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 the 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. Gregersen and Nickerson, using the Sheldon somatotype system, found that ectomorphs, endomorphs and mesomorphs tended to have different BV to body weight ratios. 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. 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 associates since we were not able to obtain an adequate number of extremely underweight but otherwise normal subjects. Four of

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*SA = Wt. \( 0.405 \times Ht. \times 71.84^1)
Keys' subjects developed significant anemia after weight reduction and their data are not included in the present series.

We selected subjects to obtain a spectrum of body weights ranging from underweight to extremely obese and a wide distribution of height. These individuals, who were not hospitalized, underwent a history and physical examination and gave voluntary and informed consent prior to study.

The physical characteristics of all 160 subjects are summarized in table 1. Weight was measured with minimum indoor clothing and corrected to the nude state by subtracting 1 kg. In all cases weight had been stable for at least two months prior to measurement of BV. Height was measured without shoes. Age ranged from 18 to 61 years, height varied from 138.4 to 193.0 cm; weight from -38.7 to 210.8% of desirable weight; and blood volume from 2.89 to 9.65 L.

**BV Calculation**

Measurements were made in the postabsorptive state with the subject in the supine position for a minimum of 45 minutes. BV was estimated from the zero time plasma concentration of radioiodinated human serum albumin (RISA-131, Abbott Laboratories) obtained by semilogarithmic extrapolation of values measured in samples secured 10, 20, 30, 40 and 50 minutes after injection of the radioisotope; and from the hematocrit reading, according to the considerations of Noble and Gregersen. The hematocrit was measured by centrifuging aliquots of each sample in Win-trobe hematocrit tubes for 55 minutes at 3000 rpm (International, Model SBV). The average of the five readings (which included the buffy coat) was corrected for trapped plasma and adjusted to body hematocrit.

Repeated determinations of blood volume were performed in five men and five women one hour after the original measurement to assess the reproducibility of this technique. The mean of the first determination did not differ significantly from the mean of the second. The deviation of the second measurement from the first varied from 1.6 to 4.8%, regardless of sign, with an average of 3.8%.

Blood volumes presented in Keys' study were recalculated by correcting the tabulated peripheral hematocrits for trapped plasma and adjusting them to mean body hematocrit.

**Determination of Desirable Weight**

Desirable weight was determined from a reference curve adapted from the standard Metropolitan Life Insurance Company Desirable Weight tables. We required a curve which would give a specific weight at a specific height and which could be read to 0.1 kg. The Metropolitan tables, however, give a range of weights, at any specific height, for each of three frame types (small, medium and large). Hence these tables could not be used in unmodified form to designate a specific desirable weight for a given height.

We therefore constructed reference curves from these data (fig. 1), one each for women and for men, in the following manner:

1. The midrange weight value of each medium frame

| Table 1. Summary of Physical Characteristics and Blood Volumes Encountered in 100 Normal Subjects |
|------------------------------------------|----------|----------|----------|
| Women & Men                            | N        | Mean     | sd       | Range    |
| age                                     | 80       | 37 yr    | ± 10.9   | 19 - 61  |
| weight                                  |          | 86.1 kg  | ± 25.4   | 40.1 - 157.6 |
| deviation desirable weight              |          | 58.5 %   | ± 45.8   | - 15.9 - +210.8 |
| height                                  |          | 159.7 cm | ± 7.8    | 138.4 - 177.8 |
| surface area                            |          | 1.87 m²  | ± 0.26   | 1.30 - 2.52 |
| blood volume                            |          | 4.57 L   | ± 0.95   | 2.80 - 7.24 |
| blood volume/m²                         |          | 2.44 L/m²| ± 0.26   | 2.07 - 3.24 |
| blood volume/kg                         |          | 55.1 ml/kg| ± 8.88  | 40.0 - 83.0 |

*108 observations.

Abbreviations: cm = centimeter; kg = kilogram; L = liter; m² = square meter; ml = milliliter; N = number of subjects; sd = standard deviation; yr = years.
group for women was determined by averaging the tabulated range limits.

2. A specific weight for minimal indoor clothing (2 lb) was deducted from each midrange value; 2 inches were subtracted from height for shoes.

3. The derived values were then plotted on linear graph paper and interpolated by eye to give specific values of weight to the nearest 0.1 lb at each height. Since height changes unidimensionally while body weight or mass changes three-dimensionally, the absolute increment in weight between successive increments in height must always increase. Hence, in extending the range of heights beyond that reported in the Metropolitan tables (56-70 inches) we determined the average increment in weight per unit change in height (3.8%/inch) and appropriately augmented or diminished the corresponding weight at each change of height by this value until the range of our own observations was encompassed (54-76 inches).

