Correlation among cardiac autonomic function tests in normal subjects.

ELIZABETH CLARENCE SIMONMANUEL CLARENCE
Department of Physiology,
CHRISTIAN MEDICAL COLLEGE

Abstract:
Cardiac autonomic function tests such as the Orthostatic Challenge Test (OCT) and Valsalva Maneouvre (VM) test are popular clinical neurophysiological investigations used to diagnose autonomic disorders. Analysis of heart rate responses in OCT (3015 ratio) and VM (Valsalva ratio) evaluates the parasympathetic responses of the cardiac autonomic nervous system. The indices of short-term Heart Variability Analysis (HRV) that reflects the cardiac parasympathetic activity are pNN50, RMSSD and HF power. The current study investigated whether there was any correlation between (a) OCT 3015 ratio and Valsalva ratio (b) OCT 3015 ratio and pNN50, RMSSD and HF power (c) Valsalva ratio and pNN50, RMSSD and HF power. Towards this, the data acquired from 22 healthy male volunteers were analysed. Five min ECG and respiration were recorded for short-term HRV analysis. Following this, the OCT was performed where the subjects were instructed to stand abruptly from the supine posture. For VM the subjects were instructed to blow through a mouthpiece attached to a mercury manometer to sustain a pressure of 40mm of Hg for 10 seconds. The correlation of short-term HRV parameters and OCT 3015 ratio and Valsalva ratio was done using Spearmans correlation test. The results of our study showed that there was a weak positive correlation between the OCT and VM test results (r=0.431, p=0.045). The Valsalva ratio showed a weak but highly significant correlation with the HF power (r=0.559, p=0.007) while the OCT results showed no correlation with any of the HRV indices considered. Thus, in conclusion, though all the tests studied were evaluating the cardiac parasympathetic activity, strikingly, the OCT results showed no correlation with any of the short-term HRV indices while the VM test results showed highly significant correlation with HF power. Thus, even though VM is more difficult to perform, the Valsalva ratio appears to be better correlated with short-term HRV index of HF power.

Keyword: Orthostatic challenge test, Valsalva manoeuvre, correlation, HF power, cardiovagal activity
BACKGROUND:
Cardiac autonomic function tests such as the Orthostatic Challenge Test (OCT) and Valsalva Maneouvre (VM) test are popular clinical neurophysiological investigations used to diagnose autonomic disorders such as Primary autonomic failure, autonomic failure associated with Parkinsonism, multiple sclerosis and Diabetic neuropathy. Analysis of heart rate (HR) responses in OCT and VM evaluates the parasympathetic responses of the autonomic nervous system. During OCT the subject is made to stand abruptly from the supine posture. The VM is performed by forceful exhalation against a closed airway. In OCT, immediately on standing, the heart rate increases due to vagal withdrawal produced as a result of the exercise reflex initiated by the process of standing up. In addition, the fall in blood pressure (BP) due to gravitational effects and other factors results in a further increase in heart rate which peaks around 15 seconds. Meanwhile, the baroreceptor mediated increase in sympathetic tone produces a transient overshoot in BP causing a baroreceptor mediated decrease in HR, due to vagal stimulation. These sequences of events results in a slowing of the HR around the 30th second after standing up. The results of the OCT is expressed as the 30:15 ratio which is the ratio of the longest RR interval around the 30th beat after standing up to the shortest RR interval around the 15th beat after standing up. As per published literature the normal value for the OCT 30:15 ratio is 1.04. The normal response of the Valsalva manoeuvre has four phases. During the first few seconds in phase I there is an increase in blood pressure caused by increased intrathoracic pressure, leading to a baroreceptor mediated reflex decrease in heart rate. The phase II has two sub-phases; during the early phase the venous return decreases due to an increase in intrathoracic pressure, leading to a reduction in cardiac output and blood pressure. There is an increase in heart rate due to baroreceptor unloading and vagal withdrawal in the early phase and due to sympathetic stimulation in the late phase II. During Phase III the release of strain causes fall in intrathoracic pressure and rise in pulmonary venous capacitance and therefore pooling of blood in the pulmonary circulation, reduced venous return to the left ventricle and a decrease in cardiac output causing a decrease in BP. Phase IV occurs a few seconds after the cessation of strain. Prolonged sympathetic stimulation causes an overshoot of BP leading to a baroreceptor mediated bradycardia in phase IV. The result of the study of the heart rate response to the VM is expressed as the Valsalva ratio which is the ratio of the longest R-R interval after the manoeuvre to the shortest R-R interval during the manoeuvre. The normal value for the Valsalva ratio is 1.21. Both the OCT 30:15 ratio and the Valsalva ratio measure the same autonomic parameter, namely the cardiovagal activity. However, while the OCT is a simple procedure which can be done at the bedside without the need of any specialised equipment other than the set up for measuring ECG continuously, the VM test requires arrangements to measure the pressure against which the patient is expiring. Further, the test involves active participation by the patient and is dependent on patient effort. All these make the VM test more complicated to perform than the OCT. Further, precautions have to be taken while performing the test in elderly patients and in patients with retinopathies. Another mode for studying the cardiovagal activity is through heart rate.
variability analysis (HRV), which is the analysis of the beat to beat variations in milliseconds of adjacent RR intervals by using statistical methods and mathematical algorithms such as the Fast Fourier transformation. The output of the short-term HRV analysis of 5-min of ECG is given in terms of various indices of which the time domain indices pNN$_{50}$ (the proportion derived by dividing NN$_{50}$ by the total number of NN intervals, where NN$_{50}$ is the number of interval differences of successive NN intervals greater than 50 ms) $^3$ and RMSSD (the square root of the mean of the sum of the squared differences of successive NN intervals) and frequency domain index, the HF (High frequency) power. The HF power represents parasympathetic activity and is therefore generally considered to be a marker of cardiovagal activity $^3$. The present study aimed to investigate the relationship between the heart rate response results of OCT and VM tests, both of which assess parasympathetic activity and the short-term HRV analysis indices which reflect cardiovagal activity, namely pNN$_{50}$, RMSSD and HF power.

