A New, Noninvasive Technique for Inducing Post-extrasystolic Potentiation during Echocardiography

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SUMMARY Left ventricular function was evaluated in 34 patients with the echocardiogram, and an external mechanical cardiac stimulator was used to induce a ventricular premature contraction (VPC) noninvasively. Extent of post-extrasystolic potentiation (PESP) was determined by comparing systolic dimensional shortening and ejection fraction of the sinus beat preceding the VPC to that of the potentiated beat which followed it. Using this technique, a VPC could be introduced into the cardiac cycle of 30 of the 34 patients, six of whom were free of obvious cardiac disease and 24 of whom had valvular, coronary or myopathic heart disease. The only complication observed was mild breast ecchymosis in a female patient. Systolic dimensional shortening and ejection fraction increased from control values by an average of 21% and 17% respectively, with a range of 0–100%. The degree of PESP was very reproducible in repeat studies and when the same patients were subsequently evaluated during a spontaneously occurring or catheter-induced VPC. This technique can safely and reliably induce post-extrasystolic potentiation during echocardiography and is a potentially important adjunct to the noninvasive evaluation of left ventricular function.

THE AUGMENTATION OF MYOCARDIAL CONTRACTILITY that occurs in the normally conducted beat following a ventricular extrasystole is referred to as post-extrasystolic potentiation (PESP). Evaluation of the effect of PESP on ventricular contraction (determined by ventriculographic study of left ventricular wall motion) has demonstrated that areas of ventricular wall that exhibit absent or diminished motion during regular cardiac cycles often exhibit augmented contraction during the post-extrasystole beat. In patients with coronary artery disease, the degree of regional and global improvement of left ventricular function with PESP (measured by augmentation of axis shortening and ejection fraction) has proven useful in predicting: 1) which areas of myocardium supplied by stenosed coronary arteries are reversibly rather than irreversibly damaged, and hence suitable for myocardial revascularization; and 2) which patients with depressed ventricular function have the greatest amount of contractile reserve, and thus are more likely to tolerate myocardial revascularization. The effects of PESP in other forms of heart disease have also been studied by ventriculography in our laboratory, but no firm conclusions as to the clinical value can be made at present.

If a technique were available to measure the effects of PESP on left ventricular function noninvasively, it could complement — and hopefully replace — similar ventriculographic studies in some patients. Such a technique would have to combine noninvasive methods both for evaluating left ventricular function and introducing ventricular premature contractions safely into the cardiac cycle. At present, echocardiography is one of the most widely used noninvasive techniques for evaluating left ventricular function, but until recently no noninvasive method for consistently and safely eliciting ventricular premature contractions has been available. In 1976, Zoll et al. reported studies utilizing an external mechanical stimulator capable of introducing ventricular beats into the cardiac cycle. They used the device as an external emergency pacemaker, but in the present report it was employed to induce ventricular premature contractions, thereby allowing evaluation of the effects of PESP on left ventricular function. Specifically, in these initial studies, the effects of PESP were determined during echocardiography by measuring induced changes in systolic dimensional shortening and ejection fraction.

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reproducing similar degrees of augmentation with repeat studies. We also correlated the extent of augmentation of ventricular performance induced with the external stimulator and that resulting from spontaneously occurring or catheter-induced ventricular premature contractions during both echocardiography and cine left ventriculography.

Materials and Methods

Patient Selection

Three criteria were used in selecting subjects for this study: 1) the clinical condition was stable; 2) the patient was in regular sinus rhythm (without left bundle branch block); and 3) a technically adequate echocardiographic tracing of the basal septum and posterior wall could be recorded reproducibly with the patient lying supine or rotated slightly to the left. The 34 patients who were studied ranged in age from 19 to 76 years (mean 52 years); 33 were male. Six patients had no heart disease, 16 had coronary artery disease, six had valvular heart disease and six had primary myocardial disease. All patients gave informed consent for these studies.

