The Relationship between Isolated Dizziness/Vertigo and the Risk Factors of Ischemic Stroke: A Case Control Study

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Abstract-

Purpose: Dizziness/vertigo are important public heath care issues especially in elderly patients. Isolated dizziness/vertigo without neurological deficits has seldom been considered a symptom/sign due to vascular origin. Recently, some studies have suggested that vascular origin should be considered in cases of positional vertigo and isolated vertigo or dizziness when the etiology remains unclear. In this study, we tried to delineate the correlation of dizziness/vertigo and risk factors of stroke.

Methods: We collected adult subjects receiving health screening of the brain at their own expense. All subjects had undergone brain magnetic resonance imaging (MRI), magnetic resonance angiography (MRA) and carotid duplex. The chief complaints, body height, body weight, waist circumference and blood pressure of all subjects were recorded. Most received blood tests including fasting sugar, total cholesterol, low density lipoprotein, high density lipoprotein (HDL), triglycerides, and uric acid (UA). The relationships between dizziness/vertigo and blood test data, blood pressure, body mass index (BMI), waist circumference, metabolic syndrome, carotid duplex, silent brain infarction, leukoaraiosis and MRA were analyzed.

Results: After exclusion, a total of 170 out of 210 subjects were collected. The analysis revealed that dizziness/vertigo had a significant correlation to age, UA , BMI, male HDL and female waist circumference. Among them, female waist circumference had the highest statistical significance (P = 0.001). Leukoaraiosis on brain MRI also had a close relationship with dizziness/vertigo.

Conclusion: After careful examination and approach, a vascular origin should be considered in dizzy patients of unknown etiology.

Key Words: dizziness, vertigo, metabolic syndrome, leukoaraiosis

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BACKGROUND

After eliminating the misleading symptoms or gait disturbance, "dizziness" usually means either faintness (presyncope) or vertigo (an illusory or hallucinatory sense of movement of the body or environment, most

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often a feeling of spinning)[1]. Dizziness/vertigo are important public heath care issues and dizziness in elderly patients is very common in family practice[2,3]. Isolated dizziness/vertigo without neurological deficits has seldom been considered as a symptom/sign due to vascular origin. In the emergency department, isolated dizziness, vertigo, or imbalance also strongly predicts a noncerebrovascular cause[4].

A large proportion of dizzy elderly patients in family practice remain undiagnosed. In recent years, there have been studies suggesting that a vascular origin should be considered in cases of positional vertigo and isolated vertigo or dizziness when the etiology remains unclear[5]. In addition, the involved brain sites are not necessarily infra-tentorial[6,7].

In this study, we collected the subjects with the chief complaint of dizziness/vertigo undergoing brain magnetic resonance imaging (MRI) and analyzed the relationship between the symptoms and silent brain infarcts/leukoaraiosis[8,9]. In addition, we analyzed the relationship between the dizziness/vertigo and risk factors of cerebrovascular accident (CVA).

METHODS

We collected 210 adult subjects aged above 18 years old receiving health screening of the brain at their own expense from January to October 2008 at Chang Gung Memorial Hospital (CGMH)-Kaohsiung. Among them, 176 subjects received serum blood tests for fasting blood sugar, total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride (TG) and uric acid (UA). All 210 subjects had records of body height, body weight, waist circumference and blood pressure. The chief complaints and abnormal neurological examination findings of the subjects were recorded if they existed.

Metabolic syndrome (MetS) was defined according to the modifications of the Third Report of the National Cholesterol Education Program's Adult Treatment Panel (ATP III 2005)[10,11]. The ATP III 2005 defines MetS as the presence of three or more of the following: fasting plasma glucose ≥ 100 mg/dl, serum triglycerides ≥ 150 mg/dl, serum HDL-cholesterol < 40 mg/dl in men and < 50 mg/dl in women, blood pressure ≥ 130/85 mmHg, or waist circumference > 90 cm in men and > 80 cm in women.

The exclusion criteria included brain tumors, hydrocephalus and vertebrobasilar dolichoectasia in the brain MRI[12]. Subjects taking the anti-platelet, anti-coagulant, statin drugs and anti-histamine medicine for dizziness/vertigo were also excluded. Those with concurrent focal neurological deficits implying brain lesions, past history of CVA or the chief complaint of syncope were excluded[13-15]. Those with obvious ear diseases such as otitis media or severe systemic disease were also excluded.

