COMPUTER SCIENCES

Ventricular Performance in Congenital Left-to-Right Shunt: Temporal Fourier Analysis of Gated Blood-Pool Data

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Using global time-activity curves, the phase and amplitude at fundamental frequency were calculated, and emptying patterns of the right and left ventricles (RV,LV) were evaluated by phase difference [D(phase) = RV phase minus LV phase] and RV/LV amplitude ratio [R(amp)]. In 21 subjects with normal cardiac function, D(phase) was minimal (mean 2.2 ± 6.1°), regardless of heart rate, and R(amp) was distributed from 0.31 to 0.92 (mean 0.57 ± 0.20). In 19 patients of ventricular septal defect (VSD), R(amp) remained within the normal range, whereas D(phase) became larger in proportion to the ratio of pulmonary-to-systemic blood flow, Qp/Qs ($p < 0.001$). Especially, cases with Qp/Qs over 2.0 showed a significant RV phase lag. By contrast, nine patients with patent ductus arteriosus (PDA), showed no RV phase lag, but—particularly in cases with Qp/Qs > 2.0—R(amp) was smaller than normal ($p < 0.001$). Thus this method is valuable for pathophysiologic investigation of diseases with L-to-R shunt, and can help in the noninvasive differential diagnosis between VSD and PDA.

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In recent years many advances have been made in nuclear cardiology regarding assessment of ventricular functions. The application of temporal Fourier analysis to multigated cardiac blood-pool data, first proposed by Adam et al. (*1*), is a new method for evaluating ventricular emptying patterns. Many authors have investigated left-ventricular (LV) function in patients with conduction abnormalities (*2–7,10*), ischemic heart disease (*2,8–11*), and cardiomyopathy (*12*), etc. The present paper describes ventricular emptying performance in patients having congenital heart disease with left-to-right (L-to-R) shunt, studied by means of this method.

MATERIALS AND METHODS

Fifty subjects, ages 7 mo to 49 yr, were studied by multigated cardiac blood-pool imaging. There were 21 subjects with normal cardiac function and 29 patients with congenital L-to-R shunts. Except for four volunteers, all subjects underwent cardiac catheterization and contrast angiocardiography to establish a diagnosis. The ratio of pulmonary to systemic blood flow (Qp/Qs) was calculated from oxymetry data at the time of cardiac catheterization. The ratio of pulmonary to systemic blood pressure (Pp/Ps) was obtained from the mean pressures in the main pulmonary artery and the aorta.

The 50 cases were divided into three groups. Group 1 included 21 subjects with normal cardiac function: Kawasaki disease ten; spontaneous closure of ventricular septal defect four; Takayasu's arteritis one; innocent murmur two; volunteers four. Normal function was proved by electrocardiogram, echocardiogram, cardiac catheterization, and contrast cineangiogram.

Group 2 included nine patients with patent ductus arteriosus (PDA) but intact ventricular septum. All patients had L-to-R shunt with or without pulmonary hypertension (PH), defined here as mean pulmonary arterial pressure higher than 20 mm Hg. There was no

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case with reversed shunt (R-to-L) in this group. Group 2 was subdivided into two subgroups according to the severity of L-to-R shunt. Subgroup 2a consisted of four cases with small L-to-R shunt (Qp/Qs ≤ 2.0) and subgroup 2b included five cases with a large L-to-R shunt (Qp/Qs > 2.0).

Group 3 included 20 patients with ventricular septal defect (VSD) without other cardiac anomaly. Nineteen cases in this group had L-to-R interventricular shunt of various degrees with or without PH. One case, however, was diagnosed as Eisenmenger type VSD with reversed (R-to-L) shunt and severe PH. Group 3 was subdivided into three subgroups according to the amount of L-to-R shunt. Subgroup 3a consisted of ten cases with small L-to-R shunt (Qp/Qs ≤ 2.0) and subgroup 3b included nine cases with large L-to-R shunt (Qp/Qs > 2.0). Subgroup 3c consisted of one case of Eisenmenger type VSD with mixed L-to-R and R-to-L shunts.

Patients who had conduction abnormalities by ECG were excluded—for example, many with atrial septal defect and incomplete right bundle branch block.

