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Research Article

Correlation Between Systolic Blood Pressure Variability and Global Longitudinal Strain in Patients with Parkinson's Disease and Dysautonomia

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ABSTRACT

Background: Patients with Parkinson's disease (PD) and dysautonomia often present elevated blood pressure (BP) variability. However if the elevate BP variability is correlated with subclinical echocardiography abnormalities have been poorly investigated yet. Our aim was to evaluate the correlation between indices of left ventricular function and 24/h BP variability in patients with PD.

Methods: We studied 21 patients with diagnosed PD and autonomic dysfunction and 20 hypertensive age-matched subjects. All patients underwent 24/h ambulatory blood pressure monitoring (ABPM) and echocardiography. Left ventricular (LV) systolic function was evaluated by ejection fraction (EF), tissue Doppler s wave and global longitudinal strain (GLS). BP variability was evaluated through average real variability.

Results: At ABPM, patients with PD had an higher occurrence of nocturnal hypertension, orthostatic hypotension and post-prandial hypotension compared to hypertensive subjects. GLS, tissue Doppler s velocity, LVEF, LV mass index, and E/e' ratio were similar between the patients with PD and those with hypertension. In patients with PD there was a significant correlation between GLS and 24/h systolic BP variability (r= 0.44; p=0.01). a trend through significance between 24 systolic BP variability and tissue Doppler s velocity (r= -0.31; p=0.06).

Conclusions: In PD patients, short-term BP variability was inversely related to GLS. GLS seems to be an early detector of LV dysfunction in patients with PD and autonomic dysfunction.

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INTRODUCTION

Blood pressure (BP) variability, has demonstrated a relevant clinical and prognostic impact, beyond BP values, in different clinical contexts[1,2]. In particular, an elevated short-term BP variability, evaluated by 24/h BP monitoring (ABPM), is also a recognised risk factor for target organ damage in the general population[3,4], ed hypertension [5]. Some clinical conditions, including diabetes mellitus and Parkinson's disease, characterized by high cardiovascular risk and elevated short-term BP variability, share the common background of dysautonomia[6-8]. Clinical implications of an elevated short-term variability have been elucidated in dysautonomic patients with diabetes [9]. Conversely whether the elevated short-term BP variability observed in Parkinson's disease (PD) with dysautonomia is associated with subclinical left ventricular (LV) abnormalities remain still unknown. Among parameters estimating LV function, global longitudinal strain (GLS), assessed by two-dimensional speckle-tracking echocardiography, has recently gained a growing interest for its greater accuracy when compared to other indices[10]. GLS permitted to identify earlier LV dysfunction when other parameters such as LV ejection fraction and tissue Doppler imaging were still normal [11]. To our knowledge there are no data about GLS values in patients with PD and dysautonomia and their correlation with BP variability.

This study had two main objects: a) to investigate the relationship between short-term BP variability and indices of LV function in patients with PD b) to compare the echocardiography pattern of non-hypertensive patients with PD with that of hypertensive subjects.

METHODS

The study was conceived as cross-sectional. Population included 21 patients with PD with already diagnosed dysautonomia, and 20 age-matched subjects with arterial hypertension. Exclusion criteria were: history of heart failure; known valve heart diseases and/or coronary artery disease; reduced LV ejection fraction (below 50%); poor acoustic window. Patients with PD who had also hypertension were excluded. Subjects with hypertension ho had secondary or resistant hypertension were also excluded. PD group included patients with idiopathic Parkinson's disease in the mid-late stage of the disease enrolled in another clinical study (NCT 03843944); they were on stable treatment with levodopa and rasagiline for at least 4 weeks prior the study start, and had a median duration of the disease of 8.0±2.8 years. The hypertension group included subjects who had a diagnosis of grade I-II uncomplicated hypertension according to ESC guidelines for at least one year and were treated with less than three anti-hypertensive drugs. The study protocol was approved by the local ethical committee. All subjects underwent echocardiography and 24/h ABPM.

Echocardiography was performed using Acuson SC 2000 Prime ultrasound system (Siemens) with a 4.0-MHz transducer by two experienced sonographers. All participants were examined with conventional two-dimensional echocardiography and colour tissue Doppler. We used 2-D echocardiography to measure chambers, wall thickness and LV mass through area-length method from short axis view. LV ejection fraction was measured with the Simpson's method. Colour tissue Doppler tracings were obtained with the range gate placed at the lateral mitral annular segments in the 4-chamber view. Speckle-tracking echocardiography was performed in the 2, 3 and 4-chamber apical views with an average of 4 cycles. Images were processed offline. The endocardial border was traced by an automated function that defined a region of interest at the end-systole. The investigator visually assessed the detected regions and if necessary, manually modified them to ensure correct tracking of the speckle.