After exclusion, we analyzed the subjects with the chief complaint of dizziness/vertigo. The other subjects were classified as the control group. The distribution of the subjects with the complaint of dizziness/vertigo is illustrated in Figure 1. The relationships between dizziness/vertigo and sex, age, the level of blood sugar, TC, LDL, HDL, TG, UA, systolic blood pressure (SBP), diastolic blood pressure (DBP), body mass index (BMI), waist circumference and MetS were analyzed (Table 1). HDL and waist circumference was analyzed separately by sex.

All subjects had undergone brain MRI, magnetic resonance angiography (MRA) and carotid duplex examination. The MRI and MRA films were read by experienced neuroradiologists blinded to the results of the clinical conditions. The relationships between dizziness/vertigo and brain infarcts, leukoaraiosis, abnormal intracra-

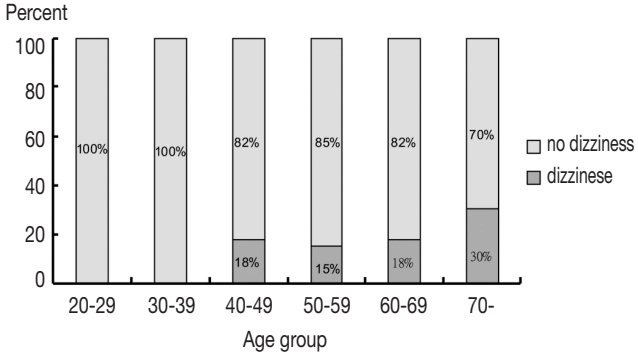

Figure 1. The distribution of dizzy subjects by age group (n = 170).

nial MRA and duplex findings were analyzed (Table 2).

Brain infarction was defined as focal hyperintensity on T2-weighted images and corresponding hypointensity on T1-weighted images. Leukoaraiosis was defined as hyperintense lesions in periventricular or subcortical regions, or in the pons, on fluid-attenuated inversion recovery MRI sequences[16,17]. As the subjects with symptomatic brain infarctions were excluded, the brain infarctions found in the chosen subjects were silent infarctions. The peak systolic velocity (PSV) of internal carotid arteries (ICA) > 140 centimeter per second was considered as ICA stenosis > 50%[18]. A PSV of the vertebral artery (VA) > 140 centimeter per second or reversal of VA flow was considered as abnormal VA[18,19].

In addition, we furthered analyzed the subjects with the chief complaints of headache, neck pain, insomnia and miscellaneous complaints. The relationship between the above complaints and leukoaraiosis is illustrated in Table 3.

Chi-square and Fisher's exact tests allowed comparisons of categorical variables between groups. The Student t test was used for comparisons of means, and the Mann-Whitney U test was used for ordinal variables. All statistical analyses used SPSS 15.0 for Microsoft Windows (SPSS Inc., Chicago, IL). Two-sided values of $p < 0.05$ were considered significant.

Table 1. The relationship between dizziness/vertigo and sex, age, blood pressure BMI, waist circumference, serum laboratory data and metabolic syndrome

	Dizzy (n = 28)	Non-dizzy (n = 142)	*P*-value
(1) Sex			
Male	14 (50)	73 (51)	1
Female	14 (50)	69 (49)	
(2) Age	58.2 (±11.5)	52.6 (±12.8)	0.035*
(3) Blood pressure (mmHg)			
Systolic	132.5 (±17.4)	128.2 (±19.0)	0.271
Diastolic	78.5 (±8.5)	78.5 (±9.5)	0.963
(4) BMI (kg/m^2)	25.6 (±3.0)	23.9 (±3.6)	0.015*
(5) Waist circumference (cm)			
Male	88.0 (±6.1)	87.0 (±8.2)	0.681
Female	91.9 (±8.4)	81.9 (±9.8)	0.001*
(6) Serum laboratory data$^\delta$ (fasting)	(n = 25)	(n = 120)	
Glucose (mmol/L)	5.76 (±1.16)	5.55 (±1.18)	0.219
Total cholesterol (mmol/L)	5.24 (±0.97)	5.14 (±1.00)	0.392
LDL (mmol/L)	3.26 (±0.91)	3.09 (±1.33)	0.181
HDL (mmol/L)			
Male	1.13 (±0.19)	1.35 (±0.36)	0.041*
Female	1.52 (±0.36)	1.55 (±0.37)	0.926
Triglycerides (mmol/L)	1.53 (±0.59)	1.40 (±1.03)	0.086
Uric acid (μmol/L)	368.9 (±83.3)	339.1 (±83.3)	0.018*
(7) Metabolic syndrome$^\delta$			
Yes	12 (48)	34 (28)	0.062
No	13 (52)	86 (72)	

Data are expressed as mean (±SD), n (%) or *P*-value.

