Noninvasive Stress Testing
Methodology for Elimination of the Phonocardiogram

DAVID H. SPODICK, M.D., D.SC., AND VERONICA QUARRY LANCE, M.S.

SUMMARY Measurement by systolic time intervals (STI) of cardiac responses requires extremely careful recording during actual stress test performance. Previous work indicated no significant changes in the pulse transmission time (PTT) during exercise and other challenges. Since external STI depend on the carotid pulse offset by the PTT as an aortic curve equivalent, stable PTT implies that timing of the carotid upstroke (CARu) and the carotid incisura (CARi) would respectively pre-ejection period (i.e., the externally calculated onset of the aortic upstroke) and the aortic incisura which is externally timed by the aortic component of S1 (IIa).

BECAUSE THE EXTERNALLY MEASURED systolic time intervals (STI) reflect corresponding hemodynamic events, they have become a well established practical tool for assessing left ventricular function and responses to physiologic and pharmacologic challenges. STIs are measured from simultaneously recorded electrocardiogram (ECG), phonocardiogram (PCG), and carotid displacement (CAR) traces. Recent work has shown that with great care the STI can be measured during the actual performance of exercise and other stress tests, rather than only in the post-stress state. A prime difficulty in making measurements during muscular effort and postural changes has been recording PCGs on which heart sounds can be timed with precision. One implication arising from our earlier studies (see below) was that STI responses during cardiocirculatory challenges could be measured without the PCG. But this remained to be demonstrated. Elimination of the PCG during stress testing would have distinct advantages: 1) reduction in sensing and recording equipment, 2) reduction in personnel needed to monitor stability of microphones and curve registration, and 3) reduction in the number of data points to arrive at the same results. Moreover, this last advantage implies reduction in sources of potential error and reduction in the time required to make measurements.

Theoretical Basis
The three commonly measured STIs include left ventricular ejection time (LVET), the timing of the aortic component of the second heart sound (q IIa), which is also known as electromechanical systole or EMS, and the pre-ejection period (PEP). Left ventricular ejection time is measured directly from the carotid pulse curve, while EMS requires a phonocardiogram to register IIa. Measuring PEP...
also requires a PCG since it is determined by the difference, i.e., PEP = EMS minus LVET. Calculation of the STI from external recordings depends entirely on the use of the carotid as a displaced aortic curve (fig. 1); this use of the carotid is made possible by two conditions: 1) both the upstroke of the aortic curve and the aortic incisura are delayed by identical or nearly identical pulse transmission time (PTT) in reaching the neck, where their respective counterparts are picked up as the carotid upstroke (CARu) and carotid incisura (CARIN) and 2) the aortic incisura is contemporaneous with the aortic second sound (IIA), which becomes its external marker. Thus, LVET is practically identical when measured from either the carotid or the aortic curve.

The externally measured PEP is the time from q to onset of ejection obtained by statistically moving the carotid upstroke backward by a period equal to the PTT so that CARu minus PTT measures the time of the aortic upstroke, i.e., the onset of ejection. Yet, this relationship is not clear from the customary “shortcut” measurement by which PEP = EMS minus LVET. It becomes apparent only if the PTT (which cancels in the shortcut measurement) is separately calculated. Thus, PEP = CARu minus PTT. Since (q → IIA) measures the timing of the aortic incisura, CARIN minus IIA measures the time between incisuras, i.e., the PTT. Differently stated,

1) PEP = EMS - LVET (i.e., EMS minus LVET).
2) PEP = (q → IIA) - (q → CARIN) - (q → CARu).

Cancelling q, since PEP = time from q to ejection onset (q → ejection),

3) PEP = IIA - (CARIN - CARu).

Rearranging terms,

4) PEP = CARu - (CARIN - IIA).

Since (CARIN - IIA) = PTT,

5) PEP = CARu - PTT.

Equation (5) implies that in circumstances during which PTT does not change, measurement of CARIn will track IIA and measurement of CARu will track PEP. These preconditions have been met during a wide variety of cardiovascular challenges during which the PTT was not changed significantly; in only one (isometric handgrip) changes in PTT were miniscule and only reached significance because they were directionally similar. It is worth emphasizing that bias was avoided in these studies because individual data points were measured blindly.

Hypothesis

It follows from the foregoing that during the challenges investigated, all of which were common stress tests with well understood physiologic responses, measurements of changes in CARu should be equivalent to the response of PEP and changes in CARIn should be equivalent to the response of EMS. Therefore if these can be independently demonstrated, then STI responses during stress testing can be accurately measured without using a phonocardiogram.

Methods

Ten healthy males with normal ECG, chest X-ray, medical history, physical examination and signed informed consent, volunteered for this study. Subjects ranged in age from 22 to 35 years and none had previously been tested in our laboratory.

