PARKINSON'S DISEASE AND CAROTID INTIMA-MEDIA THICKNESS

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PARKINSON'S DISEASE AND CAROTID INTIMA-MEDIA THICKNESS (Abstract): Reports about the impact of cerebrovascular disease (CVD) on clinical status in Parkinson's disease (PD) are rather controversial. There have been a few studies and inconsistent results regarding the coincidence of Parkinson's disease (PD) and atherosclerotic diseases, such as cerebrovascular disease. Carotid intima-media thickness (IMT) is a known marker for subclinical atherosclerosis. **Aim:** This study was done to investigate the carotid IMT between PD patients and controls. **Material and methods**: A total of 54 PD patients and 50 controls were examined. The duration of Parkinson's disease, the severity of Parkinson's disease (the Hoehn–Yahr stage) and carotid IMT were examined. **Results:** The mean Hoehn and Yahr stage was 2.78 (range 2-4). Duration of disease had a mean of 7.59 ± 0.85 years. The left CCA mean IMT was 0.900 ± 0.147 in Parkinson group and 0.828 ± 0.118 in control group (p=0.007). The right CCA mean IMT was 0.891 ± 0.176 mm in the Parkinson group and 0.860 ± 0.164 in control group (p=0.360). No relationship between the Hoehn and Yahr stages or the duration of PD with the IMT were found by the Pearson's correlation test. **Conclusions:** The carotid IMT was higher in PD patients than in controls. **Keywords**: CAROTID INTIMA-MEDIA THICKNESS, PARKINSON'S DISEASE, SUBCLINICAL ATHEROSCLEROSIS

Parkinson's disease (PD) is one of the most frequent neurodegenerative disorders, characterized by progressive degeneration not only of the dopaminergic, nigrostriatal system, responsible for the core motor symptoms but also by involvement of many other neuronal systems and organs.There are multifocal neurodegenerative lesions affecting the central, peripheral, and autonomic nervous systems and many other organs (eg, adrenals, retina, heart, skin). The resulting biochemical deficits cause the heterogenous clinical picture including the variegated and often early presenting nonmotor deficit of this multisystem disorder (1). There have been a few studies and inconsistent results regarding the coincidence of Parkinson's disease and atherosclerotic diseases, such as cerebrovascular disease (CVD). Some authors reports that the pathology of vessels supplying the brain contributes to disease severity in PD patients, even without clinically manifest CVD (2). Studies have shown that carotid intima-media thickness (IMT) is an indicator of early generalized atherosclerosis and

that arterial wall thickness is associated with cardiovascular disease and stroke. The carotid IMT can be measured using Doppler ultrasound (3,4). As increased thickness in the intima media complex of the carotid artery has a clinical significance to cardiovascular comorbidity, we examined the hypothesis that patients with PD have an increased thickness of the intima-media complex of the carotid artery (5, 6).

MATERIAL AND METHODS

A prospective, descriptive study was carried out on 54 patients with PD, diagnosed according with United Kingdom Parkinson's Disease Society Brain Bank Diagnostic Criteria for Parkinson's Disease. None of the patients had vascular parkinsonism or was severely impaired by any other comorbidity. Other exclusion criteria were clinical features consistent with a diagnosis of atypical parkinsonism, such as multiple system atrophy, progressive supranuclear palsy, and corticobasal degeneration. The control group was composed of 50 healthy age- and sex-matched subjects. Extracranial carotid IMT measurements were performed according to a predetermined, standardized scanning protocol for the right and left comune carotid arteries. To evaluate carotid atherosclerosis, high-resolution B-mode ultrasonography was performed with a 7.5-MHz linear type probe (Acuson X 300, Siemens, Germany). The IMT was evaluated as the distance between the luminal intimal interface and the medial-adventitial interface, and it was measured using an electronic caliper on the frozen frame of a suitable longitudinal image. Three measurements of far-wall IMT were taken manually in each image using ultrasound calipers, and the average values of these readings were used in the analyses. The mean of left and right IMTs were used in the analyses. Statistical analysis was performed with the SPSS 13.0 statistical package program. Mean IMT of both groups, the duration of PD, and the Hoehn&Yahr scores of both groups were compared. Student's t test and Pearson's correlation analysis were used. Significance levels were set at $p<0.05$ in all cases and 95% confidence intervals (CI) were estimated.