For a multigated cardiac blood-pool study, 5–15 mCi of Tc-99m red blood cells, labeled in vivo, or Tc-99m human serum albumin was injected intravenously. After blood-pool equilibrium, the gated data were obtained with a large-field scintillation camera in 40–80° left anterior oblique projection with 20–50° craniocaudad angulation. The multigated data were stored in 64 × 64 matrix in a nuclear medicine computer system, with division of the R-R interval into 28 frames. Temporal Fourier analysis of the data was performed on a pixel-by-pixel basis (*1,3,12*). Using the fundamental frequency of the Fourier series, the values of the phase angle and amplitude were computed for each pixel's time-activity curve throughout the matrix, then displayed on a color CRT with 16 color levels. In addition, Fourier analysis was applied to the time-activity curves derived from LV and RV regions of interest outlined on the phase and amplitude images, thus permitting the global values of the fundamental frequency's phase and amplitude to be computed for each ventricle. Quantitative evaluation of global ventricular emptying pattern was done by calculating (a) the difference of phase angle between the two ventricles [D(phase) = RV phase angle minus LV phase angle], and (b) the amplitude ratio from RV to LV [R(amp)]. The phase angles were indicated in degrees.

RESULTS

Figure 1 shows the relationship of phase angle to heart rate in 21 subjects with normal cardiac function (Group 1): A for the LV and B for the RV. In both, the phase angles become larger with increasing heart rate, and the relationship is almost linear. The linear correlation coefficient for the LV is 0.921, and for the RV it is 0.904. However, it is clearly shown in Fig. 1, (bottom), that in normal hearts the values of D(phase) are minimal, ranging −7° to +12° (mean 2.2°), being independent of heart rate.

Figure 2 presents the values of D(phase) for Groups 1–3, separating the subgroups for 2 and 3. For each group or subgroup the mean D(phase) is shown near the left side. For Subgroup 2a the mean D(phase) does not differ significantly from that of Group 1. By contrast, in Subgroup 2b the values of D(phase) tend to be smaller than those in Subgroup 2a, with a mean of −6.2 ± 11.3°. In Subgroup 3a the mean D(phase) shows no significant difference from that of Group 1. In Subgroup 3b, however, a definitive RV phase lag is detected in all nine

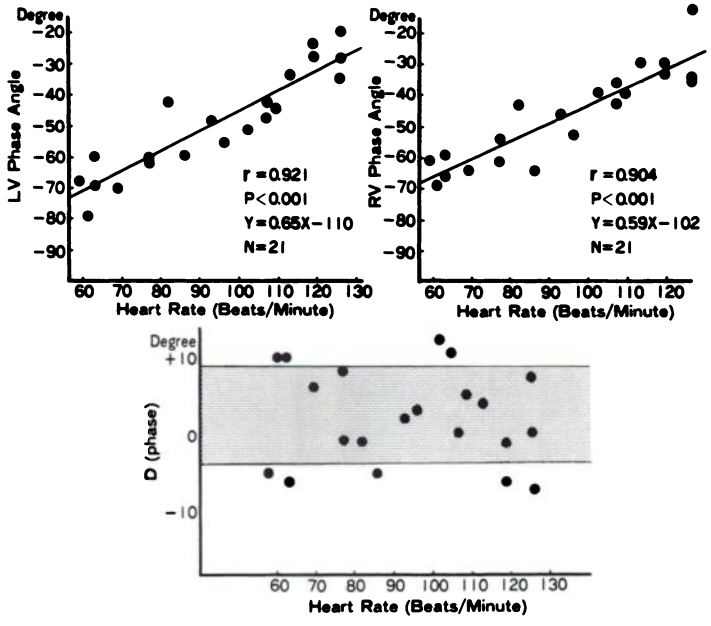
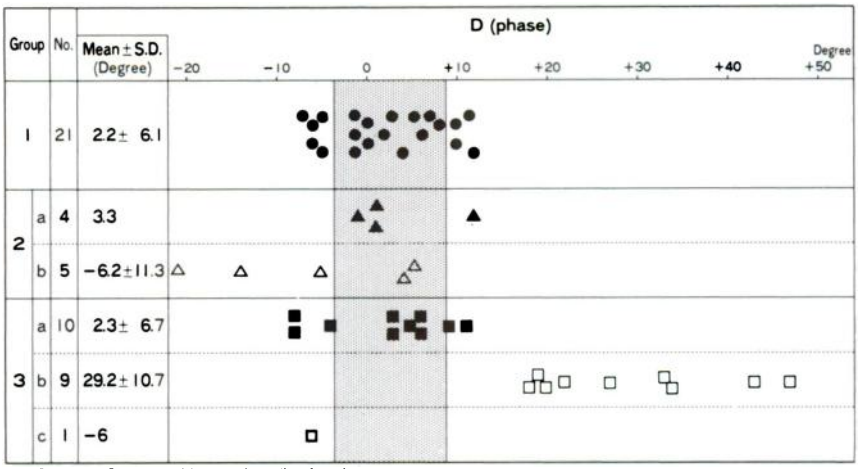


