A Study of Cardiac Parameters using Impedance Plethysmography (IPG) in Healthy Volunteers


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A Study of Cardiac Parameters using Impedance Plethysmography (IPG) in Healthy Volunteers

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Abstract

Impedance plethysmography is non-invasive technique to measure blood flow in any part of the body like heart (Impedance Cardiography), arteries or veins. As only heart rate and blood pressure is not sufficient to access a person’s hemodynamic status, cardiac output and other cardiac parameters measured by this simple technique will help further to access heart’s functional status with avoidance of all complications associated with previous catheter related invasive techniques. Main aim of the study was to measure cardiac parameters noninvasively in healthy volunteers of all age groups of both sex using impedance cardiography and then compare them between different age groups. Study was done in 5 age groups (16 – 25 yrs, 26 – 35 yrs, 36 – 45 yrs, 46 – 55 yrs and > 55 yrs) and in total 400 subjects. Each group was of 80 healthy volunteers of either sex. It was carried out on Nivomon Series computerized software in Bhavnagar region. Cardiac parameters measured were SV – Stroke Volume, SI - Stroke Volume Index, CO – Cardiac Output, CI – Cardiac Index, LVET – Left Ventricular Ejection Time, SVR – Systemic Vascular Resistance and SVRI - Systemic Vascular Resistance Index. Normative baseline laboratory data obtained from 400 healthy volunteers were as: SV - 65.15 ± 13.18 ml / beat, SI - 38.16 ± 7.64 ml / beat / m², CO - 4.94 ± 1.09 lit. / min, CI - 2.91 ± 0.51 lit. / min / m², LVET - 357.35 ± 46.32 msecs, SVR - 1500.95 ± 305.45 dyne•sec / cm⁵ and SVRI - 2507.75 ± 441.63 dyne•sec / cm⁵ / m². These values were found to be consistent with normal reference range. So now these baseline normative data will be helpful in many future research studies related to heart function in Bhavnagar region for this novel instrument. Significant differences were found for all parameters between different age groups. LVET and SVR were found on higher side in later ages due to atherosclerosis and other age related changes. Positive correlation was found between BSA and SV, CO. Negative was the case for BSA and SVR. In case of gender difference in last age group, Zo was found to be extremely higher in females due to higher fat proportion. Also SV was significantly lower and SVR was higher in females but no difference was there for CO and LVET. Overall, cardiac parameters were measured with this impedance technique accurately. Although there were some

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limitations, this technique was found to be simple, cheap and effective. If this technique is further validated and established, than it can be used widely for many physiological and pharmacological studies on human heart. Further, it can be used in ICU, in clinical set up for many heart disease patients, and also in CCU or in emergency trauma centres for other critically ill patients.

**Keywords:** Impedance plethysmography, impedance cardiography, cardiac output, non – invasive

**Introduction**

Plethysmography is a technique of measuring volume changes of an organ, the volume may be due to blood, water or air. It is of many types like Photo electric Plethysmography, Pneumo (Body or Chamber) Plethysmography, Inductive Plethysmography, Impedance Plethysmography, Magnetic Susceptibility Plethysmography, Strain Gauge Plethysmography (Peck Y et al. 2003) The concern of our study is Impedance Plethysmography that measures volume changes of blood in chest, calf or any other region of the body by sensing electrical resistance changes in respective area. Impedance Plethysmography (IPG) measures blood flow in Arteries. Occlusive Impedance Plethysmography (OIP) measures blood flow in Veins. Impedance Cardiography (ICG) measures blood flow in major vessels of Cardiac region from which Stroke Volume is obtained. Impedance Plethysmography can also be used in measurement of cerebral blood flow, Intra Thoracic Fluid Volume and Determination of Body Composition. Our study consist of measuring Cardiac Parameters like Stroke volume (SV), Cardiac output (CO), Systemic Vascular Resistance (SVR) and many others using the principle of Impedance Plethysmography that is ICG. ICG is in vague term, means Electrical Resistance. Resistance (R) means as according to Ohm’s law, voltage (V) to current (I) ratio. Zo indicates basal body Impedance.

\[ V = I / R \]

When current is constant, sinusoidal, means frequency component is there, then resistance R is called Impedance Z. Constant DC current is for resistance measurement and constant amplitude sinusoidal current is for impedance measurement. Known amount of current is passed (1 mA – 4 mA), amount of voltage is measured by voltage sensing electrodes and so this voltage to current ratio gives value of Impedance. Whenever constant current is passed through any body segment, it will choose the path with least resistance. Major arteries offer less resistance, E.g. brachial artery in arm, femoral artery in thigh. In case of chest region, the current will pass through aorta. During systole, more blood flow will give least resistance to the current due to alignment of cells in a vessel as shown in next figure. Least resistance will in turn be recorded as a positive upward wave in the graph. Less blood flow as during diastole will lead to misalignment of cells, which in turn give more resistance to the current and there will be a wave in the graph with less
amplitude as compared to that during systole. Graph during diastole is smaller, but amplitude is there because though less as compared to systole, but pressure is present during diastole.