RESULTS

No significant differences in the ages or gender were observed between the two groups. The age of parkinsonian patients ranged between 32 and 85 years with a mean of 66.37±8.90 years while the mean age of controls was a little smaller 63.92±12.63 years. The mean Hoehn and Yahr stage was 2.78 (range 2-4). Duration of disease varied from 1 to 32 years with a mean of 7.59 ± 0.85 years (tab. I**).**

TABLE. I

Demographic data of patients with Parkinson's disease and controls

	Parkinson (n=54)	**Controls (n=50)**	**P**
Age, years	66.37±8.90	63.92±12.63	0.253
Sex, male	61%	56%	0.121
Duration of disease	7.59 ± 0,85		
Hoehn–Yahr stage	2.78±0.79		

Data are mean ± SD or number (%).

Analyses of the left CCA revealed a mean IMT of 0.900 ± 0.147 in Parkinson group and 0.828 ± 0.118 in control group while the right CCA was found to have mean IMT of 0.891 ± 0.176 mm in the Parkinson group and 0.860 ± 0.164 in control group. The difference was statistically significant only for the left side (tab. II, III, fig.1).

TABLE II

Descriptive data of IMT on study groups

Interval	N	Average	Std. Deviation	Std. Error	Confidence interval		Min	Max
					- 95%CI	+95%CI		
IMT right								
Parkinson	54	0.891	0.176	0.024	0.843	0.939	0.5	1.4
Control	50	0.860	0.164	0.023	0.813	0.907	0.5	1.2
IMT left								
Parkinson	54	0.900	0.147	0.020	0.860	0.940	0.6	1.2
Control	50	0.828	0.118	0.017	0.795	0.861	0.7	1.1

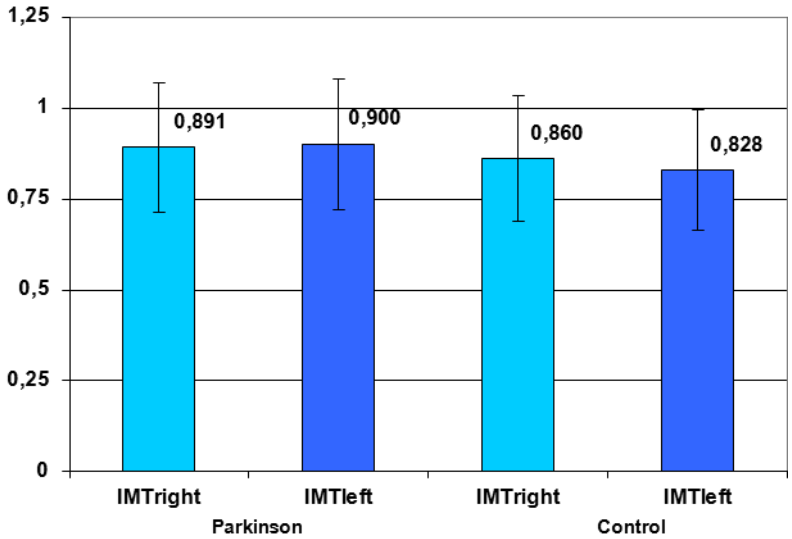

Fig. 1. Average values of IMT (mm) between study groups

TABLE III

Correlation of mean values of IMT between study groups

IMT	Control group Mean ± SD	Parkinson group Mean ± SD	*P* value Two-tailed probability
Right	0.860 ± 0.164	0.891 ± 0.176	0.360
Left	0.828 ± 0.118	0.900 ± 0.147	0.007*

*Significant (P<0.05)

No relationship between the Hoehn and Yahr stages or the duration of PD with the IMT were found by the Pearson's correlation test. (tab. IV)

TABLE IV

Pearson's correlation between IMT. duration of disease and Hoehn and Yahr stage

Correlations		Duration of disease	Hoehn Yahr stage
IMTright	Pearson Correlation	-.175	-.015
	Sig. (2-tailed)	.206	.914
	N	54	54
IMTleft	Pearson Correlation	-.144	-.130
	Sig. (2-tailed)	.298	.350
	N	54	54

