OLDER AGE, HIGHER BODY MASS INDEX AND INFLAMMATION INCREASE THE RISK FOR NEW-ONSET DIABETES AND IMPAIRED GLUCOSE TOLERANCE IN PATIENTS ON PERITONEAL DIALYSIS

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◆ **Objectives:** To identify predictors of new-onset diabetes and impaired glucose tolerance (IGT) events in patients undergoing peritoneal dialysis (PD) based on baseline and time-dependent covariates, respectively.

◆ **Methods:** In this prospective, single center-based cohort, all non-diabetic incident PD patients between August 2003 and August 2011 were included. All demographic and laboratory data were recorded at baseline. Repeated measurements for laboratory, dialysis prescription, and nutrition parameters were recorded at regular intervals. Multivariable Cox regression models built from baseline and time-dependent variables respectively were used to calculate the hazard ratio (HR) of potential predictors for new-onset diabetes and IGT (NODI).

◆ **Results:** Of the 612 PD patients, 25 (4.1%) and 7 (1.1%) patients were identified with NODI, respectively, during a mean follow-up period of 32.4 (12.9–60.8) months. Using multivariable Cox regression analysis, age and body mass index (BMI) at baseline were significantly associated with NODI after adjustment for potential confounders. During follow-up, time-dependent BMI and serum high-sensitive C-reactive protein (HS-CRP) independently predicted the risk for NODI. Patients with NODI had significantly elevated plasma glucose concentrations and BMI from the start of PD therapy, with serum HS-CRP maintained at high levels. Dietary/dialysate energy intake and other laboratory parameters were not correlated with NODI risk either as baseline or time-dependent variables.

◆ **Conclusions:** Traditional and uremic-related risk factors, such as older age, higher BMI, and inflammation, contribute to new-onset diabetes and impaired glucose tolerance in PD patients.

new-onset diabetes and IGT (NODI) is a common complication among patients on dialysis (4–6,8), it is important to explore the potential risk factors for this complication. However, published data on this issue are limited in dialysis populations.

To our knowledge, traditional risk factors, such as age, male gender, obesity, hypertension, and hyperlipidemia, have been recognized to increase the risk for new-onset diabetes in the general population (9–11). These traditional factors, as well as uremia-related factors including malnutrition, inflammation, and comorbidities, have previously shown to be associated with new-onset diabetes, IGT, or fasting hyperglycemia in dialysis patients in 2 cross-sectional (4,8) and 2 longitudinal cohort datasets, respectively (6,7). However, the above parameters were collected at baseline or at a single timepoint in these studies, which makes it impossible to analyze the association between time-varying variables and outcomes. In addition, glucose is inevitably used as an osmotic agent in all commercial solutions for PD patients in China, accounting for about 20% of total energy intake (12,13). A previous study has indicated the potential side effects of dialysate glucose including a tendency for hyperglycemia and hyperinsulinemia in a dose-dependent manner in PD patients (14). However, 2 recent papers did not compare the higher risk for new-onset diabetes in PD populations with their hemodialysis (HD) counterpart (6,7). It is therefore of interest to explore the potential effect of the amount of dietary energy intake and glucose absorption via dialysate on the incidence of NODI in PD patients.

All of the above mentioned contributors actually exist at the start of PD therapy and then vary to different degrees during follow-up. To determine the critical contributors to NODI, baseline characteristics and time-dependent variables need to be analyzed in Cox regression models. In this paper, we report a prospective cohort study to explore the incidence and risk factors for NODI, taking baseline and time-dependent covariates into account.

METHODS

SUBJECT SELECTION

All the non-diabetic incident patients on chronic PD between August 2003 and August 2011 were enrolled in this

Perit Dial Int 2016; 36(3):277–283 epub ahead of print: 04 Feb 2016
<http://dx.doi.org/10.3747/pdi.2015.00182>

KEY WORDS: Peritoneal dialysis; PD; inflammation; diabetes; impaired glucose tolerance; IGT; new-onset diabetes/IGT; NODI.

New-onset diabetes and impaired glucose tolerance (IGT) have been shown to be associated with increased cardiovascular events and risk of death in the general population (1–3) and in patients undergoing dialysis (4–7). Since

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Received 29 July 2015; accepted 10 August 2015.

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study. All patients visited with a physician at least once every 3 months. All subjects began the PD program within 1 month after catheter implantation and were given lactate-buffered glucose dialysate with a twin-bag connection system (Baxter Healthcare, Guangzhou, China). This study was approved by the Medical Ethics Committee of Peking University. Written informed consent was obtained from each patient.