Induction of Premature Ventricular Contractions

The ventricular premature contractions were induced with the external mechanical cardiac stimulator positioned on the precordium, either at or near the point of maximum impulse, but not over the nipple (fig. 1). The stimulator was a modified electrically powered stapling gun attached to a control box containing potentiometers and synchronizing switch. Thus, electrical current could be used to produce mechanical stimuli of varying force (calibrated from 0.7 to 1.5 joules). Before the stimulator was discharged on the precordium, it was first discharged on the patient's palm to prepare him for the sensation. On the precordium, the stimulator was discharged manually when the inscription of the T wave was observed on an oscilloscope. (Electronic triggering of the stimulator should be possible on future models of the device.) No patient experienced more than five attempts at inducing ventricular extrasystoles.

Echocardiographic Procedures

Echocardiograms were recorded using M-mode scans (figs. 2 and 3) with the patients either supine or rotated slightly to the left. A Smith Kline Instruments Ekoline 20 System (employing a 2.25 MHz transducer) coupled to an Irex Continutrace 101 Multichannel Recorder was utilized for all studies. Left ventricular dimensions were measured from the left septal to the posterior endocardial echo at or near the point where the most apical echoes of the mitral valve were registered. Onset of the QRS complex was used as a marker for end-diastolic diameter; end-systolic diameter was measured as the point of maximal posterior wall excursion. Systolic dimensional shortening was defined as end-diastolic diameter minus end-systolic diameter divided by end-diastolic diameter (multiplied by 100%). Left ventricular end-diastolic and end-systolic volumes and ejection fraction were calculated as described by Teichholz et al. To determine the degree of PESP, systolic dimensional shortening and ejection fraction of the postextrasystolic beat was compared to that of the sinus beat preceding the ventricular premature contraction. Within 24 hours of the initial echocardiographic studies, seven patients were restudied by echocardiography during cardiac catheterization just prior to angiocardiography. During the second echocardiographic evaluation, a pacing catheter inserted into the right ventricular cavity was used to induce ventricular extrasystoles either by rotating it against the ventricular wall or by connecting it to an R-wave coupled stimulator.

Cardiac Catheterization Procedures

Ventricular premature contractions were induced during left ventriculography in eight patients by again rotating a pacing catheter against the right ventricular wall, by con-

Figure 1. Technique for introducing ventricular extrasystoles during echocardiography. The external mechanical cardiac stimulator is positioned on the precordium and is manually triggered by the physician when the T wave is inscribed on the oscilloscope.
necting it to an R-wave coupled stimulator, or as a result of the power injection of angiographic contrast medium. Left ventriculography was performed with multiholed angiographic catheters using power injections of 35–50 ml of 76% meglumine sodium diatrizoate over a 3–4 second period and recorded on 16 mm or 35 mm cine film. Ventricular volumes and ejection fractions were determined from sequential end-diastolic and end-systolic silhouettes of the left ventricle in either a single plane (30° right anterior oblique) projection or biplane (30° right anterior oblique and 60° left anterior oblique) projections using a grid calibration system and the area-length formula for a prolate ellipsoid. To determine the degree of PESP, the ejection fraction of the sinus beat just preceding the ventricular premature contraction was compared to the ejection fraction of the post-extrasystolic beat. (It was not possible to reproduce PESP with the external mechanical stimulator during left ventriculography because the device would obscure a part of the ventriculographic image.)

Analyses of echocardiographic and ventriculographic data obtained during cardiac catheterization were performed without knowledge of the result of the noninvasive echocardiographic studies.