BMI: body mass index; LDL: low density lipoprotein; HDL: high density lipoprotein

δ: not all subjects had serum laboratory data; *: statistically significant.

Table 2. The relationship between dizziness/vertigo and brain MRI(A), carotid duplex findings

	Dizzy group (n = 28)	Control group (n = 142)	*P*-value
Brain MRI(A) findings			
Silent infarct	3 (11)	9 (6)	0.420
Leukoaraiosis	10 (35)	26 (18)	0.047*
Abnormal intracranial MRA			
Any intracranial MRA	6 (21)	23 (16)	0.582
Abnormal MCA	6 (21)	14 (10)	0.105
Abnormal VBA	3 (11)	8 (6)	0.393
Carotid duplex findings			
Any abnormal Duplex	21 (75)	90 (63)	0.282
ICA stenosis > 50%	1 (4)	2 (1)	0.419
Abnormal vertebral artery	0^c (0)	5 (4)	0.592

Data are expressed as n (%) or *P*-value.

MRI: magnetic resonance imaging; MRA: magnetic resonance angiography

MCA: middle cerebral artery; VBA: vertebrobasilar artery; ICA: internal carotid artery; c: using a correction of 0.5 in every cell that contains a zero.

Table 3. The relationship between chief complaint other than dizziness/vertigo and leukoaraiosis

All subjects	Leukoaraiosis (n = 36)	No Leukoaraiosis (n = 134)	*P*-value
(1) Headache	3 (8)	31 (23)	0.06
(2) Neck pain	1 (3)	16 (12)	0.127
(3) Insomnia	3 (8)	6 (4)	0.401
(4) Miscellaneous complaints	14 (39)	50 (37)	0.894

Data are expressed as n (%) or *P*-value.

RESULTS

Among the subjects excluded, brain MRI(A) revealed one large cerebral tumor, one superior vermis tumor, one left cerebellopontine angle tumor, one hydrocephalus and dolichoectasia in six subjects. Two subjects with obvious ear disease and one subject with severe anemia were also excluded. Four subjects had the chief complaint of syncope. Two subjects had focal neurological deficits implying acute stroke and another two subjects had a history of old stroke. Four subjects had taken antihistamine drugs for dizziness/vertigo, three subjects had taken statin medicines and twelve subjects had taken anti-platelet drugs.

After exclusion, a total of 170 out of 210 subjects were collected. Among the 170 chosen subjects, the mean age was 53.6 years with 88 males and 82 females. Twenty-eight (16%) subjects had the chief complaint of dizziness/vertigo regardless of onset or duration. The incidence of dizziness increased with increasing age (Figure 1). The gender percentage of dizzy subjects was the same with 14 males and 14 females (Table 1). When comparing the dizzy subjects with controls, the mean age was older with statistical significance in the dizzy group (Table 1).

Serum laboratory data revealed higher levels in the dizzy group except for HDL. Higher SBP was also observed in the dizzy group. The lower HDL level in dizzy male subjects reached statistical significance. In contrast, the higher UA level in the dizzy group reached statistical significance especially in the female subjects (P = 0.004). Higher BMI and waist circumference in female subjects also bore statistical significance compared to the control group (Table 1). As for MetS, a higher percentage of dizzy subjects had MetS and borderline significance was noted.

When comparing the dizzy subjects to ischemic lesions found in the brain MRI, although infarction lesions were more common in the dizzy group, there was no statistical significance. Moreover, leukoaraiosis was also more common in the dizzy group and it reached statistical significance (Table 2). Among intracranial MRA findings, the abnormal middle cerebral artery (MCA) had the closest relationship to dizziness/vertigo. In contrast, there was little relationship between carotid duplex findings and dizziness/vertigo.

The other common complaints included headache, neck pain and insomnia. We also analyzed the relationship between leukoaraiosis and headache, neck pain, insomnia and miscellaneous complaints (Table 3).