FIG. 1. Relation between ventricular phase angle and heart rate in 21 subjects with normal cardiac function. Top left: LV phase angle compared with heart rate; top right: RV phase angle compared with heart rate; bottom: difference between LV and RV phase angles, D(phase), compared with heart rate. Shaded zone shows mean value ±1 s.d.



Group 1 Subjects with normal cardiac function
Group 2 PDA with L-to-R shunt (a: with small shunt (Qp/Qs≦2.0), b: with large shunt (Qp/Qs>2.0))
Group 3 VSD (a: with small L-to-R shunt (Qp/Qs≦2.0), b: with large L-to-R shunt (Qp/Qs>2.0), c: with R-to-L shunt)

FIG. 2. D(phase), = RV phase angle minus LV phase angle, plotted for three groups of subjects. Group 1: with normal hearts. Group 2: patent ductus arteriosus with L-to-R shunt; 2a, Qp/Qs ≤ 2.0; 2b, Qp/Qs > 2.0. Group 3: ventricular septal defects with small and large L-R shunts (Qp/Qs) as in Group 2. Group 3c: subject with R-to-L shunt. Shaded zone shows mean and ±1 s.d. for normal cardiac function (Group 1).

cases, with a mean value of 29.2 ± 10.7°, significantly larger than normal ($p < 0.05$). The one case in Subgroup 3c (Eisenmenger) shows no abnormal phase difference.

Figure 3 shows the lack of significant correlation between Qp/Qs and the value of D(phase) in patients with PDA. Figure 4 reveals the similar lack of correlation between Pp/Ps and D(phase) in PDA patients.

Figure 5 plots D(phase) against Qp/Qs for the 19 VSD patients with L-to-R shunt (Subgroups 3a and 3b). There is a highly significant correlation between these two variables, with a linear correlation coefficient (r) of 0.903 ($p < 0.001$). In cases with Qp/Qs > 2.0 (Subgroup 3b), the values of D(phase) become larger than 18° in almost direct proportion to the amount of L-to-R shunt.

Figure 6 shows the relation between Pp/Ps and D(phase) in the same two VSD subgroups. Here the correlation is less striking, with r = 0.715 ($p < 0.001$). Cases with Pp/Ps > 0.4 (all in Subgroup 3b) show significant RV phase lag of over 18°.

In order to learn which of these two variables, Qp/Qs or Pp/Ps, is more closely related to D(phase) in patients with VSD, individual partial correlation coefficients were calculated by multivariate analysis. The partial correlation coefficient between Qp/Qs and D(phase) was 0.81, whereas that between Pp/Ps and D(phase) was 0.12.

