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Blood Pressure Variability and Its Relationship with Cognitive Function in Elderly Patients with Essential Hypertension and Type 2 Diabetes

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ABSTRACT

Objective: To investigate blood pressure variability of Elderly hypertensives with type 2 diabetes and its relationship with cognition. **Methods:** A total of 143 elderly hypertensives were enrolled and divided into diabetic group (59 cases) and non-diabetic group (84 cases). The difference of general clinical characteristics, biochemical parameters, carotid ultrasound, a neuropsychological Scales and 24-hour ambulatory blood pressure (24hABPM) parameters between the two groups of subjects were compared. Then, the two groups (diabetic group and non-diabetic group) were further divided into (Mild cognitive dysfunction) subgroup (MMSE>26) and normal cognition subgroup (MMSE≤26), respectively. On the basis of MMSE scores, the difference of the parameters of ABPM between the two subgroups was analyzed. **Results:** Compared with the control group, 24hSBP, 24hPP, dSBP, dPP, nSBP, nPP, 24hSSD, dSSD, nSSD, 24hSCV, dSCV and nSCV were significantly higher in the diabetic group ($p<0.05$). However, cognition was lower in the diabetic group. No significant difference was found in the circadian pattern of blood pressure between the two groups. 24hSSD, dSSD, nSSD, 24hSCV, dSCV, nSCV were significantly higher in the MCI subgroup than normal cognition subgroup in both diabetic and non-diabetic groups ($p<0.05$), and they were negatively associated with scores of MMSE, the correlation coefficient were -0.235, -0.246, -0.341, -0.158, -0.222, -0.238 ($0.001\leq P<0.05$). **Conclusion:** The study showed that in the elderly with hypertension, the mean systolic blood pressure and blood pressure variability were both higher in the diabetic group, and the cognition was lower instead. Whether or not with diabetes, blood pressure variability was always higher in the MCI subgroup. Blood pressure variability increased in patients with diabetes, and was associated with cognitive decline.

1. Introduction

With the changes in modern lifestyles, the prevalence of diseases such as diabetes and high blood pressure is increasing. The World Health Organization estimates that

approximately 1.5 billion adults worldwide are affected by high blood pressure, which accounts for more than one-third of the adult population worldwide, and that the proportion increases with age. At present, the number of hypertension patients in China has exceeded 330 million,

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with one in every three adults suffering from hypertension. The resulting heart disease and stroke can cause 9.4 million deaths worldwide each year. According to the latest statistics from the International Diabetes Federation (IDF) in 2013, the global prevalence of diabetes in adults aged 20-79 is 8.3%, and the number of patients has reached 382 million ^[1]. In 2013, a total of 5.1 million people worldwide died of diabetes-related diseases, accounting for 8.39% of all deaths. In China, the prevalence of diabetes has nearly doubled in the past decade. In 2010, the prevalence of adult diabetes in China was 9.7%. The total number of patients has exceeded 90 million. China has become the world's largest country with diabetes.

At the same time, with the improvement of material life and medical conditions and the extension of life expectancy, the aging of the population in modern society is accelerating, and the incidence of Alzheimer's disease is also increasing year by year. According to statistics, there are currently 5 million Alzheimer's patients in China, accounting for about 1/4 of the total number of cases in the world. The incidence rate of people over 55 years old is close to 3%, and the incidence rate of people over 65 years old is more than 5% ^[2]. Following cardiovascular and cerebrovascular diseases and cancer, senile dementia has become a major disease threatening the health of the elderly. Because of the lack of interventions, the treatment of advanced Alzheimer's disease is not effective. Therefore, the early diagnosis and treatment of Alzheimer's disease is particularly important.