Results

Ventricular premature contractions could be induced using the external mechanical cardiac stimulator in 30 of the 34 patients. These beats were usually of the right bundle branch block configuration (suggesting left ventricular origin) and demonstrated a widened QRS complex with a T wave vector opposite to that of the QRS and a full compensatory pause. In one additional patient, only interpolated beats could be induced and in the remaining three patients, all of whom were thick-chested by subjective evaluation, no ventricular premature contractions could be induced despite three to five attempts in each patient. Only one of the 34 patients was female; mild ecchymoses developed in the breast at the site of mechanical stimulation and subsequently it was decided to confine the studies to males. In no patients did serious complications such as repetitive ventricular arrhythmias or angina occur, nor was there more than minimal and transient chest wall discomfort. The interval

Figure 2. Echocardiogram demonstrating augmentation of septal (S) and posterior (P) wall motion following a noninvasive externally induced ventricular premature contraction (VPC). In this patient, systolic dimensional shortening and ejection fraction of the control beat preceding the VPC were 14% and 0.27, respectively, and increased to 19% and 0.38 in the potentiated beat following the VPC. MVA = mitral valve apparatus; Art = artifact indicating external mechanical stimulus and onset of VPC. Arrows (from top to bottom) = right septum, left septum, posterior endocardium, posterior epicardium.

Figure 3. Effects of mechanically-induced and spontaneous ventricular premature contractions (VPC). In this patient, systolic dimensional shortening increased from 18% to 28% following an externally induced VPC and ejection fraction increased from 0.36 to 0.53 (panel A) compared to increases of 18% to 27% and 0.36 to 0.51 following a spontaneously occurring VPC (panel B).
between the R wave of the sinus beat and the onset of the ventricular premature contraction induced by the mechanical stimulator averaged 434 ± 23 msec (mean ± SEM).

**Effect of PESP on Ventricular Function**

1) **Overall Group**

The difference in echocardiographic diameters (i.e., end-diastolic diameter minus end-systolic diameter) in the sinus beats preceding the ventricular extrasystolic (i.e., the control beat) averaged 1.5 cm and increased to 1.9 cm with PESP. Similarly, the derived values for systolic dimensional shortening and ejection fraction increased from 28% ± 2 to 34% ± 2 (P < 0.001*) and 0.52 ± 0.03 to 0.61 ± 0.03 (P < 0.001), respectively. This augmentation of systolic dimensional shortening and ejection fraction above control values averaged 21% and 17%, respectively, and ranged from 0% to 100%.

2) **Subgroups (table 1 and fig. 4)**

Six of the 30 patients had no obvious cardiac disease and served as the control group. Two of these patients were felt to have functional heart murmurs on the basis of clinical and noninvasive examination and four others had a chest pain syndrome with normal coronary arteriograms demonstrated at catheterization. During PESP, the difference between diastolic and systolic diameters increased from 1.7 to 2.0 cm (table 1) and systolic dimensional shortening increased by 33% ± 1 to 38% ± 2 (P < 0.001). Ejection fractions (fig. 4) rose from an average of 0.61 ± 0.02 to 0.68 ± 0.02 (P < 0.001); the increases averaged 12% over a narrow range (9% to 19%) of the control level.

The responses of the 24 patients with cardiac disease diagnosed by clinical, noninvasive and/or cardiac catheterization procedures are described according to type of cardiac disease. Five patients had primary myocardial disease (including one with idiopathic hypertrophic subaortic stenosis and four with congestive cardiomyopathy). During PESP, the difference between diastolic and systolic diameters increased from 1.2 to 1.7 cm and systolic dimensional shortening increased from 19% ± 5 to 26% ± 4 (P < 0.01). Ejection fractions increased from an average of 0.40 ± 0.08 to 0.50 ± 0.08 (P < 0.01); the increases averaged 25% and unlike control subjects ranged from 9% to 47% of the control level.

Five patients had valvular heart disease (including three with predominant aortic valve disease and two with mitral valve disease). During PESP, the difference between diastolic and systolic diameters increased from 2.1 to 2.5 cm and there was an increase in systolic dimensional shortening from 32% ± 5 to 37% ± 4 (P < 0.05). Ejection fraction increased from 0.58 ± 0.07 to 0.65 ± 0.06 (P < 0.05); the increases averaged 12% and ranged from 0% to 46%.