Fig. 1: Path of current through vessels.

In this technique, the Electrical Impedance of any part of the body is measured by constant current method and variations in the impedance are recorded as a function of time as a Graph. Since blood is a good conductor of electricity, the amount of blood in a given body segment is reflected inversely in the electrical impedance of the body segment. Pulsatile blood volume by heart, which is systemic blood circulation, causes proportional decrease in the electrical impedance. Variation in the electrical impedance thus gives adequate information about the blood circulation in any part of the body, either Heart or any other Blood Vessels. Difference between the instantaneous electrical impedance and initial value of electrical impedance (Zo) indicates blood volume in that particular region. Value of rate of change of this impedance will give us different measured cardiac parameters for blood volume changes in thoracic major blood vessels, especially aorta. A typical impedance plethysmograph system is comprised of a sine wave generator followed by voltage to current converter. This constant current 4 mA is passed through the body segment of interest with the help of 2 surface electrodes, called as the current electrodes (I1, I2). These electrodes may be in the form of banded wire, loop around the body or may be typical surface stick on type of ECG electrodes. Voltage signal developed along the current path is sensed with the help of another pair of electrodes, called as the voltage electrodes (V1, V2) (Babu JP et al. 1990).

The amplitude of the signal sensed is directly proportional to the electrical impedance of the body segment. Amplification and detection of this signal gives instantaneous electrical impedance Z of the body segment. Difference between the instantaneous electrical impedance (Dynamic impedance) and initial value of electrical impedance (Zo – basal impedance) gives variation in the impedance as a function of time, called the ∆Z(t) waveform. First time derivative of the impedance (dZ/dt) is obtained to give the rate of change of impedance. With the help of this dZ/dt, used in Kubicek’s equation, stroke volume can be measured (Kubicek WG et al. 1974).

Fig. 2: Electrodes placement for measuring cardiac parameters and path of current through aorta.

There are various types of electrodes and their method of placement across the chest wall. The Cardiac Output Monitor by Bhabha Atomic Research Centre (BARC) uses the four band...
electrodes using vertical method (also called as Neck abdomen method) of electrode placement. This method requires special type of band electrodes made out of braided silver (Barde P et al. 2006). In our study, placement of electrodes are in the form of standard stick - on type surface ECG electrodes which has replaced now band electrodes used earlier for cardiac parameters determination using non-invasive Impedance Cardiography. The four electrodes are placed above and other four below the chest wall, inner four are voltage sensing electrodes while outer four are stimulating or current injecting electrodes. The graph recorded is as follows:

**Table1**: Timing of various notches in the first derivative impedance signal in Impedance Cardiography

<table>
<thead>
<tr>
<th>Event in the cardiac cycle</th>
<th>Notch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial contraction</td>
<td>A</td>
</tr>
<tr>
<td>Closure of tricuspid valve</td>
<td>B</td>
</tr>
<tr>
<td>Closure of aortic valve</td>
<td>X</td>
</tr>
<tr>
<td>Closure of pulmonic valve</td>
<td>Y</td>
</tr>
<tr>
<td>Opening snap of mitral valve</td>
<td>O</td>
</tr>
<tr>
<td>Third heart sound</td>
<td>Z</td>
</tr>
</tbody>
</table>

BCX is called the systolic wave (C wave) and XYOZ is called the diastolic wave (O wave). Left Ventricular Ejection Time (LVET) is measured as shown in next figure:

![Fig. 4: LVET measurement.](image)

B corresponds to the first heart sound.
X corresponds to the second heart sound.
BX corresponds to Left Ventricular Ejection Time (LVET).

(dZ / dt ) max is measured as the height of the curve from B to the peak of the systolic wave (C) (Babu JP et al. 1990 ).

Stroke Volume (SV) is measured by the impedance signal recorded from the inner pair of electrodes using Kubicek’s equation (Shyu LY et al. 2000) as,

\[ \text{Stroke volume (SV)} = k \, p \, (L / Zo)^2 \, \text{[LVET (dZ / dt) max]} \]

where \( k \) is a constant which accounts for variation in body composition based on age, gender, relative fat content, chest circumference;

\( \frac{dZ}{dt} \) max is the maximum rate of change of the impedance in \( \Omega / s \);

LVET is the left-ventricular-ejection time in seconds;

\( L \) is the inter - electrode distance in cm;
\( Zo \) is the basal impedance in \( \Omega \);
\( p \) is the blood specific resistivity computed using hematocrit as \( [13.5 + (4.29 \times \text{Hematocrit})] \) in \( \Omega \cdot \text{cm} \).