Studies were conducted on each subject on two separate mornings in the postabsorptive state. One morning included change in posture, prompt and sustained squatting and isometric handgrip exercise while the other morning was used for bicycle ergometry.

Posture Series. 1) Supine position: recorded after 15 minute rest period in supine position. 2) Sitting: recording taken two minutes after transition from supine to sitting position. 3) Standing: recording taken two minutes after transition from sitting to standing position. 4) Squat: recording taken at onset of squat (prompt squat, i.e., abrupt transition from standing to squatting position) and again after two minutes of uninterrupted squatting.

Isometric Handgrip (IHG). IHG was accomplished by having the subjects squeeze a rolled pressure cuff. Fifteen minute rest periods followed by control recordings preceded each IHG. Recordings of IHG were taken without interrupting the exercise at four minutes of 30% maximum voluntary contraction (MVC) and at one minute of 50% MVC. All control and IHG recordings were taken with subjects seated on a cushioned chair.

Bicycle Ergometry. Subjects exercised at 50, 100 and 150 watt loads. The procedure for each bout of exercise was identical: twenty minute rest period followed by control recordings; four minutes of bicycle exercise with recordings taken at the fourth minute without interrupting the exercise,
TABLE 1. PEP versus CARu during Cardiocirculatory Challenges

<table>
<thead>
<tr>
<th></th>
<th>Slope (msec/msec)</th>
<th>Intercept (msec)</th>
<th>Correlation coefficient (r)</th>
<th>Coefficient of determination (r^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posture series</td>
<td>1.01</td>
<td>35.85</td>
<td>+0.91</td>
<td>0.82</td>
</tr>
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<td>IHG—controls</td>
<td>0.98</td>
<td>54.03</td>
<td>+0.88</td>
<td>0.77</td>
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<tr>
<td>IHG</td>
<td>0.90</td>
<td>39.55</td>
<td>+0.80</td>
<td>0.64</td>
</tr>
<tr>
<td>Bicycle—controls</td>
<td>1.03</td>
<td>33.18</td>
<td>+0.92</td>
<td>0.85</td>
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<tr>
<td>Bicycle—exercise</td>
<td>0.98</td>
<td>42.17</td>
<td>+0.87</td>
<td>0.76</td>
</tr>
<tr>
<td>Bicycle—recovery</td>
<td>0.91</td>
<td>48.63</td>
<td>+0.97</td>
<td>0.94</td>
</tr>
<tr>
<td>Combined series</td>
<td>0.92</td>
<td>46.67</td>
<td>+0.92</td>
<td>0.94</td>
</tr>
<tr>
<td>without IHG</td>
<td>0.94</td>
<td>45.78</td>
<td>+0.98</td>
<td>0.96</td>
</tr>
</tbody>
</table>

and recovery recordings with subjects seated on the bicycle taken at 30 seconds, and one and five minutes.

Recordings. The ECG, PCG and CAR were simultaneously recorded on an eight channel Hewlett Packard recorder No. 568-100A. The bipolar ECG was recorded via disposable electrodes over the upper and lower sternal borders with a ground electrode on the subject's side. The PCG was recorded at the mesoapect via a Hewlett Packard model A/B contact microphone at a nominal filter frequency of 50 Hz. The CAR was recorded from the right carotid artery via a Hewlett Packard model A/B contact microphone and signal splitter.

Measurements and Calculations. The following points were measured from the q wave: aortic component of the second heart sound on the PCG, the CARu and CARIN. PEP was calculated as CARu - (IIa → CARIN). EMS was the time from q to IIa(q → IIa).

Five beats were measured on each of the recordings of each subject. The mean CARu, CARIN, PEP and EMS from these five beats were the values used in the statistical analyses of the data.

Statistical Analysis. The correlation coefficient \(r\), slope (b), intercept (a) and standard error of estimate (see \(SD\)) were calculated for PEP versus CARu and for EMS versus CARIN. The analysis was made for each of the following conditions: 1) posture series, 2) control recordings for IHG, 3) IHG at 30% and 50% MVC, 4) control recordings for bicycle ergometry, 5) bicycle ergometry at 50, 100 and 150 watts, 6) recovery recordings from bicycle ergometry, and 7) all six conditions above combined.

Results

The results are summarized in tables 1 and 2 and plotted in figures 2 and 3. Individual correlation coefficients were high and \(P\) values for the correlations were uniformly less than 0.001. The overall correlation was +0.97 for PEP versus CARu and +0.99 for EMS versus CARIN. Because the comparison is of nonidentical quantities, coefficients of determination \(r^2\) were also calculated to indicate the degree of covariation. For EMS vs CARIN, \(r^2\) ranged from 94 to 98% (table 2). For PEP vs CARu \(r^2\) ranged from 64 to 94%. However, the 64% value was for IHG, all other values exceeding 76%.

