Noninvasive Evaluation of Left Ventricular Function in Chronic Severe Anemia

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SUMMARY

Left ventricular function was evaluated noninvasively in cases of chronic severe anemia (CSA) by recording systolic and diastolic time intervals (STI and DTI). These time intervals were recorded in 38 patients with CSA (hemoglobin below 7 g%), without cardiac decompensation, and in 30 control subjects. STI and DTI were measured from the simultaneous recordings of the apexcardiogram, carotid arterial pulse, electrocardiogram and phonocardiogram. The left ventricular ejection time was significantly prolonged (p<0.02), and associated with marked shortening of the PEP and reduction of the PEP/LVET ratio (p<0.001 in each case) in cases of CSA as compared to controls. Regarding the DTI, there was significant shortening of total filling time, slow filling time (p<0.001 in each case) and atrial systole (p<0.01) with no appreciable change in rapid filling time and isovolumic relaxation time. The SFT/RFT ratio and a/H ratio (the amplitude of the a-wave relative to the total height of the apexcardiogram) showed significant reductions (p<0.001 in each case). These changes in STI and DTI indicate enhanced left ventricular performance during diastole followed by faster and more complete relaxation during diastole in CSA.

Additional Indexing Words:

- STI
- DTI
- Pre-ejection period
- Ejection time
- Isovolumic relaxation time
- Rapid filling time
- Slow filling time
- Atrial systole

A NEMIA is a frequently encountered clinical entity in our day to day clinical practice, particularly in tropical countries. A hyperkinetic circulatory state at rest has been reported in chronic severe anemia (CSA) when hemoglobin falls below 7 g%. Several invasive procedures have demonstrated a rapid circulation time, and an increase in stroke volume and cardiac output in an attempt to compensate for the diminished oxygen carrying capacity of the blood. These hemodynamic alterations are accompanied by increased tissue extraction of oxygen, decreased blood viscosity, and an increased preload.
and decreased afterload in CSA.\textsuperscript{1)--3)}

In view of the widespread circulatory changes in severe anemia, a study of left ventricular function is indicated. Despite the frequent occurrence of anemia in India, there are only a few studies of left ventricular function using noninvasive methods, and their results are contradictory. Using systolic time intervals as an index of left ventricular function certain workers have shown diminished left ventricular function\textsuperscript{4)--6)} whereas others have shown enhanced function.\textsuperscript{7),8)} No literature is available on the diastolic function of the heart in CSA. In the present paper we present the results of a study of both left ventricular systolic and diastolic function by measuring systolic and diastolic time intervals in CSA.

**Materials and Methods**

The present study was conducted on 38 patients suffering from chronic severe anemia without clinical evidence of cardiac decompensation. The patients were all males, 20 to 40 years of age. The cause of anemia was nutritional deficiency in all cases. The patients selected had hemoglobin levels of less than 6 g\% (mean 4.13±1.57) with at least 3 months of anemia as shown by clinical history. All patients had hemoglobin levels and type of anemia determined and bone marrow studies performed.

The control group consisted of 30 normal healthy adults, age and sex matched, with hemoglobin levels above 12 g\%. The subjects included paramedical staff and attendants of patients. The subjects received a thorough physical examination, and an ECG was done to exclude the presence of any cardiovascular disease.

*Recording of systolic time intervals:*

Simultaneous recordings of carotid arterial pulse (CAP), apexcardiogram (ACG), phonocardiogram (PCG) and ECG were made using a four channel polygraph (Polyrite INCO). Systolic and diastolic time intervals were computed from these recordings.

Studies were performed with subjects in the left lateral decubitus position. ACG was recorded through a piezoelectric crystal transducer firmly applied and strapped at the point of maximum cardiac impulse. The CAP was recorded from the right carotid artery in the neck through a funnel-shaped pickup device attached to a volume transducer which was connected to a polygraph through an amplifier. The pickup device was firmly placed over the carotid artery to get a well marked upstroke and incisura in the CAP. The phonocardiogram was recorded by placing a phonotransducer over the third left intercostal space at the parasternal border. The ECG was recorded using
lead II. In some cases in which the QRS complex was not clearly defined in lead III, other leads were employed.

**Measurements of STI:**

The following systolic time intervals were computed from simultaneous recordings of CAP, PCG and ECG (Fig. 1). Electromechanical systole (QS2) was measured from the onset of the QRS deflection of the ECG to the first high frequency vibration of the aortic component of the second heart sound. Left ventricular ejection time (LVET) was measured from the point of onset of the sudden upstroke of the CAP tracing to the trough of the incisura. The pre-ejection time (PEP) was obtained by subtracting LVET from QS2. The PEP/LVET ratio was also calculated.