DATA COLLECTION

Demographic and clinical data including age, gender, body mass index (BMI), primary renal disease, the presence of cardiovascular disease (CVD) and diabetes mellitus (DM), and Charlson index (7) were collected within the week preceding PD catheter implantation. Cardiovascular disease was recorded if any of the following conditions was present at the baseline: angina, class III-IV congestive heart failure (NYHA), transient ischemic attack, history of myocardial infarction or cerebrovascular accident and peripheral arterial disease (15). Baseline values included all measurements of blood pressure, biochemistry, dialysis adequacy, dietary and nutrition parameters in the first 3 months. All above measurements during the study period were prospectively collected and averaged for each 6-month interval to calculate time-dependent values. All patients were followed until death, transfer to HD, renal transplantation, or censoring at 30 September 2014.

Systolic and diastolic blood pressures were measured on the morning of each clinic visit according to the standard method. Mean arterial pressure was calculated. Biochemistry data including hemoglobin, serum albumin, lipids spectrum, glucose, uric, urea, creatinine, calcium, phosphate, intact parathyroid hormone (iPTH) and so on were examined using an automatic Hitachi chemistry analyzer (Hitachi Chemical, Tokyo, Japan). Serum high-sensitive C-reactive protein (HS-CRP) was measured by immune rate nephelometric analysis.

Dialysis prescription including glucose concentration and volume of instilled and drained dialysate were recorded for 1 day before each clinic visit. Dialysis adequacy, residual renal function (RRF) and glucose absorption were measured by collecting 24-hour urine and dialysate. Dialysis adequacy was defined as total Kt/V and total creatinine clearance. Glucose absorption via dialysate was calculated by subtracting glucose amounts in drained dialysate from that in instilled dialysate, expressed as grams of glucose/day, and then dialysate energy absorption was calculated as kcal of energy/day.

All patients completed 3-day diet records before their regular clinic visits that were then evaluated by a skilled dietitian. Food models were used to estimate actual amounts of foods recorded in the diet diary. Daily intakes of protein, energy, carbohydrate, fat, potassium, sodium, fiber, and so on were calculated using the PD information Management System computer application (Peritoneal Dialysis Center, Peking University, Beijing, China).

DEFINITION OF OUTCOME EVENTS

The main outcomes were defined as NODI according to the current diagnostic criteria of the American Diabetes Association for the diagnosis of diabetes and IGT in the general population (16). The composite outcome was expressed as NODI. New-onset diabetes was diagnosed if fasting plasma glucose was ≥ 7 mmol/L on 2 occasions or 2-hour plasma glucose was ≥ 11.1 mmol/L during an oral glucose tolerance test (OGTT). Patients were defined as IGT if their fasting plasma glucose was 5.6 ~ 6.9 mmol/L, or their 2-hour plasma glucose was 7.8 ~ 11 mmol/L during an OGTT. We did not use the criteria of glycosylated hemoglobin for diagnosing diabetes and IGT since the influence of dialysate glucose absorption on the measurement of glycosylated hemoglobin for continuous ambulatory PD patients was unknown.

Screening for NODI during the study period was as follows: for each visit, at least once every 3 months, all subjects had their plasma glucose measured after an overnight fast, but PD therapy was continued. Once their plasma glucose was higher than 7 mmol/L, absolute fasting status with dialysate draining for at least 10 hours was requested to complete the fasting plasma glucose for their next visits, or an OGTT at the appointment.

STATISTICAL ANALYSIS

Parametric data are presented as mean $\pm$ standard deviation (SD). Nonparametric data are presented as median values with interquartile range (IQR). Categorical variables are expressed as percentages or ratios. Comparisons between groups used the unpaired Student's *t*-test, the Mann-Whitney U test, and the chi-square test, as appropriate.

The incidence of events was estimated as a cumulative incidence rate using the Kaplan-Meier method. For the univariate analysis of the risk for NODI, the relative risks of potential parameters were calculated respectively. Only parameters showing a significant univariate relationship ($p < 0.10$) with NODI were included in Cox regression multivariable models. The calculation of time-dependent biochemistry, nutrition and dialysis parameters in the models used the half-yearly measurements. We reported the multivariable adjusted hazard ratios (HRs) with 95% confidence intervals (CIs).