Thus, in 1999, Petersen et al. proposed the concept of Mild cognitive impairment (MCI) ^[3]. MCI refers to the cognitive impairment state that cognitive function is lower than normal people of the same age and cultural background but does not reach the level of dementia, and their daily life is not affected. It is a clinically transitional state characterized by disease between normal aging and Alzheimer's disease (AD) or other early stages of dementia. Studies have shown that MCI has a large heterogeneity, and its annual conversion rate for dementia varies greatly. In 2008, Petersen ^[4] refined MCI into two types: amnesic (aMCI) and non-memory (nmMCI). Each category is divided into single-domain and multi-domain. Among them, aMCI type is considered to have a high risk of developing into AD.

More and more evidences show that vascular factors play an important role in the development and progression of Alzheimer's disease. These cardiovascular risk factors can be used as a target therapy to reduce the incidence of cognitive dysfunction and dementia. Bell RD et al. ^[5] found in brain imaging studies of human and animal models that cerebral vascular dysfunction may precede cog-

nitive decline and neurodegenerative changes. Decreased cerebral blood flow can affect the synthesis of proteins needed for learning and memory, and may eventually lead to nerve damage and nerve cell death. Genome-wide association studies confirmed that the ApoEε4 allele is the strongest genetic risk factor for AD ^[6]. Studies have shown that carriers of the ApoE ε4 allele are predisposed to hypertension and coronary heart disease. This suggests that it is related to the development of cardiovascular disease and AD ^[7]. J zhu et al. found that MCI patients with intracranial artery stenosis are more likely to progress to AD dementia ^[8]. A study conducted by Zhou Huadong et al. in Daping Hospital of the Third Military Medical University on 837 MCI patients showed that vascular risk factors could increase the risk of AD dementia ^[9]. Active intervention of VRF can improve the progression of MCI to AD dementia. The study found that patients with vascular risk factors had a higher risk of developing Alzheimer's disease than those without vascular risk factors. Controlling vascular risk factors can improve the progression of mild cognitive impairment to AD.

Hypertension causes the wall of cerebral arteries and arterioles to become thicker and harder, and the lumen to become smaller, which in turn reduces cerebral blood flow and leads to abnormal brain energy metabolism. In addition, the cerebral cortical arterial wall is glass-like, and the lumen becomes smaller, which constitutes a subcortical white matter with low perfusion. This impairs brain energy metabolism. The use of glucose in the brain decreased and local protein synthesis was abnormal. Neurotransmitters become dysfunctional and cholinergic receptors are absent, which causes neuronal damage in the white matter and hippocampus and leads to cognitive dysfunction.

Blood pressure level fluctuates constantly under the influence of various physiological, pathological, environmental and genetic factors. The degree of fluctuation of blood pressure over a certain period of time (including physiological variation, pathological variation, and drug-induced variation) is called blood pressure variability (BPV). It has been generally believed that the mean blood pressure of hypertensive patients is closely related to the damage of target organs. At the same time, the average blood pressure is also an important parameter in the clinical diagnosis and treatment of hypertension. Current major clinical guidelines also support the idea that lowering average blood pressure can reduce target organ damage. However, with the development of dynamic blood pressure monitoring technology, people's research on blood pressure fluctuations has gradually deepened. More and more clinical studies have shown that BPV is an effective predictor of target organ damage and is independent of

average blood pressure.

Recently, researchers at the Leiden University Medical Center in the Netherlands, the University of Cork in Ireland and the University of Glasgow in the United Kingdom investigated the relationship between blood pressure variability (independent of blood pressure) and cognitive function in the elderly at high risk for cardiovascular disease^[10]. The results suggest that increased blood pressure variability is inversely associated with various cognitive function tests and is associated with a higher risk of stroke. This association was independent of a variety of other cardiovascular risk factors, including blood pressure levels. The reasons are as follows: first, blood pressure variability and cognitive impairment may result from a common cause, that is, cardiovascular risk factors. Second, blood pressure variability may reflect long-term instability of blood pressure and blood flow regulation in the main organs of the body. Third, severe fluctuations in blood pressure in the brain may cause the brain to fail to receive adequate blood flow, leading to brain damage and cognitive dysfunction.