Figure 7 shows the values of R(amp) for Groups 1 through 3, with the means for each subgroup toward the left. The values for Group 1, distribute in a relatively wide range from 0.31 to 0.92, with a mean 0.57 ± 0.20. R(amp) has a tendency to be smaller in younger children: the mean in children under 12 yr old was 0.52 ± 0.18 (n = 17), whereas above age 13 it was 0.81 (n = 4). The means for Subgroups 2a, 3a, and 3b show no significant difference from that of Group 1. In Subgroup

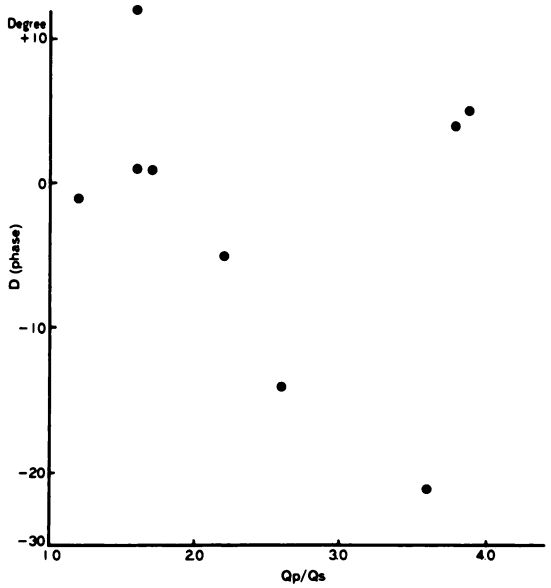


FIG. 3. Relation between Qp/Qs and D(phase) in patients with patent ductus arteriosus (PDA).

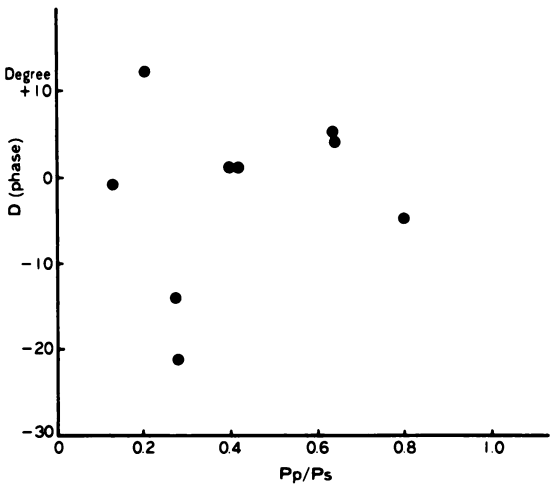


FIG. 4. Relation between Pp/Ps and D(phase) in patients with PDA.

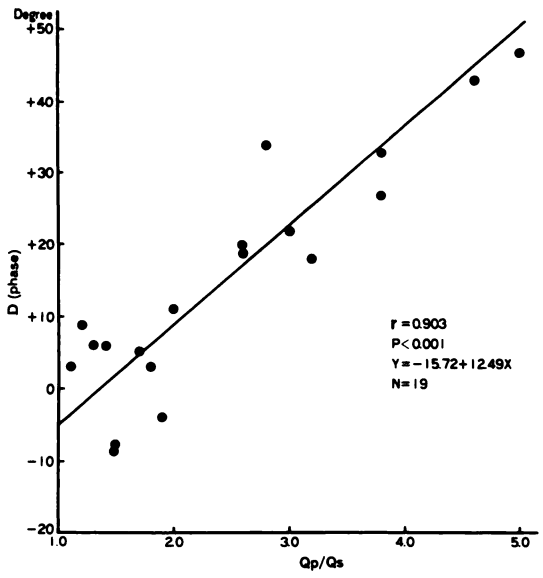


FIG. 5. Relation between Qp/Qs and D(phase) in patients with ventricular septal defects (VSD).

2b, however, R(amp) tends to be smaller than in other groups: the mean for this subgroup (0.23 ± 0.10) differs significantly from the normal value ($p < 0.001$). The patient with Eisenmenger VSD (Subgroup 3c) shows a strikingly large value of R(amp).

Figure 8 plots R(amp) against Qp/Qs for the nine cases of PDA (Group 2). Although there is no statistically significant correlation between the two variables, there seems to be a tendency for R(amp) to be smaller with increasing Qp/Qs.

DISCUSSION

Temporal Fourier analysis of gated cardiac blood-pool data, as reported by Adam et al. (*1*) and others is a new and excellent method for obtaining valuable information about ventricular function. They reported the usefulness of this method in visualizing the temporal difference between LV and RV emptying patterns in patients with conduction abnormalities, in determining the optimum position for an intracardiac pacemaker electrode (*2–7,10*), and in detecting LV regional wall-motion abnormalities in patients with ischemic heart disease and cardiomyopathy (*2,8–11*). However, there are still no reports about the ventricular emptying patterns—especially for the RV—in congenital heart disease as studied with this method.