When alternating current (AC) current is used, the capacitance component of the impedance reacts differently to the various electrical frequencies. When frequency is low (20 – 100 kHz), the reactive component may be negligible, and the specific impedance of the tissue is close to its resistivity. Under such conditions, the resistivity in ohms per centimeter is 150 for blood, 63 for plasma, 750 for cardiac muscle, 1275 for lungs, and 2500 for fat (Backer LE et al. 1989).

Purpose of this study is to measure cardiac parameters in healthy volunteers of all age groups of either sex, to compare value of each parameter between different age group and also to see gender based differences. Each parameter measured by this technique alone or in accordance with other parameters, are useful in early detection of many cardiac disease conditions. Studies in past had been done for usefulness of non-invasive methods in cardiac and other critically ill patients. Many studies in past had been done for comparison between invasive and non-invasive methods in cardiac or any other disease patients for cardiac output and other parameters measurement (Arunodaya R et al. 2008, Sullivan PJ et al. 1990, Belardini R et al. 1996). Only a few studies had been done in normal healthy volunteers and that also not in a large group.
of population (Ng HWK et al. 1991). So here in our study we have tried to establish normative baseline laboratory data of cardiac parameters in a particular region by measuring them in 400 healthy volunteers, which can be used in further future physiological, pharmacological or clinical studies related to heart function in healthy normal subjects and in patients of heart disease also. As also this is relatively new study in our country as compared to foreign countries, it is first necessary to obtain normative baseline laboratory data in particular region. Also as the instrument used is relatively new, it is necessary first to check the compatibility of this instrument by measuring parameters in healthy volunteers and then by comparing these with standard normal values of the same.

Materials and Methods

Present study was carried out at Cardiovascular Laboratory, Department of Physiology, Government Medical College; Sir T. General Hospital and Old Age Home, Bhavnagar after obtaining ethical clearance from Institutional Review Board of our Government Medical College, Bhavnagar. This study was done to obtain normative data of cardiac parameters in following five age groups: 1st: 16 – 25 yrs, 2nd: 26 – 35 yrs, 3rd: 36 – 45 yrs, 4th: 46 – 55 yrs and 5th: above 55 yrs. Each group was containing 80 healthy volunteers of either sex. 25 subjects were excluded due to anticipatory tachycardia. 8 subjects were excluded due to abnormal ICG waveform. It was done on Nivomon Series Product computerized software by L and T Company.

Subject preparation and recording

Subject was asked to sit comfortably, to be relaxed and reassured that the procedure is totally harmless. Informed consent and history were taken along with Blood Pressure, Height in cm and Weight in kg. Subject’s name (initials), age, sex, height, weight, ID and Bed No. if necessary were entered the instrument. Then subject were asked to rest in supine position on a comfortable bed and to be relaxed with quiet breathing. Total 8 surface electrodes were used. Among them, four were current passing electrodes (I1, I2, I1’, I2’) delivering constant current of 4 mA and other four were voltage - sensing electrodes (V1, V2, V1’, V2’). Their placements are as follows:

V1, V1’: The base of neck on each side (Cervical voltage sensing electrodes)

V2, V2’: At the level of the xiphisternum on each side at anterior axillary line (Thoracic voltage sensing electrodes)

I1, I1’: At top of the neck on each side 5 cm above the cervical sensing electrodes

I2, I2’: 5 cm below the thoracic voltage sensing electrodes on each side

Surface stick – on type of ECG electrodes were used to connect NICO cable with body surface. Electrodes placement is shown in the next figure with minimal removal of clothing and so minimal discomfort to subjects.

![Fig. 5: Electrodes placement and NICO cable connection over body surface.](image)

As shown in the previous figure, particular electrode has particular color for ease of application as: I1 – Red, V1 – Yellow, V2 – Violate and I2 - Green (RYVG). Placement of electrodes on one particular side, either left or right are as I1, V1, V2 and I2 above downwards, and vice versa on the
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other side as I1', V1', V2' and I2'. CVP was by default taken as 5 mmHg because it is not much altered in healthy subjects as compared to critically ill patients. CO and other parameters were stabilized, averaged and displayed by the instrument. All the parameters were updated for every beat. Values displayed were real time, averaged over the previous eight beats. Electrodes were carefully removed with minimum discomfort to subject after recording is over.

![Image](image.jpg)

**Fig. 6:** ICG waveform display of NIVOMON

**Results**

All data were calculated and analyzed by trial version of GraphPad InStat – [DATASET1.ISD] Statistical software. Mean age of each group were 21.12 ± 3.04, 28.26 ± 2.79, 40.05 ± 3.32, 48.52 ± 2.33 and 68.5 ± 6.9 years respectively. Number of healthy male volunteers were in each group were 75, 73, 74, 71 and 57 respectively. And those of females were 5, 7, 6, 9 and 23 respectively. As there are comparable numbers of females in last age group of more than 55 years, we had done gender based comparison of parameters in this group.