4. The midrange weight value of each medium frame group for men was determined by averaging the tabulated range limits. Two pounds was subtracted from each midrange value for minimal indoor clothing and one inch from height for shoes. The average difference between medium frame desirable weights for men and women at the same height was 107.5% (range 106-109%) throughout the published height range. The difference between midrange weight values in the central (64-67 inch) portion of the height range was exactly 108%. Hence men were assigned values which were exactly 108% of the corresponding value on the female curve at all heights. All individuals of the same sex and height were considered to have the same desirable weight.

5. All values of height and weight defined by the resulting reference curves were converted to their metric equivalents.

Each individual's desirable or reference weight at his specific height was determined from the curve, and his percent departure from desirable weight was calculated as

$$\pm\% \text{ desirable wt} = \frac{\text{actual wt} - \text{desirable wt}}{\text{desirable wt}} \times 100 \quad (1)$$

Our use of these tables to assess variations in BV assumes that individuals who differ equally from their reference weight (± percent overweight) are proportional to each other with respect to their blood volume.

**Results**

**Effect of Body Composition on BV**

The relations between blood volume and height, weight and surface area, respectively, are indicated in figure 2. While blood volume increases with the respective body dimension in each case, the regressions fail to pass through the zero intercept. Hence the ratio of blood volume to each independent variable is not a constant value.

This conclusion is confirmed by the wide and systematic variation in the ratio of blood volume to body weight indicated in figure 3 where the ratio is shown as a function of percent deviation from desirable weight. In extremely underweight but otherwise normal subjects the ratio of BV to body weight is 90–100 ml/kg. As the degree of obesity increases the ratio falls until it appears to level off at about 43 ml of blood per kg body weight. In very thin individuals the ratio is almost 2.5 times higher than it is in the presence of severe obesity. A continuous hyperbolic spectrum of BV
Accuracy of Prediction of BV

To assess the effect of these variations in BV to body weight and BV to SA ratios on the accuracy of BV prediction, we used three methods to predict blood volume for each of the subjects reported herein. The first is the conventional procedure which assumes that BV is related to each of these reference standards by a constant value. The values chosen for the BV to body weight ratio, 72.6 ml/kg for men and 66.3 ml/kg for women, represent commonly used averages of a number of reports corrected where necessary to body hematocrit by assuming an average peripheral hematocrit of 45% for men and 41% for women. The values selected for the BV to SA ratio, 2566 ml/m² for men and 2245 ml/m² for women, were taken from the study of Samet and associates and are in the range found by other investigators.

The second method of predicting BV continues to use weight and SA as reference standards, but avoids the assumption made above by employing the linear regressions of blood volume on weight (fig. 2, center panel) and on SA (fig. 2, lower panel) derived from our own data.

The third method of predicting BV uses deviation from desirable weight as the reference standard. The subject's desirable weight is derived from figure 1 on the basis of height. Deviation from desirable weight is assessed from equation 1 above. The ml/kg value corresponding to that specific degree of overweight or underweight is determined from the regression of the BV to body weight ratio on deviation from desirable weight (fig. 3) and multiplied by the subject's actual weight

\[ BV = \text{body weight (kg)} \times \text{ratio (ml/kg)}. \]  

The blood volumes predicted by this method were computed from a regression curve which could be read to 0.1 ml/kg and 0.2% deviation from desirable weight. Table 2 comprises a series of values of BV to body weight ratio and percent deviation from desirable weight which define the regression. Comparison was made between the observed BV and values predicted by the three methods outlined. The respective correlation coefficients, the standard errors of estimate as well as the significance of difference between sequential standard errors (assessed from the F distribution) are summarized in table 3.

When BV is predicted from body weight or SA by assuming a constant ratio (method 1) the standard errors of estimate are ± 1529 and ± 684 ml respectively. A significant
improvement in BV prediction ($P < 0.005$) results when the estimating equations are used (method 2). The lowest standard error ($\pm 465$ ml or $\pm 9$ percent of the mean) is obtained by predicting BV from deviation from desirable weight (method 3). While this value does not differ significantly from that resulting from the use of the SA estimating equation, it is significantly smaller ($P < 0.05$) than that obtained with the body weight estimating equation.

Systematic errors of prediction result from the use of method 1. The disparity between observed and predicted blood volumes (body weight reference standard) is displayed in figure 5, upper panel, as a function of the subject's deviation from desirable weight. BV is overestimated in obese and underestimated in lean individuals. The error of predicting BV from SA is similarly illustrated in figure 5, center panel. This reference standard predicts blood volume best in average to slightly overweight subjects. SA tends to underpredict BV in both underweight and obese individuals.

The error of predicting BV from deviation from desirable weight (method 3) is indicated in figure 5, lower panel. Accuracy of prediction is uniform throughout all weight ranges. Prediction on the basis of the regression equations (method 2) results in a similar uniform distribution.

Another source of systematic error is apparent when the disparity between observed blood volumes and those predicted by these three methods is analyzed as a function of height. The body weight reference (fig. 6, upper panel) is associated with a strikingly wide scatter of values at all height ranges. The SA reference (method 1) underpredicts BV in both short and tall subjects (fig. 6, center panel). The estimating equations relating BV to either body weight or SA (method 2) underpredict BV to a significant degree ($P < 0.001$ and $P < 0.005$, respectively) in men as height increases. Only prediction from deviation from desirable weight (fig. 6, lower panel) results in a uniformly narrow band of difference from observed values throughout the height range.

Table 2. Corresponding Values of Blood Volume to Body Weight Ratios and Degree of Deviation from Desirable Weight Which Define the Regression in Figure 3

<table>
<thead>
<tr>
<th>Blood volume to body weight ratio (ml/kg)</th>
<th>Deviation from desirable weight (±%)</th>
<th>Blood volume to body weight ratio (ml/kg)</th>
<th>Deviation from desirable weight (±%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>99.7</td>
<td>-40</td>
<td>97.1</td>
<td>-37</td>
</tr>
<tr>
<td>97.1</td>
<td>-37</td>
<td>94.4</td>
<td>-34</td>
</tr>
<tr>
<td>94.4</td>
<td>-34</td>
<td>91.2</td>
<td>-30</td>
</tr>
<tr>
<td>91.2</td>
<td>-30</td>
<td>87.9</td>
<td>-26</td>
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<tr>
<td>87.9</td>
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<td>80.6</td>
<td>-17</td>
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<td>80.6</td>
<td>-17</td>
<td>77.0</td>
<td>-12</td>
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<td>-12</td>
<td>73.2</td>
<td>-6</td>
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<tr>
<td>73.2</td>
<td>-6</td>
<td>69.9</td>
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<td>66.6</td>
<td>+ 6</td>
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<td>+ 6</td>
<td>63.9</td>
<td>+12</td>
</tr>
<tr>
<td>63.9</td>
<td>+12</td>
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<td>+19.0</td>
</tr>
<tr>
<td>61.2</td>
<td>+19.0</td>
<td>58.9</td>
<td>+26</td>
</tr>
</tbody>
</table>

Table 3. Comparison Between 188 Observed Values of Blood Volume in 160 Normal Subjects and Values Predicted from Body Weight, Surface Area and Deviation from Desirable Weight

<table>
<thead>
<tr>
<th>Method of prediction</th>
<th>Reference standard</th>
<th>Correlation coefficient</th>
<th>Standard error of estimate (ml)</th>
<th>Significance of reduction in standard error</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. constant ratio</td>
<td>body weight</td>
<td>0.773</td>
<td>±1529 ml</td>
<td>---</td>
</tr>
<tr>
<td>2. linear regression</td>
<td>body weight</td>
<td>0.864</td>
<td>±684 ml</td>
<td>---</td>
</tr>
<tr>
<td>3. curvilinear regression</td>
<td>surface area</td>
<td>0.842</td>
<td>±531 ml</td>
<td>$P &lt; 0.005$</td>
</tr>
<tr>
<td></td>
<td>deviation from desirable weight</td>
<td>0.856</td>
<td>±510 ml</td>
<td>$P &lt; 0.005$</td>
</tr>
</tbody>
</table>

*P value indicates significance of reduction from preceding standard error.

Discussion

In the large population described in this study, encompassing a wide range of body types from extremely lean to grossly obese, BV is not related by a constant ratio to height or weight alone, nor to the combination of height and weight expressed as SA. This undoubtedly reflects variations in body composition which are not included by absolute height or weight.

While the role of body composition as a major determinant of BV has long been appreciated, its assessment has hitherto involved techniques which are sufficiently cumbersome to preclude their routine application. More recently, mean skinfold thickness (assessed in 10 locations with a caliper) has proven to be a useful index of total body adiposity. While we have been able, with even greater ease, to assess the degree of obesity in each of our subjects by reference to a simple pair of curves derived from the Metropolitan Life Insurance Company Desirable Weight tables. A continuous spectrum of BV to body weight populations has been demonstrated which can be identified on the basis of a subject's deviation from desirable (or ideal) weight.

As the severity of obesity increases, blood volume does not increase proportionally to the increase in body weight. The BV to body weight ratio falls toward an asymptotic value of approximately 45 ml/kg. The blood content of adipose tissue has been estimated to range from 18 to 47 ml/kg. Part of the increased weight in extreme obesity, however, reflects an increase in supportive tissue, such as muscle, which contains a larger volume of blood than does fat alone. Hence the actual blood content of adipose tissue must lie below the 40-43 ml/kg suggested by our data.

At the other end of the spectrum, the ratio of BV to body weight in individuals who are 25 to 35% overweight ranges from 95-105 ml/kg. These data are consistent with the report by Muldowney on lean body mass and blood volume.

These considerations explain the wide range of average normal ml/kg values (62-86 ml) for BV reported by different investigators. Such studies were usually performed on randomly selected normal individuals. However, the
range of 62–86 ml/kg corresponds (fig. 3) to population groups which vary from 25% underweight to 16% overweight. Hence the variation in reported values suggests that the populations selected at random actually differed significantly in their average composition with respect to body habitus.

The variation in BV to SA ratios encountered in the present study is also greater than has been reported previously. Analysis of the dispersion of these values with respect to deviation from desirable weight (fig. 4) indicates that the scatter is relatively small only within the narrow range near

![Figure 5](image1.png)

**Figure 5.** Graphic representation of the relationship between the difference between observed and predicted values of blood volume (expressed as a percent of the observed value), on the ordinate, and the subject’s degree of deviation from ideal (desirable) weight, on the abscissa in percent. Prediction from body weight (method 1) appears in the upper panel, from surface area (method 1) in the center panel and from deviation from ideal (desirable) weight (method 3) in the lower panel. One hundred eighty-eight observations in 80 normal women (circles) and 80 normal men (triangles) are included. The zero isopleth on each ordinate represents complete agreement between observed and predicted values.

![Figure 6](image2.png)

**Figure 6.** Graphic representation of the relationship between the difference between observed and predicted values of blood volume (expressed as a percent of the observed value), on the ordinate, and the subject’s height (in centimeters) on the abscissa. Prediction from body weight (method 1) appears in the upper panel, from surface area (method 1) in the center panel and from deviation from ideal (desirable) weight (method 3) in the lower panel. One hundred eighty-eight observations in 80 normal women (closed circles) and 80 normal men (open triangles) are included. The zero isopleth on each ordinate represents complete agreement between observed and predicted values.
desirable weight where previous examinations of the normal BV have been conducted. Within this limited range our data are quite consistent with previous findings.

Others have also considered the effect of body composition on BV. Allen has developed a method of prediction, based on the study of a group of Taiwanese subjects, which involves weight and cubic function of height. A high degree of correlation between observed and predicted values was found in this limited population. When this formulation was applied to the diverse population reported in the present study the accuracy of prediction achieved was better than that of the body weight reference standard (method 1) but not as accurate as that obtained by using the surface area reference (method 1).

Wennesland and associates studied 201 males of average proportions and developed a series of multiple regression equations for BV prediction derived from height and weight. They noted, even in their relatively uniform group, that the accuracy of BV prediction decreased as individuals whose dimensions differed from the center of their height-weight scatter diagram were considered. They also recognized that their equations should not be applied to dimensions beyond those within their relatively uniform population.

Gregersen and Nickerson, and Moore also used separate equations for obese, normal and lean subjects. However, no simple criteria were reported for classification according to these subgroups. With the deviation from desirable weight reference standard it is possible, however, to determine BV to body weight ratios for a continuum of subgroups rather than for two or three groupings such as obese, lean and normal and to give exact criteria for identification of these subgroups on the basis of weight and height alone.

The measurement of BV has limited clinical usefulness without an accurate method for predicting normal values. The present study indicates that the smallest error of estimate is obtained by using deviation from desirable weight (method 3) as the reference standard (± 465 ml or ± 9% of the mean). This value is substantially lower than those obtained by assuming a constant ratio between BV and either body weight or SA. It is also significantly lower than that resulting from the use of the body weight estimating equation (P < 0.05). It does not differ significantly, however, from the standard error of the SA estimating equation. Nevertheless, the desirable weight reference is the sole estimator of BV which is apparently free from systematic bias throughout the entire spectrum of adult body configurations.

