Direct Correlation of External Systolic Time Intervals with Internal Indices of Left Ventricular Function in Man

By C. Edwin Martin, M.D., James A. Shaver, M.D., Mark E. Thompson, M.D., P. Sudhakar Reddy, M.D., and James J. Leonard, M.D.

SUMMARY

Direct correlation of externally measured systolic time intervals with internally measured indices was obtained using catheter-tip micromanometers in six patients who had normal coronary arteriograms. Simultaneous recordings were made of central aorta and left ventricular pressure, maximum rate of rise in left ventricular pressure (dp/dt), external carotid pulse, external and internal sound, and electrocardiogram. Acute interventions were used to vary the indices by a variety of mechanisms including changes in contractility, preload, afterload, and heart rate. The initial values and the changes in these values produced by acute interventions are identical for left ventricular ejection time (LVET) whether measured externally (range 175 to 385 msec) or internally (range 169 to 392), r = 0.99. Although the absolute values differed for internally measured isovolumic contraction time (internal ICT), externally measured ICT, and preejection time (PEP), there was good linear correlation between the changes observed in these values following the interventions. Changes in PEP and internal ICT showed excellent linear correlation (r = 0.94) and were also alike in absolute value following the interventions. The interval from the Q wave of the electrocardiogram to rise in left ventricular pressure (electrical-mechanical delay) did not change significantly during these interventions. During a period of spontaneous isorhythmic dissociation there was close tracking between beat-to-beat changes in PEP and internal ICT and between externally and internally measured LVET. Following acute interventions PEP and left ventricular dp/dt changed inversely.

Externally measured systolic time intervals have therefore been shown in man to correlate well with directly measured internal indices, both in steady-state conditions and during a series of acute interventions. This convenient and atraumatic method has been shown to be a valid and sensitive measure of myocardial performance.

Additional Indexing Words:
Electrical-mechanical delay Isovolumic contraction time
Left ventricular dp/dt Left ventricular ejection time Preejection period

Although systolic time intervals were studied and defined some years ago by Wiggers1, 2 and by Lombard and Cope,3 there has been a recent resurgence of interest in studying these as well as other noninvasive techniques in the evaluation of myocardial

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of externally measured systolic time intervals

with internally measured indices of

myocardial performance be made both at rest

and with acute interventions. Externally measured

preejection period has been correlated

with internally measured isometric time and

left ventricular dp/dt in anesthetized dogs

although external and internal ejection times

were not studied. The present study was

designed to make these direct correlations in

man, both at rest and following a variety of

acute interventions.

Materials and Methods

Six adult male patients were studied during

coronary arteriography and left heart catheteriza-
tion. The nature of the procedure was explained

and consent was given in each case. Hemodynamic

data were normal in five patients. One patient

had valvular aortic stenosis. All coronary arterio-
grams were normal. There were no electrocardio-

graphic conduction abnormalities. The clinical
data are summarized in table 1. Central aorta

pressure events were measured by a catheter-tip

pressure transducer on a no. 5 catheter (Model

P866)* which was passed percutaneously via the

right femoral artery. Left ventricular pressure and

its first derivative dp/dt were recorded by an

Allard-Laurens Teleo catheter-tip micromanometer

introduced via a right brachial arteriotomy. This

system has a uniform amplitude response to

frequencies up to 200 cycles per second with no

significant time delay. Both catheters were

initially placed in the central aorta and made

equisensitive to the fluid-filled side arm of the

Teleo which was attached to a P23Db strain
gauge.* For recording, one catheter was passed

into the left ventricle, and the other was left in

the ascending aorta just above the valve. External

phonocardiograms were recorded with a contact

microphone* placed on the chest wall for optimal

pickup of the first heart sound (S₁) and aortic

component of the second heart sound (A₂). The

indirect carotid pulse was obtained from a

standard funnel-shaped pickup connected to a

P23Db strain gauge. This was positioned to

record the discrete onset of the carotid arterial

pulse and a sharp dicrotic notch. A standard limb

tead of the electrocardiogram was selected which

showed a sharp onset of the QRS complex,

preferably with a small septal Q wave. All data

were recorded on a multichannel recorder at a

paper speed of 100 mm/sec with time lines

indicating 20 msec (fig. 1).