Followings were parameters and other values with unit of measurement; those were obtained from Nivomon, tabulated and then analyzed by statistical software:

- Zo (ohms),
- Body Surface Area (m²),
- Stroke Volume (ml/beat),
- Stroke volume Index (ml/beat/m²),
- Cardiac Output (lit./min ),
- Cardiac Index (lit./min/m²),
- Left Ventricular Ejection Time ( msecs ),
- Systemic Vascular Resistance (dyne·sec/cm⁵),
- Systemic Vascular Resistance Index (dyne·sec/cm⁵/m²)

Mean ± SD values of cardiac parameters overall and within each group are shown in the Tables 1, 2.

One way ANOVA (ANalysis Of Variance) with post test was used to compare parameters within 5 age groups. Individual group comparisons for each parameter with p values are shown in the next table. Linear (Pearson) correlation coefficient \( r \) indicates positive (+) or negative (-) correlation between 2 parameters. Its value is up to ± 1. + 1 indicates strong positive correlation. It means, when 1 parameter is increased or decreased, other parameter is also strongly increases or decreases respectively. –1 indicates strong negative correlation. It means, when 1 parameter is increased, other parameter is strongly decreases and vice versa. Values of ‘r’ in each age group for correlation between BSA with each that of SV, CO, SVR and Zo are shown in the following Table. As there are maximum and so comparable number of females in last age group (more than 55 yrs: n = 23), we have done comparison of parameters between male and female using unpaired t – test with Welch correction in this group. Mean ± SD values of parameters, p value and significance are displayed in the following table.
Table 2: Mean ± SD values overall (n = 400)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean ± SD</th>
<th>Parameters</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>SV</td>
<td>65.15 ± 13.18</td>
<td>LVET</td>
<td>357.35 ± 46.32</td>
</tr>
<tr>
<td>SI</td>
<td>38.16 ± 7.64</td>
<td>SVR</td>
<td>1500.95 ± 305.45</td>
</tr>
<tr>
<td>CO</td>
<td>4.94 ± 1.09</td>
<td>SVRI</td>
<td>2507.75 ± 441.63</td>
</tr>
<tr>
<td>CI</td>
<td>2.91 ± 0.51</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Mean ± SD values in 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup> and 5<sup>th</sup> group

<table>
<thead>
<tr>
<th>Group → Parameters ↓</th>
<th>(1) (16 - 25) yrs</th>
<th>(2) (26 - 35) yrs</th>
<th>(3) (36 - 45) yrs</th>
<th>(4) (46 - 55) yrs</th>
<th>(5) More than 55 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zo</td>
<td>26.37 ± 3.5</td>
<td>27.46 ± 3.38</td>
<td>26.12 ± 3.46</td>
<td>28.61 ± 4.04</td>
<td>30.16 ± 5.34</td>
</tr>
<tr>
<td>BSA</td>
<td>1.72 ± 0.18</td>
<td>1.76 ± 0.17</td>
<td>1.68 ± 0.18</td>
<td>1.67 ± 0.14</td>
<td>1.63 ± 0.17</td>
</tr>
<tr>
<td>SV</td>
<td>63.8 ± 12.99</td>
<td>65.91 ± 9.2</td>
<td>70.23 ± 15.83</td>
<td>63.72 ± 11.86</td>
<td>62.06 ± 13.86</td>
</tr>
<tr>
<td>SI</td>
<td>36.14 ± 7.77</td>
<td>36.72 ± 7.23</td>
<td>41.84 ± 8.74</td>
<td>38.17 ± 5.72</td>
<td>37.95 ± 7.26</td>
</tr>
<tr>
<td>CO</td>
<td>4.99 ± 0.96</td>
<td>5.06 ± 0.85</td>
<td>5.23 ± 1.37</td>
<td>4.6 ± 1.02</td>
<td>4.83 ± 1.09</td>
</tr>
<tr>
<td>CI</td>
<td>2.9 ± 0.4</td>
<td>2.88 ± 0.42</td>
<td>3.09 ± 0.67</td>
<td>2.75 ± 0.48</td>
<td>2.95 ± 0.49</td>
</tr>
<tr>
<td>LVET</td>
<td>340.87 ± 42.85</td>
<td>347.75 ± 41.18</td>
<td>360.75 ± 41.85</td>
<td>366.87 ± 55.22</td>
<td>370.5 ± 43.07</td>
</tr>
<tr>
<td>SVR</td>
<td>1451.6 ± 240.62</td>
<td>1448.16 ± 239.85</td>
<td>1412.8 ± 317.19</td>
<td>1595.83 ± 319.9</td>
<td>1596.35 ± 348.17</td>
</tr>
<tr>
<td>SVRI</td>
<td>2463.01 ± 317.13</td>
<td>2526.2 ± 377.77</td>
<td>2347.01 ± 481.43</td>
<td>2629.22 ± 439.6</td>
<td>2573.31 ± 518.58</td>
</tr>
</tbody>
</table>