DISCUSSION

In this study, the age of the dizzy subjects was significantly higher than those without dizziness. This might explain the higher levels of serum glucose, TC, LDL, UA and SBP in the dizzy group. The incidence of MetS was also much higher in the dizzy group[20]. A lower level of HDL was noted in the male dizzy subjects reaching statistical significance. A significantly higher level of UA was noted in the dizzy group, especially in the female dizzy subjects. Recent studies have concluded that hyperuricemia may modestly increase the risks of both stroke incidence and mortality[21,22]. However, the median level of UA in the dizzy group was still within normal range. In contrast, studies discussing the relationship between HDL and stroke are sparse. Due to the correlation of plasma homocysteine to cerebral white matter hyperintensity on MRI, it might be worthwhile including plasma homocysteine for comparison[23].

Other categories of statistical significance included BMI and female waist circumference. The significantly higher level of BMI and waist circumference might also

explain the higher serum laboratory levels in the dizzy group. Elevated BMI increases the risk of both ischemic and hemorrhagic stroke incidence, and stroke mortality in Chinese adults[24,25]. Increasing levels of general or abdominal adiposity consistently predict increased risk of stroke in predominantly non-obese Chinese women[26].

Isolated dizziness/vertigo is usually considered as peripheral vestibulopathy but seldom as vascular origin. Recent studies have suggested that a vascular origin should be considered in cases of positional vertigo and isolated vertigo or dizziness when the etiology remains unclear[5]. Although seldom encountered, one report showed three cases of small brain infarctions in the lateral wall of the fourth ventricle presenting with central paroxysmal positional vertigo[6]. In our study, the complaints of the dizzy subjects were either acute, subacute or chronic.

One study has discussed the correlation between non-specific neurological complaints and silent cerebral infarctions, with non-specific complaints including headache, dizziness and forgetfulness[27]. In this study, we tried to correlate the dizziness/vertigo to cerebral infarctions or leukoaraiosis. Statistical significance was noted between the correlation of dizziness/vertigo and leukoaraiosis rather than infarctions (Table 2).

Other complaints including headache, neck pain, insomnia and miscellany revealed no correlation with leukoaraiosis (Table 3). This might indicate a remote relationship between neurosis and leukoaraiosis, because neurotic patients are prone to having multiple non-specific complaints.

Several studies have discussed the relationship of cerebral leukoaraiosis to small-vessel disease[28-30]. Leukoaraiosis shares common pathophysiological mechanisms with stroke and, because it is likely an expression of the same disease, must be regarded as an intermediate surrogate of stroke rather than a true stroke risk factor.

In neurological or other clinical practice, dizziness/vertigo is a frequently encountered complaint. The patients with the complaint of dizziness/vertigo are usually older. The significant relationship of dizziness with HDL, UA, BMI, waist circumference and leukoaraiosis may indicate the linkage of dizziness and cerebral ischemic lesions. After careful examination and approach, a vascular origin should be considered in cases of positional vertigo and isolated vertigo or dizziness when the etiology remains unclear.

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REFERENCES

1. Daroff R. Dizziness and vertigo. In: Fauci A, Braunwald E, Kasper D, Hauser S, Longo D, Jameson J, Loscalzo J. Eds. Harrison's Principles of Internal Medicine. 17th edition. McGraw-Hill, 2008,144-147.
2. Gopinath B, McMahon CM, Rochtchina E, Mitchell P. Dizziness and vertigo in an older population: the Blue Mountains prospective cross-sectional study. Clin Otolaryngol 2009;34:552-556.
3. Maarsingh OR, Dros J, Schellevis FG, van Weert HC, Bindels PJ, Horst HE. Dizziness reported by elderly patients in family practice: prevalence, incidence, and clinical characteristics. BMC Fam Pract 2010;11:2.
4. Kerber KA, Brown DL, Lisabeth LD, Smith MA, Morgenstern LB. Stroke among patients with dizziness, vertigo, and imbalance in the emergency department: a population-based study. Stroke 2006;37:2484-2487.
5. Cloutier JF, Saliba I. Isolated vertigo and dizziness of vascular origin. J Otolaryngol Head Neck Surg 2008;37:331-339.
6. Hosomi M, Matsumoto K, Kageyama Y, Ichikawa K. Three cases of small brain infarction in the lateral wall of the fourth ventricle presenting with paroxysmal positional vertigo and vomiting. Rinsho Shinkeigaku 2008;48:709-712.
7. Murai N, Oda N, Hori I, Shabana M, Kurozawa Y, Funabiki K. The relationship between cerebral T2 hyperintensity and fixation suppression of vestibulo-ocular reflex in elderly patients with dysequilibrium symptoms. Auris Nasus Larynx 2007;34:165-171.
8. Mäntylä R, Aronen HJ, Salonen O, Pohjasvaara T, Korpelainen M, Peltonen T, Standertskjöld-Nordenstam CG, Kaste M, Erkinjuntti T. Magnetic resonance imaging