**Aims and Objectives:** The aim of the present study was to investigate whether there was any correlation between (a) OCT 30:15 ratio and Valsalva ratio (b) OCT 30:15 ratio and pNN$_{50}$, RMSSD and HF power c) Valsalva ratio and pNN$_{50}$, RMSSD and HF power.

**Methods: Subjects:** Twenty two healthy male volunteers (age 30.08 ± 4.94 yrs) without any co-morbidity as assessed by medical history and medical examinations were recruited as part of an ongoing study in the department. Tobacco chewers and sniffers, and subjects who consume alcohol were excluded. All the subjects who were recruited were normotensive and none of them were on any chronic medica-
till a reading of 40mm of Hg was attained and the subject was required to maintain the same for 10 seconds. A small air leakage was incorporated to ensure that the expiratory pressure came from the chest and that the subject did not blow with his cheeks. The ECG was recorded continuously during, and for a short interval after the end, of the manoeuvre. The test was done twice with a rest period of 2 minutes in between.

The analogue signals were acquired at a sampling rate of 1 KHz and stored as a digital data in a personal computer using a data acquisition system (BIOPAC Systems, Inc., CA 93117, USA).

**Data analysis:**
For the 30:15 ratio, the longest RR interval around the 30\textsuperscript{th} beat after standing up (noted from the event marker/noise in ECG due to the movement) to the shortest RR interval around the 15\textsuperscript{th} beat after standing up was calculated. For the Valsalva ratio the longest RR interval within 20 beats after stopping the manoeuvre to the shortest RR interval during the manoeuvre was computed.

The 5 min ECG recordings were examined for ectopic beats and noises and the R-R interval was analysed for short-term HRV using Nevrocard aHRV software version 1.1 (Medistar, Slovenia). The short-term HRV indices that were considered for analysis in the present study were as follows:

- **Time domain indices:**
  1. RMSSD (ms) – the square root of the mean of the sum of the squared differences of successive NN intervals.

  2. pNN\textsubscript{50}: the proportion derived by dividing NN\textsubscript{50} by the total number of NN intervals, where NN\textsubscript{50} is the number of interval differences of successive NN intervals greater than 50 ms. Frequency domain indices: The RR interval tachogram obtained from the five minute ECG recording was subjected to Fast Fourier Transformation (FFT) where the variability of the NN intervals is resolved into its frequency components to obtain the magnitude of variability in different frequency bands\textsuperscript{4,5}.

