Heart rate variability: Response to graded head up tilt in healthy men

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Abstract

Background: Heart rate variability is actually a misnomer for R to R variability in cardiac cycle. Variation in successive cycle length is called the heart rate variability (HRV). Head-up tilt is a model of studying cardiovascular haemodynamics, which reflects in heart rate variability (HRV).

Objectives: To study the effect of 10° and 70° head-up tilt on HRV.

Materials and methods: The study was done in the Department of Physiology using graded head up tilt (passive orthostatism). HRV measurement was done at 10° and 70° tilt and compared with supine using standardised methods on 30 consenting healthy males (age 25.37±3.89 years). The HRV variables across postures were compared by ANOVA and Bonferroni test.

Results: The heart rate increased at 70° compared to 10° and supine (70.48±8.17 Vs 70.22±8.67 and 88.51±12.84 bpm, p<0.001). The 70° tilt decreased vagal HRV indicators compared to 10° and supine: SDNN (31.13±8.12 Vs 38.07±11.29 and 38.13±10.89 ms, p<0.05), RMSSD (20.06 ±8.47 Vs 34.23±14.22 and 36.16±12.22 ms, p<0.001), NN50 count (13.03±20.58 Vs 45.07±44.44 and 55.27±44.10, p<0.01), pNN50 (3.28±6.08 Vs 14.06±15.65 and 16.65±14.23, p<0.01), HF power (197.20±143.76 Vs 218.17±155.85 and 216.87±150.98 Hz, p<0.05), HFnu unit (24.28±14.16 Vs 45.48±16.34 and 47.67±19.89, p<0.001). The 70° tilt increased LF power% (197.20±143.76 Vs 218.17±155.85 and 216.87±150.98, p<0.001). LFnu unit (75.72±14.76 Vs 54.52±16.34 and 52.32±19.89, p<0.001), LF: HF (4.96±4.08 Vs 1.53±1.138 and 1.69±1.67, p<0.001) compared to 10° and supine.

Conclusion: At 70° tilt, HRV measures, reflecting vagal contribution to cardiac-cycle length, decreased with reciprocal increase in sympathetic activity compared to 10° or supine leading to increase in sympathetic predominance. A 10° tilt, which is almost equivalent to lying down with pillow, did not change HRV from supine.

Key words: Cardiac cycle, cardiovascular haemodynamics, head-up-tilt, heart rate variability, sympathetic activity, parasympathetic activity

It is commonly perceived that a regular heartbeat is a sign of good cardiac health. However, sinus rhythm, the rhythm of healthy heart, or the successive cardiac cycle length is characterised by significant variability. Therefore, normal heart rate is not characterised by clockwise regularity. In fact, preferably regular cardiac cycle length may signify disease condition. Variation in successive cycle length is called the heart rate variability (HRV). The heart rate fluctuates with phase of respiration: cardio-acceleration during inspiration and cardio inhibition during expiration. The relationship between heart rate (HR) and heart rate variability (HRV) are not simple but, both depend on autonomic nervous system; so they are not independent variables. The quantification of HRV is influenced by HR level. So, heart rate and heart rate variability variables represent quite different characteristics of autonomic nervous activity.

Measurement: Time domain and frequency domain analysis.

Time domain analysis

In a continuous electrocardiograph (ECG) record, successive QRS complexes (R peaks) detected and intervals between are called normal to normal (NN) intervals.
Statistical methods: The most commonly used measure derived from interval differences include RMSSD (the square root of the mean squared differences of successive NN intervals), NN 50, the number of interval differences of successive NN intervals greater than 50 ms, and pNN50 (percentage NN50 count). Geometrical methods: The geometrical method uses the sequence of RR intervals to construct a certain geometrical forms and extract the assessment of HRV from this. e.g. Lorenz plot or Poincare plot SD1, which represents the short term HRV and SD2, which represents long term HRV.

Frequency domain (Power spectrum) analysis
In the frequency domain measure, power spectral densities of R-R intervals are plotted and different frequency components are identified. It includes the high frequency (HF) components (0.15-0.40 Hz) its power, percentage and normalized unit value that represents vagal modulation of HRV; and low frequency (LF) components (0.03-0.15 Hz) and its power, percentage and normalized unit value that represents sympathetic modulation. LF/HF ratio represents sympathovagal balance.