For clarity, the illustrations show only three kinds of sym-

TABLE 2. IIa (EMS) versus CARin during Cardiocirculatory Challenges

<table>
<thead>
<tr>
<th></th>
<th>Slope (msec/msec)</th>
<th>Intercept (msec)</th>
<th>Correlation coefficient (r)</th>
<th>Coefficient of determination (r^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posture series</td>
<td>0.97</td>
<td>49.49</td>
<td>+0.97</td>
<td>0.94</td>
</tr>
<tr>
<td>IHG—controls</td>
<td>0.96</td>
<td>51.24</td>
<td>+0.98</td>
<td>0.96</td>
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<tr>
<td>IHG</td>
<td>0.99</td>
<td>32.03</td>
<td>+0.97</td>
<td>0.94</td>
</tr>
<tr>
<td>Bicycle—controls</td>
<td>1.05</td>
<td>19.40</td>
<td>+0.99</td>
<td>0.98</td>
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<tr>
<td>Bicycle—exercise</td>
<td>1.05</td>
<td>26.12</td>
<td>+0.99</td>
<td>0.98</td>
</tr>
<tr>
<td>Bicycle—recovery</td>
<td>0.97</td>
<td>48.62</td>
<td>+0.99</td>
<td>0.98</td>
</tr>
<tr>
<td>Combined series</td>
<td>0.97</td>
<td>48.35</td>
<td>+0.99</td>
<td>0.98</td>
</tr>
</tbody>
</table>

FIGURE 2. Pre-ejection period (PEP) plotted against corresponding timing of carotid incisura (CARu) for each data point. Each series consolidated to one symbol for clarity (see table 1). Exercise data appear at the lower ranges of PEP and CARu and fit the regression curve as well as do the other points.

FIGURE 3. Electromechanical systole (EMS = q → IIa) plotted against corresponding time of carotid incisura (CARIN) for each data point. Each series consolidated to one symbol for clarity (see table 2). Exercise data appear at the lower ranges of EMS and CARIN and fit the regression curve as well as do the other points.
bol. Accordingly, the exercise data points have the smallest numeric coordinates on both the ordinate and the abcissa.

Discussion

The results demonstrate that the carotid upstroke closely tracks the pre-ejection period and that the carotid incisura closely tracks the aortic component of the second heart sound. The tracking relationships show slopes and correlation coefficients close to 1.00. Figures 2 and 3 show that the data at all points have very little scatter from the regression line. The most scatter was during IHG. This is reflected in its relatively low coefficients. Thus, measurements of CARu and CARIN can be used, respectively, in place of PEP and EMS (IIa) in certain stress tests, with the exception of IHG during which CARu varies with PEP but predicts it to a too limited (64%) extent. Indeed, if the combined series is recalculated without IHG, the overall values improve as shown in the last line of table 1. (The near-perfect correlations for EMS in table 2 make calculation redundant.) Conversion to PEP and EMS is readily performed by using the data in tables 1 and 2 as regression equations for the appropriate control or challenge state. For PEP, the general formula for this is:

$$\text{PEP} = \frac{\text{CARu} - a}{b}$$

and for EMS:

$$\text{EMS} = \frac{\text{CARIN} - a}{b}$$

References

5. Quarry VM, Spodick DH: Cardiac responses to isometric exercise: Comparative effects with different postures and levels of exertion. Circulation 49: 905, 1974

The Incidence of Bacteremia in Pediatric Patients Following Tooth Extraction

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SUMMARY Procedures which produce bacteremias may lead to bacterial endocarditis in the susceptible patient. Recent work has suggested that bacteremia does not occur in children following extraction of teeth as it does in adults. One hundred and seven children were divided into four groups. Group 1, which consisted of children who had nondiseased primary teeth extracted, had 35% positive blood cultures. Group II consisted of children who had diseased primary and permanent teeth removed. The incidence of positive blood cultures was 53%. Group III, which consisted of patients who had extractions of nondiseased permanent teeth, had a 61% incidence of positive blood cultures. Group IV served as a negative control. Bacteremias do occur in children following the extraction of normal and diseased primary and permanent teeth. Therefore, the susceptible pediatric patient who is to undergo a dental extraction procedure must be given prophylactic antibiotics.

THE ASSOCIATION of the bacteremia which follows tooth extraction with subsequent subacute bacterial endocarditis (SBE) was recognized forty-five years ago. However, evidence from experimental work which firmly established the causal relationship between the bacteremia and the onset of SBE has only recently been reported. Although direct evidence in man is lacking, the fact that the bacteremia following dental extraction may result in SBE in the susceptible patient must be seriously considered. The patient most susceptible to SBE following a bacteremia is the one with underlying valvular heart disease. Congenital and rheumatic heart diseases are the most common predisposing factors, but other types of heart disease which result in turbulent blood flow in the heart may also predispose a patient to the disease. The administration of prophylactic antibiotics to reduce the probability of the occurrence of SBE in the susceptible patient who is to undergo
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