Twenty-four/h ABPM was obtained with an oscillometric device (BP one, United Kingdom); patients were instructed to maintain their usual activities and medications. Data were accepted if at least 75 % of the measurements were obtained successfully. Data from 24-h, daytime (from 6.00 A.M. to 10.00 P.M.) and night-time (from 10.00 p.m. to 6.00 a.m.) systolic and diastolic BP were evaluated. BP variability was evaluated through average real variability[12].

***Statistical Analysis*:** Results were expressed as median ± standard deviation (SD). The between groups comparison was performed with the unpaired *t* test or the Mann-Whitney rank sum test. The relationship

between variables was assessed either the Pearson correlation or the Spearman rank test.

RESULTS

Baseline data of the study population are summarized in Table 1. The two groups of patients were well matched according to age ad gender distribution. Body mass index was higher in the hypertensive group than in the PD. All subjects with PD had a nondipper profile at ABPM. Nocturnal hypertension, orthostatic hypotension and post-prandial hypotension were more often observed in the PD compared to hypertension group. The majority (82.6%) of hypertensive subjects were taking two anti-hypertensive drugs. 24/h systolic BP, diurnal systolic and diastolic BP, were significantly lower in the PD group compared to hypertension group. Conversely, nocturnal systolic and diastolic BP values were similar between the two groups. Patients with PD had higher 24/h and nocturnal systolic BP variability than hypertensive patients. Diastolic BP variability was similar between the two groups. GLS, tissue Doppler s (sm) velocity, LV mass index, LVEF, and E/e' ratio were similar between the two groups. There was a significant correlation between GLS and 24/h systolic BP variability (r= 0.44; p=0.01) (Figure 1) and a trend through significance between 24/h systolic BP variability and tissue Doppler s velocity (r= -0.31; p=0.06). LVEF was not correlated with systolic BP variability.

DISCUSSION

The main result of this preliminary study is the demonstration of an inverse correlation between 24/h systolic BP variability and GLS in a small group of normotensive patients with advanced PD and dysautonomia who were free from other cardiac diseases. This is a new finding: to our knowledge no previous studies have assessed LV function by two-dimensional speckle tracking echocardiography in PD. Conversely a correlation between GLS and short-term BP variability has recently been described in 94 hypertensive subjects[14]. PD has been associated to a high cardiovascular risk and to an higher risk of heart failure occurrence compared to age-matched subjects without PD [15]. Subclinical echocardiography alterations have already been described in PD. Günaydın et al.[16] found increased aortic stiffness and impaired diastolic function, compared to healthy individuals, in patients with PD under L-dopa treatment. Our results are compatible with prior studies demonstrating that short-term BP variability was related to subclinical target organ damage in hypertension and diabetes [5,13]. However given the small sample size and the cross-sectional design of our study, we think further longitudinal investigations are needed in order to establish if a cause-effect relation between BP variability and GLS abnormalities exists also in PD. Interestingly, in our study, GLS was the only echocardiography parameter, among those estimating LV function, to be significantly correlated with BP variability. Speckle tracking echocardiography enables the assessment of myocardial strain, providing detailed information on global and regional active

Table 1. Statistical comparison of patients with Parkinson's disease and with hypertension.

	Parkinson disease (N=21)	Hypertension (N=20)
Age, years	72.3 ± 8.4	70.2±11.2
Male/female	16/5	9/2
BSA, m^2	1.54±0.3*	1.66±0.5
BMI, kg/m^2	22.1±6.4	28.7±9.6
Number of anti-hypertensive drugs	-	1.9±0.7
Echocardiography		
LV volume, ml		
End diastolic	63.9±9.6	64.4±11.6
End systolic	27.1±12.0	27.8±10.4
LV mass, index, g/m^2	127.6 ±31.3	131.8±27.4
LVEF, %	61.4±8.3	60.6±7.7
LA volume indexed , ml/ m^2	49.6±13.5	51.3±11.2
Global strain, %		
GLS	19.6±2. 5	20.1.8±3.3
GCS	23.4±3.3	23.9±2.7
GRS	22.1±3.7	21.9±3.0
Tissue Doppler velocity, cm/s		
S^m	10.2±2.1	9.7±2.3
$E^m/A^m < 1$	17/4	17/3
E/ e^m	10.6±4.5	11.4±4.7
Ambulatory BP monitoring,		
Nondipper profile, (y/n)	21/0	8/12
Nocrurnal hypertension, (y/n)	18/3	3/17
Orthostatic hypothension, (y/n)	11/10	4/16
Post-prandial hypotension, (y/n)	15/6	3/17
BP values, mmHg		
24/h Systolic BP	121.4±10.3*	134.7±19.6
Diurnal Systolic BP	120.8±12.9*	138.1±22.8
Nocturnal Systolic BP	121.7±11.5	125.1±20.4
24/h Diastolic BP	73.6±7.5	82.7±13.9
Diurnal diastolic BP	74.2±10.1*	88.7±15.3
Nocturnal diastolic BP	73.3±5.7	78.4±11.8
BP variability, mmHg		
24/h Systolic BPV	8.9±2.3*	6.4±3.6
Diurnal Systolic BPV	8.5±1.9	7.0±2.2
Nocturnal Systolic BPV	10.2±3.7*	6.1±2.8
24/h Diastolic BPV	3.7±1.6	3.3±0.9
Diurnal diastolic BPV	3.8±1.2	3.6±1.0
Nocturnal diastolic BPV	3.3±1.8	3.0±1.8