Fourteen patients had coronary artery disease. During PESP, the difference between diastolic and systolic diameters increased from 1.6 to 2.1 cm and there was an increase in systolic dimensional shortening from 29% ± 3 to 34% ± 3

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**TABLE 1. Effect of PESP on Echocardiographic Dimensions**

<table>
<thead>
<tr>
<th>Patient group</th>
<th>LVD (cm)</th>
<th>LVS (cm)</th>
<th>LVD-LVS (cm)</th>
<th>SDS (%)</th>
<th>%† in SDS with PESP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C</td>
<td>P</td>
<td>C</td>
<td>P</td>
<td></td>
</tr>
<tr>
<td>Normals (6)</td>
<td>5.1 ± 0.1*</td>
<td>5.2 ± 0.1</td>
<td>3.4 ± 0.1</td>
<td>3.2 ± 0.1</td>
<td>1.7 ± 0.1</td>
</tr>
<tr>
<td>PMD (5)</td>
<td>6.2 ± 0.4</td>
<td>6.3 ± 0.6</td>
<td>5.0 ± 0.7</td>
<td>4.6 ± 0.6</td>
<td>1.2 ± 0.2</td>
</tr>
<tr>
<td>VHD (5)</td>
<td>6.6 ± 0.5</td>
<td>6.7 ± 0.5</td>
<td>4.5 ± 0.6</td>
<td>4.2 ± 0.6</td>
<td>2.1 ± 0.2</td>
</tr>
<tr>
<td>CAD (14)</td>
<td>5.4 ± 0.3</td>
<td>5.5 ± 0.3</td>
<td>3.8 ± 0.4</td>
<td>3.4 ± 0.4</td>
<td>1.6 ± 0.4</td>
</tr>
</tbody>
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*All statistical comparisons are by paired t-tests.

**FIGURE 4. Effect of noninvasively induced post-extrasystolic potentiation (PESP) on echocardiographic ejection fraction (EF) in 30 subjects. Panel A depicts the changes in EF from the regular sinus beat (RSR) to the potentiated beat following the extrasystole in six control patients free of obvious cardiac disease (NORMAL). Panel B the response of 14 patients with coronary artery disease (CAD), panel C the response of five patients with valvular heart disease (VHD) and panel D the response of five patients with primary myocardial disease (PMD). Twenty-nine of the 30 patients demonstrated PESP, but the degree of response varied from 5-86% of control values.
Ejection fractions increased from an average of 0.52 ± 0.05 to 0.60 ± 0.04 (P < 0.01); these increases averaged 15% and ranged widely from 6% to 86% of the control level.

Several responses in individual patients were of particular interest. Only one patient in the study had no demonstrable augmentation of ventricular function. He had recently ruptured chordae tendineae resulting in severe mitral regurgitation and was presumably utilizing near maximal contractile reserve (control ejection fraction was 0.69). In the other 29 patients, the rise in the ejection fractions varied considerably when cardiac disease was present, as has been observed in earlier ventriculographic studies. Also of special interest were the six patients with markedly depressed resting ejection fractions (<0.40). In these patients, the increases in echocardiographic ejection fraction above the control value ranged from 30% to 86% (or in absolute values from 0.06 to 0.19) despite similar degrees of congestive heart failure clinically. One of these six patients, a 59-year-old man with severe aortic and mitral regurgitation had a resting ejection fraction of 0.35 which increased by 46% to 0.51 with noninvasively-induced PESP. Following replacement of the aortic and mitral valves, there was striking clinical improvement despite the depressed preoperative ejection fraction in the basal state. Of the other five medically treated patients, the patient with the longest follow-up had primary myocardial disease and an ejection fraction which rose from 0.27 to 0.38 (41%). This patient’s clinical course has stabilized in the six months since study despite the poor ventricular function in the basal state.

Reproducibility of Noninvasively-Induced PESP

In five patients, two ventricular premature contractions with sinus beat coupling intervals differing by less than 100 msec were induced several minutes apart with the external mechanical cardiac stimulator. In these five patients, the increase in systolic dimensional shortening calculated from the first series of PESP measurements averaged 24% ± 5 compared to 25% ± 4 resulting from the second series of measurements (r = 0.88). The individual responses in ejection fraction are plotted in figure 5 and also demonstrate good reproducibility (r = 0.95).

