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Cardiac Autonomic Dysfunction in Day and in Night Time Possible Predictor of Functional Outcome in Post-Acute Ischaemic Stroke

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Introduction

Cardiac Autonomic dysfunction frequently occurs after an acute cerebrovascular accident and it is often asymptomatic (1). Predominance of sympathetic activity is common in patients with acute ischemic stroke, while autonomic unbalance has been associated with worse clinical and functional outcome. Aim of the study is to evaluate autonomic unbalance in post-stroke patients as assessed by selected Heart Rate Variability (HRV) measures. Besides, the role of such HRV parameters as possible predictors of functional outcome in the post-acute setting of stroke was also assessed.

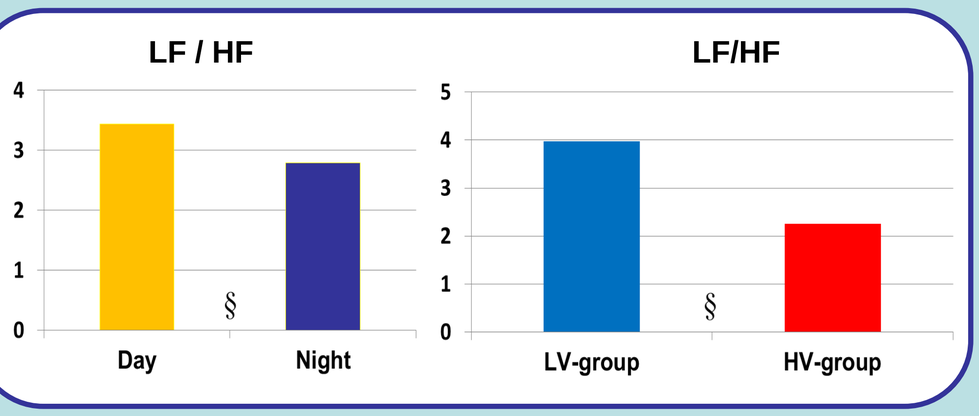
Methods

Cerebral Stroke Patients (rMSSD-day measure HM)	All Group n. 45	HV- group n.23(51%)	LV- group n.22 (49%)
	Demographic Characteristics		
Age, years, mean SD	63.6 11.6	62.4 11.9	64.8 11.4
Males, n (%)	24 (53)	12 (52)	12 (55)
On Admission	**Clinical and Functional Evaluation**		
Right-side of lesion, n (%)	27 (60)	17 (74)	10 (45)*
Barthel Index, median – moda	40 - 35	40 - 35	38 - 35 *
	Autonomic Measures		
24 hours SDNN, mean SD	116 22	114 23	118 20
24 hours rMSSD, mean SD	34,4 20	46,3 21	22,1 07
24 hours SDNN≤100, n (%)	14 (31)	10 (43)	04 (18)
24 hours SDNN / rMSSD	4,3 2	2,9 2	5,8 2
3 hours SDNN-day, mean SD	81,5 25	92,1 25	70,5 19 *
3 hours rMSSD-day, mean SD	31,8 23	47,1 24	15,6 04 *
3 hours SDNN-night, mean SD	71,6 20	68,9 18	74,4 23
3 hours rMSSD-night, mean SD	32,8 21	40,4 24	24,4 15

One-way ANOVA was employed to assess LV-group and HV-group differences on admission.

* p<0.001 - p<0.05

Results



STUDY DESIGN

Forty-six Consecutive patients reporting to the rehabilitation institute for acute stroke (in a 2.5-year period) were screened and included in the study only if they fulfilled the inclusion criteria (n.962). The presence of major concurrent medical conditions potentially interfering with HRV were carefully excluded in all patients. Patients in a sub-acute stage (within 15 days from the index event) after their first-ever acute stroke were recruited for the present study.

24-hours holter monitoring (HM) was performed to characterize HRV. Moreover, HRV values in time and frequency domine were achieved from selected and stabilized period (3 hours) from HM recording, during the day (06:00-13:00, not in supine position) and night (23:00-06:00).

Functionality on admission was assessed by the **Barthel Index (BI) Scale**

Global cognitive performance attention shifting and language disorders were evaluated

Neuroimaging studies (MRI, CT) were performed on admission to confirm brain infarct size and localization (modified ellipsoid method).