Table 4: ANOVA - p values and significance for Basal Impedance (Zo), Stroke Volume (SV), Stroke Volume Index (SI), Cardiac Output (CO), Cardiac Index (CI), Left Ventricular Ejection Time (LVET), Systemic Vascular Resistance (SVR) and Systemic Vascular Resistance Index (SVRI)

<table>
<thead>
<tr>
<th>Parameters → Groups ↓</th>
<th>Zo</th>
<th>SV</th>
<th>SI</th>
<th>CO</th>
<th>CI</th>
<th>LVET</th>
<th>SVR</th>
<th>SVRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 and 2</td>
<td>p</td>
<td>p</td>
<td>p</td>
<td>p</td>
<td>p</td>
<td>p</td>
<td>p</td>
<td>p</td>
</tr>
<tr>
<td>1 and 3</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>1 and 4</td>
<td>&lt; 0.01**</td>
<td>&lt; 0.05*</td>
<td>&lt; 0.001***</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&lt; 0.05*</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>1 and 5</td>
<td>&lt; 0.001***</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&lt; 0.001***</td>
<td>&lt; 0.05*</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>2 and 3</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&lt; 0.001***</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>2 and 4</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>2 and 5</td>
<td>&lt; 0.001***</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&lt; 0.05*</td>
<td>&lt; 0.05*</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>3 and 4</td>
<td>&lt; 0.001***</td>
<td>&lt; 0.05*</td>
<td>&lt; 0.05</td>
<td>&lt; 0.01**</td>
<td>&lt; 0.001***</td>
<td>&gt; 0.05</td>
<td>&lt; 0.01**</td>
<td>&lt; 0.001***</td>
</tr>
<tr>
<td>3 and 5</td>
<td>&lt; 0.001***</td>
<td>&lt; 0.001***</td>
<td>&lt; 0.01**</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&lt; 0.001***</td>
<td>&lt; 0.01**</td>
</tr>
<tr>
<td>4 and 5</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
</tr>
</tbody>
</table>

Note: p < 0.05 = significant. p > 0.05 = not significant. *significant, **very significant, ***extremely significant.

Table 5: r values for Body Surface Area (BSA) with Stroke Volume (SV), Cardiac Output (CO), Systemic Vascular Resistance (SVR) and Basal Impedance (Zo)

<table>
<thead>
<tr>
<th>BSA and</th>
<th>SV</th>
<th>CO</th>
<th>SVR</th>
<th>Zo</th>
</tr>
</thead>
<tbody>
<tr>
<td>→</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16 – 25 yrs</td>
<td>+ 0.66</td>
<td>+ 0.69</td>
<td>- 0.63</td>
<td>+ 0.04</td>
</tr>
<tr>
<td>26 – 35 yrs</td>
<td>+ 0.42</td>
<td>+ 0.49</td>
<td>- 0.45</td>
<td>+ 0.05</td>
</tr>
<tr>
<td>36 – 45 yrs</td>
<td>+ 0.37</td>
<td>+ 0.57</td>
<td>- 0.44</td>
<td>+ 0.11</td>
</tr>
<tr>
<td>46 – 55 yrs</td>
<td>+ 0.59</td>
<td>+ 0.62</td>
<td>- 0.57</td>
<td>+ 0.06</td>
</tr>
<tr>
<td>&gt; 55 yrs</td>
<td>+ 0.53</td>
<td>+ 0.68</td>
<td>- 0.42</td>
<td>- 0.08</td>
</tr>
</tbody>
</table>

Significance: YES YES YES NO

Note: r value, + positive and - negative correlation.
Discussion

We have tried to establish normative baseline laboratory data of all cardiac parameters for Bhavnagar region. Table No. 2 is showing mean values of all parameters in whole study group containing 400 healthy volunteers. Most of values are consistent with normal reference range (Guyton, Ganong, Harrison). So all parameters were measured effectively by this new instrument. These data will be helpful in many further future physiological, pharmacological or clinical studies.