To assess the RV function, many authors (*13–16*) have used first-pass radionuclide angiocardiography rather than the multigated cardiac blood-pool approach, because the former is better at separating the RV, temporally and spatially, from the LV and the right and left atria. Some investigators, however, have selected the multigated blood-pool study as a method of choice (*17–21*). Holman et al. (*20*) reported on the accuracy of measurement of RV ejection fraction by means of the equilibrium radionuclide angiogram, and remarked that the best possible separation of the RV from right atrium and LV could be obtained when a gated cardiac blood-pool study is performed in a modified left anterior oblique position with 30° caudad tilting, using a 30° slant-hole collimator. Bargeron et al. (*22*) had proposed a "hepatoclavicular position" for contrast cineangiocardiography to project the images of the four cardiac chambers "en face without mutual superimposition." In our radionuclide study, the detector closely approaches the "hepatoclavicular position."

Links et al. (*3*) stated that phase angle at fundamental frequency would be affected by the length of isovolumic diastole (diastasis), which is dependent upon heart rate. As shown in Figs. 1, (top left, top right), in normal subjects it is true that the phase angle changed with heart rate in almost linear fashion. However, the difference of phase angle between the two ventricles [D(phase)] was independent of heart rate (Fig. 1, bottom), and showed values within a limited range. We have therefore used the D(phase) as the temporal parameter to investigate global ventricular emptying pattern.

In cases with VSD (Group 3), significant RV phase lag—i.e., over 18°, which is beyond the mean value plus two s.d. for normal subjects—was detected under two major conditions: when Qp/Qs was greater than 2.0 (Figs. 2 and 5), or when Pp/Ps was larger than 0.4 (Fig. 6). In general, pulmonary hypertension will accompany increasing severity of L-to-R shunt in patients with VSD. It may be difficult, therefore, to determine which factor, Qp/Qs or Pp/Ps, is mainly responsible for the phenomenon of RV phase lag. The value of D(phase) increased more directly in proportion to the amount of

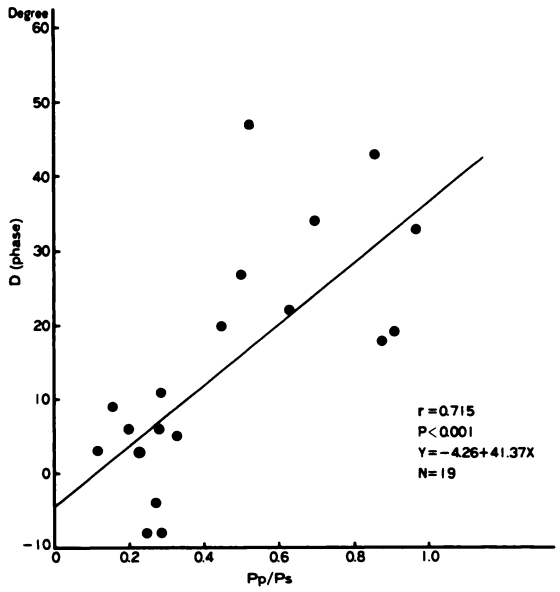


FIG. 6. Relation between Pp/Ps and D(phase) in patients with VSD.