Changes in plasma glucose, BMI, HS-CRP, and dietary and dialysate energy intake over time were also compared between groups using a mixed model analysis of variance, with bootstrap covariance accounting for correlation among repeated measures within a patient. We chose the 3-year period of observation here since the median time to NODI was around 3 years in this cohort. Sensitivity analysis was performed with adjustment for patients' age and gender in the model. In addition, changes in outcome variables over time were also assessed within each group.

Statistical analyses were performed using the SPSS software package version 20.0 (SPSS, Chicago, IL, USA). All probabilities were 2-tailed, and the level of significance was set at 0.05 to reject the null hypothesis.

RESULTS

BASELINE CHARACTERISTICS AND FOLLOW-UP

A total of 612 non-diabetic PD patients were enrolled, with a mean age of 55.5 ± 16.8 years and a BMI of 22.6 ± 3.7 kg/m²; CVD was present in 32.4% of subjects at baseline. The median Charlson index scores were 3 (2 – 5). Chronic glomerulonephritis was the most common primary disease (38.1%), followed by hypertensive nephropathy (26%).

The median follow-up time was 32.4 (12.9 – 60.8) months. At the end of the study, 213 (34.8%) patients died, 87 (14.2%) transferred to HD, 87 (14.2%) received a transplant, 12 (2.0%) lost to follow-up and 213 (34.8%) maintained PD therapy. There were 25 and 7 patients diagnosed with NODI, respectively. The cumulative incidence rates of NODI were 0.8% at 1 year, 2.3% at 3 years, 3.9% at 5 years, 4.6% at 7 years, and 5.2% at 10 years. The median time to new-onset diabetes or IGT was 30.8 (12.6 – 56.9) months. Of 25 patients with new-onset diabetes, mean fasting plasma glucose and 2-hour plasma glucose in OGTTs were 8.1 ± 0.6 mmol/L and 16.9 ± 2.3 mmol/L, and 48% and 52% of them were prescribed insulin and drugs such as acarbose and fastic respectively. Seven patients were diagnosed as IGT since their fasting plasma glucose and 2-hour plasma glucose in OGTTs were 6.8 ± 0.5 mmol/L and 10.3 ± 0.7 mmol/L respectively. They were taught to control their glucose levels by dietary restriction and aerobic exercise.

As depicted in Figure 1, the changing trend of plasma glucose concentrations was significantly different between groups after adjusting for age and gender ($p < 0.001$). Patients

Figure 1 — Plasma glucose concentration in 36-month observation period in patients with and without NODI on PD. Markers represents the mean, and lower and upper bar boundaries are 95% CI; p value comparing the 2 groups over time was obtained from the linear mixed model with bootstrap covariance accounting for correlated measures within a subject. IGT = impaired glucose tolerance; NODI = new-onset diabetes and IGT; PD = peritoneal dialysis; CI = confidence interval.

with NODI showed an increasing trend in plasma glucose levels compared with those without, and they also had significantly higher plasma glucose concentrations than the control group at baseline and subsequent half-yearly timepoints during follow-up ($p = 0.001 - 0.05$).

COMPARISONS OF CLINICAL DATA IN PATIENTS WITH AND WITHOUT NODI AT BASELINE

As shown in Table 1, patients with NODI were more likely to be older and overweight as indicated by a higher BMI at baseline. Serum creatinine concentration was significantly lower in patients with NODI. Serum HS-CRP was significantly higher in these patients. Other clinical data such as gender, CVD history, Charlson index scores, primary kidney disease, blood pressure, other biochemistry data, total Kt/V, and RRF at baseline were not different between groups.

RISK FACTORS FOR NODI

The relative risks of univariates for NODI events at baseline are listed in Table 2. For univariate regression analysis, the relative risk of older age, time-dependent BMI, and log-transformed HS-CRP were each significantly contributing factors. Time-dependent serum high-density lipoprotein (HDL) and creatinine only showed weak associations with risk of NODI. Because of the large sample size and small number of endpoints in this cohort, only potentially significant ($p < 0.1$) predictors of NODI in Table 2 were included in the final model. By using a multivariable Cox regression model, the coexistence of age, time-dependent BMI, and log-transformed HS-CRP were identified as independent predictors for NODI, with HRs 1.03 (1.00 – 1.06), 1.12 (1.02 – 1.22), and 2.23 (1.03 – 4.85), respectively. Conversely, time-dependent dietary energy intake and dialysate energy absorption could not predict NODI occurrence, nor could other laboratory variables, dialysis adequacy, or RRF.