We can study physiological factors (Sherwood A et al. 1998, Brown CVR et al. 2005) and pharmacological drugs (Aust PE et al. 1982, Sharman DL et al. 2004) affecting these cardiac hemodynamic parameters. These can be used for screening of susceptible subjects; and then life style modification, change of treatment or any other intervention (Treister N et al. 2005) can be suggested accordingly. ICG waveform can be used to aid in diagnosis of certain valvular (Schieken RM et al. 1981) or other cardiac diseases (Hubbard WN et al. 1986) and then to evaluate medical or surgical treatment for the same. It can be used to detect early signs of developing myocardial ischemia (Mohr R et al. 1986). It can be helpful in autonomic function testing also (Schondorf R et al. 1993). Cardiac output measurement can be used for the monitoring of other diverse cardiovascular conditions and for other purposes, like pacemaker setting during implantation (Tse HF et al. 2003). It can also be used in trauma centre and emergency for early detection of shock and so appropriate management (Asensio JA et al. 2006). CONTINUOUS CO monitoring is very useful in ICU set up (Albert NM et al. 2004). It can also be used for hemodynamic monitoring during haemodialysis. So if this non invasive technique is established, then it will be a great milestone in history of medical sciences.

We would able to avoid complications like infection, hemorrhage or arrhythmia associated with invasive catheter related CO measurement techniques like dye – dilution, fick’s principle or thermodilution. Further it requires minimal removal of clothing. So it is comfortable on the patient side also. As it is cheap and easy non invasive technique with portability of instrument, a trained staff can also take required data instead of a qualified doctor. So it is helpful with the problem of man – power and funding also, particularly in developing countries.

Table 6: Male and Female comparison in 5th group – Mean ± SD values, p values and significance

<table>
<thead>
<tr>
<th>Para.</th>
<th>Male (n = 57)</th>
<th>Female (n = 23)</th>
<th>p value</th>
<th>Signi.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zo</td>
<td>28.24 ± 4.34</td>
<td>34.9 ± 4.63</td>
<td>&lt; 0.0001</td>
<td>Extremely</td>
</tr>
<tr>
<td>BSA</td>
<td>1.65 ± 0.17</td>
<td>1.58 ± 0.15</td>
<td>0.076</td>
<td>Not quite</td>
</tr>
<tr>
<td>SV</td>
<td>64.32 ± 14.77</td>
<td>56.46 ± 9.44</td>
<td>0.0062</td>
<td>Very</td>
</tr>
<tr>
<td>SI</td>
<td>38.83 ± 7.6</td>
<td>35.75 ± 5.91</td>
<td>0.058</td>
<td>Not quite</td>
</tr>
<tr>
<td>CO</td>
<td>4.96 ± 1.17</td>
<td>4.52 ± 0.8</td>
<td>0.058</td>
<td>Not quite</td>
</tr>
<tr>
<td>CI</td>
<td>2.98 ± 0.51</td>
<td>2.86 ± 0.44</td>
<td>0.29</td>
<td>Not quite</td>
</tr>
<tr>
<td>LVET</td>
<td>374.21 ± 39</td>
<td>361.3 ± 51.64</td>
<td>0.28</td>
<td>Not</td>
</tr>
<tr>
<td>SVR</td>
<td>1543.12±343.8</td>
<td>1728.26±329.99</td>
<td>0.03</td>
<td>Yes</td>
</tr>
<tr>
<td>SVRI</td>
<td>2510.14±495.48</td>
<td>2729.86 ± 552.1</td>
<td>0.1</td>
<td>Not</td>
</tr>
</tbody>
</table>

Note: p values are two tailed.

Distribution of different parameters within each age group

Table No. 3 is showing Mean ± SD values of parameters in each group. As there are more than 2 age groups for comparison of different parameters, one way ANOVA statistical test was used.

Mean values of Basal Impedance Zo in each age group were 26.37 ± 3.5, 27.46 ± 3.38, 26.12 ± 3.46, 28.61 ± 4.04 and 30.16 ± 5.34 respectively. Table no. 4 and chart below indicate that Zo values in group 5 were significantly higher than group 1, 2 and 3. There is no significant difference between group 4 and 5. Also Zo values in group 4 were significantly higher than group 1 and 3. Zo depends on contents of blood, plasma and tissues like that of lungs, muscle and more important is fat.
Higher values in group 4 and 5 are due to higher proportion of fat as there are more number of females and peoples of later ages. So we can conclude that the instrument measures basal impedance accurately.

Mean values of stroke volume in each age group were $63.8 \pm 12.99$, $65.91 \pm 9.2$, $70.23 \pm 15.83$, $63.72 \pm 11.86$ and $62.06 \pm 13.86$ respectively. Table no. 4 and chart below indicate that stroke volume was significantly higher in group 3 than groups 1, 4 and 5. There is no significant difference between group 2 and 3. Stroke volume is dependent on many factors. But here we can say that in older ages SV is decreased mostly due to increased peripheral resistance (afterload) indicating atherosclerosis. In group 1, SV may be low due to low metabolic rate, small heart size or may be due to any other factor. Exact reason can’t be ruled out.

Mean values of stroke volume index in each age group were $36.14 \pm 7.77$, $36.72 \pm 7.23$, $41.84 \pm 8.74$, $38.17 \pm 5.72$ and $37.95 \pm 7.26$ respectively. Table no. 4 and next chart indicate that significance is same as that of stroke volume except, stroke index is significantly higher in group 3 than group 2. So stroke volume index should be preferably used over stroke volume to exclude variation due to BSA.