** Correlation is significant at the 0.01 level (2-tailed).

DISCUSSION

Increased carotid intima-media thickness is a noninvasive marker of systemic atherosclerosis and relates to the risk of future cerebrovascular disease attacks (7).There have been some previous studies of carotid IMT in PD (8.9.10). One reported that the IMT in PD patients was significantly greater than those in controls (4). Others reported that carotid IMT did not correlate with PD duration or severity and others proved that IMT is thinner in parkinsonian patients (2). In our study we founded that IMT is thicker in parkinsonian patients on both carotids arteries but only for the left side statistically significance was reached. We did not find any relationship between Hoehn and Yahr stage and IMT. or between duration of Parkinson disease and IMT of the carotid artery. It is not clear whether increased IMT of the carotid artery is a cause or a result of the severity of Parkinsonism. One possible mechanism by wich subclinical vascular impairment can accelerate the evolution of Parkinson disease is the deleterious effect of otherwise subclinical hypoperfusion on regions made vulnerable by the degenerative process (13.14.15). On the other hand. other mechanisms may link PD with a higher risk of atherosclerosis. L-dopa treatment may promote secondary hyper- homocysteinemia. which may induce atherosclerosis but these hypertrophic changes were observed primarily in patients with a Hoehn-Yahr stage of 3-5 (4). In our study patients were Hoehn-Yahr stage of 2-4 and not all of them had treatment with L-dopa.

CONCLUSIONS

We conclude that patients with PD are at an increased risk for thickening of the intima media of the carotid artery. Due to the small sample size of this study we weren't able to say if this concomitant vascular pathology may contribute to a less favorable course in PD patients. Larger studies are needed to precisely establish the role of vascular factors in PD.

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REFERENCES

1. K. A. Jellinger : Neuropathology of Sporadic Parkinson's Disease: Evaluation and Changes of Concepts. *Mov Disord*. 2012; 24: 793–800.
2. J.M. Lee. K.W. Park. W.K. Seo. M. H. Park. C. Han : Carotid Intima-Media Thickness in Parkinson's Disease. *Mov Disord.* 2007; 22: 657–671.
3. K. Nakaso. K. Yasui. H. Kowa. M. Kusumi. K. Ueda. Y. Yoshimoto. T. Takeshima. K. Sasaki. K. Nakashima : Hypertrophy of IMC of carotid artery in Parkinson's disease is associated with L-DOPA. homocysteine. and MTHFR genotype. *J Neurol Sci*. 2003 15; 207(1-2): 19-23.
4. Oncel C. Ince B. Apaydin H. Ozekmekçi S. Uludüz D : Hypertrophy of intima media of the carotid artery due to L-dopa therapy in Parkinson's disease. *Adv Ther*. 2008; 25(3): 201-7.
5. Rektor I. Goldemund D. Sheardova K. Rektorova I. Michalkova Z. Dufek M. Vascular pathology in patients with idiopathic Parkinson's disease. *Parkinsonism Relat Disord* 2009; 15: 24–29.
6. Rektor I.. Goldemund D.. P. Bednarik P.. Sheardova K. Michalkova Z. Telecka S. Dufek M. Rektorova I: Impairment of Brain Vessels May Contribute to Mortality in Patients With Parkinson's Disease. *Mov Disord.* 2012;27:982–993
7. Bots ML. Hoes AW. Koudstaal PJ. Hofman A. Grobbee DE.Common carotid intima-media thickness and risk of stroke and myocardial infarction: the Rotterdam Study. *Circul* 1997; 96: 1432–1437.
8. Gorell JM. Johnson CC. Rybicki BA. Parkinson's disease and its comorbid disorders: an analysis of Michigan mortality data. 1970 to 1990. *Neurol* 1994; 44: 1865–1868.
9. Horner S. Niederkorn K. Ni XS. et al. : Evaluation of vascular risk factors in patients with Parkinson syndrome. *Der Nervenarzt* 1997; 68:967–971.
10. Struck LK. Rodnitzky RL. Dobson JK. : Stroke and its modification in Parkinson's disease. *Stroke* 1990;21:1395–1399.
11. Nataraj A. Rajput AH. : Parkinson's disease. stroke. and related epidemiology. *Mov Disord* 2005;20:1476 –1480.
12. Papapetropoulos S. Ellul J. Argyriou AA. Talelli P. Chroni E. Papapetropulos T. : The effect of vascular disease on late onset Parkinson's disease. *Eur J Neurol* 2004; 11: 231–235.
13. Hughes AJ. Daniel SE. Kilford L. Lees AJ. : Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. *J Neurol Neurosurg Psychiatry 1992*; 55: 181–184.
14. Jellinger KA. : The neuropathologic diagnosis of secondary parkinsonian syndromes. In: Battistin L. Scarlato G. Caraceni T. Ruggieri S.(eds). *Advanced Neurology*. New York. NY: Raven; 1996
15. Rektor I. Rektorova I. Kubova D.: Vascular parkinsonism: an update. *J Neurol Sci* 2006; 248: 185–191.