In recent years, studies have shown that long-term hyperglycemia in diabetes can cause vascular endothelial function and platelet agglutination dysfunction, resulting in lacunar cerebral infarction and cerebral thrombosis and other complications. Marioni et al.^[11] showed that the increase of plasma viscosity in patients with type 2 diabetes was positively correlated with the decline of cognitive function. At the same time, the blood-brain barrier integrity is impaired, cerebral blood flow and cerebral vascular surface area are reduced, resulting in reduced transport of essential nutrients to nerve tissue, which in turn affects synaptic function. Abnormal glucose metabolism can lead to cardiovascular autonomic nervous system dysfunction in the body, aggravating essential hypertension and causing structural and functional abnormalities of the cardiovascular system. BPV reflects the effect of cardiovascular autonomic nerve on hemodynamics. At present, there have been many studies on cognitive function in patients with hypertension and type 2 diabetes. However, there are few studies on the effect of blood pressure variability of diabetes mellitus combined with hypertension on cognitive function.

In this study, the 24-hour dynamic blood pressure and neurocognitive scale of 59 patients with hypertension with type 2 diabetes and 84 patients with simple hypertension were measured respectively to study the correlation. The relationship between blood pressure variability and cognitive function in elderly patients with hypertension and type 2 diabetes mellitus was investigated.

2. Materials and Methods

2.1 Research Object

(1) Cases Resource

A total of 143 patients with hypertension were admitted to the Geriatrics Department of the Sixth People's Hospital of Shanghai from August 2012 to December 2013.

(2) Case Grouping

These patients were divided into the elderly hypertension group (diabetes group, 59 cases) and the elderly simple hypertension group (control group, 84 cases). According to the cognitive function, the diabetic group was divided into the subgroup with normal cognitive function of hypertension and diabetes mellitus (MMSE>26, 16 cases) and the subgroup with mild cognitive impairment of diabetes mellitus (diabetes MCI subgroup, MMSE ≤26, 43 cases). The control group was also divided into non-diabetic cognitive function subgroup (MMSE>26, 41 cases) and non-diabetic mild cognitive dysfunction subgroup (non-diabetic MCI subgroup, MMSE≤26, 43 cases) according to cognitive function.

(3) Inclusion Criteria

"China Guidelines for the Prevention and Treatment of Hypertension 2010 Edition"^[12] Diagnostic Criteria: Blood pressure was measured 3 times on different days without antihypertensive drugs. Patients with primary hypertension were diagnosed with systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg.

Diagnostic criteria for type 2 diabetes use the 2010 edition of the Chinese Type 2 DM prevention guidelines diagnostic criteria^[13]: Fasting blood glucose (FPG) ≥ 7.0mmol / L or 2h after meal (2hPG) ≥ 11.1mmol / L, while eliminating secondary diabetes. Or the patient has been diagnosed with diabetes in the past. Although the blood glucose level has not reached the diagnostic criteria, the patients who have been treated with hypoglycemic.

The level of education is university and above.

(4) Exclusion Criteria

A. Patients with secondary hypertension caused by renal hypertension, neuroendocrine disorders, mechanical blockage of blood flow, and poor blood pressure control, systolic blood pressure > 180 mmHg and / or diastolic blood pressure > 110 mmHg;

B. Patients with severe heart and lung disease;

C. Patients with acute complications of diabetes such as tumors, infectious diseases, hypoglycemia coma, diabetic ketoacidosis, non-ketotic hyperosmolar coma;

D. Stroke, Parkinson's disease, brain trauma, persistent episodes of epilepsy, vitamin B12 deficiency, hypothyroidism, obstructive respiratory sleep apnea;

E. Depression patients with a score greater than 10 on

the geriatric depression scale;

F. Patients with impaired daily living ability who scored more than 20 on the daily living ability scale;

G. Patients taking drugs that improve cognitive function (cholinesterase inhibitors: including huperzine A, donepezil, rivastigmine tartaric acid, galantamine, etc.; excitatory amino acid receptor antagonist: Ebixa).