Mean values of cardiac output in each age group were $4.99 \pm 0.96$, $5.06 \pm 0.85$, $5.23 \pm 1.37$, $4.6 \pm 1.02$ and $4.83 \pm 1.09$ respectively. Table no. 4 and next chart indicate that cardiac output is significantly higher in group 3 than that of group 4. Otherwise there is no any significant difference between any other pair of groups. So the difference seen earlier in SV is neutralized by changes in heart rate, because CO depends on both SV and HR.

It indicates that whatever SV is there, CO is maintained within normal range here in wide range of ages by adjusting HR to supply each and every part of the body tissues for continuous supply of necessary elements. Also the cardiac output is regulated throughout life almost directly in proportion to the overall bodily metabolic activity. Therefore, the declining cardiac output and index is indicative of declining metabolic activity with age (Guyton).
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Mean values of cardiac index in each age group were 2.9 ± 0.4, 2.88 ± 0.42, 3.09 ± 0.67, 2.75 ± 0.48 and 2.95 ± 0.49 respectively. Table no. 4 and chart below indicate that results are same as that of CO. Only significant difference is seen between group 3 and 4 (higher value in group 3). Cardiac index is widely used for early detection of shock. Declining cardiac index with ageing is indicative of declining bodily activity and so basal metabolic rate (BMR) with age (Guyton).

Mean values of LVET in each age group were 340.87 ± 42.85, 347.75 ± 41.18, 360.75 ± 41.85, 366.87 ± 55.22 and 370.5 ± 43.07 respectively. Table no. 4 and chart below indicate that mean value of LVET was significantly higher in group 3, 4 and 5 than that of group 1. Further it was also significantly higher in group 5 than that of group 2. There is no significant difference between group 2, 3 and 4. It states that in old ages, LVET is on higher side; and in younger subjects, it is on lower side.

The data obtained in previous study showed that most of the variability in the duration of LVET in normal children can be explained by the HR differences (Spitaels S et al. 1974). So a regression equation is applied for study of LVET to exclude effect of HR differences (Weissler AM et al. 1961). LVET increases with maturity mainly because of a slower HR (Spitaels S et al. 1974). Values of LVET in our study are thus consistent with earlier study in which the duration of the left ventricular ejection was derived from the indirect carotid artery tracing. LVET was defined there as the interval between the beginning of the upstroke and the trough of the incisura (Spitaels S et al. 1974, Willems J et al. 1970).

Mean values of SVR in each age group were 1451.6 ± 240.62, 1448.16 ± 239.85, 1412.8 ± 317.19, 1595.83 ± 319.9 and 1596.35 ± 348.17 respectively. Table no. 4 and chart below indicate that the value of SVR was significantly higher in group 4 and 5 than those of group 1, 2 and 3. Mean arterial pressure increases (afterload) and so CO decreases due to atherosclerotic changes in later ages. As SVR depends on MAP (numerator) and CO (denominator), it increases in later ages. Low and high SVR are associated with many disease conditions (Peters J et al. 2000).
Mean values of SVRI in each age group were 2463.01 ± 317.13, 2526.2 ± 377.77, 2347.01 ± 481.43, 2629.22 ± 439.6 and 2573.31 ± 518.58 respectively. Table no. 4 and next chart indicate that the value of SVRI in group 4 and 5 are higher than those of group 3. There is no significant difference between group 1, 2, 4 and 5. So most of significant differences observed in SVR were neutralized in SVRI due to exclusion of BSA effect. So it is always better to use indices than that of actual value to avoid differences arising due to BSA.

Correlation between parameters

Now we consider correlation of BSA with other parameters. Pearson correlation coefficient ‘r’ was calculated for the same. Values of ‘r’ are shown in Table no. 5. It states that significant correlation was there between BSA and SV, CO, SVR.

There was no significant correlation between BSA and Zo. As Zo depends on fat, muscle and other tissues, it is independent of BSA. That means a person with more BSA have more or less fat distribution. It is shown as scattered diagram.
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Table no. 6 and next chart indicate that, SV was significantly higher in males but no difference for SI. That was mainly due to effect of increased metabolic activity. Zo was extremely higher in females indicating more fat proportion as compared to males.

**Gender based physiological difference**

Table no. 6 shows the comparison of parameters between male and female in last age group (> 55 yrs) using unpaired t test. Although numbers of male and female were not same, numbers of female were maximum in this group. And so we have selected this group for the same.

Further Table no. 5 indicates that ‘r’ was significantly negative for BSA with SVR. This is because increased BSA is associated with increase CO which in turn is associated with low SVR. So we can say that this instrument measures SVR appropriately. It is shown in the form of scattered diagram below:

**Chart 11:** Significant Positive Correlation between Body Surface Area (BSA) and Cardiac Output (CO) e.g. in 1\textsuperscript{st} group.