Following control tracings the following inter-

ventions were performed: (1) amyl nitrite was

given by inhalation; (2) phenylephrine (50–100

µg/min) and (3) isoproterenol (1–2 µg/min) were

given intravenously until significant heart

rate and blood pressure responses occurred;

(4) sustained hand grip was performed by

having the patient maximally squeeze the rolled

cuff of a sphygmomanometer for 45 sec with

instructions to continue relaxed breathing so as to

avoid a Valsalva maneuver; (5) right atrial

pacing was performed at increasing rates until

*Statham Instruments, Inc., Hato Rey, Puerto

Rico.

†Carolina Medical Electronics, P. O. Box 307, King,

North Carolina.

‡Electronics for Medicine, White Plains, New

York.

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Capture could no longer be obtained, and steady-state measurements were made 5–10 min after each increase in pacing rate; and (6) spontaneous isorhythmic dissociation was studied in one patient, in whom the P-R interval varied from 0 to 230 msec while the ventricular rate remained constant.

For each control and each intervention at least five complexes were counted and averaged. The following mean values were calculated for each group of complexes: (1) R-R and P-R interval of the electrocardiogram; (2) external left ventricular ejection time, measured from the rapid upstroke to the nadir of the incisura of the external carotid pulse tracing; (4) the interval from the Q wave of the electrocardiogram to the onset of rapid left ventricular pressure rise, this interval representing "true" electrical-mechanical delay; (5) the interval from the Q wave of the electrocardiogram to A₂; (6) the interval from the first high amplitude vibration of S₁ to A₂; (7) true isovolumic contraction time, measured from the onset of the rapid rise of left ventricular pressure to the upstroke of the central aorta pressure; and (8) maximal rate of rise in left ventricular pressure (dp/dt).

Two external indices were derived as follows: (1) Preejection period (PEP) was designated as the Q-A₂ interval minus external ejection time. (2) External isovolumic contraction time, designated as the S₁-A₂ interval minus external ejection time. Intervals were counted to the nearest 4 msec.

Illustrative tracing from which data were obtained (patient T.B.). Simultaneous recording of electrocardiogram, LV pressure and its first derivative, dp/dt, external and internal ejection time, and external and internal sound. The duration of ejection time measured from the external carotid pulse is identical to that measured directly from the central aorta. Note however the delay in the upstroke and incisura in the external carotid tracing as compared to the central aorta tracing. The central aorta incisura corresponds exactly to the aortic closure sound. Intervals were counted to the nearest 4 msec. Paper speed 100 mm/sec. Times lines = 20 msec.

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## Summary of Hemodynamic Data

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<th>∆I-LVET (msec)</th>
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Abbreviations: Q-LV = interval from Q wave to rapid onset of LV pressure rise; I-LVET = internal left ventricular ejection time measured from central aorta with micromanometer; E-LVET = external LVET from carotid pulse; PEP = preejection period (Q to A) – (E-LVET); ICT = internally measured isovolumic contraction time; E-ICT = externally measured ICT (M to A) – (E-LVET); C = control; P = phenylephrine; AN = amyl nitrite; I = isoproterenol; HG = sustained hand grip; ID = isorhythmic dissociation.

*P-R interval of 0 serves as control. ∆ refers to deviation of values from control as P-R interval varies.

† In this instance, a common control value is used for P infusion (early and late responses) and AN inhalation.

‡ Spontaneous rate of 64/min serves as control state. ∆ refers to deviation from control at the indicated pacing rates.

