Mehrotra R, Molnar MZ, et al. Glycemic control and survival in peritoneal dialysis patients with diabetes mellitus. *Clin J Am Soc Nephrol.* 2011;6(5):1041–8.
6. Freedman BI, Shihabi ZK, Andries L, et al. Relationship between assays of glycemia in diabetic subjects with advanced chronic kidney disease. *Am J Nephrol.* 2010;31(5):375–9.
7. Coelho S, Rodrigues A. Hemoglobin A1c in patients on peritoneal dialysis: how should we interpret it? *Ther Apher Dial.* 2014;18(5):375–82.
8. Zhou JJ, Schwenke DC, Bahn G, Reaven P, VADT Investigators. Glycemic variation and cardiovascular risk in the veterans affairs diabetes trial. *Diabetes Care.* 2018;41(10):2187–94.
9. Takenouchi A, Tsuboi A, Kurata M, Fukuo K, Kazumi T. Carotid intima-media thickness and visit-to-visit HbA1c variability predict progression of chronic kidney disease in type 2 diabetic patients with preserved kidney function. *J Diabetes Res.* 2016;2016:3295747.
10. Noyes JD, Soto-Pedre E, Donnelly LA, Pearson ER. Characteristics of people with high visit-to-visit glycaemic variability in Type 2 diabetes. *Diabet Med.* 2018;35(2):262–9.
11. Li S, Nemeth I, Donnelly L, Hapca S, Zhou K, Pearson ER. Visit-to-Visit HbA1c variability is associated with cardiovascular disease and microvascular complications in patients with newly diagnosed type 2 diabetes. *Diabetes Care.* 2020;43(2):426–32.
12. Rohlfing CL, Wiedmeyer HM, Little RR, England JD, Tennill A, Goldstein DE. Defining the relationship between plasma glucose and HbA(1c): analysis of glucose profiles and HbA(1c) in the Diabetes Control and Complications Trial. *Diabetes Care.* 2002;25(2):275–8.
13. Fryer AA, Holland D, Stedman M, et al. Variability in Test Interval Is Linked to Glycated Haemoglobin (HbA1c) Trajectory over Time. *J Diabetes Res.* 2022;2022:7093707.
14. Zhang X, Wu H, Fan B, et al. The role of age on the risk relationship between prediabetes and major morbidities and mortality: Analysis of the Hong Kong diabetes surveillance database of 2 million Chinese adults. *Lancet Reg Health West Pac.* 2022;30:100599.
15. Ceriello A, Monnier L, Owens D. Glycaemic variability in diabetes: clinical and therapeutic implications. *Lancet Diabetes Endocrinol.* 2019;7(3):221–30.
16. Hoshino J, Abe M, Hamano T, et al. Glycated albumin to glycated hemoglobin ratio and mortality in diabetic patients on dialysis: a new association. *Nephrol Dial Transplant.* 2023;38(5):1309–17.
17. Afghahi H, Nasic S, Peters B, Rydell H, Hadimeri H, Svensson J. Long-term glycemic variability and the risk of mortality in diabetic patients receiving peritoneal dialysis. *PLoS One.* 2022;17(1):e0262880.
18. Seng JJB, Monteiro AY, Kwan YH, et al. Population segmentation of type 2 diabetes mellitus patients and its clinical applications - a scoping review. *BMC Med Res Methodol.* 2021;21(1):49.
19. Chan KE, Maddux FW, Toloff-Rubin N, Karumanchi SA, Thadhani R, Hakim RM. Early outcomes among those initiating chronic dialysis in the United States. *Clin J Am Soc Nephrol.* 2011;6(11):2642–9.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