Head up tilt
Head up tilt is one of the experimental models of orthostatic test commonly used for autonomic test including HRV. On moving from supine to erect position there is large gravitational shift of the blood away from the chest to the distensible venous capacitance system below the diaphragm. So during head up tilt, a hydrostatic venous pooling in the extremities occurs owing to gravity. In addition, with prolonged standing, the high capillary transmural pressure in dependant parts of the body causes filtrations of protein free fluid in to the interstitial spaces. It is estimated that this results in 15-20% (700 ml) decrease in the plasma volume in 10 minutes in healthy adult humans. As a consequence of this, venous return to heart is reduced resulting in the rapid diminution of cardiac filling pressure and, thereby decrease in stroke volume. Despite decreased cardiac output, a fall in mean arterial pressure is prevented by a compensatory vasoconstriction of the resistance and capacitance vessels in the splanchnic, musculo-cutaneous, and renal vascular beds within a minute. Vasoconstriction of the systemic blood vessels is the key factor in the maintenance of arterial blood pressure in the upright posture. There is pronounced HR increase to maintain cardiac output. These rapid short terms adjustment to orthostatic stress is mediated exclusively by the autonomic nervous system. During prolonged orthostatic stress, additional adjustments are mediated by the hormonal limb of the neuroendocrine system.

Recording procedure: The subjects were instructed not to take tea or coffee at least for 4 hours before test. Alcohol was forbidden 24 hours prior to test. The recording was done in morning hours between 08:00 to 12:00 hours after 15 min of supine rest. The resting ECG with spontaneous respiration at three positions first at supine followed by 10º and 70º were recorded for 5 minutes in the computer. The ECG signals for HRV were captured using Coulbourn Instrument and its software Windaq pro/pro+. From this software R-R intervals were obtained, which were manually checked and edited. Then from R-R intervals different parameters of time and frequency domain measure of HRV were calculated by using HRV analysis software 1.1.

Statistical analysis: Descriptive and inferential
statistics of all the variables of the time domain and frequency domain measure of HRV were done along with age, BMI, respiratory rate, blood pressure. Multiple comparisons among the variables were analyzed by one way ANOVA and Bonferroni tests of multiple comparisons using software SPSS version 10.2.

**Results**
The mean age of the subjects was 25.37±3.89 years and their BMI ranged from 18.11 to 24.72 kg/m² (mean= 20.77±2.1 kg/m²)

**Effect of graded head up tilt on cardiopulmonary variables**
No significant difference in respiratory rate and systolic blood pressure in response to 10º or 70º tilt were observed in the present study. The diastolic blood pressure was significantly increased in response to 70 degree tilt compared to 10 degree (81.07±6.94 vs. 75.87±8.10 mmHg, p< 0.05) tilt and supine (81.07±6.94 vs. 74.13±7.3 mmHg, p<0.01). The difference in heart rate was not significant in response to 10 degree head up tilt. Whereas, in response to 70 degree tilt as compared to supine, it increased significantly (88.51±12.84 vs. 70.48±8.17 bpm, p<0.001), the increases in heart rate at 70º was also significant compared to 10º tilt (88.51±12.84 vs. 70.22±8.67 bpm, p<0.001).

**Effect of graded head up tilt on HRV**
The 70º tilt significantly decreased the following vagal HRV indicators compared to 10º and supine: RMSSD, NN50, pNN50, SDNN. (Table 2)

The 70º tilt significantly decreased HF power, HF unit compared to 10º and supine where as the same 70º tilt increase LF power %, LF normalised unit, and LF: HF ratio compared to 10º and supine. (Table 3).

### Table 1: Cardiopulmonary variables

<table>
<thead>
<tr>
<th>Variables</th>
<th>Supine</th>
<th>At 10° tilt</th>
<th>At 70° tilt</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP, mmHg</td>
<td>118.60±8.98</td>
<td>118.07±9.50</td>
<td>121.20±9.46</td>
<td>NS</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>74.13±7.30</td>
<td>75.87±8.10</td>
<td>81.07±6.94</td>
<td>p&lt;0.05 (70° vs. 10°) p&lt;0.01(70° vs. supine)</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>70.48±8.17</td>
<td>70.22±8.67</td>
<td>88.51±12.84</td>
<td>NS (10° vs. supine ) p&lt;0.001 (70° vs. Supine) p&lt;0.001 (70° vs. 10°)</td>
</tr>
<tr>
<td>Respiratory rate, per minute</td>
<td>18.03±2.04</td>
<td>18.27±2.58</td>
<td>19.20±3.17</td>
<td>NS</td>
</tr>
</tbody>
</table>

SBP: Systolic blood pressure, DBP: diastolic blood pressure, bpm: beats per minute.