white matter hyperintensities and mechanism of ischemic stroke. Stroke 1999;30:2053-2058.
9. Inzitari D. Leukoaraiosis: an independent risk factor for stroke? Stroke 2003;34:2067-2071.
10. Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). JAMA 2001; 285:2486-2497.
11. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, Gordon DJ, Krauss RM, Savage PJ, Smith SC Jr, Spertus JA, Costa F; American Heart Association; National Heart, Lung, and Blood Institute. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation 2005; 112:2735-2752.
12. Passero SG, Rossi S. Natural history of vertebrobasilar dolichoectasia. Neurology 2008;70:66-72.
13. Rancurel G. Transient ischemic attacks in the elderly: new definition and diagnostic difficulties. Psychol Neuropsychiatr Vieil 2005;3:17-26.
14. Davidson E, Rotenbeg Z, Fuchs J, Weinberger I, Agmon J. Transient ischemic attack-related syncope. Clin Cardiol 1991;14:141-144.
15. Khurana V, Gambhir IS, Srivastava A, Kishore D. Dizziness and collapse? It's a steal! Lancet 2009;374:1472.
16. Vermeer SE, Hollander M, van Dijk EJ, Hofman A, Koudstaal PJ, Breteler MM; Rotterdam Scan Study. Silent brain infarcts and white matter lesions increase stroke risk in the general population: the Rotterdam Scan Study. Stroke 2003;34:1126-1129.
17. Putaala J, Kurkinen M, Tarvos V, Salonen O, Kaste M, Tatlisumak T. Silent brain infarcts and leukoaraiosis in young adults with first-ever ischemic stroke. Neurology 2009;72:1823-1829.
18. Hwang CS, Shau WY, Tegeler CH. Doppler velocity criteria based on receiver operating characteristic analysis for the detection of threshold carotid stenoses. J Neuroimaging 2002;12:124-130.
19. Buckenham TM, Wright IA. Ultrasound of the extracranial vertebral artery. Br J Radiol 2004;77:15-20.
20. Lin CC, Liu CS, Lai MM, Li CI, Chen CC, Chang PC, Lin WY, Lee YD, Lin T, Li TC. Metabolic syndrome in a Taiwanese metropolitan adult population. BMC Public Health 2007;7:239.
21. Chien KL, Hsu HC, Sung FC, Su TC, Chen MF, Lee YT. Hyperuricemia as a risk factor on cardiovascular events in Taiwan. The Chin-Shan Community Cardiovascular Cohort Study. Atherosclerosis 2005;183:147-155.
22. Kim SY, Guevara JP, Kim KM, Choi HK, Heitjan DF, Albert DA. Hyperuricemia and risk of stroke: a systematic review and meta-analysis. Arthritis Rheum 2009;61:885-892.
23. Tseng YL, Chang YY, Liu JS, Su CS, Lai SL, Lan MY. Association of plasma homocysteine concentration with cerebral white matter hyperintensity on magnetic resonance images in stroke patients. J Neurol Sci 2009;284:36-39.
24. Rexrode KM, Hennekens CH, Willett WC, Colditz GA, Stampfer MJ, Rich-Edwards JW, Speizer FE, Manson JE. A prospective study of body mass index, weight change, and risk of stroke in women. JAMA 1997;277:1539-1545.
25. Bazzano LA, Gu D, Whelton MR, Wu X, Chen CS, Duan X, Chen J, Chen JC, He J. Body mass index and risk of stroke among Chinese men and women. Ann Neurol 2010;67:11-20.
26. Zhang X, Shu XO, Gao YT, Yang G, Li H, Zheng W. General and abdominal adiposity and risk of stroke in Chinese women. Stroke 2009;40:1098-1104.
27. Hougaku H, Matumoto M, Irino T, Hashimoto H, Handa N, Kamada T. Non-specific neurological complaints and silent cerebral infarction. Nippon Ronen Igakkai Zasshi 1996; 33:460-464.
28. Coşkun O, Yildiz H, Emre U, Akin U, Uçler S, Ergun U, Tunç T, Inan EL. Leukoaraiosis in stroke patients. Int J Neurosci 2003;113:915-922.
29. Hénon H, Vroylandt P, Durieu I, Pasquier F, Leys D. Leukoaraiosis more than dementia is a predictor of stroke recurrence. Stroke 2003;34:2935-2940.