LONGITUDINAL CHANGES IN BMI, HS-CRP, AND DIETARY AND DIALYSATE ENERGY INTAKE IN PATIENTS WITH AND WITHOUT NODI

During the 3-year follow-up, longitudinal changes in the above parameters were compared between patients with and without NODI. As shown in Figure 2, after adjusting for age and gender, BMI increased over time in patients with NODI ($p = 0.007$) as well as in those without NODI ($p < 0.001$). This increasing BMI trend was significantly higher in NODI patients ($p = 0.003$). After adjusting for age and gender, the change in serum HS-CRP over time between groups was also significantly different ($p < 0.001$). As can be seen in Figure 3, serum HS-CRP levels in patients with NODI was maintained at a high level ($p = 0.71$), but was gradually increased in those without ($p = 0.006$). Comparisons of changes in dietary energy intake and dialysate energy absorption were not significant between groups ($p > 0.05$).

TABLE 1
Baseline Clinical Characteristics and Biochemistry Data of Non-Diabetic Patients on PD with and without NODI

Variables	NODI group	Control	<i>p</i> values
N	32	580	—
Age, years	61.0±12.5	55.2±15.4 ^a	0.02
Male (%)	28.1	44.1	0.09
BMI, kg/m ²	24.3±4.1	22.5±3.6 ^a	0.01
CVD history (%)	37.5	32.2	0.56
Charlson index scores	4 (2~5)	2 (2~5)	0.25
Primary disease			0.15
CGN	18.8	39.8	
Hypertension	37.5	25.7	
CTIN	21.9	13.5	
Others	21.8	21.0	
Systolic blood pressure, mmHg	134.3±21.5	133.5±17.9	0.52
Diastolic blood pressure, mmHg	79.3±14.1	81.3±12	0.21
Triglycerides, mmol/L	1.97±1.04	1.67±0.89	0.06
Total cholesterol, mmol/L	4.9±0.9	4.8±1.1	0.55
HDL, mmol/L	1.1±0.3	1.2±0.4	0.2
LDL, mmol/L	2.4±0.8	2.6±0.8	0.25
Albumin, g/L	37.6±3.8	35.9±4.8	0.06
Hemoglobin, g/dL	103.8±15	100.1±16.7	0.2
Uric acid, mg/dL	384.9±77.4	395.7±97.7	0.69
Urea nitrogen, mmol/L	21.3±5.2	23.2±6.6	0.12
Creatinine, μmol/L	655.9±151.7	758.9±246.3 ^b	0.001
Calcium, mmol/L	2.3±0.3	2.2±0.2	0.08
Phosphate, mmol/L	1.6±0.4	1.6±0.4	0.41
Parathyroid hormone, pg/mL	272.8 (87.7, 539.4)	194.5 (80.8, 386.6)	0.13
HS-CRP, mg/L	4.2 (2.2, 9.9)	1.9 (0.7, 5.4) ^a	0.02
Total Kt/V	2.1±0.6	1.9±0.5	0.08
RRF, mL/min	7.9 (5.7, 11.1)	4.7 (3.2, 7.2)	0.15

PD = peritoneal dialysis; NODI = new-onset diabetes/impaired glucose tolerance; BMI = body mass index; CVD = cardiovascular disease; CGN = chronic glomerulonephritis; CTIN = chronic tubulointerstitial nephropathy; HDL = high-density lipoprotein; LDL = low-density lipoprotein; HS-CRP = high-sensitive C-reactive protein; RRF = residual renal function.

^a *p* < 0.05 compared with the NODI group.

^b *p* < 0.01 compared with the NODI group.

Values are expressed as mean ± standard deviation, median with interquartile range, or percentages or ratios.

DISCUSSION

The cumulative incidence of NODI was 5.2% at 10 years in this PD cohort. This is similar to the prevalence of new-onset diabetes as reported in PD patients from previous reports, which ranged between 1.6% and 5% (8,17,18), but lower than the cumulative incidence of new-onset diabetes in HD patients (7.6% at 3 years) from USRDS data (5), and in combined PD and HD patients (21% at 9 years) in a report from Taiwan (6).