  The power spectral analysis so done gives the spread of the power in ms\textsuperscript{2} per Hz in the different frequencies. Of the spectral indices, the HF power was considered for analysis. HF power is the High Frequency Power in ms\textsuperscript{2}, obtained by integrating the area under the curve between 0.15 – 0.40 Hz.

**Statistical analysis:**
The correlation of short-term HRV parameters and OCT 30:15 ratio and Valsalva ratio was done using non-parametric tests. The data was checked for normality and was found to be not normally distributed. Thus, Spearman’s correlation was applied for analysis with the help of SPSS version 18.0. The value of:

- a. +1 to 0 indicated positive correlation
- b. 0 indicated no correlation
- c. -1 to 0 indicated negative correlation

**Results:**
The OCT 30:15 ratio and the Valsalva ratio for all the subjects showed a weak, but statistically significant correlation (r=0.431, p=0.045) between each other (Refer Table 1). The OCT 30:15 ratio did not show any significant correlation with any of the HRV parameters (Refer Table 1).
The Valsalva ratio showed a highly statistically significant correlation with the HF power ($r = 0.559$, $p = 0.007$), but no significant correlation with the other HRV parameters (Refer Table 2).

**Table 1:** Correlation between OCT 30:15 ratio and Valsalva ratio; and OCT 30:15 ratio and the Short-term HRV indices

<table>
<thead>
<tr>
<th>Parameter</th>
<th>OCT 30:15 ratio</th>
<th>Valsalva ratio</th>
<th>RMSSD (ms)</th>
<th>pNN50 HF (ms$^2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r value</td>
<td>p value</td>
<td>r value</td>
<td>p value</td>
</tr>
<tr>
<td>Valsalva ratio</td>
<td>0.431</td>
<td>0.045*</td>
<td>0.32</td>
<td>0.146</td>
</tr>
<tr>
<td>RMSSD (ms)</td>
<td>0.32</td>
<td>0.146</td>
<td>0.395</td>
<td>0.069</td>
</tr>
<tr>
<td>pNN50 HF (ms$^2$)</td>
<td>0.395</td>
<td>0.069</td>
<td>0.395</td>
<td>0.069</td>
</tr>
</tbody>
</table>

* $p < 0.05$

Discussion:
The current study explored the correlation between two commonly performed cardiac autonomic function tests that reflect the integrity of the cardiac parasympathetic activity, namely the OCT and the VM test. The correlation between HF power, a short-term HRV index of parasympathetic cardiac autonomic activity and the results of the OCT and VM test were also studied. All the data was collected in normal healthy male subjects. The OCT and VM test results were all within normal limits. The results of our study showed that there is a weak positive correlation between the OCT result values and the VM test results with regard to heart rate responses ($r=0.431$, $p=0.045$). As both these tests study the same arm of the autonomic nervous system, we had expected a stronger and more significant correlation between the test results. However, a strong correlation was not evident from our study results. This may be because of the variability in the results obtained from the VM test, as the test value depends upon the performance and effort put in by the subject, unlike the OCT result. The Valsalva ratio showed a weak but highly significant correlation with the frequency domain index reflecting parasympathetic activity, namely the HF power ($r=0.559$, $p =0.007$). This is as expected, as the Valsalva ratio also reflects the cardiovagal activity. However, the Valsalva ratio did not show any correlation with any of the time domain indices reflecting parasympathetic activity. This may be because the time domain indices are better markers of autonomic activity in Long-term HRV analysis. Strikingly, the OCT results showed no correlation with any of the short-term HRV parameters of cardiovagal activity while the VM test results showed highly significant correlation with the HRV parameter, HF power. Thus, even though Valsalva manoeuvre is more difficult to perform, the Valsalva ratio appears to be better correlated with short-termHRV index of HF power. Further, the VM test is reported to be a more sensitive test than the OCT. In conclusion, the results of our study showed a weak positive correlation between the test values of two popularly used cardiac autonomic function tests that study the cardiovagal activity. Further our study showed a positive correlation between VM test values and the HF power, an HRV index of cardiovagal activity.
References:


