LETTERS TO THE EDITOR

Echo Assessment of PVR

To the Editor:

We wish to congratulate Dr. Hirschfeld and his colleagues1 for their study on the echocardiographic assessment of pulmonary arterial pressure and pulmonary vascular resistance; they have provided a valuable approach to the noninvasive evaluation of pulmonary vascular disease. However, we wish to take issue with some of their statistical handling of the data and to mention some other problems.

The authors stated that they did not have sufficient data to evaluate whether age or heart rate is the dominant factor in influencing right sided systolic time intervals. Although more normal values would lead to greater accuracy of prediction, the data that they published can be analyzed by multiple linear regression techniques2 to give:

\[
\text{PEP} = 99.6 + 0.42 \text{ age} - 0.32 \text{ heart rate}, \quad (1) \\
\text{RVET}_c = 378 + 2.6 \text{ age} - 1.1 \text{ heart rate} \quad (2)
\]

where the subscript 'c' indicates the predicted value of the time interval. Because heart rates are larger numbers than ages (in years), the heart rate is more important than age in each of these prediction formulas. The coefficient for age in predicting PEP is small and not statistically different from zero, and so can be disregarded to produce a simpler formula relating PEP to heart rate:

\[
\text{PEP} = 109.6 - 0.39 \text{ heart rate}. \quad (3)
\]

On the other hand, age cannot be disregarded in estimating RVET since its coefficient, though small, is significantly different from zero. The standard deviations from regression were 10.9 for PEP and 14.9 for RVET.

The authors also related the PEP/RVET ratio to pulmonary vascular resistance (Rv, in mm Hg·L·min⁻¹·m⁻²) and fitted a straight line to the points (their fig. 6) by varying a horizontal scale. They obtained a linear correlation coefficient of 0.66; however, there is a significant curvilinear relationship between these variables that can be expressed as:

\[
\frac{\text{PEP}}{\text{RVET}} = 0.192 + 0.030 \text{ Rv} - 0.000833 \text{ Rv}^2. \quad (4)
\]

The second order equation reduced residual variation significantly from 50% to 27%. The standard deviation from regression of the PEP/RVET ratio was 0.063 for linear regression and 0.046 for curvilinear regression, and the multiple correlation coefficient increased to 0.85.

There are even more problems with the authors' figure 6 and its interpretation. Using the PEP/RVET ratio to predict Rv from a given PEP/RVET ratio requires inverse prediction (by bioassay methods) and not the usual confidence limits obtained from standard regression analysis. Thus our figure 1 shows a line of best fit from their figure 6 with 95% confidence limits for points. At any value of Rv in figure 1 top shown by the solid line the 95% confidence limits for RPEP/RVET are shown by the dotted lines and are quite narrow. However, for an observed RPEP/RVET ratio shown by the solid line in figure 1 bottom, the 95% confidence limits of Rv (shown by the dotted lines) are wide. Exact methods of calculating these limits are available but will not be given here.

Turning from the statistical analysis of the data, we would like first to point out that as yet we do not know if the prediction formulas relating the right sided time intervals to age and heart rate are influenced by left-to-right shunts with their larger than normal stroke volumes. This is all the more important because in many types of congenital heart disease there is an increase in pulmonary blood flow, and it is in these patients that it is particularly important to evaluate the pulmonary arterial pressure and vascular resistance.

Secondly, in our experience, the pulmonary valve opening signal can be more easily identified than the whole pulmonary valve echo signal in most patients so that the use of PEP alone would be more practical. This right ventricular pre-ejection period, normalized for heart rate, has previously been related to pulmonary arterial end-diastolic pressure by Nanda et al.,3 but only a minority of their patients had congenital heart disease. We therefore examined the relationship of the PEP normalized for heart rate by equation 3 to the pulmonary vascular resistance/m² body surface area and to pulmonary arterial pressures in the 50 patients described by Hirschfeld et al.1 The PEP was not linearly related to pulmonary vascular resistance, but when PEP was above 125 msec the pulmonary vascular resistance was over 3 mm Hg·L·min⁻¹·m⁻² in all but one patient (fig. 2). The relationships between PEP and either pulmonary arterial mean or diastolic pressures were less satisfactory.