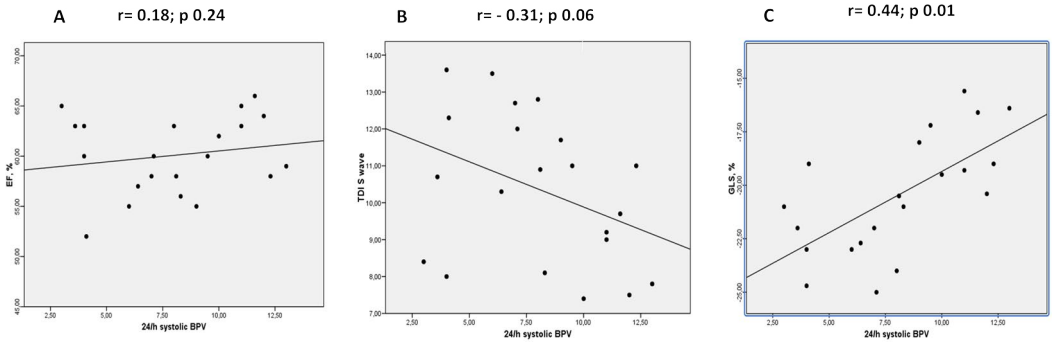

Figure 1. Correlation between 24/systolic BP variability and ejection fraction (A), S wave (B) and GLS (C) in patients with Parkinson's disease.

LV deformation. Early changes induced on myocardial fibers by high BP variability could decrease GLS, but it may not be detectable by LV ejection fraction. Therefore, we might hypothesize that the assessment of GLS in PD patients with dysautonomia otherwise considered to be with normal LV function, could enable physicians to discover very early signs of subclinical LV impairment. GLS has already been reported to enable an early detection of LV dysfunction in different populations with normal LV ejection fraction [5,17].

In this study PD patients showed several echocardiography similarities with hypertensive subjects, including indices of systolic and diastolic function, LV mass index and left atrial size. Data on cardiac structural abnormalities in PD are lacking and we did not find previous direct confrontations with hypertension. Recently, Piqueras-Flores et al.[18] found that PD patients had higher left ventricular mass index and larger left atrium compared to healthy controls. Since in our study patients with PD and dysautonomia were normotensive, we postulated that the increase of LV mass in this group was BP variability-mediated. Our hypothesis is supported by the current literature: the presence of high short-term BP variability has been associated with the increase of LV mass in subjects with hypertension independently from BP values[19]. Moreover dysautonomia has itself been associated with the LV hypertrophy and diastolic dysfunction in normotensive Type 1 diabetic patients[20].

Limitations: This study is limited by the small sample size and this do not allow to us to draw a formal conclusion. Our results are limited to PD patients with an advanced stage of the disease and dysautonomia; therefore, they cannot be extended to the whole population of PD patients. Finally, being a cross-sectional study, the progression of LV dysfunction was unknown. Longitudinal clinical follow-up will be required in future studies to determine the prognostic value of GLS abnormalities in PD.

Conclusions: we observed an inverse significant correlation between GLS and 24/h systolic BP variability in PD. Moreover, we observed a similar echocardiography pattern in patients with PD and in those with hypertension. Further studies are needed in order to clarify the impact of high BP variability in PD and the clinical utility of two-dimensional speckle tracking echocardiography in the early diagnosis of LV dysfunction in PD.