§ Maximal left ventricular dp/dt. Results are expressed as percentage change from control value.
### Results

The hemodynamic data are shown on table 2. A tabulation was made of externally and internally measured LVET, PEP, internal ICT, external ICT, and electrical-mechanical delay. Changes in each of these intervals and in left ventricular $\frac{dp}{dt}$, produced by the interventions, are shown. From this data no attempt was made to define normal responses to the interventions, since more than one

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<th>PEP (msec)</th>
<th>Δ PEP (msec)</th>
<th>ICT (msec)</th>
<th>Δ ICT (msec)</th>
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<td>-3</td>
<td></td>
</tr>
<tr>
<td>-119</td>
<td>110</td>
<td>+8</td>
<td>70</td>
<td>+14</td>
<td>35</td>
<td>-3</td>
<td></td>
</tr>
<tr>
<td>-135</td>
<td>109</td>
<td>+7</td>
<td>70</td>
<td>+14</td>
<td>47</td>
<td>+9</td>
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</tr>
</tbody>
</table>
intervention was used in each patient, usually at 10- to 15-min intervals. Attention was directed primarily to the correlation between changes in externally and internally measured indices produced by the interventions.

**Comparison of Externally and Internally Measured Left Ventricular Ejection Time**

The durations of internally and externally measured left ventricular ejection times are plotted on figure 2. The absolute values are essentially identical, ranging from 175 to 395 msec for externally measured ejection time and from 169 to 392 msec for internally measured ejection time. Following interventions, the resultant changes in ejection times were also identical whether measured externally or internally (fig. 3). Ejection times were prolonged by phenylephrine infusion and, during isorhythmic dissociation, by an appropriate P-R interval when a P-R interval of 0 was used as the control. Left ventricular ejection time was shortened by nitrite inhalation, sustained hand grip, isoproterenol infusion, and by right atrial pacing at increasing rates. Using right atrial pacing (fig. 4), it was possible to shorten left ventricular ejection time from a resting value of 309 to 169 msec (measured internally) and to 174 msec (measured externally). Close correlation between changes in internally and externally measured ejection time occurred throughout this range of values.

**Comparison of Preejection Period and External Isovolumic Contraction Time with True Isovolumic Contraction Time**

Two externally measured preejection events, external isovolumic contraction time and preejection period, were compared with internally measured or true isovolumic contraction time. The absolute values differed for each of these three parameters both at rest and following interventions. The average duration was 47 msec for external isovolumic contraction time, 63 msec for true isovolumic contraction time, and 99 msec for preejection period. Absolute values for preejection period were compared with those for true isovolumic contraction time (fig. 5). Values for preejection period range from 50 to 139 msec while the range of values for true isovolumic contraction time is from 26 to 100 msec. Although the absolute values differ, there is a

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**Figure 2**

Comparison of internally and externally measured ejection times, showing nearly identical values. Control values and those following interventions are included. The interventions are identified by symbols. The line on each side of the regression line is one standard deviation (±1 s.d.); R = correlation coefficient.

**Figure 3**

Correlation of changes in externally and internally measured ejection time produced by the various interventions. Each point represents the change from control value produced by that intervention.
Effect of right atrial pacing at increasingly rapid rates on externally and internally measured left ventricular ejection time. As the pacing rate increases, externally and internally measured ejection times shorten to the same degree, with the absolute values remaining identical.

**Figure 4**

![Graph showing the effect of right atrial pacing on left ventricular ejection time.](image)

A close correlation between pre-ejection period and true isovolumic contraction time ($r = 0.90$). A significant correlation of absolute values is also shown between external isovolumic contraction time and true isovolumic contraction time ($r = 0.75$) (fig. 6).

In order to examine more closely the comparative effects of the various interventions on pre-ejection period and true isovolumic contraction time and on external isovolumic contraction time and true isovolumic contraction time, only the changes produced by the interventions are plotted on figures 7 and 8. A high correlation between changes in pre-ejection period and true isovolumic contraction time was found ($r = 0.94$). In addition the magnitude of the change produced by the various interventions is nearly identical for pre-ejection period and isovolumic contraction time. A similar comparison between changes in external isovolumic contraction time and true isovolumic contraction time shows a significant correlation ($r = 0.77$).

