Mechanocardiographic assessment of left ventricular function in coronary artery disease*

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SUMMARY Multiple regression analysis was used in order to evaluate the independent contribution and combined use of mechanocardiographic indices for assessing cardiac function in 23 patients with coronary artery disease.

Three indices were derived from the quantitative displacement left apex cardiogram: the time from the onset of electrical depolarisation to the peak of the first derivative (t peak dD/dt) and the first derivative normalised for the amplitude of the displacement (dD/dt/D) using for D total and developed displacement. From the external carotid pulse the ratio pre-ejection period to the ejection time (PEP/LVET) was calculated. Several invasive isovolumic and ejection phase indices of left ventricular function were calculated and used as dependent variables in the multiple regression analysis. The non-invasive indices were used as dependent variables. The index dD/dt/D of the left apex cardiogram was significantly partially correlated with all invasive indices and demonstrated the highest t values. For PEP/LVET the t values were smaller and not always significant. No significant partial correlation was found for (t peak dD/dt). The combined use of PEP/LVET and dD/dt/D resulted in a better differentiation between normal and abnormal left ventricular function.

It is concluded that quantitative apex cardiography is superior to systolic time intervals for assessing left ventricular function in coronary artery disease though both methods offer independent information and should be considered complementary.

Systolic time intervals and indices derived from the left apex cardiogram have become established methods for the non-invasive evaluation of left ventricular function in man.1–11

There is no general agreement as to the value of these indirect methods for assessing myocardial function at rest in patients with coronary heart disease. Moreover, it is largely unknown to which degree each of these methods independently contributes to the assessment of left ventricular function. It may be postulated that the combined use of both non-invasive methods might result in a better evaluation of left ventricular performance.

In order to clarify this problem, comparisons were made with both angiographic and isovolumic indices of contractility in a group of patients with chronic coronary artery disease. All indices, invasive and non-invasive, were obtained during the same catheterisation procedure and were correlated with each other by means of multiple linear regression analysis.

Methods

Twenty-three patients, two women and 21 men, with a mean age of 49 ± 11 (±SD) years were selected for the study. Chronic coronary artery disease, defined as stable angina pectoris, with or without previous myocardial infarction, was present in all patients. None of them had valvular lesions. All patients had regular sinus rhythm. Informed consent was obtained before the procedure.

Techniques

A selective coronary arteriography and a left
Mechanocardiology

ventriculogram in a 30 degree right anterior oblique position were performed in all patients. At least 15 minutes after the angiographic procedure a high-fidelity catheter tip micromanometer was introduced in the left ventricle (Telco or Millar Instruments).

Reference tracings were recorded through a side opening by means of an Elema EMT 456 strain gauge. The zero level was mid-thoracic.

The first derivative of left ventricular pressure (dP/dt) was obtained through resistance-capacitance differentiating circuits providing linear differentiation up to 45 Hz.

A calibrated displacement (D) left apex cardiogram was recorded by means of a piezoelectric crystal microphone (Elema-Schönander) with a time constant of four seconds. A description of the apparatus and the calibration procedure has been reported previously.\(^8\)\(^\text{11}\)

The right external carotid pulse tracing was recorded by the same transducer.

Lead II of the electrocardiogram and the internal phonocardiogram, obtained by appropriate high-pass filtering from the micromanometer, were recorded simultaneously. The internal phonocardiogram was used for the determination of the onset of the high-frequency vibrations of the aortic component of the second heart sound (A2). Recordings were made on an eight-channel ink-jet recorder (Elema 81) at a paper speed of 250 mm/s. Before and after each experiment the simultaneity of the channels of the recorder was controlled.

**Calculations**

The following invasive indices were derived from the left ventricular pressure (LVP):

- the peak value of the first derivative of LVP: peak dP/dt (mmHg/s),
- maximum value of the ratio of the first derivative of LVP to the corresponding total pressure (Pd): (dP/dt/Pd)\(_\text{max}\) also called Vpmax,
- the linear extrapolation of this ratio to zero pressure called VmaxPd,
- the ratio of the first derivative of LVP to the corresponding developed pressure (Pd=the instantaneous left ventricular pressure minus left ventricular end-diastolic pressure): dP/dt/Pd. The value of dP/dt/Pd at the time of peak dP/dt was represented (peak dP/dt)/Pd,
- the polynomial extrapolation of dP/dt/Pd to zero pressure using Pd values >10 mmHg was called VmaxPd. As the c and k constants of the series elasticity were ignored, these indices were expressed per second.