2.2 Research Method

The age, sex, smoking history, and antihypertensive medication use of all subjects were recorded. In the morning, the patient's blood is drawn to measure fasting plasma glucose (FPG). Based on 24h ambulatory blood pressure monitoring (24hABPM) and neuropsychological scale measurement (including MMSE, GDS, ADL scale), 2-hour postprandial blood glucose (P2hPG), hemoglobin A1C (HbA1C), alanine transaminase (ALT), serum creatinine (Scr), thyroid function (FT3, FT4, TSH), vitamin B12 (Vit B12), cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL), low density lipoprotein (LDL) were detected.

(1) Assessment of smoking history: According to the World Health Organization smoking survey standards, a minimum of one cigarette per day before the hospitalization, continuous smoking lasts for more than one year, or long-term smoking but smoking cessation for less than half a year is positive for smoking.

(2) Blood biochemical testing: ALT, Scr, TC, TG, HDL-C, LDL-C, FPG, and P2hPG were detected by an automated biochemical analyzer (U.S., Backman LX20). The FT3, FT4, and TSH were tested by the Roche Cobas 6000. The VitB12 is tested by Siemens ADVIA centaur XP. HbA1C is detected by the UK's DREW-DS5 high pressure liquid phase analyzer.

(3) Ambulatory blood pressure monitoring: Noninvasive portable cuff blood pressure monitor (SPACELABS Healthcare 90217) was used to measure the left upper limb artery pressure for 24 hours. The blood pressure is measured automatically at intervals of 30 minutes during the day and 1 hour during the night, and the patient's activity is not restricted during the monitoring period. 24 hours later, the data were analyzed: 8:00~23:00 is blood pressure of the day, and 23:00~8:00 is the blood pressure at night. The computer automatically analyzed the mean value of systolic and diastolic blood pressure, pulse pressure, standard deviation, and 24-hour blood pressure circadian rhythm in patients with 24-hour blood pressure effective reading >80% of each time period (24 hours, day, night).

(4) Observation indicators: Daytime systolic pressure standard deviation (dSSD), daytime diastolic pressure

standard deviation (dDSD), nighttime systolic pressure standard deviation (nSSD), nighttime diastolic pressure standard deviation (nDSD), and 24-hour systolic blood pressure, diastolic blood pressure weighted standard deviation (24hSSD, 24hDSD). The calculation formula is: 24-hour systolic blood pressure weighted standard deviation (24hSSD) = [(dSSD×14)+ (nSSD×6)]/20, 24 hours diastolic pressure plus weight standard deviation (24hDSD) = [(dDSD×14) +(nDSD×6)]/20. According to the blood pressure coefficient of variation $CV = SD / \text{blood pressure mean} \times 100\%$, the 24h systolic blood pressure variation coefficient (24hSCV), 24h diastolic blood pressure variation coefficient (24hDCV), daytime systolic blood pressure variation coefficient (dSCV), daytime diastolic blood pressure variation coefficient (dDCV), nighttime systolic blood pressure variation coefficient (nSCV), and nighttime diastolic blood pressure variation coefficient (nDCV) were calculated respectively.

(5) Minimum Mental State Examination (MMSE):

The Minimum Mental State Examination (MMSE) was compiled by Folstein in 1975. It is one of the most widely used screening tools for cognitive impairment. The scale assessment items include: time orientation, location orientation, language immediate memory, attention and calculation, short-term memory, naming, language retelling and understanding and expression, spatial structure. The total score is 30 points. The lower the score, the worse the cognitive assessment. Subjects with a college degree or above were included, and their MMSE>26 was classified as normal cognition, while 26 was defined as MCI.