The median's value of rMSSD has been used to divide the population in two sub-group: subjects with lower values (LV-group) and higher ones (HV-group). The rMSSD measure is the root mean square differences of successive R-R interval in the ECG, it is considered parasympathetic measure. The main method to investigate sympathetic/vagal balance is LF/HF measure of HRV, while SDNN/rMSSD measure is a good surrogate of such evaluation (2, 3).

LV-group **HV-group**

The final outcome of a 60 days rehabilitation program was defined as favourable or unfavourable on the basis of the final Barthel score at discharge (cut-off=75). A two-way ANOVA (2x2) was employed to assess night and day differences. Moreover, multiple regressions were used to predict the functional outcome after rehabilitation treatment.

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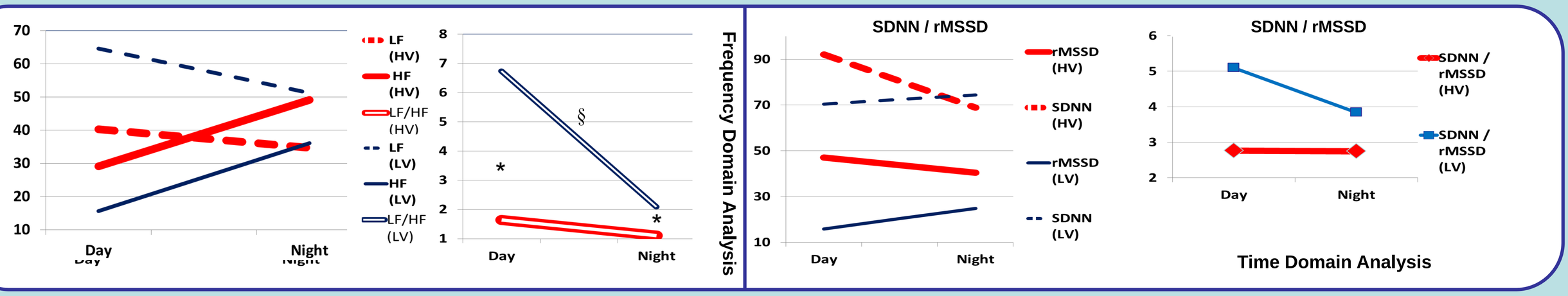
Holter monitoring HRV assess cardio-autonomic control with calculations based on statistical operations on R-R intervals. **Time-domain measures** of HRV, including standard deviation of all normal-to-normal RR intervals (SDNN) and root-mean-square of differences of adjacent normal-to-normal RR intervals (rMSSD); **frequency-domain** measures are respectively assessed by the power of low and high frequency (HF, HF) components of the spectrum of the beat by beat interval.

Cognitive Global cognitive performance, attention shifting and language disorders were evaluated respectively by Mini Mental State Examination (MME), Trail Making Test (TMT), Batteria per l'analisi dei deficit afasici (B.A.D.A.).



Discussion

We used here several parasympathetic measure to characterize post stroke patients. When using the rMSSD-day, patients with similar clinical and demographic characteristic could be divided in two subgroups: those with LV and those with HV. As expected, over night, all patients revealed a prevalence of parasympathetic tone. However, this increase of parasympathetic tone was significantly lower in HV than LV in patients. This suggests that HV patients suffer from a form of cardiac-autonomic dysregulation, which might have a relevant clinical impact on the patients' status. This interpretation is supported by the poorer clinical outcome observed in HV patients at the end of a standardized rehabilitation program. There are several pathophysiological explanations for this potential relationship between autonomic dysregulation and poorer clinical outcome (4). First, autonomic dysregulation may affect the perfusion of various tissues and organs, including brain (with a possible impact on cognitive performance) and muscles. Additionally, several brain structures are known to control both autonomic and cognitive functions, as previously reported (5). Future studies including assessment of anatomical localisation of brain lesions are needed to clarify this aspect.

Barthel Index At Discharge			
	after 60 days of Treatment		
	All group	HV-group	HV-group
media–moda	65 - 65	55 - 55	75 - 65
> 75, n (%)	17(38%)	06 (26%)	11 (50%) § §

Barthel Index at discharge	Beta	P value
LF/HF - day	0.32	< 0.05
Barthel Index on admission	0.63	< 0.01

Conclusion

This study suggests the importance of defining the presence or absence of HRV alterations in stroke patients candidates for neuro-rehabilitation. Indeed, HRV measures allow to obtain information on potential rehabilitation outcome, with relevant implications for patient' clinical management.

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