From the left ventriculogram the following indices of myocardial function were calculated using the area-length method\(^\text{18}\):

- the ejection fraction (EF): the ratio of stroke volume to end-diastolic volume. In our laboratory the lower limit of normal (mean normal value minus 2 SD) for the EF was 0.64,
- the mean velocity of circumferential fibre shortening according to the method of Karliner et al.\(^\text{19}\)

This index is expressed in circumferences per second (circ/s).

![Fig. 1 Calculation of indices of left ventricular function from the quantitative displacement left apex cardiogram (QLAC).](http://heart.bmj.com/)

**D** apical displacement; **dD/dt**, first derivative of QLAC; **dD/dt/Ds**, normalised first derivative of QLAC using total displacement (D\(_s\)); **Dd**, developed displacement; **C**, onset of systolic rise; **O**, protodiastolic nadir; **ECG**, electrocardiogram; **Phono**, phonocardiogram.
The quantitative left apex cardiogram provided the non-invasive indices listed below:

— the time from the onset of electrical depolarisation to the peak value of the first derivative (t peak dD/dt), expressed in milliseconds (ms),

— the normalised first derivative of the left apex cardiogram (dD/dt/D) using for D both total (D1) and developed (D2) displacement. D1 is measured with the 0 point (protodiastolic nadir) and D2 with the C point (onset of systolic contraction) of the apex cardiogram as reference zero point (Fig. 1). dD/dt/D1 is calculated electronically by means of a logarithmic amplifier and differentiator and the maximum value is termed (dD/dt/D1)max. dD/dt/D2 is measured manually and its value at the time of peak dD/dt is called (peak dD/dt)/D2. Both indices are expressed per second.

From the right external carotid pulse tracing the ratio pre-ejection period to left ventricular ejection time, PEP/LVET, was calculated. The beginning of the upstroke of the carotid pulse was determined by extending the systolic rising and the diastolic descending limb of the preceding complex. The intersection was considered as the exact onset of the upstroke.14 The nadir of the incisura was determined by simple inspection. PEP was measured as (Q-A2) minus LVET, where (Q-A2) represents the time interval from the beginning of the QRS complex to the first high-frequency vibrations of A2.

**STATISTICAL CALCULATIONS**

In order to evaluate and to quantify the independent contribution of a non-invasive index, taking into account the interaction with others, multiple linear regression analysis was performed. Four non-invasive parameters were used as independent variables: (dD/dt/D1)max, (peak dD/dt)/D2, t peak dD/dt, and PEP/LVET. All invasive indices were successfully used as dependent variables in the regression model.

The insignificant independent variables were deleted stepwise until only significant variables remained.

**Results**

The mean values (± SD) of all invasive and non-invasive indices are listed in Table 1. A normal left ventricular function (EF > 0.64 and absence of segmental contraction abnormalities) was found in seven patients.

In the multiple regression analysis the same four non-invasive indices are used as independent variables. All the invasive indices are successively used as dependent variables.

Multiple regression analysis with ejection fraction as dependent variable reveals a significant t value for (dD/dt/D1)max and PEP/LVET. The apex cardiographic index presents the highest t value (Table 2). With peak dD/dt of the left ventricular pressure similar results are obtained (Table 3). The individual values and the single linear correlations of these indices are shown in Fig. 2 and 3. The lower limits of normal (mean normal value minus 2 SD) for (dD/dt/D1)max, PEP/LVET, peak dD/dt, and EF are also indicated. (dD/dt/D1)max incorrectly categorised eight patients out of 23 and PEP/LVET incorrectly categorised six patients.