(6) The Geriatric Depression Scale (GDS):

The Geriatric Depression Scale (GDS) was created by Brink et al. (1982). This is a depression screening form for the elderly. Brink et al. (1982), Yesavage et al. (1983), Hyer and Blount (1984) tested GDS, respectively. The results show that GDS has good reliability and validity, and has a high correlation with commonly used depression scales such as SDS, HRSD and BDI.

(7) Activities of Daily Living (ADL):

By asking the patients or their families for scores, the medical staff can assess the patients' daily life functions. The assessment program includes 20 daily living abilities. In each category, 1 = can do it oneself, 2 = have some difficulty, 3 = need help, and 4 = can't do it at all. The total score of 20 is normal. The total score of >26 or more than two functional loss is considered deficiency in daily living ability.

2.3 Statistical Treatment

SPSS 17.0 statistical software was used to process the data. Measurement data are expressed as (\pm s). The nor-

mality test is performed on the measurement data. The test results show that the measurement data conforms to the normal distribution ($P > 0.05$), and the homogeneity of the posterior difference is tested. $P > 0.05$ indicated homogeneity of variance, and t test was used. $P < 0.05$ means heterogeneity of variance, and t' test is adopted. Qualitative data are described by rate (or constituent ratio). The χ^2 test was used to compare the rate (or composition ratio) of each group. Multivariate correlations were analyzed using Pearson correlation. $P < 0.05$ was considered statistically significant.

3. Results

3.1 General Clinical Data

143 patients were enrolled. There were 59 patients in the diabetic group, including 45 males (84.33±4.39 years old) and 14 females (83.86±3.95 years old). There were 84 patients in the control group, including 64 males (83.55±4.69 years old) and 20 females (84.65±5.56 years old). The age, sex, smoking history, antihypertensive medication type, ALT, Scr, TC, TG, HDL-C, LDL-C, Vit B 12, folic acid, FT3, FT4, TSH were compared between the two groups. The difference was not statistically significant ($P > 0.05$). The FPG, P2hPG and HbA1C in the diabetic group were compared with the control group, and the difference was statistically significant ($P < 0.05$). The baseline balance of the two groups was consistent and the comparability was good, as shown in Tables 1 and 2.

Table 1. Comparison of general conditions between diabetic group and control group

Item	Diabetes group n=59	Control group n=84	t or χ^2	P
Age	84.22±4.58	83.81±4.90	0.507	0.613
Gender (male/female)	45/14	64/20	0.000	0.991
Smoking history	6.06±0.76	6.13±0.84	1.811	0.178
ALT(u/l)	37.43±25.87	40.56±31.23	0.632	0.528
Scr (mmol/l)	81.40±23.22	79.40±30.57	0.423	0.672
TC (mmol/l)	4.20±0.98	4.13±0.94	0.430	0.668
TG (mmol/l)	1.34±1.07	1.21±0.66	0.115	0.391
HDL (mmol/l)	1.44±0.85	1.70±0.98	0.131	0.100
LDL (mmol/l)	2.27±0.86	2.06±0.91	0.999	0.168
Vit B ₁₂ (ng/L)	878.97±232.56	905.43±214.35	0.701	0.484
Folic acid (ug/l)	12.12±3.45	13.06±3.62	1.558	0.121
FT ₃ (pmol/L)	4.14±1.15	4.03±0.96	0.621	0.535
FT ₄ (pmol/L)	18.69±4.56	19.04±3.98	0.487	0.626
TSH (mIU/l)	3.88±0.98	3.96±0.87	0.513	0.608
FPG (mmol/l)	5.99±1.70	5.48±0.87	0.000	0.041*

P2hPG(mmol/l)	9.18±2.88	7.70±2.18	0.005	0.001*
HbA _{1C}	6.86±1.19	5.99±0.87	0.052	0.000**

Note: * indicates $0.001 < P < 0.05$ compared with the control group. ** indicates $P < 0.001$ compared with the control group.

