

SUPPLEMENTARY TABLES

Supplementary Table 1. Association of the risk factors of dementia and MMSE score in PD, DM and PD-DM patients.

Model	Predictor variables	B	SE	β	p	R ²	Adjusted R ²	F	p
PD	FBG<5.00 (mmol/L)	-1.052	0.433	-0.126	0.016	0.185	0.173	14.469	<0.001
	HCY>15.00 (μ mol/L)	-1.336	0.595	-0.115	0.026				
	Age	-0.140	0.019	-0.376	< 0.001				
	Cys C>0.95 (mg/L)	-0.908	0.452	-0.103	0.046				
	Hyperlipidemia	-1.232	0.641	-0.098	0.056				
PD-DM	Fibrinogen>4.00 (g/L)	-1.857	0.663	-0.174	0.006	0.290	0.275	19.383	<0.001
	LDL-C<2.00 (mmol/L)	-1.876	0.674	-0.173	0.006				
	Age	-0.171	0.032	-0.342	< 0.001				
	SAE	-2.196	0.640	-0.216	0.001				
DM	AST>40 (IU/L)	-3.278	1.023	-0.141	0.001	0.319	0.310	34.277	<0.001
	Cys C>0.95 (mg/L)	-1.878	0.690	-0.119	0.007				
	Anxiety or depression	-1.579	0.531	-0.135	0.003				
	Male	-1.182	0.398	-0.131	0.003				
	Age	-0.163	0.015	-0.481	< 0.001				

B- Unstandardized coefficient; β - Standardized coefficient; R² represents the model explanatory power with according standardized β weights, showing the contribution of each independent variable to the proposed model; SE- Standard Error; MMSE- mini mental state examination; PD- patients with Parkinson disease without type 2 diabetes mellitus; PD-DM- patients with Parkinson disease and type 2 diabetes mellitus; DM- type 2 diabetes mellitus without Parkinson disease; FBG- Fasting blood glucose; HCY- homocysteine; Cystatin C- Cys C; LDL-C- low density lipoprotein cholesterol; SAE- subcortical arteriosclerotic encephalopathy; AST- Aspartate transaminase.

Supplementary Table 2. Differences of risk factors among PDD, DMD and PD-DMD groups.

Clinical variables	PDD (n=31)	DMD (n=35)	PD-DMD (n=31)	p*	Multiple comparisons **
Age, years	69.0(59.0,79.0)	68.0(57.0,74.0)	79.0(72.0,84.0)	< 0.001	PD-DMD>PDD=DMD
<55, n (%)	3(9.68)	7(20.00)	0	-	-
55-70, n (%)	16(51.61)	14(40.00)	5(16.13)	-	-
>70, n (%)	12 (38.71)	14(40.00)	26(83.87)	< 0.001	PD-DMD>PDD=DMD
Male, n (%)	18(58.06)	27(77.14)	16(51.61)	0.080	-
PD duration, month	60(24,84)	-	36(12,72)	-	-
Dementia, n (%)	31 (100.00)	35 (100.00)	31 (100.00)	0.094	-
Use of drugs, n (%)					
Atorvastatin	6(19.35)	14(40.00)	20(64.52)	0.001	PD-DMD>PDD
Metformin	-	14(40.00)	9(29.03)	-	-
Insulin	-	8(22.86)	14(45.16)	0.055	-
Acarbose	-	17(48.57)	18(58.06)	0.441	-
L-Dopa	28(90.32)	-	26(83.87)	-	-
MDS-UPDRS (I)	3.0(2.0,5.0)	-	5.0(3.0,6.0)	0.006	PD-DMD>PDD
MDS-UPDRS (II)	8.0(6.0,11.0)	-	14.0(12.0,18.0)	< 0.001	PD-DMD>PDD
MDS-UPDRS (III)	17.0(15.0,23.0)	-	23.0(21.0,29.0)	< 0.001	PD-DMD>PDD
MDS-UPDRS (Total)	26.0(24.0,38.0)	-	44.0(37.0,54.0)	< 0.001	PD-DMD>PDD
H&Y	3.0(2.0,4.0)	-	3.0(3.0,4.0)	0.072	-
NMSS	26.0(17.0,32.0)	-	32.0(28.0,34.0)	0.003	PD-DMD>PDD
MMSE	15.0(13.0,17.0)	15.0(9.0,19.0)	13.0(11.0,17.0)	0.613	-
MoCA	12.0(9.0,14.0)	12.0(7.0,15.0)	9.0(8.0,13.0)	0.205	-
Anxiety or depression	17(54.84)	13(37.14)	19(61.29)	0.124	-
Vascular and inflammatory risk factors					
SBP mmHg	120.0(118.0,135.0)	146.0(128.0,153.0)	132.0(120.0,152.0)	-	-