**Table 1** Indices of left ventricular function (mean ± SD)

<table>
<thead>
<tr>
<th>Invasive indices</th>
<th>Mean</th>
<th>± SD</th>
<th>Non-invasive indices</th>
<th>Mean</th>
<th>± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak dP/dt (mmHg)</td>
<td>1466.00</td>
<td>567.00</td>
<td>t-peak dD/dt (msec)</td>
<td>56.83</td>
<td>14.96</td>
</tr>
<tr>
<td>(dP/dt/Pmax t-1)</td>
<td>32.01</td>
<td>13.66</td>
<td>(dD/dt/D1)max (s-1)</td>
<td>30.05</td>
<td>9.85</td>
</tr>
<tr>
<td>(peak dP/dt)/P2 (s-1)</td>
<td>29.49</td>
<td>10.31</td>
<td>(peak dD/dt)/D2 (s-1)</td>
<td>32.22</td>
<td>9.14</td>
</tr>
<tr>
<td>Vmax P1 (s-1)</td>
<td>42.09</td>
<td>14.88</td>
<td>PEP/LVET</td>
<td>0.497</td>
<td>0.132</td>
</tr>
<tr>
<td>Vmax P2 (s-1)</td>
<td>78.27</td>
<td>26.05</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EF</td>
<td>0.511</td>
<td>0.207</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Vcf (circ/s)</td>
<td>1.028</td>
<td>0.691</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

For abbreviations of different indices see text.

**Table 2** Multiple regression equation between ejection fraction (EF) and mechanocardiographic indices of left ventricular function (n = 23)

<table>
<thead>
<tr>
<th>EF = 0.64 + 0.013 (dD/dt/D1)max + 3.02**</th>
</tr>
</thead>
<tbody>
<tr>
<td>= 0.003 (peak dD/dt)/D2</td>
</tr>
<tr>
<td>= 0.001 t-peak dD/dt</td>
</tr>
<tr>
<td>= 0.711 PEP/LVET</td>
</tr>
<tr>
<td>R = 0.78</td>
</tr>
<tr>
<td>0.50 + 0.012 (dD/dt/D1)max + 3.92***</td>
</tr>
<tr>
<td>= 0.699 PEP/LVET</td>
</tr>
<tr>
<td>R = 0.77***</td>
</tr>
</tbody>
</table>

R = multiple correlation coefficient; n = number of patients; t = computed t value of partial correlation; *p < 0.05; **p < 0.01; ***p < 0.001. For other abbreviations see text.
However, an abnormality in one or two of these measurements was associated with an abnormal ejection fraction in 22 out of the 23 patients. In 11 out of 23 patients at least one non-invasive index and in nine patients both indices correctly differentiated between normal and abnormal values of peak dP/dt (Fig. 3). There is no significant linear correlation between PEP/LVET and (dD/dt/Dt)max \((r = -0.16 \text{ NS})\).

Using mean Vcf as dependent variable an independent significant contribution is found only for \((dD/dt/Dt)\text{max} \) (Table 4). The same holds for the multiple correlation with Vpm (Table 5).

Table 6 summarises all the significant partial correlations found in the multiple regression analysis. Whether an injection phase index or an isovolumic pressure index is used as dependent variable, the normalised first derivative of the left apex cardiogram is always significantly correlated with the index under consideration and demonstrates the highest t values. The ratio PEP/LVET presents a significant partial correlation only with EF, peak dP/dt, and peak dP/dt/Dp. No significant partial correlation can be demonstrated for the index t peak dP/dt.

**Discussion**

Assessment of cardiac dynamics and myocardial function using external pulse tracings remains an important goal in non-invasive diagnostic cardiology. Among these the external carotid pulse and the left apex cardiogram are certainly the most commonly used. The apex cardiogram has been used as a substitute for pressure in timing left ventricular events,11–18 and constructing pressure dimension loops.17 When the delay for pulse wave transmission is taken into account, the external carotid pulse closely resembles the aortic pressure.6,14

Morphological changes of these tracings already offer many diagnostic possibilities as to valvular lesions and cardiac performance. Both tracings also provide a quantitative estimate of left ventricular function. Both methods, however, also have their limitations: for the left apex cardiogram, the absence of a true zero level and a still incomplete understanding of the determinants of its time course and morphology; for systolic time intervals, the change in opposite direction of some determinants of these intervals during changes in the inotropic state of the heart.19

