Reduced Variability in Pulse Wave Velocity in Depressed Patients with Suicidal Ideation

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Abstract

Recently arterial stiffness was found to be associated with depression. The aim of this study was to investigate the association between arterial pulse wave velocity (PWV) and Major Depressive Disorder (MDD) with or without suicidal ideation. Twenty unmedicated MDD patients with a history of suicidal ideations (Age: 32.37±9.53 years) and 20 unmedicated MDD patients without any history of suicidal ideations (Age: 36.84± 8.66) were recruited for this study at a psychiatric clinic in the UAE. Depression severity was assessed with the Hamilton Depression Rating Scale and the Beck Depression Inventory. Pulse wave velocity (PWV) was estimated from the ratio of half of the height and Pulse Transit Time which is defined as the time delay between the R-wave of the ECG and the arrival of the pulse wave in the index finger respectively. MDD Patients with suicidal ideation were found to have reduced low frequency (LF) and high frequency (HF) power of PWV compared to MDD patients without suicidal ideations. Suicidal score was negatively correlated ($r=-0.54; p<0.05$) with LF power and positively ($r=0.54; p<0.01$) with HF power. No difference in the average PWV was found between the two groups of participants. Reduced variability in pulse wave velocity in MDD patients with suicidal ideation may lead to arterial stiffness and higher risk of future cardiovascular disease.

1. Introduction

Studies of Global Burden of Disease (GBD) from 1990 and 2010 identified depression to be the leading cause of burden, as depressive disorders are associated with increased functional disability and mortality [1]. The socioeconomic costs of depression in the European Union alone were estimated at €92 billion in 2010 [2]. Several studies have suggested that the endothelial dysfunction and ensuing arterial stiffness is the common mechanism linking depressive symptoms and coronary artery disease (CAD) [3,4]. CVD and depression appear to have bidirectional relationship [5]. Taking into account and controlling for pre-existing cardiovascular risk factors, a recent systematic meta-analysis estimated a combined overall relative risk of 1.54 for the contribution of depression to the onset of CAD [6]. Patients diagnosed with acute myocardial infarction run an increased mortality risk even when they suffered from low levels of depression, compared to their nondepressed cohorts [7]. Increased arterial stiffness adversely affects the brain, with high pulsatile flow damaging cerebral microvessels, leading progressively to edema, hemorrhage and inflammation [8-9]. As a result, increased arterial stiffness is associated with both cerebral lacunar infarction and cortical functions [10,11].Fifteen percent of clinically depressed patients die by suicide [12].Patients with suicidal tendencies exhibited significant and more pronounced cardiac vagal withdrawal compared to healthy counterparts, as well as MDD patients without suicidal ideation [13]. Another study suggested that suicidal ideation is related to altered serotonergic functions [14]. We hypothesize that suicidal ideation in depression may be associated with arterial stiffness as measured by pulse wave velocity (PWV). Therefore, the aim of this study was to investigate the association of PWV with severity of suicidal ideation in MDD patients.

2. Methods

2.1. Data

Forty patients with a primary diagnosis of MDD were included in this study. Participants were recruited from the outpatient clinic at American Center for Psychiatry and Neurology in Abu Dhabi. The study was approved by

Al Ain District Ethics Committee, and all participants provided written informed consent. Diagnoses including history of suicidal ideation were made by a consultant Psychiatrist (Veena Luthra) using the Mini-International Neuropsychiatric Interview (MINI) [15]) and the severity of clinical depression was assessed using the structured interview guide for the Hamilton Depression Rating Scale (HAM-D) [16]. The scale of suicidal ideation consists of 19 items which was used to evaluate a patient's suicidal intention [17]. The minimum score was zero and maximum score was38. Higher scores indicate greater suicidal ideation. All participants completed the Depression Anxiety and Stress Scales (GAD 7 and PHQ 9), a reliable and valid self-report measure of depression, anxiety, and stress severity (Table 1).