DBP mmHg	80.0(78.0,81.0)	85.0(80.0,95.0)	78.0(69.0,87.0)	-	-
Smoking history, n (%)	2(6.45)	7(20.00)	3(9.68)	-	-
Drinking history, n (%)	0	5(14.29)	1(3.23)	-	-
BMI	23.0(22.0,25.0)	24.0(22.0,26.0)	24(21,25)	-	-
LDL-C (mmol/L)	2.5(2.3,3.2)	2.7(1.9,3.1)	1.9(1.6,3.0)	0.094	-
LDL-C<2.00 (mmol/L), n (%)	2(6.45)	12(34.29)	15(48.39)	0.001	PD-DMD=DMD>PDD
D-Dimer (mg/L)	0.6(0.3,1.1)	0.4(0.3,0.9)	0.6(0.4,1.4)	-	-
D-Dimer>0.50 (mg/L), n (%)	10(32.26)	8(22.86)	10(32.26)	0.618	-
Fibrinogen (g/L)	3.5(2.8,4.0)	3.3(3.0,4.6)	4.1(3.5,5.1)	0.012	PD-DMD>PDD
Fibrinogen>4.00 (g/L), n (%)	6(19.35)	9(25.71)	15(48.39)	0.033	PD-DMD>PDD
WBC (g/L)	6.1(5.0,7.2)	7.3(6.0,9.5)	7.4(6.1,9.9)	-	-
Lymphocyte (%)	30.7(24.2,34.8)	25.3(18.6,32.1)	20.5(12.2,28.0)	0.001	PD-DMD<PDD
Neutrophil (%)	58.6(52.5,67.5)	64.0(58.3,70.2)	71.5(61.6,82.8)	<0.001	PD-DMD>PDD
hs-CRP (mg/L)	0.6(0.6,2.0)	3.6(1.5,7.1)	4.5(0.7,47.1)	0.036	-
hs-CRP>3.00 (mg/L), n (%)	2(6.45)	11(31.43)	8(25.81)	0.039	DMD>PDD
Hyperlipidemia	7(22.58)	3(8.57)	2(6.45)	-	-
Brain infarction	13(41.94)	27(77.14)	26(83.87)	0.001	PD-DMD=DMD>PDD
SAE	9(29.03)	5(14.29)	18(58.06)	0.001	PD-DMD>DMD
WMLs, n (%)	12(38.71)	17(48.57)	18(58.06)	0.313	-
Fazekas 1	5(16.13)	2(5.71)	2(6.45)	-	-
Fazekas 2	7(22.58)	12(34.29)	15(48.39)	0.103	-
Fazekas 3	0	3(8.57)	1(3.23)	0.322	-
Metabolic risk factors					
AST>40(IU/L), n (%)	0	5(14.29)	3(9.68)	0.091	-
ALT	15.0(9.0,22.0)	22.0(15.0,28.0)	14.0(11.0,30.0)	-	-
Albumin	40.3(38.0,41.8)	39.3(36.2,42.9)	36.9(36.0,42.1)	0.204	-
Albumin<35.00 (g/L), n (%)	2(6.45)	4(11.43)	7(22.58)	0.187	-
Calcium (mmol/L)	2.3(2.2,2.4)	2.2(2.2,2.3)	2.2(2.1,2.3)	0.329	-
Calcium<2.10 (mmol/L), n (%)	5(16.13)	6(17.14)	8(25.81)	0.569	-
Potassium (mmol/L)	3.8(3.6,4.1)	3.9(3.6,4.0)	3.8(3.4,4.3)	0.911	-
MCV (fL)	92.7(91.1,97.4)	87.2(83.5,93.3)	89.9(88.2,93.2)	<0.001	PDD>PD-DMD=DMD
MCV>90.00 (fL), n (%)	25(80.65)	13(37.14)	14(45.16)	0.001	PDD>PD-DMD=DMD
HCY (μmol/L)	15.8(12.0,17.8)	11.3(8.5,15.3)	12.3(8.7,18.0)	-	-
HCY>15.00 (μmol/L), n (%)	9(29.03)	5(14.29)	5(16.13)	0.270	-
Hyperhomocysteinemia	4(12.90)	0	1(3.23)	0.041	-
Cys C (mg/L)	1.1(1.0,1.2)	1.0(0.9,1.1)	1.0(0.9,1.5)	0.551	-
Cys C>0.95 (mg/L), n (%)	15(48.39)	8(22.86)	7(22.58)	0.039	-
FBG (mmol/L)	4.7(4.3,5.1)	7.6(5.8,11.6)	7.1(6.1,10.0)	<0.001	PD-DMD=DMD>PDD
FBG<5.00 (mmol/L), n (%)	23(74.19)	5(14.29)	1(3.23)	<0.001	PD-DMD=DMD<PDD
HbA1c (%)	5.7(5.2,5.9)	7.3(6.3,8.9)	6.4(6.0,7.4)	-	-