The time interval from the onset of electrical depolarisation to the peak of the first derivative of the left apex cardiogram has been proposed as a quantitative index in assessing left ventricular function on the apex cardiogram.2,20 Subsequently the concept of ‘amplitude normalisation’ was introduced. It was found that the left ventricular pressure plays a predominant role in shaping the morphology of the left apex cardiogram21 and that a distinct similarity in slope exists between the left apex cardiogram and the left ventricular pressure during isovolumic contraction.2 In view of these findings the left apex cardiogram was calibrated and its first derivative was normalised for the amplitude of the apical impulse. Recent studies from our laboratory demonstrated the clinical value and advantages of the calibrated apex cardiogram and its normalised first derivative.6,11

Several authors have correlated systolic time intervals with other measurements of cardiac performances.3,4,6,9 The index PEP/LVET is used
and Garrard et al.\textsuperscript{4} have shown the highest correlation coefficient with the angiographic ejection fraction ($r = -0.90$). In the latter study various forms of heart disease were included, with extreme values for ejection fraction (ranging from 0.08 to 0.84). When, however, it was applied to patients with coronary artery disease the correlation coefficients were smaller.\textsuperscript{9, 22, 23}

At present there is no single undisputed invasive index for assessing myocardial contractility in man. Both isovolumic and ejection phase indices of contractility are susceptible to criticism and have their advantages and limitations.\textsuperscript{24, 25} In order to evaluate the usefulness and the relative importance of calibrated apex cardiography and systolic time intervals for assessing left ventricular function in coronary artery disease, comparisons were made with both invasive methods. Multiple linear
regression analysis was used to quantify the individual contribution of each non-invasive index.

From the statistical results it is clear that most important indirect information on left ventricular function is provided by the normalised derivative of the apex cardiogram. This is true whether angiographic or pressure indices of cardiac performance are used as dependent variables. When developed pressure is used in the calculation of the isovolumic indices, the corresponding apex cardiographic indices based on developed displacement are involved, since the 0-C amplitude of the left apex cardiogram reflects left ventricular end-diastolic pressure. Furthermore, the concept of normalisation of the first derivative, also termed 'normalised velocity', can be considered as a general index for assessing cardiac performance, equally applicable to invasive and non-invasive methods.

The ratio PEP/LVET also provides independent significant information, as shown by the regression equation with the EF and peak dP/dt of the left ventricular pressure. It should be noted that the present investigations were limited to resting frequencies. Though better identification of abnormal cardiac function in coronary artery disease during exercise is reported using systolic time intervals, the overall correlations with invasively determined indices of cardiac performance have improved only a little.

It is noteworthy that in this group of patients and with this regression model, no significant independent information on left ventricular function is provided by the index t peak dD/dt. The most logical explanation appears to be that the pre-ejection period and the normalised first derivative of the left apex cardiogram already contain most of the information provided by this index.

From our data it can be concluded that quantitative apex cardiography is a useful non-invasive tool for the evaluation of cardiac function in patients with coronary artery disease. In the group of patients studied, it is superior to systolic time intervals.

Although each method alone is not a strong indication of the state of the left ventricle in chronic coronary artery disease, both methods contain useful independent information and should be used together.

Table 6 Multiple regression analysis between invasive and non-invasive indices of left ventricular function in patients with chronic coronary artery disease (n = 23)

<table>
<thead>
<tr>
<th>Dependent variables</th>
<th>Independent variables</th>
<th>(dD/dt)/Dmax</th>
<th>(peak dD/dt)/Dmax</th>
<th>t peak dD/dt</th>
<th>PEP/LVET</th>
<th>Correlation coefficient (R, r)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF</td>
<td>***</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0-77***</td>
</tr>
<tr>
<td>Mean Vcf</td>
<td>**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0-61**</td>
</tr>
<tr>
<td>(dD/dt/Pa) max or Vpm</td>
<td>***</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0-71**</td>
</tr>
<tr>
<td>Vmax Pa</td>
<td>**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0-62**</td>
</tr>
<tr>
<td>peak dP/dt</td>
<td>***</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0-78**</td>
</tr>
<tr>
<td>(peak dP/dt)/Pa</td>
<td>**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0-83**</td>
</tr>
<tr>
<td>Vmax Pa</td>
<td>**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0-57**</td>
</tr>
</tbody>
</table>

*p < 0-05; **p < 0-01; ***p < 0-001. For abbreviations of different indices see text.

References

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