Of note, baseline and subsequent plasma glucose levels were elevated even before NODI diagnosis. The trend of plasma glucose concentration increased over time and was significantly greater among patients with NODI. This finding supports the theory that individuals with hyperglycemia have an increased risk for future diabetes in the general population (19). In addition, similar to previous studies, patients with higher fasting glucose or NODI in our cohort are possibly

sicker at baseline since they are older individuals with more extensive inflammation (4,8). This could partly explain these patients' higher risk for cardiovascular events and mortality rates reported in previous literature (2–4). Therefore, hyperglycemia at baseline, even in those not achieving NODI criteria, or the increasing trend of plasma glucose levels after PD therapy commencement should garner more attention in PD patients. Whether clinicians should take action to initiate lifestyle modifications, such as exercise training, weight loss, and dietary counseling, to prevent the occurrence of diabetes in these subjects is unknown (20,21). The target of plasma glucose control for these patients before NODI is also to be determined by exploring the association between glucose level and outcomes from large-scale multi-center cohort studies.

To the best of our knowledge, this is the first study exploring risk factors of NODI in a PD cohort based on baseline and time-dependent variables. Age and time-dependent fat

TABLE 2
Risk Factors for NODI in Non-Diabetic Patients on Peritoneal Dialysis

Covariates ^a	Univariate analysis		Multivariable analysis	
	HR (95% CI)	p values	HR (95% CI)	p values
Age, years	1.04 (1.01–1.07) ^b	0.008	1.03 (1.00–1.06) ^b	0.03
Male (%)	1.36 (0.63–2.92)	0.42	—	
CVD history (%)	1.33 (0.65–2.74)	0.42	—	
Charlson index scores	1.08 (0.96–1.21)	0.18	—	
BMI, kg/m ²	1.15 (1.06–1.26) ^b	0.001	1.12 (1.02–1.22) ^b	0.01
Systolic blood pressure, mmHg	1.08 (0.96–1.13)	0.28	—	
Diastolic blood pressure, mmHg	0.96 (0.92–1.15)	0.32	—	
Triglycerides, mmol/L	1.12 (0.88–1.41)	0.36	—	
Total cholesterol, mmol/L	0.84 (0.61–1.18)	0.33	—	
HDL, mmol/L	0.29 (0.08–1.19)	0.09	—	
LDL, mmol/L	0.83 (0.52–1.33)	0.44	—	
Albumin, g/L	0.94 (0.87–1.02)	0.15	—	
Hemoglobin, g/dL	0.95 (0.85–1.23)	0.34	—	
Uric acid, mg/dL	0.99 (0.99–1.00)	0.63	—	
Creatinine, μ mol/L	0.99 (0.99–1.00)	0.06	—	
Calcium, mmol/L	0.59 (0.10–3.49)	0.57	—	
Phosphate, mmol/L	0.50 (0.16–1.52)	0.22	—	
Parathyroid hormone, pg/mL	1.00 (0.99–1.00)	0.54	—	
HS-CRP ^c , mg/L	2.72 (1.43–5.20) ^d	0.008	2.23 (1.03–4.85) ^b	0.04
Total Kt/V	1.81 (0.64–5.11)	0.26	—	
RRF, mL/min	1.00 (0.98–1.02)	0.94	—	
Dietary energy intake, kcal/d	1.00 (0.998–1.006)	0.27	—	
Dialysate energy absorption, kcal/d	0.999 (0.998–1.00)	0.24	—	

NODI = new-onset diabetes/impaired glucose tolerance; HR = hazard ratio; CI = confidence interval; CVD = cardiovascular disease; BMI = body mass index; HDL = high-density lipoprotein; LDL = low-density lipoprotein; HS-CRP = high-sensitive C-reactive protein; RRF = residual renal function.

^a Covariates were shown as time-dependent variables except for age, gender, CVD history, and Charlson index scores.

^b $p < 0.05$, hazard ratio (HR) for NODI risk.

^c HS-CRP values were log-transformed.

^d $p < 0.01$, hazard ratio (HR) for NODI risk.

mass evaluated by BMI were confirmed as predictors of NODI in this cohort. The trend of increasing BMI in patients with NODI after the initiation of PD should be noted. Prior to our studies, age and BMI were commonly recognized to be associated with hyperglycemia or NODI in the general population (22,23), but less confirmed in incident dialysis patients (6,7). Inflammation is recognized as a critical predictor of NODI in the general population (24–26), which was also determined in this PD cohort when time-dependent HS-CRP was considered. Of note, patients having maintained inflammation status are potential high-risk subjects for NODI. This phenomenon can be explained by the fact that pro-inflammatory cytokines in chronic inflammation can interfere with insulin signaling in peripheral tissues or induce B-cell dysfunction and subsequent insulin deficiency (27). Based on the above findings, we suggest that PD patients may share a common pathway to the incidence of NODI as indicated in the general population. However, the lack of association between serum lipids and the risk for NODI in PD patients should also be stated.