PDD- patients with Parkinson disease with dementia; DMD- type 2 diabetes mellitus with dementia; PD-DMD- patients with Parkinson disease and type 2 diabetes mellitus and dementia; L-Dopa- Levodopa and Benserazide; MDS-UPDRS- Movement Disorder Society–Unified Parkinson’s Disease Rating Scale; H&Y- the modified Hoehn and Yahr staging scale; NMSS- Non-Motor Symptoms Scale for Parkinson’s Disease; MMSE- mini mental state examination; MoCA- Montreal Cognitive Assessment; SBP- systolic blood pressure; DBP- diastolic blood pressure; BMI- body mass index; LDL-C- low density lipoprotein cholesterol; WBC- White blood cell count; hs- CRP- hypersensitive C-reactive protein; SAE- subcortical arteriosclerotic encephalopathy; WMLs- White matter lesions; AST- Aspartate transaminase; ALT- Alanine transaminase; MCV- mean corpuscular volume; HCY- homocysteine; Cystatin C- Cys C; FBG- Fasting blood glucose; HbA1c- glycated hemoglobin. *The Bonferroni method was used to adjust the significance level to perform multiple testing. **If statistically significant, continuous variables were analyzed by Kruskal-Wallis test followed by post-hoc analysis with Bonferroni adjustment to compare differences among PDD, DMD and PD-DMD groups and were prior adjusted for age using multivariate linear regression. Mann-Whitney U test were used to compare differences between PDD and PD-DMD groups. Categorical parameters were analyzed using χ^2 -test with Bonferroni adjustment for multiple testing.

Supplementary Table 3. Multivariable logistic regression analysis for risk factors of dementia in PD patients.

(a)

Variables	Univariate		Multivariate model	
	OR (95%CI)	p	Adjusted OR (95% CI)	p
FBG<5.00 (mmol/L)	2.704(1.171,6.241)	0.020	4.380(1.748,10.975)	0.002
HCY>15.00 (μ mol/L)	2.684(1.156,6.231)	0.022	3.131(1.243,7.888)	0.015
Hyperlipidemia	2.448(0.980,6.119)	0.055	3.075(1.142,8.277)	0.026
Age	1.035(1.000,1.071)	0.050	1.043(1.003,1.084)	0.034
Cys C>0.95 (mg/L)	2.122(1.008,4.468)	0.048	2.157(0.979,4.752)	0.056

(b)

Variables	Univariate		Multivariate model	
	OR (95%CI)	p	Adjusted OR (95% CI)	p
HCY>15.00 (μ mol/L)	2.684(1.156,6.231)	0.022	2.522(1.042,6.104)	0.040
Hyperlipidemia	2.448(0.980,6.119)	0.055	2.638(1.018,6.840)	0.046
Age	1.035(1.000,1.071)	0.050	1.030(0.992,1.069)	0.124
Cys C>0.95 (mg/L)	2.122(1.008,4.468)	0.048	2.057(0.947,4.464)	0.068
Hypoglycaemic episodes (FBG \leq 3.9mmol/L)	1.594(0.186,13.690)	0.671	2.949(0.308,28.262)	0.348

PD- patients with Parkinson disease without type 2 diabetes mellitus; OR- odds ratio; CI- confidence interval; FBG- fasting blood glucose; HCY- homocysteine; Cys C- Cystatin C.

Supplementary Table 4. Multivariable logistic regression analysis for risk factors of dementia in DM patients.

Variables	Univariate		Multivariate model	
	OR (95% CI)	p	Adjusted OR (95% CI)	p
AST>40(IU/L)	6.074(1.913,19.286)	0.002	6.472(1.147,36.533)	0.034
Cys C>0.95 (mg/L)	3.864(1.584,9.424)	0.003	4.905(1.399,17.206)	0.013
Anxiety or depression	3.239(1.535,6.833)	0.002	3.750(1.220,11.526)	0.021
Male	2.549(1.125,5.775)	0.025	3.480(1.109,10.918)	0.033
Hypoglycaemic episodes (FBG \leq 3.9mmol/L)	5.062(1.208,21.212)	0.027	7.013(0.903,54.463)	0.063
Neutrophil (%)	1.054(1.017,1.093)	0.004	1.151(0.983,1.348)	0.080
Brain infarction	5.511(2.429,12.500)	<0.001	2.485(0.788,7.834)	0.120
Calcium<2.10(mmol/L)	5.414(1.892,15.490)	0.002	3.464(0.694,17.294)	0.130
Lymphocyte (%)	0.935(0.896,0.974)	0.001	1.144(0.960,1.364)	0.133
Potassium (mmol/L)	0.381(0.149,0.977)	0.045	0.500(0.145,1.725)	0.273
WMLs	4.450(2.166,9.142)	<0.001	2.812(0.439,18.002)	0.275
hs-CRP>3.00 (mg/L)	2.512(1.160,5.439)	0.019	1.850(0.573,5.974)	0.303
LDL-C<2.00(mmol/L)	2.103(0.996,4.440)	0.051	1.712(0.615,4.770)	0.303
SAE	5.421(2.618,11.224)	<0.001	1.460(0.249,8.548)	0.675
D-Dimer>0.50(mg/L)	3.698(1.522,8.986)	0.004	1.309(0.318,5.383)	0.709
Albumin<35.00(g/L)	5.339(1.513,18.846)	0.009	1.207(0.207,7.026)	0.834
Fibrinogen>4.00 (g/L)	2.431(1.066,5.543)	0.035	1.098(0.306,3.947)	0.886
Age	1.033(1.005,1.062)	0.022	0.998(0.957,1.042)	0.931