Table 2. Comparison of antihypertensive drugs between diabetic group and control group

Antihypertensive drugs	Diabetes group n=59	Control group n=84	χ^2	P
Long-acting CCB	34	52		
ARB	28	40		
ACEI	13	19		0.364
β receptor blockers	8	14	0.784	
Diuretic	8	12		
Others	2	3		

Note: Long-acting CCB: long-acting calcium antagonist; ARB: angiotensin receptor antagonist; ACEI: angiotensin-enzyme conversion agent

3.2 Comparison of Mean Blood Pressure Between Diabetic Group and Control Group

The levels of 24hSBP, 24hPP, dSBP, dPP, nSBP and nPP in the diabetic group were higher than those in the control group. The differences were statistically significant ($P < 0.05$). The comparison of mean blood pressure between the diabetic group and the control group is shown in Table 3.

Table 3. The comparison of mean blood pressure between the diabetic group and the control group

Observation index	Diabetes group n=59	Control group n=84	t	P
24hSBP(mmHg)	126.97±18.70	119.82±15.35	2.501	0.014*
24hDBP(mmHg)	61.79±10.05	61.74±8.25	0.235	0.972
24hPP(mmHg)	65.19±14.52	57.82±12.18	0.228	0.001*
dSBP(mmHg)	127±18.89	119.90±14.72	0.019	0.017*
dDBP(mmHg)	61.87±10.25	62.27±8.56	0.306	0.800
dPP(mmHg)	65.12±14.73	57.66±12.03	0.235	0.001*
nSBP(mmHg)	128.66±21.99	119.60±20.47	0.987	0.045*
nDBP(mmHg)	61.29±11.39	60.42±11.90	1.000	0.663
nPP(mmHg)	65.37±16.46	59.17±16.98	0.739	0.031*

Note: * indicates $0.001 < P < 0.05$ compared with the control group.

3.3 Comparison of Blood Pressure Variability between Diabetic Group and Control Group

The results of 24hSSD, dSSD, nSSD, 24hSCV, dSCV, and nSCV were compared between the two groups, and the diabetic group was higher than the control group ($p < 0.05$). The comparison of blood pressure variability between di-

abetic group and control group is shown in Table 4.

Table 4. The comparison of blood pressure variability between diabetic group and control group

Observation index	Diabetes group n=59	Control group n=84	t	P
24hSSD	14.03±5.17	11.31±2.83	0.290	0.000 **
24hDSD	7.59±1.96	7.96±2.05	0.849	0.283
dSSD	13.60±3.67	11.33±2.94	0.095	0.000 **
dDSD	7.56±2.24	7.89±2.35	0.811	0.409
nSSD	13.34±3.47	11.27±3.95	0.154	0.001 *
nDSD	7.66±2.58	8.13±3.00	0.234	0.328
24hSCV	11.27±4.61	9.51±2.41	0.024	0.009 *
24hDCV	12.50±3.47	13.12±3.87	0.549	0.331
dSCV	10.91±3.27	9.53±2.53	0.081	0.005 *
dDCV	12.40±3.73	12.94±4.41	0.249	0.440
nSCV	10.80±3.32	9.54±3.36	0.549	0.028 *
nDCV	13.06±5.49	13.51±5.49	0.929	0.630

Note: * indicates 0.001 < P < 0.05 compared with the control group. ** indicates P < 0.001 compared with the control group.

3.4 Comparison of Blood Pressure Circadian Rhythm between Diabetic Group and Control Group

There was no significant difference between the two groups (P>0.05). Comparison of blood pressure circadian rhythm between diabetic group and control group is shown in Table 5.

Table 5. Comparison of blood pressure circadian rhythm between diabetic group and control group

Blood pressure circadian rhythm	Diabetes group n=59	Control group n=84	χ^2	P
Dipper	9	14	0.051	0.821
Non dipper	50	70		

3.5 Comparison of Cognitive Function between Diabetic Group and Control group

There was a statistically significant difference in cognitive function between the two groups (0.001 < P < 0.05). Comparison of cognitive function between diabetic group and control group is shown in Table 6.