**Effect of Interventions on Left-Sided Electrical-Mechanical Delay (Q to LV Pressure Rise Interval)**

The time from the Q wave to the onset of rise in left ventricular pressure did not change significantly with the various interventions. The control values and those following the interventions are tabulated on table 2.
The changes in pre-ejection period (Δ PEP) produced by the various interventions are plotted on the ordinate against the changes in internally measured ICT (Δ “true” ICT) plotted on the abscissa. Note the high correlation (R = 0.94) as well as the similarity in magnitude of the changes in these two indices produced by the various interventions.

Figure 7

The average control value was 35 msec (SEM = ±2.8). The average time for Q to left ventricular pressure rise was then determined for two groups of interventions: (1) those which shortened and (2) those which lengthened preejection time. The first group of interventions included isoproterenol infusion, amyl nitrite inhalation, and a P-R interval of 0.75 to 0.200 msec, when a P-R interval of 0 was used as control during spontaneous isorhythmic dissociation. These interventions shortened preejection period by an average of 23 msec, true isovolumic contraction time by 21 msec, and external isovolumic contraction time by 12 msec. The time from the Q wave to LV pressure rise following this group of interventions was 36 msec (SEM = ±2.1).

Figure 8

The changes in externally measured ICT (Δ external ICT) produced by the various interventions are plotted on the ordinate against Δ “true” ICT plotted on the abscissa. A significant correlation is found with a correlation coefficient (R = 0.75).

Figure 9

Tracking of externally measured indices is demonstrated as the absolute values are changed on a beat-to-beat basis in a patient (C.R.) with isorhythmic dissociation. An appropriate PR interval, 75–200 msec, prolongs ejection time and shortens isovolumic contraction time. Note that the change in ejection time is greater than in preejection period and isovolumic contraction time, the net result being prolongation in total duration of systole. Each point represents the average value for 10 complexes at the PR interval indicated on the abscissa.

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DIRECT CORRELATION OF TIME INTERVALS

Q-A
Q-A2
QA
nsc
IP/
P
f
PR
msec
H -
RR
= 940
RR
= 960
msec
A
Figure 10
Tracing taken during a period of spontaneous isorhythmic dissociation (patient C.R.) showing beat-to-beat changes in indices as a function of the PR interval. As PR interval changes from 180 msec to 0 there is identical shortening of externally and internally measured ejection time and identical prolongation of PEP and true ICT. Note also the drop in dp/dt associated with an inappropriate PR interval.

showing no significant change from the control time of 35 msec. Interventions prolonging preejection time were phenylephrine infusion, sustained hand grip, and to a minimal extent, right atrial pacing. The time from the Q wave to the onset of left ventricular pressure rise with these interventions averaged 40 msec (SEM = ±1.8) and did not differ significantly from the control value (P > 0.20).

Effect of a Varying P-R Interval on Beat-to-Beat Changes in Externally and Internally Measured Indices

Changes in internally and externally measured preejection time and ejection time and dp/dt were correlated during a period of spontaneous isorhythmic dissociation in one patient. Successive beats were grouped according to P-R interval, and values for preejection period, true isovolumic contraction time, and externally and internally measured ejection time were plotted (fig. 9). There was close tracking of the increase in internally and externally measured ejection time as the P-R interval prolonged beyond 75 msec. Concurrently, there was parallel shortening of preejection period and isovolumic contraction time. Total systole (measured externally) and mechanical systole (measured internally) prolonged in parallel fashion with lengthening of the P-R interval beyond 75 msec. A sample of the tracing from which these measurements were made is shown in figure 10. Three successive beats are shown having P-R intervals of 180, 84, and 0 msec. As the P-R interval decreases from an optimal duration of 180 msec to 0, internally and externally measured ejection times are seen to shorten identically while PEP and ICT lengthen. Simultaneously, the
Figure 11

The changes in pre-ejection period (Δ PEP) produced by the interventions are plotted (in msec) on the ordinate against changes in left ventricular dp/dt (Δ dp/dt) which is expressed as percent change from the control value. Interventions are shown to change PEP and dp/dt in an inverse manner.