**Measurement of diastolic time intervals:**

Total diastole (TD) was measured from the beginning of the first high frequency vibration of the second heart sound (S2) to the beginning of the sudden upstroke of the ACG. Isovolumic relaxation time (IVRT) was measured from the beginning of the first high frequency vibration of the second heart sound to the nadir of the 'O' point on the ACG. Total ventricular filling time (TFT) was found by subtracting IVRT from TD. Rapid filling time (RFT) was measured from the nadir of the 'O' point of the ACG to the 'F' point. Slow filling time (SFT) was calculated by subtracting RFT...
plus the duration of atrial systole from TFT. Atrial systole (AS) is the duration from the beginning to the end of the a-wave of the ACG. The SFT/RFT ratio was also calculated.

The recordings were taken at a paper speed of 50 mm/sec. Only clearly defined tracings were analysed. Measurements were made on 10 cycles and the averages calculated. The results were expressed in milliseconds. The heart rate (HR) was determined from the ECG by measuring the RR interval.

Statistical analysis:

The mean values, SD and SE were calculated for each time interval. Student's t-test was applied to determine the significance of the differences between the mean values of different groups. The correlation coefficient (r) between each value and HR was determined and regression equations worked out. These regression equations (on our own data) were used to correct the values of STI and DTI to zero heart rate (using the procedure described by Richterich9).

RESULTS

Heart rate:

In the present series an appreciable increase in resting heart rate (p<0.001) was observed in cases of anemia (mean 92.08±18.19 beats/min) as compared to controls (mean 75.40±12.50 beats/min).

Systolic time intervals:

There was a significant negative correlation between HR and QS2, and between HR and LVET in normal subjects as well as in those with anemia. A negative correlation between HR and PEP was observed only in normal subjects. The correlation coefficients and regression equations are given in Table I. The figures for rate corrected STI (designated with the subscript 'I') are given in Table II. It is seen that LVET was significantly prolonged in cases of anemia (mean 352.48±23.73, p<0.02) as compared to controls (mean 344.26±15.24). This was associated with marked shortening of PEP (Fig. 2A) and reduction of the PEP/LVET ratio in anemics (p<0.001 in each case). However, QS2 showed no significant change.

Table I. Regression Data of Systolic Time Intervals in Controls and in Cases of Anemia

<table>
<thead>
<tr>
<th>STI</th>
<th>Controls</th>
<th>Anemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>QS2</td>
<td>QS2+1.39×HR</td>
<td>QS2+1.50×HR</td>
</tr>
<tr>
<td></td>
<td>r = −0.76 p&lt;0.001</td>
<td>r = −0.69 p&lt;0.001</td>
</tr>
<tr>
<td>LVET</td>
<td>LVET+0.90×HR</td>
<td>LVET+1.11×HR</td>
</tr>
<tr>
<td></td>
<td>r = −0.59 p&lt;0.001</td>
<td>r = −0.65 p&lt;0.001</td>
</tr>
<tr>
<td>PEP</td>
<td>PEP+0.48×HR</td>
<td>PEP+0.25×HR</td>
</tr>
<tr>
<td></td>
<td>r = −0.39 p&lt;0.02</td>
<td>r = −0.28 NS</td>
</tr>
</tbody>
</table>

NS = not significant.
Diastolic time intervals:

The various diastolic time intervals (except IVRT and RFT) were influenced by HR. The correlation coefficients and regression data are given in Table III. The values of DTI corrected for HR are given in Table IV, where they are expressed as indices.

The comparison of diastolic time interval indices between controls and anemics is shown in Table IV. The results show that there was significant shortening in the duration of TD, TFT, SFT (p<0.001 in each case) and AS.

Table II. Rate Corrected Systolic Time Intervals in Controls and in Anemia

<table>
<thead>
<tr>
<th>Diastolic time intervals</th>
<th>Equations employed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>Anemia</td>
</tr>
<tr>
<td>Total diastole (TD)</td>
<td>TD + 7.5 × HR</td>
</tr>
<tr>
<td>r = −0.85 p &lt; 0.001</td>
<td>r = −0.80 p &lt; 0.001</td>
</tr>
<tr>
<td>Total filling time (TFT)</td>
<td>TFT + 7.62 × HR</td>
</tr>
<tr>
<td>r = −0.84 p &lt; 0.001</td>
<td>r = −0.76 p = 0.001</td>
</tr>
<tr>
<td>Rapid filling time (RFT)</td>
<td>RFT + 0.16 × HR</td>
</tr>
<tr>
<td>r = −0.09 NS</td>
<td>r = −0.23 NS</td>
</tr>
<tr>
<td>Slow filling time (SFT)</td>
<td>SFT + 6.73 × HR</td>
</tr>
<tr>
<td>r = −0.82 p &lt; 0.001</td>
<td>r = −0.69 p &lt; 0.001</td>
</tr>
<tr>
<td>Atrial systole (AS)</td>
<td>AS − 0.69 × HR</td>
</tr>
<tr>
<td>r = −0.38 p &lt; 0.05</td>
<td>r = −0.45 p &lt; 0.01</td>
</tr>
</tbody>
</table>