Correlation Between Noninvasively-Induced PESP and Spontaneously Occurring or Catheter-Induced PESP

In five of the 30 patients in whom PESP was elicited by external mechanical stimulation, the effects of PESP were redetermined by echocardiography using a right ventricular catheter to induce single ventricular premature contractions. Two other patients had spontaneously occurring ventricular premature contractions of left ventricular origin and are included with the other five for the purpose of comparing the degree of PESP induced with spontaneously occurring or catheter-induced ventricular premature contractions to that obtained with the external mechanical cardiac stimulator. Echocardiographic recordings of one of these patients are depicted in figure 3. In each patient, the catheter-induced or spontaneous ventricular premature contraction with the sinus beat coupling interval closest to that obtained in the same patient with the stimulator was used for comparison. The increase in systolic dimensional shortening following the externally-induced extrasystoles averaged 35% ± 11 of the control value compared to 35% ± 10 following those that were catheter-induced or spontaneous (r = 0.94). The similarity of responses in ejection fraction to the two methods of inducing extrasystoles (which differed in their sites of origin) are shown in figure 6 (r = 0.92).
Six of the 30 patients had single ventricular premature contractions induced with a right ventricular catheter during the first five beats of the ventriculographic study. Two other patients had spontaneous ventricular premature contractions of left ventricular origin in the course of cine left ventriculography. These two patients are included with the other six patients for purposes of comparing the effects of PESP induced by external mechanical stimulation and determined by echocardiography with catheter-induced or spontaneous PESP determined by left ventriculography. Four patients had single plane and four had biplane ventriculographic studies. Five of the eight patients had coronary artery disease (including four with wall motion abnormalities), one patient was a normal control, one had valvular heart disease and one had a cardiomyopathy. The individual responses are plotted about the line of identity in Figure 7 and show a close relationship (r = 0.89) despite different sites of origin of the ventricular premature beats, and different methods used in determining ventricular volumes.

Discussion

PESP was first demonstrated by Langendorff in 1885. It represents a potent inotropic stimulus which is now considered to be a fundamental characteristic of both normal and depressed mammalian myocardium. It has recently been shown in an animal model that PESP is superior to pharmacologic inotropic stimulation in identifying poorly perfused but viable myocardium. In subsequent studies carried out on patients with coronary artery disease utilizing left ventriculography, it was demonstrated that PESP is useful in differentiating between areas of ventricular wall that are totally fibrotic and areas composed of a mixture of viable muscle and scar tissue, or containing only ischemic muscle. The mechanism by which a premature contraction stimulates the subsequent enhanced contraction of the intact ventricle is not fully known, but it probably results from three components: 1) an augmentation of myocardial contractility, similar to that which occurs in isolated isometrically contracting muscle and probably related to an augmentation of calcium influx into the myocardium; 2) the augmented filling during the compensatory pause following the extrasystole; and 3) a reduction in afterload due to the decline in aortic pressure during the compensatory pause. In comparison with the use of other inotropic stimuli in the catheterization laboratory, such as infused l-epinephrine, PESP has the advantage of requiring only a single ventriculogram to obtain both the control and stimulated beat. Furthermore, the degree of augmentation of both normal and ischemic but viable tissue appears to be greater than that obtained with 1-epinephrine. The effects of nitroglycerin and PESP on abnormal wall motion appear to be similar, although the mechanism of action of nitroglycerin is to reduce both afterload and preload rather than exerting a direct inotropic effect like PESP or l-epinephrine. Like l-epinephrine, however, a second ventriculogram is necessary.

The clinical importance of determining the effects of PESP on the ventriculograms of patients with coronary artery disease is twofold. First, PESP can help identify poorly contracting but viable myocardium and thus help to indicate which areas of myocardium are suitable for revascularization. Secondly, PESP can also supplement data obtained from determinations of the ejection fraction in the basal state. The latter measurement is a readily obtained index of ventricular performance that is a useful prognostic guide in patients with coronary artery disease, whether treated medically or surgically. The degree of augmentation of ejection fraction with PESP has been demonstrated to be of additional value in this regard, since it reflects the contractile reserve of the ventricle. In other cardiac diseases, only limited data are available.