Q-A₂ interval shortens, and maximal left ventricular dp/dt decreases while the R-R interval remains essentially constant.

Comparison of Changes in Pre-ejection Period and Maximal Left Ventricular dp/dt Following Interventions

Changes in preejection period were correlated with changes in maximal rate of left ventricular pressure rise (dp/dt) following interventions. The data obtained from four patients is shown in figure 11. There was an inverse relationship between changes in dp/dt and preejection period, the response being most evident following isoproterenol infusion.

Discussion

Noninvasive methods have been widely used to measure left ventricular ejection time. During steady-state conditions they have been found to correlate with internal measurements using fluid-filled catheter systems. However, it is possible that acute interventions might change this static relationship. Changes in velocity and acceleration of flow and changes in vessel compliance might change internally and indirectly measured ejection time to a different degree. There is also a variable delay in ejection time measured from the external carotid pulse, dependent on the pulse wave velocity. This delay, the interval from the aortic second sound to the nadir of the incisura of the external carotid pulse tracing, measures from 10 to 35 msec. It varies between different individuals and may also vary in a given patient under various physiologic conditions.

This study was designed to clarify these issues in the following manner. First, the interventions were selected to alter systolic time intervals through various mechanisms including changes in contractility, preload, afterload, heart rate, or a combination of these. Contractility and rate, for example, are altered markedly by isoproterenol. Preload and stroke volume were varied on a beat-to-beat basis by changing the P-R interval. Afterload was acutely decreased by amyl nitrite inhalation and increased by sustained hand grip and phenylephrine. All of the interventions used in this study are understood to have modes of action in addition to those listed above. Secondly, the problem of time delay was studied using catheter-tip micromanometer for central measurements. Using this catheter we found, as have others, that the nadir of the central aorta pressure incisura corresponds exactly to the internally and externally recorded A₂. This point is delayed from A₂ when measured by a fluid-filled catheter system, even when recorded in the central aorta.

The results of this study show that the initial values for ejection times, and the changes in these values produced by acute interventions, are identical when measured internally or externally. This correlation establishes the validity of measuring true ejection time from the external carotid pulse tracing under dynamic as well as steady-state conditions. The onset of left ventricular ejection can be determined from a high-quality external carotid pulse tracing by correcting for delay, which is the interval from the aortic second sound to the nadir of the carotid tracing incisura. This delay should be measured for
each complex and should not be assumed to remain constant under dynamic conditions.

Of the two externally measured preejection intervals, preejection period and external isovolumic contraction time, the former was found to correlate more closely with internally measured true isovolumic contraction time. Since preejection period is an indirect measure of the total electromechanical preejection time (Q to S₂ - LVET), it is longer in duration than true isovolumic contraction time which measures only mechanical preejection time. External isovolumic contraction time measures that portion of isovolumic contraction time following the first heart sound. The interventions used in this study theoretically might have altered only the premechanical component of preejection time (Q - onset of LV pressure rise), mechanical preejection only, or both components. The results showed nearly identical changes in preejection time and true isovolumic contraction time during the interventions, suggesting that only the mechanical component was significantly altered. The time from the Q to the onset of left ventricular pressure rise was not changed by the interventions. In particular, this interval showed no tendency to shorten during those interventions which significantly shortened other preejection intervals. This interval encompasses the time required for left ventricular activation and electrical-mechanical coupling. Since only the mechanical component of preejection period is changed by the interventions, it is concluded that changes in preejection period are identical to changes in internal or true isovolumic contraction time.