DM- patients with type 2 diabetes mellitus; OR- odds ratio; CI- confidence interval; AST- Aspartate transaminase; Cystatin C- Cys C; FBG- Fasting blood glucose; WMLs- White matter lesions; hs-CRP- hypersensitive C-reactive protein; LDL-C- low density lipoprotein cholesterol; SAE- subcortical arteriosclerotic encephalopathy.

Supplementary Table 5. Multivariable logistic regression analysis for risk factors of dementia in PD (with and without DM) patients and the interaction of risk factors with the existence of DM.

Variables	Univariate		Multivariate Model		Interaction p
	OR (95%CI)	p	Adjusted OR (95% CI)	p	
Fibrinogen>4.00 (g/L)	3.002(1.677,5.374)	<0.001	3.259(1.674-6.345)	0.001	
With DM	3.613(2.266,5.761)	<0.001	3.204(1.247,8.233)	0.016	0.979
Without DM	0.277(0.174,0.441)	<0.001	3.267(1.059,10.082)	0.039	
LDL-C<2.00 (mmol/L)	2.129(1.142,3.969)	0.017	1.544(0.783,3.043)	0.210	
With DM	2.586(1.594,4.197)	<0.001	3.347(1.305,8.585)	0.012	0.022
Without DM	0.387(0.238,0.627)	<0.001	0.384(0.078,1.890)	0.239	
SAE	2.458(1.428,4.231)	0.001	1.566(0.848,2.894)	0.152	
With DM	1.469(1.001,2.156)	0.049	3.952(1.566,9.971)	0.004	0.028
Without DM	0.681(0.464,0.999)	0.049	0.855(0.312,2.343)	0.761	
FBG<5.00 (mmol/L)	1.100(0.638,1.895)	0.732	2.364(1.153,4.848)	0.019	
With DM	0.108(0.067,0.175)	<0.001	0.323(0.036,2.905)	0.313	0.025
Without DM	9.232(5.728,14.880)	<0.001	5.116(1.879,13.931)	0.001	
HCY>15.00 (μmol/L)	1.925(1.005,3.687)	0.048	1.724(0.848,3.503)	0.132	
With DM	0.907(0.554,1.1.486)	0.699	0.940(0.283,3.130)	0.920	0.163
Without DM	1.102(0.673,1.804)	0.699	2.828(1.068,7.492)	0.036	
Hyperlipidemia	1.302(0.610,2.780)	0.495	1.391(0.618,3.133)	0.425	
With DM	1.035(0.612,1.752)	0.898	0.717(0.146,3.506)	0.681	0.141
Without DM	0.966(0.571,1.635)	0.898	2.996(1.048,8.561)	0.041	
Diabetes	1.685(0.991,2.863)	0.054	1.168(0.573,2.384)	0.669	
Cys C>0.95 (mg/L)	1.350(0.775,2.353)	0.290	1.267(0.681,2.355)	0.455	
With DM	0.722(0.493,1.057)	0.094	0.467(0.155,1.405)	0.175	0.022
Without DM	1.385(0.946,2.028)	0.094	2.360(1.014,5.495)	0.046	
Age	1.051(1.024,1.078)	<0.001	1.044(1.010,1.078)	0.010	
With DM	1.082(1.062,1.103)	<0.001	1.059(0.999,1.123)	0.055	0.854
Without DM	0.924(0.907,0.942)	<0.001	1.052(1.007,1.099)	0.024	

PD- patients with Parkinson disease without type 2 diabetes mellitus; DM- type 2 diabetes mellitus without Parkinson disease; OR- odds ratio; CI- confidence interval; LDL-C- low density lipoprotein cholesterol; SAE- subcortical arteriosclerotic encephalopathy; FBG- fasting blood glucose; HCY- homocysteine; Cys C- Cystatin C.