Two factors that may contribute to the error of estimate afforded by the desirable weight method merit consideration. We have not included a description of frame type in our assessment of body habitus. For simplicity, our modification of the Metropolitan Life Insurance Company Desirable Weight tables uses only medium frame data for both women and men at each height. It may be possible to reduce the standard error by including this factor more completely in the prediction. However, we have been advised that assessments of body frame “require both special skills and special instruments” (personal communication), and hence have refrained from doing so. Similarly, this study employs a technique of BV determination that assumes a constant ratio of peripheral to body hematocrit. It is conceivable that this correction factor might change in grossly obese subjects. The simultaneous use of plasma and red cell tags to assess blood volume independent of the ratio may also reduce the standard error to some extent.

A method for predicting blood volume which is both accurate and free of systematic bias should prove a useful tool in managing a variety of disease states.

Acknowledgment

We wish to thank Ms. Mariam Heath for her help in preparing this manuscript.

References

The Enlargement of Small Pulmonary Arteries by Preliminary Palliative Operations

JOHN W. KIRKLIN, M.D., L. M. BARGERON, JR., M.D., AND ALBERT D. PACIFICO, M.D.

SUMMARY  Four patients with tetralogy of Fallot, three of whom had congenital pulmonary atresia, were treated by initial palliative operations to enlarge left and right pulmonary arteries which were considered too small for complete repair. Two to four years later the right and left pulmonary arteries had enlarged sufficiently to allow complete repair.

DIFFUSELY VERY SMALL right and left pulmonary arteries, which occur infrequently, are not amenable to direct surgical enlargement as is the main pulmonary artery, and thus are potentially a contraindication to complete repair of classical tetralogy of Fallot and tetralogy of Fallot with pulmonary atresia, as well as other malformations with severe pulmonary stenosis or atresia. For some years, surgeons have proposed that increasing pulmonary blood flow by patch graft enlargement of the pulmonary valve ring (leaving the ventricular septal defect open) or by a systemic-pulmonary artery shunt would increase the size of the right and left pulmonary arteries sufficiently to allow later definitive repair. The truth of this proposal has not been well documented.

We present four patients in whom enlargement of diffusely small arteries has occurred after palliative operations which increased pulmonary blood flow and presumably intraluminal pulmonary artery pressure. Three of the four have now undergone successful complete repair.

Material and Methods

Four patients, ranging in age from 1.7 to 6.1 years, have undergone initial palliative operations to enlarge very small right and left pulmonary arteries. All four patients had tetralogy of Fallot, one with severe stenosis of the right ventricular infundibulum, pulmonary valve and pulmonary valve ring, and a very small main pulmonary artery, and three with congenital pulmonary atresia. One of the patients with pulmonary atresia had nonconfluent right and left pulmonary arteries and previously had undergone a side-to-end ascending aortic-right pulmonary artery anastomosis (table 1). The other patients had confluent right and left pulmonary arteries.

In one patient (case 2) the palliative operation was done using cardiopulmonary bypass, profound hypothermia to 26°C, and low flow (0.5 L/min·m²) during the repair. An incision in the right ventricular infundibulum was carried across the pulmonary valve ring and to the bifurcation of the main pulmonary artery. The parietal and portions of the septal band were excised, the free wall of the right ventricle mobilized, and most of the pulmonary valve excised. A preclotted, measured woven dacron patch was sewed into the incision to enlarge the entire area. In case 1 ascending aorta to both right and left pulmonary artery anastomoses were done through a median sternotomy, after finding the left and right pulmonary arteries too small for the planned repair. Cases 3 and 4 had end-to-side subclavian-pulmonary artery (Blalock-Taussig) anastomoses.

All patients were studied by cardiac catheterization and selective angiography before the palliative operation, and two to five years after it (table 2).

Results

The right and left pulmonary arteries were considerably larger at the time of the postoperative study in all four patients (figs. 1–4). We considered them to be large enough to permit complete repair in all four.

Three of the four patients have successfully undergone complete repair including repair of the ventricular septal defect (tables 1 and 2). In case 1, a heterograft-valved external conduit between right ventricle and the confluence of the pulmonary arteries was used in the repair. Peak pressures after repair were 50 mm Hg in pulmonary artery, 75 in right ventricle, and 85 in left ventricle. In case 2, at the final repair the palliative outflow patch was replaced with a new patch.

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Received March 16, 1977; revision accepted May 16, 1977.
Prediction of the normal blood volume. Relation of blood volume to body habitus.
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Circulation. 1977;56:605-612
doi: 10.1161/01.CIR.56.4.605
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1977 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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