The clinical importance of determining the effects of PESP on the echocardiogram in patients with coronary artery disease remains to be determined and represents one of the principal long-range goals of our investigations. It is recognized that echocardiographic evaluation of left ventricular function is best suited for disease states that affect the ventricle uniformly, such as valvular heart disease or the congestive cardiomyopathies. Although useful information about localized abnormalities of wall motion (as in coronary artery disease) can also be obtained with the echocardiogram, there are limitations in relating ventricular volumes and ejection fractions derived by echocardiographic methods to those obtained in the same patients using ventriculography, especially when the ventricle is involved in a nonuniform manner. Whether the prognostic importance that can be attached to the ejection fraction determined by echocardiography is comparable to that determined by ventriculography in patients with coronary artery disease is not yet established, but it is suggested by a recent study from our laboratory demonstrating that patients with reduced echocardiographic ejection fractions (≤0.40) almost always had reduced ventriculographic ejection fractions. Consequently, it is possible that additional studies in such patients...
demonstrating the effects of PESP on the calculated echocardiographic ejection fraction or on directly measured systolic dimensional shortening may prove to be of clinical importance. However, reliance on the fortuitous occurrence of spontaneous ventricular premature contractions would obviously not be a practical way of evaluating PESP during echocardiography — hence, the need for a safe, noninvasive method of inducing ventricular extrasystoles. The present study indicates that the instrument devised by Professor Igor Paul of the Massachusetts Institute of Technology and used by Zoll et al, for external cardiac pacemaking provides such a method.

External mechanical stimulation has long been used as an initial emergency procedure in the treatment of ventricular standstill. In the external mechanical cardiac stimulator in current use, the mechanical stimuli are produced by the activation of a solenoid with an electric current which makes a small linear artifact in the electrocardiogram, thus providing accurate timing of the impulse. Current is released by a manually operated trigger. Observing the oscilloscopic transcription of the T wave, stimuli can be introduced at various intervals after an R wave (fig. 1). In his initial studies with this device in animals and in patients requiring emergency cardiac pacemaking, Zoll found the lowest threshold at which ventricular premature contractions could be obtained on the precordium to vary between 0.4 and 0.7 joules, using a 250 gram projectile with an impact surface 2 cm in diameter. Repetitive responses, such as ventricular tachycardia and fibrillation, were not observed. Thus, initial observations with this device in humans indicated that external mechanical stimulation of the heart is a safe, easily applied, effective and well tolerated method of temporary cardiac stimulation. Our present experience confirms this impression. To minimize discomfort, stimuli of 0.7 to 1.5 joules were utilized and no more than five attempts to induce ventricular premature contractions were made in any patient. Even with these restrictions, ventricular premature contractions failed to be induced with this technique in only three of 34 patients; all three of these patients appeared to have thick chest walls. In a fourth patient, only interpolated beats could be induced. Because of our experience in one female patient who developed a mild mammary ecchymosis, we have temporarily deferred using the device in women in order to determine whether the information obtained outweighs this potential disadvantage.

The results of the present study indicate that: (1) this external mechanical method of stimulating the heart can induce PESP in patients with a wide variety of cardiac disease; (2) the degree of noninvasively-induced PESP varied considerably when cardiac disease was present, but was reproducible in the same patient; (3) the degree of noninvasively-induced PESP correlated well with the degree of PESP following spontaneously occurring or catheter-induced ventricular premature contractions when echocardiography was used to measure wall motion; and (4) the augmentation of the ejection fraction induced noninvasively, and recorded echocardiographically, correlated well with that following spontaneously occurring or catheter-induced extrasystoles during left ventriculography. (Further studies in asynergic ventricles are needed to confirm this latter finding, however.)