Female (n = 23)

**Chart 12:** Significant Negative Correlation between Body Surface Area (BSA) and Systemic Vascular Resistance (SVR) e.g. in 1\textsuperscript{st} group.

**Chart 13:** Comparison between male and female for Basal Impedance (Zo), Stroke Volume (SV) and Stroke Volume Index (SI).

Table no. 6 and chart below indicate that, there is no significant difference for BSA. So we can say, this group is appropriate for comparison due to absence of confounding factor. Also there was no significant difference found for CO and CI.

**Chart 14:** Comparison between male and female for Body Surface Area (BSA), Cardiac Output (CO) and Cardiac Index (CI).

Table no. 6 and chart below indicate that, although SVR was significantly higher in females, no significant difference was there for SVRI. So
again it indicates that indices should always be considered than actual values to avoid differences arising from BSA variation. There was no significant difference found for LVET between male and female.

![Chart 15: Comparison between male and female for Left Ventricular Ejection Time (LVET), Systemic Vascular Resistance (SVR) and Systemic Vascular Resistance Index (SVRI).](image)

**Applications of ICG**

- To study the effect of factors like posture, stress, exercise, diurnal variation on Cardiac parameters for physiological research purposes.
- To study the effect of drugs like beta blockers; arteriodilators (After load reducer) like hydralazine, calcium channel blockers; venodilators (Pre load reducer) like nitrates or mixed dilators (both pre and after load reducer) like ACE inhibitors on CO and other parameters for pharmacological research.
- To detect worsening of CO or other parameters in heart disease patients early by screening, and then for suggesting change of treatment or any other intervention.
- To study the effect of all chronic and ischemic heart diseases on Cardiac parameters for clinical research.
- For screening of susceptible subjects like those with family history of HT or other heart disease, smokers, alcoholics and then suggesting life style modification accordingly.
- ICG waveform is used to aid in diagnosis, medical or surgical treatment and evaluation of that same treatment of certain valvular and other cardiac diseases.
- CO, SVR and MAP together are used to detect early signs of developing myocardial ischemia in patients with suspected ischemic heart disease. These could also be used for ischemia detection in various conditions, such as silent ischemia or ischemia during exercise testing.
- CO measurement can be used for the monitoring of other diverse cardiovascular conditions and also for intra - aortic balloon pump optimization.
- CO, CI measurement are used in emergency trauma centre and casualty for early detection of shock and then management.
- For continuous CO monitoring at ICU set up in patients of MI, LVF or CCF, and in post cardiac surgery patients, or at CCU in other critically ill patients.

**Limitations of ICG**

The method indeed has some disadvantages. These include the errors caused by aortic valve insufficiency, severe mitral valve insufficiency, and shunts in the circulation for example, in septal defects or tetralogy of Fallot. The method does not give any indication of the presence of these pathologies, and they must therefore be diagnosed by other means. The method is also difficult to apply in patients with atrial fibrillation. As it mainly detects changes of blood flow in aorta, in conditions like coarctation of aorta, its validity is still questioned. Also increased thoracic fluid volume may interfere with impedance signal and give false results (Mathews L et al. 2008).

ICG is affected by number of factors:
- Changes in tissue fluid volume
- Respiration induced changes in the volume of pulmonary artery and pulmonary venous blood flow (“noise” must be filtered out from the desired changes in volumetric blood flow of the aorta)
- Changes in electrode contact or position
- Arrhythmias - the LVET may be falsely determined and so SV, CO
- Acute changes in tissue water, for example, pulmonary or chest wall edema or pleural effusions

Difficulties may arise with dysrhythmias, tachycardia (heart rate greater than 150 beat / min), metal in the chest or chest wall, sepsis and hypertension. Mechanical ventilation did not appear to be a problem (Appel P et al. 1986). Increased
sweating due to increased body temperature, extremely oily skin or any other reason may prevent effective contact of electrodes with the skin and thus gives false results. Same is the case with hairy skin. Impedance cardiography cannot detect exact pathology like other non-invasive Echocardiography or Colour Doppler, but these techniques require a qualified radiologist or cardiologist. And again advantage of continuous CO monitoring remains with impedance plethysmography only (Northridge DB et al, 1990, Critchley LA et al. 1988).

Conclusion

Our aim was to establish normative baseline laboratory data but numbers of females in all age group were less (5, 7, 6, 9 and 23 only respectively in group 1, 2, 3, 4 and 5). So, further validation is still required. Thus here we conclude that, if impedance cardiography is further validated and then established, it is advantageous and helpful in many ways and can be widely used either for research purposes or in clinical set up.

Conflict of Interest Disclosures – None

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