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CONFLICT OF INTEREST

Authors have no conflict of interest

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REFERENCES

1. Rothwell PM, Howard SC, Dolan E, O'Brien E, Dobson JE, Dahlöf B, et al. Prognostic significance of visit-to-visit variability, maximum systolic blood pressure, and episodic hypertension. Lancet. 2010;375:895-905.
2. Mancia G, Bombelli M, Facchetti R. Long term prognostic value of blood pressure variability in the general population: results of the Pressioni Arteriose Monitorate e Loro Associazioni Study. Hypertension 2007;49:1265–1270.
3. Sega R, Corrao G, Bombelli M, Beltrame L, Facchetti R, Grassi G, et al. Blood pressure variability and organ damage in a general population: results from the PAMELA study (Pressioni Arteriose Monitorate E Loro Associazioni). Hypertension. 2002;39:710-4.
4. Schutte AE, Schutte R, Huisman HW, van Rooyen JM, Fourie CM, Malan NT, et al. Blood pressure variability is significantly associated with ECG left ventricular mass in normotensive Africans: the SABPA Study. Hypertens Res. 2011;34:1127-34.
5. Tatasciore A, Zimarino M, Tommasi R, Renda G, Schillaci G, Parati G, et al. Increased short-term blood pressure variability is associated with early left ventricular systolic dysfunction in newly diagnosed untreated hypertensive patients. J Hypertens. 2013;31:1653-61.
6. Verrotti A, Prezioso G, Scattoni R, Chiarelli F. Autonomic neuropathy in diabetes mellitus. Front Endocrinol (Lausanne). 2014;5:205.
7. Kanegusuku H, Silva-Batista C, Peçanha T, Silva-Junior N, Queiroz A, et al. Patients with Parkinson disease present high ambulatory blood pressure variability. Clin Physiol Funct Imaging. 2017;37530-535.
8. Scorza FA, Fiorini AC, Scorza CA, Finsterer J. Cardiac abnormalities in Parkinson's disease and Parkinsonism. J Clin Neurosci. 2018;53:1-5.
9. Spallone V. Blood Pressure Variability and Autonomic Dysfunction. Current diabetes report. 2018;18:137.
10. Zhang KW, French B, May Khan A, Plappert T, Fang JC, Sweitzer NK, et al. Strain improves risk prediction beyond ejection fraction in chronic systolic heart failure. J Am Heart Assoc. 2014;3:e000550.
11. Hou-juan Zuo H, Yang X, Liu Q, Zhang Y, Zeng H, Yan J, et al. Global Longitudinal Strain at Rest for Detection of Coronary Artery Disease in Patients without Diabetes Mellitus. Current Medical Science. 2018;38:413-21.
12. Mena L, Pintos S, Queipo NV, Aizpúrua JA, Maestre G, Sulbarán T. A reliable index for the prognostic significance of blood pressure variability. J Hypertension. 2005;23:505-11.
13. Manios E, Tsagalis G, Tsivgoulis G, Barlas G, Koroboki E, Michas F, et al. Time rate of blood pressure variation is associated with impaired renal function in hypertensive patients. J Hypertens. 2009;27(11):2244-8.
14. Tsai WC, Lee WH, Liu YW. P1270Effects of blood pressure variability on layer-specific longitudinal strain in hypertension. Eur Heart J Cardiovasc Imaging. 2016;1;17(suppl_2):ii270-ii276.
15. Zesiewicz TA, Strom JA, Borenstein AR, Hauser RA, Cimino CR, Fontanet HL, et al. Heart failure in Parkinson's disease: analysiss of the United States medicare current beneficery survey . Parkinsonism relat dis. 2004;190(7):417-420.
16. Günaydın ZY, Özer FF, Karagöz A, Bektaş O, Karataş MB, Vural A, et al. Evaluation of cardiovascular risk in patients with Parkinson disease under levodopa treatment. J Geriatr Cardiol. 2016;13(1):75-80.
17. Conte L, Fabiani I, Barletta V, Bianchi C, Maria CA, Cucco C, et al. Early detection of left ventricular dysfunction in diabetes mellitus patients with normal ejection fraction, stratified by BMI: A preliminary speckle tracking echocardiography study. J Cardiov Ech. 2013;23;73-80.
18. Piqueras-Flores J, López-García A, Moreno-Reig Á, González-Martínez A, Hernández-González A, Vaamonde-Gamo J, et al. Structural and functional alterations of the heart in Parkinson's disease. Neurol Res. 2018;40:53-61.
19. Mustafa ER, Istratoaie O, Musetescu R. Blood Pressure Variability and Left Ventricular Mass in Hypertensive Patients. Curr Health Sci J. 2016;42:47-55.
20. Taskiran M, Rasmussen V, Rasmussen B, Fritz-Hansen T, Larsson HB, Jensen GB, et al. Left ventricular dysfunction in normotensive Type 1 diabetic patients: the impact of autonomic neuropathy. Diabet Med. 2004;21:524-530.

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