In conclusion, this technique may be potentially useful in evaluating contractile reserve in patients with cardiac disease who have markedly depressed ejection fractions by echocardiography and thus overall reduced left ventricular performance. The data from the present series include only six such patients and therefore cannot be considered as more than preliminary results. Long-term follow-up studies with additional medically and surgically treated patients are necessary before the prognostic value of these echocardiographic responses can be compared to those reported in prior ventriculographic studies from our hospital that suggest, at least in patients with coronary artery disease and a depressed ejection fraction, that prognosis appears to be a function of the degree of augmentation of the ejection fraction. (5) This technique also may be useful in serially evaluating the contractile reserve of local regions of the heart observed by stenosed coronary arteries. Its use in characterizing both overall and regional ventricular performance would be even greater if it could be adapted to other noninvasive methods of assessing left ventricular function that visualized more areas of myocardium than the single-plane M-mode echocardiogram, i.e., radioisotopic ventriculography and real-time two-dimensional B-mode echocardiographic scanning. (2) Finally, the introduction of a ventricular premature contraction may provoke or intensify outflow tract obstruction in patients with idiopathic hypertrophic subaortic stenosis, and may also be helpful diagnostically when used with both echocardiography and indirect carotid pulse tracings in patients suspected of having this disease.

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Prediction of the Normal Blood Volume

Relation of Blood Volume to Body Habitus

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SUMMARY Predictions of blood volume (BV) assume the existence of a constant ratio between BV and body weight or surface area (SA).* We examined the validity of this assumption by calculating BV from plasma volume and body hematocrit in 160 normal volunteers whose weights ranged from -38.7 to 210.8% of desirable weight (assessed by a modification of the Metropolitan Life Insurance Company Desirable Weight tables).

BV is not a constant fraction of body weight or SA in this population. Its prediction from such constant ratios results in a large error of estimate which is systematically biased with respect to height and weight. BV prediction from the observed regressions of that parameter on weight and SA reduces the error substantially but remains biased with respect to height. BV prediction from the subject's degree of deviation from desirable weight affords a smaller error of estimate which is apparently free from systematic bias.

THE CLINICAL VALUE of blood volume (BV) measurements depends upon the accuracy with which a determination can be related to the expected normal value for a specific subject. Two methods for prediction of normal BV are widely used at present. One relates BV to body weight, while the other relates BV to body surface area (SA).* The latter has been shown to be a significantly better predictor of BV than the former.** Both methods, however, assume that the ratio of BV to the pertinent reference standard is constant. Observed variations in these values are considered to be random within a uniform population; accordingly, obese individuals should have the same ratios as lean subjects or those of normal body habitus.

Several studies cast doubt on the validity of this assumption. Alexander has reported that otherwise normal subjects weighing more than 300 lbs had an average ratio of BV to body weight of 46 ml/kg while nonobese individuals were characterized by an average ratio of 86 ml/kg.6 Gregersen and Nickerson, using the Sheldon somatotype system, found that ecomorphs, endomorphs and mesomorphs tended to have different BV to body weight ratios.6 Keys reduced the weight of 32 normal male volunteers over a six month period of dietary restriction until their weights stabilized at a level 25-35% below control values.7 Blood volume was determined before and after weight reduction. Calculations based on these data indicate that BV was 101.3 ml/kg after weight reduction, while control values averaged 84.4 ml/kg. These findings suggest that the ratio of BV to body weight does not remain constant.

The present study was undertaken to test the hypothesis that only individuals of similar proportions or equal degrees of deviation from desirable (or "ideal") weight might be expected to have similar ratios of BV to body weight.

Methods

Patient Selection

Measurements obtained in 80 normal men and 80 normal women form the basis of this report. One hundred and twenty-eight subjects were studied by us. Data of the remaining 32 are drawn from the report of Keys and associates8 since we were not able to obtain an adequate number of extremely underweight but otherwise normal subjects. Four of

*SA = Wt.\(^{0.409}\) × Ht.\(^{0.708}\) × 71.84.1

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