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**Fig 1:** ECG graph showing R-R intervals
### Table 2: Time domain variables

<table>
<thead>
<tr>
<th>Variables</th>
<th>Comparison among variables with mean ± SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean RR (ms)</td>
<td>Supine = 831.23±162.30 At 10° tilt = 869.17±103.27 At 70° tilt = 687.07±94.81</td>
<td>NS</td>
</tr>
<tr>
<td>SD of RR (ms)</td>
<td>Supine = 38.13±10.89 At 10° tilt = 38.07 ± 11.29 At 70° tilt = 31.13 ± 8.12</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>RMSSD (ms)</td>
<td>Supine = 36.16±12.22 At 10° tilt = 34.23±14.22 At 70° tilt = 20.06±8.47</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>NN50 count</td>
<td>Supine = 55.27± 44.10 At 10° tilt = 45.07±44.44 At 70° tilt = 13.03±20.58</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>pNN50</td>
<td>Supine = 16.65±14.23 At 10° tilt = 14.06±15.65 At 70° tilt = 3.28±6.08</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>SD1</td>
<td>Supine = 25.93±8.72 At 10° tilt= 24.55±10.14 At 70° tilt= 14.73±6.14</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>SD2</td>
<td>Supine= 56.40±18.23 At 10° tilt= 57.33±18.34 At 70° tilt= 49.18±13.24</td>
<td>NS</td>
</tr>
</tbody>
</table>

Mean RR: Mean of RR intervals, SD of RR: Standard deviation of RR intervals, RMSSD: The root mean square of differences of successive RR intervals, NN50: No. of RR intervals that differ by more than 50 ms, pNN50: The percentage value of consecutive RR intervals that differ by more than 50 ms.

### Table 3: Frequency domain variables

<table>
<thead>
<tr>
<th>Variables</th>
<th>Comparison among variables with mean ± SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VLF peak, Hz</td>
<td>Supine = 0.023 ± 0.008 At 10° tilt=0.02±0.07 At 70° tilt=0.023±0.006</td>
<td>NS</td>
</tr>
<tr>
<td>VLF power, ms²</td>
<td>Supine = 96.97 ± 81.38 At 10° tilt=121.93±117.32 At 70° tilt=67.9±50.36</td>
<td>NS</td>
</tr>
<tr>
<td>VLF power %</td>
<td>Supine =18.88 ± 7.87 At 10° tilt=23.76±10.59 At 70° tilt=21.25±11.13</td>
<td>NS</td>
</tr>
<tr>
<td>LF peak, Hz</td>
<td>Supine= 0.09±0.33 At 10° tilt0.083±0.03 At 70° tilt=0.082±0.15</td>
<td>NS</td>
</tr>
<tr>
<td>LF power, ms²</td>
<td>Supine= 216.87±150.98 At 10° tilt=218.17±155.85 At 70° tilt=197.20±143.76</td>
<td>NS</td>
</tr>
<tr>
<td>LF power %</td>
<td>Supine = 41.61±14.29 At 10° tilt=40.73±11.58 At 70° tilt=59.52±14.50</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>LF nu</td>
<td>Supine = 52.32±19.89 At 10° tilt=54.52±16.34 At 70° tilt=75.72±14.76</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>HF peak, Hz</td>
<td>Supine= 0.26±0.72 At 10° tilt=0.25±0.067 At 70° tilt=0.24±0.69</td>
<td>NS</td>
</tr>
<tr>
<td>HF power, ms²</td>
<td>Supine= 207.67±181.22 At 10° tilt=189.57±167.81 At 70° tilt=72.70±101.17</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>HF power %</td>
<td>Supine = 39.57±18.54 At 10° tilt=35.49±15.75 At 70° tilt=19.31±13.25</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>HF nu</td>
<td>Supine = 47.67±19.89 At 10° tilt=45.48±16.34 At 70° tilt=24.28±14.16</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>LF/HF</td>
<td>Supine = 1.69±1.67 At 10° tilt=1.53±1.138 At 70° tilt=4.96±4.08</td>
<td>p&lt;0.001</td>
</tr>
</tbody>
</table>

VLF: very low frequency, LF: low frequency, HF: high frequency, nu: normalized unit
Discussion
Heart rate variability, which routinely used in
the assessment of haemodynamics in the western
countries is a tool established in 1980s for assessment
of autonomic regulation of cardiac rhythm. It can
delineate sympathetic and parasympathetic contribution
to heart rate regulation, thus making it very sensitive to
diagnose autonomic neuropathy in its sub-clinical stage
in diabetes mellitus. The HRV has special significance
in risk stratification of post-myocardial infarction. It is
an independent predictor of sudden cardiac death.