Table III. Equations Used in Computing the Diastolic Time Intervals for Heart Rate Correction in Controls and Anemics

Table IV. Mean Values of Diastolic Time Interval Indices (msec) in Controls and in Anemics (corrected for heart rate)

<table>
<thead>
<tr>
<th>Diastolic time intervals</th>
<th>Controls</th>
<th>Anemia</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TDI</td>
<td>1078.20 ± 57.77</td>
<td>810.08 ± 64.24</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>TFTI</td>
<td>976.57 ± 60.28</td>
<td>692.25 ± 62.20</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>RFTI</td>
<td>107.19 ± 20.49</td>
<td>110.38 ± 25.31</td>
<td>NS</td>
</tr>
<tr>
<td>SFTI</td>
<td>761.10 ± 57.81</td>
<td>420.81 ± 59.90</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>ASI</td>
<td>105.54 ± 20.68</td>
<td>93.43 ± 16.77</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>SFTI/RFT ratio</td>
<td>2.78 ± 1.38</td>
<td>1.86 ± 1.43</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>a/H ratio</td>
<td>13.00 ± 3.13</td>
<td>11.00 ± 2.4</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>
(p<0.01) in cases of anemia as compared to controls. The maximum reduction observed in SFT was 44.71% (Fig. 2B).

IVRT and RFT were not corrected to zero HR as they did not have a significant correlation with HR.

The SFT/RFT ratio and a/H ratio (amplitude of a-wave in relation to the total outward movement seen on the apexcardiogram, expressed as a percentage) were significantly reduced (p<0.01 in each case) in cases of CSA as compared to controls.

**DISCUSSION**

Systolic time intervals are accepted as a measure of left ventricular performance. Increased ventricular filling is indicated by lengthening of LVET and shortening of PEP\textsuperscript{10,11} while QS2 remains unaltered. Shortening of PEP and decrease in the PEP/LVET ratio reflect increased cardiac output and increased myocardial contractility.\textsuperscript{12} The present study shows that in patients of CSA there is an increase in LVET and a decrease in PEP and in the PEP/LVET ratio, a pattern that is associated with high cardiac output and
enhanced myocardial contractility. These findings are in agreement with those of Abdullah\(^7\)) and of Florenzano,\(^8\) but are in contrast to those of Man-
chanda\(^4\)) and of Srivastava\(^5,6\)) who found left ventricular function to be de-
pressed in CSA. Warrier et al\(^13\)) found left ventricular function to be normal.

It is necessary to examine the reasons for the discrepancies in the observa-
tions of various groups of workers. With the onset of anemia the oxygen
carrying capacity of blood is reduced. The body would be expected to com-
pensate for this by increasing left ventricular filling, and by increasing myo-
cardial contractility. Over a period of time, however, these compensatory
mechanisms would begin to fail, ending in clinically observable cardiac de-
compensation. Thus a given case of anemia could show variations in cardiac
function extending all the way from normal to good compensation, and finally
to decompensation. Considered in this light it is obvious that the majority
of the patients studied in this series were in a stage where cardiac compen-
satory mechanisms were effective, this being reflected in mean STI values
indicative of increased left ventricular performance. In contrast, the patients
studied by Manchanda\(^4\)) and by Srivastava\(^5\)) would appear (as a group) to
have advanced towards the stage of decompensation, even though this was
not clinically apparent. This view is supported by the fact that in our series
the patients with CSA showed an increased heart rate whereas the subjects
studied by Manchanda\(^4\)) and by Srivastava\(^5\)) did not (as a whole) show any
significant increase in heart rate.

Although there are no reports on diastolic time intervals in CSA, some
conclusions regarding the changes to be expected can be arrived at by com-
parison with studies of DTI in other disorders. It is well known that im-
paired myocardial relaxation is indicated by prolongation of IVRT. This
has been observed in ischemic heart disease,\(^14\)) hypertension\(^15\)) and in aging.\(^16\))
Shortening of the RFT in relation to the SFT, and the presence of a SFT/
RFT ratio greater than 2.8±0.5 signifies the same.\(^17\)) A prolonged and pro-
minent a-wave\(^18,19\)) and an a/H ratio greater than 15.0/14,20) also reflect
decreased compliance of the left ventricle. Changes opposite to the above
would be expected in the presence of increased left ventricular compliance.
In the present study we have observed a significant shortening of AS, TFT
and SFT with no change in RFT and IVRT in our cases of CSA as com-
pared to controls. In addition, decreases in the SFT/RFT ratio and the a/H
ratio have been observed. All these changes suggest faster and more com-
plete relaxation of the left ventricle. It is significant that these changes are
observed in spite of the presence of tachycardia, which has been shown to
produce incomplete relaxation.\(^21\)) Our findings on the DTI in cases of CSA,
therefore, supplement those of the STI and show that in our cases left ven-
tricular efficiency is increased during both systole and diastole.

REFERENCES