Propensity-Matched Comparison of New Onset Diabetes Mellitus between Incident Peritoneal Dialysis and Hemodialysis Patients

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Background

New-onset diabetes mellitus (NODM) is associated with poor outcome in patients treated with hemodialysis (HD) or peritoneal dialysis (PD). PD patients were exposed to extra glucose load from daily dianeal dwelling. We ask the question "Are PD patients more prone to develop NODM after dialysis?". We used a propensity score(PS) matching approach to study this subject. We aim to compare the incidence and outcome of NODM by intention-to-treat analysis in a propensity score-matched HD and PD cohorts.

Methods

All HD and PD patients in Taiwan Renal Registry Database (include all patients who survived ≥ 1M after dialysis) were analyzed from 1997 to 2005. Patients were followed until death, renal transplantation or up to December 31, 2008. We attempted to correct for differences between patient characteristics using a PS-matching method. We matched each PD patient with 4 HD patients having a similar PS. PS accounted for factors recorded in the database, including age, sex, body weight, primary renal disease and co-morbidity(Fig.1) . The risk for NODM was determined using competing-risks analysis. We compared the incidence and survival outcomes of NODM in PD and PS-matched HD patients. Predictors of NODM and mortality were studied using Cox models. All statistical analysis was performed with Stata version 12 SE (Statacorp, Texas, USA). P < 0.05 was considered as significant.

Results

We analyzed 2548 non-DM incident PD patients and 10192 PS-matched HD patients with 5.9±3 years follow up. Mean age of PD patients were 50.2± 14.7y vs. 50.2± 14.4y of PS-matched HD patients. During follow up , 13% of PD patients and 22% of PS-matched HD patients developed NODM (Table 1). The crude incidence of NODM was 2.4/100 patient-years for PD patients and 4/100 patient- years for HD patients (p<0.001). The risk of developing NODM after starting dialysis is approximately 50% lower (HR 0.48) for patients treated with PD. Male gender, a lower serum albumin and lower hematocrit were independently linked to increased NODM risks. After adjusting for covariates, regardless of dialysis modality, patients who developed NODM had increased overall mortality (HR 3.628, p<0.001) than those did not.

Conclusions

In a PS-matched Chinese cohort, incident patients receiving HD carry a higher risk of developing NODM than those receiving PD. The patients with NODM are associated with increased overall mortality reardless of dialysis modality chosen.

Discussion

Why more NODM in HD patients?

We speculate that PD patients may have better physical activities in their daily life than HD patients. Increased physical activities may prevent the development of diabetes. In addition, the blood-membrane interaction during HD may induce cytokine production, such as C-reactive protein and interleukins-6. Chronic inflammation induced by blood-membrane interaction may play a critical role in the development of diabetes in HD patients.

References

1. Tien KJ, Lin ZZ, Chio CC et al. Epidemiology and Mortality of New-Onset Diabetes Mellitus After Dialysis: Taiwan national cohort study. *Diabetes Care* 2013.
2. Verduijn M, Grootendorst DC, Dekker FW et al. The analysis of competing events like cause-specific mortality--beware of the Kaplan-Meier method. *Nephrol Dial Transplant* 2011; **26**: 56-61.
3. Haubitz M, Brunkhorst R, Wrenger E et al. Chronic induction of C-reactive protein by hemodialysis, but not by peritoneal dialysis therapy. *Perit Dial Int* 1996; **16**: 158-62.
4. Pradhan AD, Manson JE, Rifai N et al. C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. *JAMA* 2001; **286**: 327-34.