The effect of dialysate glucose load on hyperglycemia in PD patients has previously been shown (14), and high dietary glycaemic load has also demonstrated a robust relationship with

the risk for type 2 diabetes in the general population based on meta-analyses (28). However, our data did not support the harmful effect of glucose load via dietary and dialysate on the risk for NODI in PD patients based on baseline or time-dependent analysis. These paradoxical findings might be explained as follows: first, the background characteristics of the patients, such as age, high BMI, and inflammation, are stronger than post-dialysis glucose load for predicting NODI. Secondly, we cannot exclude the possibility that a positive result would appear if the observation period were prolonged. Thirdly, the net energy balance is not only dependent on energy intake via dietary and dialysate, but also on basal energy expenditure, physical activity, and anabolic/catabolic hormone levels, which were not examined in the present study. We therefore cannot determine whether the risk for NODI is further influenced by net energy balance. Similar to our data, Szeto *et al.* reported that glucose load was not significantly different between PD patients with various extents of hyperglycemia in the first year of PD (8). Moreover, 2 recent papers have shown that PD therapy is not associated with a higher risk for new-onset diabetes compared with HD based on findings using the Taiwan National Database (6,7).

Figure 2 — Body mass index in 36-month observation period in patients with and without NODI on PD. Markers represent the mean; lower and upper bar boundaries are 95% CI; p value comparing the 2 groups over time was obtained from the linear mixed model with bootstrap covariance accounting for correlated measures within a subject. IGT = impaired glucose tolerance; NODI = new-onset diabetes and IGT; PD = peritoneal dialysis; CI = confidence interval.

Figure 3 — High-sensitive C-reactive protein in 36-month observation period in patients with and without NODI on PD. Markers represent the median; lower and upper bar boundaries are 95% CI; p value comparing the 2 groups over time was obtained from the linear mixed model with bootstrap covariance accounting for correlated measures within a subject. IGT = impaired glucose tolerance; NODI = new-onset diabetes and IGT; HS-CRP = high-sensitive C-reactive protein; PD = peritoneal dialysis; CI = confidence interval.

This study has several advantages. For instance, this is the first study to explore risk factors for NODI in PD patients based on time-dependent Cox regression models. Both traditional risk factors in the general population and uremic-related risk factors of NODI were taken into account. The impact of glucose load via dietary and dialysate intake on NODI risk as we explored has not been investigated in prior studies.

All non-diabetic subjects were repeatedly tested for incident NODI during long-term follow-up if their fasting glucose was higher than 7 mmol/L for timely diagnosis. Genuine fasting plasma glucose was measured and an OGTT administered for each suspected subject in this study. Glucose absorption via dialysate was directly calculated from the net glucose balance based on a 24-hour dialysate collection rather than any estimated equation.

We are also aware of the drawbacks of this study. For example, the number of endpoints was small despite the large sample size and relatively long-term follow-up. The potential effects of serum HDL and creatinine on the risk of NODI could not be observed due the limited power of the study. Moreover, there was no information about net energy balance, which led to the impossibility of exploring its association with the risk for NODI. Another limitation that needs to be highlighted is that a large number of tests were performed in the univariate analyses with no adjustment for multiple testing, increasing the chances of false positive results.

In conclusion, our data indicated that older age, higher BMI, and inflammation increase the risk for NODI in PD patients. We should pay more attention to this risk as early as possible, especially when baseline plasma glucose is relatively high or there is an increasing trend of plasma glucose and BMI right after the initiation of PD therapy. Our findings suggest PD patients may have the same probability of glucose abnormalities as indicated in the general population. However, the impact of glucose absorption via dietary and dialysate intake on NODI risk cannot be concluded until net energy balance is investigated for detailed mechanisms underlying NODI development in PD patients.

ACKNOWLEDGMENTS

The authors express their appreciation to the patients, doctors, and nursing staff of the peritoneal dialysis center of Peking University First Hospital, Division of Nephrology of Peking University Third Hospital, for their participation in this study.

Author Contributions: JD designed the study and wrote manuscript; YC researched the data; ZKY contributed to discussion.

DISCLOSURES

This study was in part supported by New Century Excellent Talents from the Education Department, China, ISN Research Award from ISN GO R&P Committee, and Capital Characteristic Clinic Research Grant from Beijing Science & Technology Committee. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. The authors have no financial conflicts of interest to declare.

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