Table 1: Patients' demographics and psychiatric scores

	MDD_Suicidal	MDD_NonSuicidal
N	20	20
Gender male,%	5(25%)	4(20%)
Age (yrs)	32.37±9.53	36.84±8.66
Waist Cirmc (cm)	88.28±14.76	86.55±16.43*
Height (cm)	162.16±9.26	164.74±8.43
Weight (kg)	71.84±17.47	71.10±16.25
BMI	27.17±5.76	30.64±23.33
SBP (mmHg)	112.63±12.84	112.10±14.37
DBP (mmHg)	72.1±8.55	72.63±7.33
BDI	38.55±11.23	32.60±11.40
GAD7	17±6.33	16.30±8.83
PHQ9	20.80±5.15	19.70±11.13
Suicidal Score	16.95±8.00	1.75±3.07*

All patients underwent a supine resting recording of ECG, respiration (PowerlabADInstruments) and arterial pulse blood pressure by Finometer MIDI (Finapres, Amsterdam). Phsyiological signals were recorded over 10 minutes using a lead II configuration (Powerlab ADInstruments, Australia) and captured on Labchart 7.1 with a sampling rate set at 1000 Hz and a notch filter at 50 Hz. Table 1 summarizes the clinical variables of the patient group.

A typical example of arterial pulse signal with different features that can be extracted from the signal is shown in Figure 1.

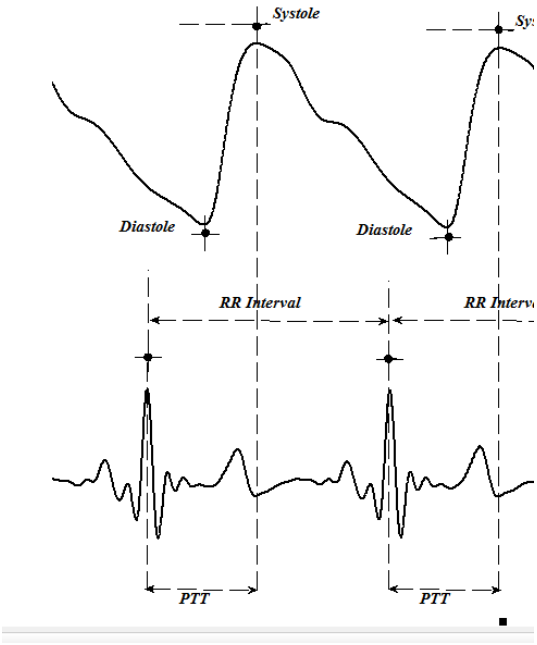

Fig. 1: ECG and arterial pulse signals

RR intervals (RR): peak-to-peak interval is defined as the time difference between two consecutive R peaks of ECG signal. The peak and trough of each cycle of the arterial pulse signal are the Systole and Diastole. The pulse transit time (PTT) was calculated as the time difference between R peaks of the ECG signals and consecutive systole points (Figure 1). The Pulse Wave Velocity (PWV) was calculated using the following formula [22]: PWV (cm/ms)= [height (cm)x BDC]/PTT (ms). BDC = body correlation factor, and height = body length. BDC is 0.5 for adults when the index finger is used for detection of the peripheral pulse wave.

Several time domain parameters were determined from the PWV features including mean, standard deviation (SDNN), Interquartile range (IQR) and the square root of the mean squared difference of the successive data points (RMSSD). Spectral analysis was performed on linearly resampled (1 Hz) time series using Welch's method [18]. The 256-point fast Fourier transform was repeatedly computed with 50% overlap between adjacent segments. Then the spectral power of each segment was computed and averaged. Hanning window was applied to avoid spectral leakage. Subsequently, spectral powers in the low frequency (LF) band (0.04–0.15 Hz) and high frequency (HF) band (0.15–0.40 Hz) were obtained by integration [12]. The normalized LF and HF powers were calculated by LF/(Total Power–VLF) and HF/(Total Power–VLF) respectively as per Task Force recommendation [task force]. The power in the very lower frequency (VLF) band was set at ≤0.04 Hz.

2.2. Statistics

In this study the nonparametric Mann-Whitney U-test was performed to determine differences of PWV features between the MDD_Suicidal and MDD_Non_Suicidal group with $p<0.05$ set for significance.