Figure 1. Scheme of study design

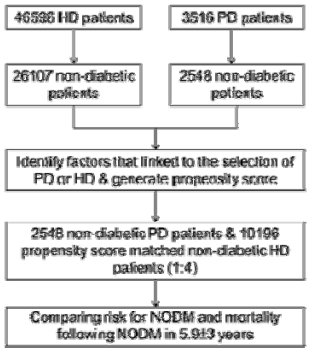

Figure 2. Risk of developing new onset diabetes mellitus in all hemodialysis (HD) patients (A) and matched HD patients (B) compared to PD patients

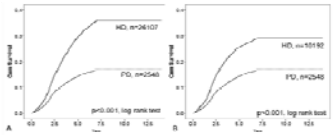

Table 1. Clinical characteristics of patients with and without new onset diabetes mellitus (NODM)

	NODM(-) n=10187		NODM(+) n=2553		P
Age (year)	48.4	±14.2	56.6	±13.7	<0.001
Follow-up (year)	6.1	±2.9	4.9	±2.8	<0.001
Male gender n(%)	3707	(36)	985	(39)	0.04
HD n(%)	7971	(78)	2221	(87)	<0.001
Mortality n(%)	2822	(28)	1276	(50)	<0.001
Weight (kg)	69.4	±5.8	70.2	±7.8	0.08
Underlying disease n(%)					
CGN	5898	(58)	1470	(58)	0.77
Hypertension	1013	(10)	298	(12)	0.01
Others	3276	(32)	785	(31)	0.17
Co-morbidity n(%)					
Hypertension	3878	(38)	870	(34)	<0.001
CHF	455	(4)	134	(5)	0.09
Ischemic heart	410	(4)	121	(5)	0.11
CVA	193	(2)	63	(2)	0.07
Liver disease	297	(3)	85	(3)	0.27
Cancer	158	(2)	42	(2)	0.73
Tuberculosis	84	(1)	22	(1)	0.85
Others	658	(6)	146	(6)	0.17
Hematocrit (%)	29.4	±3.6	28.9	±3.8	<0.001
Albumin (g/dl)	3.9	±0.4	3.8	±0.5	<0.001
Phosphate (mg/dl)	5.1	±1.3	4.9	±1.5	<0.001
Calcium (mg/dl)	9.6	±0.8	9.6	±0.8	0.14
CPP (mg/dl)²	48.9	±13.1	46.7	±14.7	<0.001
FBG (mg/dl)	96	±14	168	±69	<0.001
i-PTH (ng/dl)	262.6	±265.6	223.7	±262.3	<0.001*

HD: hemodialysis, CGN: chronic glomerulonephritis, HTN: hypertension, CHF: congestive heart failure, CVA: cerebral vascular accident, FBG: fasting blood glucose, CPP: calcium-phosphate product, i-PTH: intact parathyroid hormone
* Mann-Whitney U test

Table 2. Hazard ratio of risk factor for new-onset diabetes in chronic kidney disease patients receiving peritoneal dialysis (PD) or hemodialysis (HD) in univariate competing-risks analysis

	HR	95% C.I. for HR		p
HD (v.s. PD)	1.85	1.57	2.20	<0.001
Age	1.01	1.007	1.014	<0.001
Male gender	0.936	0.835	1.05	0.266
HTN	0.958	0.855	1.07	0.465
FBG	1.006	1.005	1.007	<0.001
Serum albumin	1.25	1.11	1.41	<0.001
Phosphorus	1.05	1.001	1.098	0.022
CPP	0.980	0.968	1.093	0.232
Hematocrit	1.02	1.001	1.03	0.031
i-PTH	1.000	0.999	1.000	0.112

FBG: fasting blood glucose, CPP: calcium-phosphate product, i-PTH: intact parathyroid hormone

Table 3. Hazard ratio of risk factor for new-onset diabetes in chronic kidney disease patients receiving peritoneal dialysis (PD) or hemodialysis (HD) in multivariate competing-risks analysis

	HR	95% C.I. for HR		p
HD (v.s. PD)	1.93	1.46	2.56	<0.001
Age	1.01	1.004	1.01	<0.001
FBG	1.01	1.005	1.01	<0.001
Serum albumin	1.36	1.14	1.62	0.001
Phosphorus	1.07	1.02	1.13	0.007
Hematocrit	1.02	0.995	1.05	0.108

FBG: fasting blood glucose