Head up tilt (orthostatic test) is the experimental
procedure of passive standing resulting in the
gravitational shift of the blood to lower extremities,
which results in reduced venous return to the heart and,
thereby decreasing stroke volume.

This study attempts to explore the HRV response
to graded 10º and 70º tilts from supine position. The
study showed no significant change in cardiovascular
parameters at 10º tilt of head up tilt compared to supine.
So, cardiovascular response at supine and 10º tilt is
statistically similar. But, cardiovascular parameters
changed in response to 70º tilt compared to supine and
10º. It is also known from the literature that there is
no change in systolic blood pressure in response to
tilt. This is consistent with our study that we did not
find significant difference in systolic blood pressure in
response to 10º or 70º of head up tilt. The heart rate in
case of higher degree of tilt involves an early rise due to
vagal withdrawal and more delayed increase over first
two minutes caused by enhanced sympathetic activity.
The heart rate increased at 70º in our study.

Effect of graded head up tilt in time domain measure
of HRV
There was corresponding decrease in HRV measure,
believed to be vagal: SDNN, RMSSD, NN50, pNN50
and SD1. Among the time domain measure, mean
RR interval was significantly decreased in response to
70º tilt as compared to 10º tilt or supine. Literature
suggests non significant decrease in SDNN intervals
with passive tilt. However, in our study the SDNN
interval decreased significantly in response to 70º tilt
as compared to 10º tilt or supine. The difference was
probable due to method applied; most of the tilt tables
used was of foot supporting type of tilt table compared to
table with only support on the centre not the foot, which
we have used. So, no skeletal muscles were involved to
support venous return in our ser up of passive standing
and hence, the difference was much pronounced. The
RMSSD is one of the most common parameters based
on interval differences that correspond to short term
HRV changes and are not dependant on day and night
variations. It was significantly decreased in response
to 70º of head up tilt as compared to 10º tilt or supine.
The NN50 count decreased significantly in response to
70º tilt compared to 10º or supine. Similarly, significant
decrease in pNN50 was observed in response to 70º of
tilt compared to 10º or supine. This pNN50 is one of
the most common parameters that correspond to short
term HRV changes. Among the geometrical methods,
Poincare plot SD1, that represents the short term HRV
was significantly decreased in response to 70º tilt as
compared to 10º or supine, whereas the Poincare plot
SD2, that represents the long term HRV, remained
unchanged among the different degree of tilt.

Effect of graded head up tilt on frequency domain
measure of HRV
It is known that in normal subjects, head up tilt leads
to decrease in high frequency components of HRV
that represents the vagal modulation to heart. At the same
time, it leads to increase in low frequency components
that represent the sympathetic modulation to heart. So, head up tilt leads to vagal withdrawal. In our study,
HF peak did not change in response to 10º or 70º tilt from supine but the HF power, its percentage
value and the HF normalized unit decreased in response
to 70º tilt as compared to 10º tilt and supine. However,
there was no significant difference in LF peak, and its
power in response to tilt to 70º, where as the LF power
percentage increased in response to 70º as compared
to 10º and supine. In the same way, the LF normalized
unit also increased in response to 70º tilt as compared to
10º and supine. LF to HF ratio has been considered as
sympathovagal balance, which changes in response to
head up tilt angle above 30 degree. Very low frequency components remained statistically
similar at supine, 10º and 70º. It was interesting to note
that changes in HRV in response to tilt occurred without
change in respiratory frequency.

Strength and limitation of the study
In cardiovascular evaluation, different degrees of tilt
are applied. However, tilt at 10º has rarely been found in
the available literature. Therefore, a 10º tilt is one of the
frequent positions used in everyday practice. Hence, it
was worth studying HRV changes in this position. But
it was found to be similar to supine posture in terms of
HRV.

This study has some limitations, the major of which is
the limitation of time, due to which this study could not
be carried out on a large sample size, besides this study
was carried out only on males. So result of the study
cannot be generalised on both sexes.

Conclusion
At 70º of head up tilt, HRV measures reflecting vagal
contribution to cardiac-cycle length decreased with
A reciprocal increase in sympathetic activity compared to 10° tilt or supine leading to increase in sympathetic predominance. LF to HF ratio, which reflects the sympathovagal balance, was found to be increased at 70° tilt. So with tilt of higher angle there is increase in sympathetic activity and decrease in parasympathetic activity. The 10° tilt, which is almost equivalent to lying down with a pillow, did not change HRV from supine. So, 10° tilt is physiologically similar to supine position. It can also be said that passive inclination to 10° tilt does not cause significant haemodynamics change to produce appreciable changes in blood pressure and HRV.

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References