If these relationships are borne out by future studies, then this
noninvasive measurement may be useful in the many patients in whom only pulmonary valve leaflet opening can be identified. It may then be possible on serial echocardiographic studies to allow more precise timing of cardiac catheterization in children in whom pulmonary vascular disease is a threat. Whatever the eventual form of echocardiographic technique used, however, this approach initiated by Hirschfeld et al. should be of great value.

NORMAN H. SILVERMAN, M.D.
JULIEN I. E. HOFFMAN, M.D.
Cardiovascular Research Institute
San Francisco, California 94143

References

The authors reply:
To the Editor:
We welcome the important comments by Drs. Silverman and Hoffman and appreciate their support of the concept and application of echocardiographic assessment of pulmonary vascular resistance. Although stepwise, multiple regression techniques would provide predictive values for the pre-ejection period, we were reluctant to publish those data because we did not have sufficient normal values for given age groups and varying heart rates, or enough patients with a constant heart rate and varying age.

We agree that a curvilinear regression analysis for the RPEP/RVET ratio to pulmonary vascular resistance would improve the correlation coefficient from 0.66 to 0.85. However, since a correlation coefficient of 0.66 is significant and since the curvilinear regression analysis would not improve the predictive value of the ratio, this analysis was not included. We did mention in the discussion that there was deviation from the linear correlation when pulmonary artery diastolic pressures were greater than 60 mm Hg.

We did not wish to imply that pulmonary vascular resistance (PVR) could be predicted from the ratio of pre-ejection period (RPEP) and right ventricular ejection time (RVET) (fig. 6). We merely wanted to indicate our observations in 35 samples that the PVR was less than 3.0 units when the RPEP and RVET ratios were less than 0.3. There was only one patient with a RPEP/RVET ratio of 0.3 or less who had a pulmonary vascular resistance of greater than 3 units (fig. 6).

We recognize that the opening movement of the pulmonary valve echo is generally detected more consistently than the closure points of the valves. However, in our experience, this has not presented a problem in those patients in whom we were particularly interested in assessing the pulmonary vascular resistance, (i.e., with increased pulmonary blood flow or pulmonary hypertension). Nevertheless, utilization of the RPEP alone may be more applicable in some patients, particularly adults.

The majority of patients in our study had left-to-right shunts and the noninvasive technique was correlated with invasive measurements of pulmonary arterial pressures and vascular resistances. Since publication of the paper, an additional 125 patients have been studied both by echocardiography and cardiac catheterization and the echocardiographic findings have continued to be supported and validated by the hemodynamic data.

In order to maintain the proper perspective of the paper, we would like to emphasize the following points: (1) The value of the RPEP/RVET ratio is its application in the serial assessment of the same patient who thus serves as his own control. Dramatic increases in the pulmonary vascular resistance will be reflected in increasing RPEP/RVET ratios which then may help the timing of cardiac catheterization. (2) It is possible to distinguish fixed pulmonary hypertension from potentially reversible vasoconstrictive influences. Echocardiographic evaluation of changes in the RPEP/RVET ratio with a patient breathing room air and 100% oxygen provides a simple, accurate, noninvasive method for obtaining this kind of information. (3) The adequacy of pulmonary artery banding in patients with large interventricular communications may be evaluated using this technique.

Clearly, further experience with this technique is needed to assess pulmonary vascular resistance. To date, application of this method has continued to support our hypothesis.

STEPHEN HIRSCHFELD, M.D.
RICHARD A. MEYER, M.D.
DAVID SCHWARTZ, M.D.
JOAN KORFHAGEN, A.R.D.M.S.
SAMUEL KAPLAN, M.D.
Children's Hospital
Cincinnati, Ohio 45229

References

Heart Sounds by Echo
To the Editor:
I would like to make a few remarks concerning a recent Editorial by Dr. Craigie (Circulation 53: 207, 1976).
Echocardiography is an elegant and interesting method which, however, is largely based on the skill of the operator (often a technician or Resident) and cannot be successfully used in all cases. We owe to echocardiography the knowledge that openings and closures of the valves are events that require a certain time. Most statements of the past mentioning "valve closure" should be amended to say "completion of valve closure."

Echocardiography should not be overemphasized in regard to the exact timing of certain valve events because of the variables introduced by the angle of the beam in regard to the plane of a leaflet, plus the changing position of the latter induced by motion of the heart due to both its dynamics and the shift induced by respiration. Therefore, it should be kept in mind that recording the motions of
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N H Silverman and J I Hoffman

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