Previous studies have shown most of the shortening of the preejection period by beta-adrenergic receptor activating agents and deslanoside (Cedilanid-D) to occur after the onset of the first heart sound. All the prolongation in preejection period accompanying pharmacologic vasoconstriction occurred after onset of the first heart sound. In the present study external isovolumic contraction time tended to shorten slightly less in most instances than either preejection period or true isovolumic contraction time. Although this difference was not statistically significant (P > 0.10), it suggests that external isovolumic contraction time does not record all of the shortening in preejection period produced by the interventions. External isovolumic contraction time was more difficult to measure because of difficulty in consistently identifying the first high-frequency component of S₁. Others have also found clear identification of S₁ to be a source of recurring difficulty in measuring external isovolumic contraction time.⁴ ⁷

Spontaneous isorhythmic dissociation with a relatively constant R-R interval provided a unique opportunity to study the relationship of beat-to-beat P-R-interval changes to preejection period, ejection time, and total duration of systole in the presence of a normal QRS complex. Externally measured indices were shown to be sensitive in that they accurately reflected the rather small beat-to-beat changes in internal measurements. Total duration of systole has been found to be variably affected by acute changes in stroke volume brought about by changes in preload. Wallace et al. found in a right heart bypass preparation that prolongation of ejection was accompanied by an equal but opposite change in isovolumic contraction time resulting therefore in no change in the total duration of systole. Katz and Wiggers found total duration of systole to prolong when stroke volume was increased by augmented venous pressure. Results of the present study support those of Harley et al. who found the total duration of systole to increase when stroke volume was augmented by an appropriate P-R interval during pacing studies in patients with complete heart block.

Preejection period was shown to correlate in an inverse manner with left ventricular dp/dt. Dp/dt was chosen as a reproducible, sensitive, and practicable direct measure of myocardial performance. Provided that preload and aortic diastolic pressure are kept constant, acute changes in left ventricular peak dp/dt reflect alterations in contractile properties of the myocardium. In the present studies, using acute interventions in awake, fully
reflexic man, no attempt was made to control these variables. Left ventricular dp/dt has been shown in animals and in man to vary directly with changes in preload, directly with heart rate due to Treppe phenomena, and directly with aortic diastolic pressure, provided only one parameter is changed while the other two are held constant. Recognizing these limitations, changes in preejection period were directly correlated with changes in dp/dt. Our results support those of Metzger et al. who found an inverse relationship between left ventricular dp/dt and true isovolumic contraction time in studies on anesthetized dogs using acute interventions. The relationship between true isovolumic contraction time or preejection period, aortic diastolic pressure, and dp/dt may be compared to a right triangle in which the base is represented by isovolumic contraction time, the height by the aortic diastolic pressure, and the hypotenuse by dp/dt. Therefore it may be stated in general that if the difference between aortic diastolic pressure and left ventricular end-diastolic pressure remains constant, acute changes in preejection period reflect inverse changes in left ventricular dp/dt.

In conclusion, externally measured systolic time intervals provide a sensitive, safe, and reproducible means for measuring myocardial performance. They accurately reflect the simultaneously measured internal counterparts and left ventricular maximal dp/dt. Of particular interest is the observation that acute interventions did not change the interval of Q to left ventricular pressure rise, substantiating the observation that changes in preejection period and true isovolumic contraction time produced by various interventions are similar. Systolic time intervals are therefore a valid method: (1) for evaluating physiologic and pharmacologic interventions; (2) for following cardiac performance during acute illness; (3) for objective evaluation of various forms of therapy; and (4) for use in other situations where repeated measurements over a period of time are desirable. When emphasis is placed on measuring changes in indices with the individual serving as his own control, the need to compare individual values to the rather broad range of variable group norms is eliminated.

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References

1. Wiggers CJ: Studies on the consecutive phases of the cardiac cycle: The duration of the consecutive phases of the cardiac cycle and the criteria for their precise determination. Amer J Physiol 56: 415, 1921
2. Wiggers CJ: Studies on the consecutive phases of the cardiac cycle: II. The laws governing relative duration of ventricular systole and diastole. Amer J Physiol 56: 439, 1921


17. Lind AR, McNicol GW: Circulatory responses to sustained hand grip contractions performed during other exercise, both rhythmic and static. J Physiol (London) 192: 595, 1967


Direct Correlation of External Systolic Time Intervals with Internal Indices of Left Ventricular Function in Man

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