Table 6. Comparison of cognitive function between diabetic group and control group

Cognitive function status	Diabetes group n=59	Control group n=84	χ^2	P
MCI	43	43	0.010	0.007 *
normal cognitive state	16	41		

Note: * indicates 0.001 < P < 0.05 compared with the control group.

4. Discussion

The autonomic function of diabetic patients is abnormal. The function of sympathetic nerve and vagus nerve in diabetic patients is disordered. The nocturnal sympathetic excitability was relatively high and the proportion of dipper was decreased. This study found that the proportion of dipper was significantly lower than that of the normal population, which was consistent with its mechanism. Insulin, as a vascular factor, can promote atherosclerosis^[14]. It can promote the hypertrophy and proliferation of arterial smooth muscle cells through insulin receptor or insulin-like growth factor, and lead to the increase of blood pressure. Insulin increases the activity of the sympathetic nervous system^[15]. Insulin enters the blood-brain barrier, binds to insulin receptors in the paraventricular nucleus and the arcuate nucleus around the ventricle, and sends excitatory signals to the sympathetic nucleus and inhibitory signals to the vagus nerve. Therefore, patients with diabetes mellitus and hypertension are more likely to have increased peripheral vascular resistance and atherosclerosis than patients with simple hypertension. The study found that the hypertension group with diabetes was higher in 24hSBP, 24hPP, dSBP, dPP, nSBP and nPP than the simple hypertension group, which was consistent with the above theory. In this study, 24hSSD, dSSD, nSSD, 24hSCV, dSCV and nSCV were also increased in the hypertension group with diabetes mellitus compared with the simple hypertension group. 24hSCV, dSCV and nSCV are independent of the mean value of mean blood pressure. This suggests that diabetes may lead to increased variability in blood pressure.

MCI (mild cognitive impairment) is a transitional state characterized by mild impairment of cognitive function between dementia and normal aging. Its daily living ability is retained and the overall cognitive function is intact. Kanemaru et al.^[16]'s 24h dynamic blood pressure study showed that short-term variability of daytime blood pressure and increased nocturnal systolic pressure were closely related to cognitive impairment. The results showed that increased blood pressure variability was negatively associated with various cognitive function tests and was associated with a higher risk of stroke. This association was independent of a variety of other cardiovascular risk factors, particularly blood pressure levels. Many recent clinical and experimental evidences suggest that diabetes may be a risk factor for MCI. In addition to regulating glucose metabolism, insulin also plays a role in promoting the neural development of embryos, promoting the formation of synapses of nerve cells, increasing cell body area and promoting the synthesis of various proteins. In diabet-

ics, the weakening of these effects of insulin is bound to lead to impaired cognitive function in the brain. Diabetes is a disease with insulin resistance as the core, which can lead to hyperinsulinemia. The study found that elderly diabetic patients with poor glycemic control performed worse in learning, reasoning and complex psychomotor functions than elderly type 2 diabetic patients with better glycemic control. At the same time, if severe hypoglycemia occurs frequently, it will also damage the higher cortex function, leading to the loss of sense of direction and consciousness and the impairment of cognitive function. Roberts RO et al.^[17] found that the course of diabetes, age of onset, blood glucose control, and presence or absence of complications all increase the risk of MCI. Our study also found that the cognitive function of the hypertension group with diabetes was significantly different from that of the simple hypertension group. This can also reflect the impairment of cognitive function in diabetes.

5. Conclusion

The results suggest that blood pressure variability increases in elderly patients with hypertension and diabetes and is associated with cognitive decline. Therefore, diabetic patients need to control blood glucose. The treatment of high blood pressure not only reduce the average blood pressure, but also should be able to smooth lowering blood pressure and blood pressure variability, in order to better prevent target organs damage and protect the cognitive function.