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3. Results

Table 2. Mean±SD of PWV features from MDD_Suicidal vs MDD_Non_Suicidalgroups. *p<0.05

		MDD_Suicidal	*MDD_Non_Suicidal*	*p-value*
PWV	*Avg.*	0.24 ± 0.05	0.25 ± 0.11	0.78
	SD	0.06 ± 0.21	0.14 ± 0.37	0.44
	RMSSD	0.08 ± 0.27	0.20 ± 0.55	0.38
	IQR	0.02 ± 0.02	0.03 ± 0.04	0.28
	LF	0.01 ± 0.05	0.02 ± 0.07	0.80
	HF	0.02 ± 0.09	0.08 ± 0.22	0.36
	LF(nu)	49.52 ± 15.89	* 39.24 ± 15.15	0.04
	HF(nu)	50.48 ± 15.89	* 60.76 ± 15.15	0.04

Table 3. Pearson Correlation Coefficients of PWV features with suicidal scores.

		r	p value
PWV	Avg.	-0.18	0.49
	SD	-0.01	0.96
	RMSSD	-0.01	0.97
	IQR	0.02	0.94
	VLF	-0.01	0.96
	LF	-0.01	0.96
	HF	-0.01	0.96
	LF(nu)	-0.54	0.03
	HF(nu)	0.54	0.03

LF(nu) and HF (nu) were found to be significantly ($p<0.05$) lower in MDD patients with suicidal ideation.

4. Discussion

Previous research has shown that vascular disease and its related brain pathologies (e.g., stroke, silent brain infarction, and subclinical brain injury) are associated with cognitive decline, dementia and depression [19]. Arterial stiffness is one of the earliest manifestations of adverse structural and functional changes within the arterial wall, due to inflammation, oxidative stress, atherosclerosis, aging or hypertension. Whether Pulse wave velocity (PWV) is considered as one of surrogate measures of arterial stiffness and the vascular involvement.

Significant correlations between suicidal scores and cardiovascular events such as low and high frequency variability in PWV were identified in this study, however,

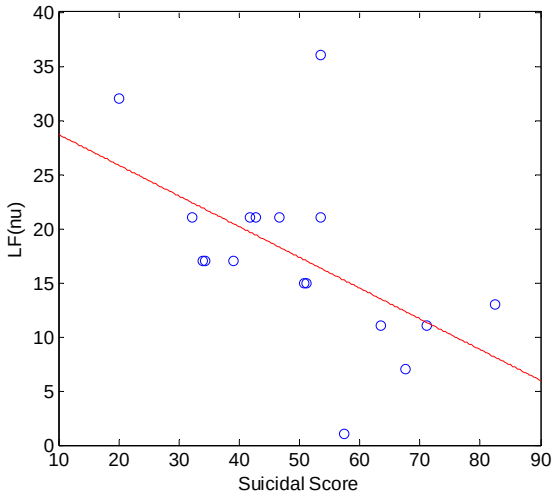

Fig. 2. Association of LF(nu) of PWV with suicidal score. Table 3 shows significant ($p<0.05$) correlations of suicidal score with LF(nu) ($r= - 0.54$).

PWV is related to a decreased arterial stiffness in these patients, is not known yet. Acute and chronic mental stresses were reported to unfavorably affecting arterial stiffness [20]. Impaired arterial stiffness also relates to depression and anxiety in that study [21]. Increased arterial stiffness was reported to be associated with increased catecholamine level during noradrenalin infusion, in a small group of patients [22]. Oulis and coworkers documented reversal of arterial stiffness in a small group severely depressed women, after 6-week antidepressant therapy [23].

It is suggested that impaired 5hydroxy-tryptamine (5-HT) function my heighten the susceptibility to CVD, as studies reveal that depressed patients who have problems with controlling impulsivity might be more at risk of developing CVD and have abnormal levels of 5-HT [19]. Tryptophan is a precursor of 5-HT and research outcomes on remitted depressed patients with suicidal tendencies revealed that highdose acute tryptophan depletion (ATD) induced increased depressive symptoms whereas lowdose ATD did not. Low HRV at baseline also correlated with the ATD induced depressive response [19]. Increased impulsivity and anxiety appear to be negatively correlated with ATD in depressed individuals with suicidal ideation [19].

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