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Increased pulse-wave velocity in patients with anxiety: implications for autonomic dysfunction

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Abstract

Decreased vagal function is associated with vascular dysfunction. In this study, we compared vascular indices and correlated heart rate and QT variability measures with vascular indices in patients with anxiety disorders and normal controls. We compared age- and sex-matched controls ($n=23$) and patients with anxiety ($n=25$) using the Vascular Profiler (VP-1000; Colin Medical Instruments, Japan), approved by the US Food and Drug Administration. Using this machine, we obtained ankle and brachial blood pressure (BP) in both arms (brachial), both legs (ankle), and carotid artery, and lead I electrocardiogram (ECG) and phonocardiogram. Using these signals, pulse-wave velocity (PWV), and arterial stiffness index % and preejection period can be calculated. We also obtained ECG sampled at 1000 Hz in lead II configuration in supine posture to obtain beat-to-beat interbeat interval (R-R) and QT interval variability for 256 s. Patients with anxiety had significantly higher carotid mean arterial pressure (MAP) %, brachial-ankle PWV (BAPWV), arterial stiffness index %, MAP, and diastolic BP of the extremities compared to controls. We found significant negative correlations (r values from .4 to .65; $P<.05$ to .007) between R-R interval high-frequency (0.15–0.5 Hz) power (which is an indicator of cardiac vagal function), and increased BAPWV and systolic BP of the extremities only in patients. We were unable to find such correlations in controls. We also found significant positive correlations between QT variability index (a probable indicator of cardiac sympathetic function) and MAP of the extremities and BAPWV only in the patient group. These findings suggest an important association between decreased vagal and increased sympathetic function, and decreased arterial compliance and possible atherosclerotic changes and increased BP in patients with anxiety.

Keywords: Arterial stiffness index; Pulse-wave velocity; Autonomic function; Atherosclerosis; Blood pressure; Cardiovascular mortality; Anxiety

Introduction

Thickening of arterial walls occurs with aging, and risk factors such as smoking, obesity, high fatty-food intake, and several genetic factors influence this process. Atherosclerosis increases blood pressure (BP) and makes the heart a less effective "pump," eventually leading to ventricular enlargement. This will lead to an increased load on the heart leading to an abnormality of cardiac electrical conduction, which may result in cardiac repolarization lability leading to serious cardiac arrhythmias. Thus, identifying these changes in the vessel walls is of paramount importance.

Pulse-wave velocity (PWV) indicates arterial stiffness and possible atherosclerosis [1,2]. The noninvasive measurement of PWV can also be used as a prognostic indicator of vascular damage [3–6]. Hence, this measure may have implications as a screening device for the general population as well [7,8]. This measure is also valuable in the evaluation of vascular damage in conditions such as diabetes [9,10].

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Similarly, carotid artery patency is an important measure, especially in the earlier stages of stenosis. Vascular Profiler (Colin Medical Instruments, Japan) uses noninvasive techniques to obtain these vascular indices and, hence, is a valuable tool to study any population that is at a higher risk for cardiovascular/cerebrovascular mortality.

Several studies suggest that people with anxiety disorders as well as depression are at a higher risk for cardiovascular mortality and sudden death [11–15]. All our previous studies mainly focused on cardiac autonomic function in anxiety and depressive disorders compared to normal controls, and our findings suggest an altered sympathovagal balance in patients with panic disorder and depression, which partly contributes to an increased risk for cardiac mortality [16–23]. Our findings generally show a decrease in heart rate variability (HRV) and an increase in QT variability (QTV) in patients with anxiety and depression [24,25].

Decreased HRV is an important predictor of sudden cardiac death in patients with cardiac disease as well as normal subjects [26–28]. Spectral power in the high-frequency (HF; 0.15–0.5 Hz) band reflects respiratory sinus arrhythmia and, thus, cardiac vagal activity. Low-frequency (LF; 0.04–0.15 Hz) power is related to baroreceptor control and is dually mediated by vagal and sympathetic systems. [29,30]. R-R LF/HF ratios may reflect cardiac sympathovagal interaction, although there is some evidence to the contrary [31,32].

Cardiac repolarization lability plays an important role in causing sudden death. An increase in sympathetic activity and a decrease in cardiac vagal activity make the myocardium vulnerable to fatal arrhythmias [33,34]. A recent measure, beat-to-beat QT interval variability appears to be an important and independent measure of cardiac mortality and severity of illness in patients with heart disease and also in coronary patients with effort angina pectoris [35–37]. We have found that beat-to-beat QT interval variability significantly increases during challenges associated with an increase in cardiac sympathetic activity including a change from supine to standing posture and administration of intravenous isoproterenol [24,38–40], suggesting an influence of sympathetic system on QT interval variability. There is also other evidence linking QTV to cardiac sympathetic function [41,42]. Several previous reports have shown abnormal sympathetic function in patients with anxiety disorders [43–47].

Our previous studies mainly dealt with cardiac autonomic function in anxiety and depressive disorders compared to normal controls, suggesting an altered sympathovagal balance in patients with panic disorder and depression, which probably contributes to an increased risk for cardiac mortality [16–22].

In this study, we compared several vascular indices including brachial-ankle PWV (BAPWV), arterial stiffness index, and BP between normal controls and age-matched patients with anxiety disorders. In addition, we also compared HRV and QT variability index (QTvi) and examined the relationship between these variables and the vascular indices.

Methods

Subjects

There were 23 normal controls (19 males and 4 females; age, 45±14 years) and 25 patients (20 males and 5 females; age, 45±13 years) with anxiety disorders. Both groups were matched for age and gender. All patients were of East Asian origin. The patients were consecutive outpatients whose complaint was mainly anxiety. Eight patients had generalized anxiety disorder, seven had panic disorder, and 10 had symptoms of both disorders. Eight of the 17 patients with a diagnosis of panic disorder had symptoms of agoraphobia. As our criterion to include subjects in the study was "anxiety," we included all these patients. All patients were diagnosed according to the *DSM III-R* criteria [48]. These patients did not have current depression or a history of previous depressive disorder. Two patients and three controls were smokers. There was no history of drug addiction, alcoholism, or any significant medical illness, especially diabetes or hypertension, and these subjects were not on any medication except for occasional nonnarcotic analgesics for at least 3 weeks prior to their participation in the study. These studies were approved by the ethical committee at the M.S. Ramaiah Hospital, Bangalore, India. The studies were explained to the patients, and informed consent was obtained prior to their participation in the studies. The noninvasive nature of the studies was particularly stressed up on before the subjects' participation to alleviate any anxiety, especially in the patient group. Table 1 shows the demographic data of the two groups.

The control subjects were recruited mainly from the same geographical area. Table 1 shows the scores on the State Anxiety Inventory (SAI) [49] for the patient and control groups. The SAI scores were similar between the three groups of patients (panic disorder, generalized anxiety disorder and patients with both conditions, and also those with and without agoraphobia). No subject in the study had an ankle-brachial index (ABI: ankle BP/brachial BP) of less than 0.9.

Data acquisition

Vascular indices

Using the Vascular Profiler-1000 (Colin Medical Instruments), one could obtain BP in carotid and all four extremities, ABI (ankle brachial index of BP), and ankle-brachial PWV. The Colin VP-1000 (Model BP203RPE II, Form PWV/ABI) was approved by the US Food and Drug Administration. The device works on a Waveform Analysis and Vascular Evaluation technology that measures arterial compliance in central (large) arteries as well as the