References

- [1] Guariguata L, Whiting D R, Hambleton I, et al. Global estimates of diabetes prevalence for 2013 and projections for 2035 for the IDF Diabetes Atlas[J]. *Diabetes Research and Clinical Practice*, 2013.
- [2] Zhen Hong. Current Situation and Prospect of Epidemiological Research on Alzheimer's Disease in China in Recent Years[J]. *Geriatrics and Health Care*, 2006, 11(4): 195-198.
- [3] Petersen R C, Smith G E, Waring S C, et al. Mild cognitive impairment: clinical characterization and outcome[J]. *Archives of neurology*, 1999, 56(3): 303-308.
- [4] Petersen R C, Negash S. Mild cognitive impairment: an overview[J]. *CNS Spectrums: The International Journal of Neuropsychiatric Medicine*, 2008, 13(1).
- [5] Bell R D, Zlokovic B V. Neurovascular mechanisms and blood-brain barrier disorder in Alzheimer's disease[J]. *Acta neuropathologica*, 2009, 118(1): 103-113.
- [6] Harold D, Abraham R, Hollingworth P, et al. Genome-wide association study identifies variants at CLU and PICALM associated with Alzheimer's disease[J]. *Nature genetics*, 2009, 41(10): 1088-1093.
- [7] Kudo T, Imaizumi K, Tanimukai H, et al. Are cerebrovascular factors involved in Alzheimer's disease? [J]. *Neurobiology of aging*, 2000, 21(2): 215-224.
- [8] Zhu, Jie, et al. "Intracranial artery stenosis and progression from mild cognitive impairment to Alzheimer disease." *Neurology* (2014): 10-1212.
- [9] Li J, Wang Y J, Zhang M, et al. Vascular risk factors promote conversion from mild cognitive impairment to Alzheimer disease[J]. *Neurology*, 2011, 76(17): 1485-1491.
- [10] Sabayan B, Wijsman L W, Foster-Dingley J C, et al. Association of visit-to-visit variability in blood pressure with cognitive function in old age: prospective cohort study[J]. *BMJ Open*, 2013, 347(f4600).
- [11] Marioni R E, Deary I J, Strachan M W, et al. Blood rheology and cognition in the Edinburgh Type 2 Diabetes Study[J]. *Age and ageing*, 2010, 39(3): 354-359.
- [12] Revision Committee of the Guidelines for the Prevention and Treatment of Hypertension in China. China Guidelines for the Prevention and Treatment of Hypertension 2010 Edition [J]. *Chinese Journal of Cardiology*, 2011,39(7):579-616.
- [13] Chinese Medical Association, Diabetes Society of Chinese Medical Association. Guidelines for the Prevention and Treatment of Type 2 Diabetes in China (2010 Edition, Discussion Draft), 2010.11.10.
- [14] Inukai T, Inukai Y, Matsutomo R, et al. Clinical usefulness of doxazosin in patients with type 2 diabetes complicated by hypertension: effects on glucose and lipid metabolism[J]. *Journal of international medical research*, 2004, 32(2): 206-213.
- [15] Zeng G, Nystrom F H, Ravichandran L V, et al. Roles for insulin receptor, PI3-kinase, and Akt in insulin-signaling pathways related to production of nitric oxide in human vascular endothelial cells[J]. *Circulation*, 2000, 101(13): 1539-1545.
- [16] Kanemaru A, Kanemaru K, Kuwajima I. The effects of short-term blood pressure variability and nighttime blood pressure levels on cognitive function[J]. *Hypertension research: official journal of the Japanese Society of Hypertension*, 2001, 24(1): 19-24.
- [17] Roberts R O, Geda Y E, Knopman D S, et al. Association of duration and severity of diabetes mellitus with mild cognitive impairment[J]. *Archives of neurology*, 2008, 65(8): 1066-1073.