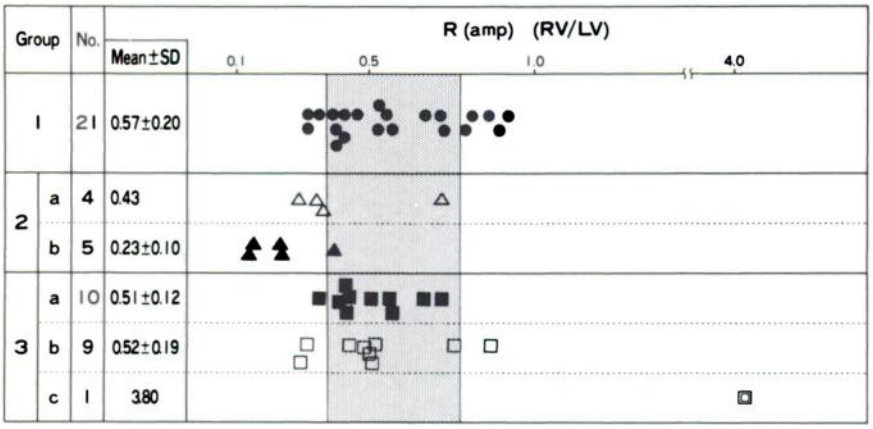


FIG. 7. R(amp), = RV amp/LV amp, as related to subject group. Shaded zone shows mean ±1 s.d. for normal cardiac function (Group 1).

L-to-R interventricular shunt than it did to the value of Pp/Ps. Furthermore, it was shown by multivariate analysis that the partial correlation coefficient between Qp/Qs and D(phase) was significantly larger than that between Pp/Ps and D(phase). In the patient with the Eisenmenger type of VSD, although Pp/Ps was greater than 1.0, no RV phase lag was noted. Moreover, in two cases with primary pulmonary hypertension—Pp/Ps >0.6, with diagnosis documented by cardiac catheterization and angiocardiography—no significant interventricular phase difference was recognized (*23*). Therefore, we conclude that in patients with VSD, RV phase lag depends mainly on the amount of interventricular L-to-R blood shunt rather than on the degree of pulmonary hypertension.

By contrast, in patients with PDA, the value of D(phase) correlated with neither Qp/Qs nor Pp/Ps and no phase lag was observed even when Qp/Qs was greater than 2.0 (Fig. 2). Rather, in those PDA patients with large L-to-R shunt (Subgroup 2b), the value of D(phase) was either in or below the normal range.

Links et al. (*3*) reported that the amplitude value at the fundamental Fourier frequency is proportional to stroke volume. Therefore, the value of R(amp) will reflect the stroke-volume ratio between both ventricles and is expected to be near unity in subjects with normal cardiac function (Group 1). In fact, however, the RV amplitude values were always smaller than those of LV in Group 1, thus making R(amp) <1.0. In cardiac blood-pool studies with a gamma camera, counts from both ventricles are subject to a variety of modifying factors. First, the distance of each ventricle from the camera cannot be geometrically equal in most cases. Second, relative to the LV, the RV shows a complicated cavity image, which may present a problem in setting a ROI. Third, as is clear from sequential observation of roentgenographic angiocardiograms, it is difficult, if not impossible, to store counts from the RV in a blood-pool study without including some from the right atrium, even after careful angulation of the camera. The contraction phases of the right atrium and RV are opposite to each other, so that at maximum systole the RV image is contaminated by counts from the large right-atrial cavity, making the "end-systolic RV count" larger than the true value. This reduces the RV stroke count (max. minus min.), which leads to R(amp) values rather smaller than 1.0 in subjects with normal cardiac functions. Younger children, in particular, seem susceptible to these effects. In subjects of Group 1, therefore, the values of R(amp) in younger children tend to be smaller than those in adolescents or adults, which are closer to 1.0.

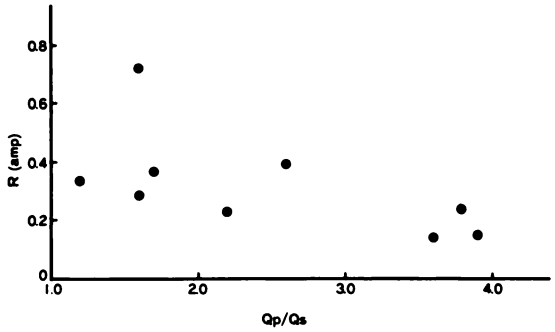


FIG. 8. Relation between Qp/Qs and R(amp) in patients with PDA.

In spite of the above-described wide range for normal R(amp) values, however, it was proved statistically that, in cases of PDA with large L-to-R shunt (Subgroup 2b) the mean value of R(amp) was significantly smaller than that of Group 1. Such significantly low values of R(amp) in Subgroup 2b may reflect the fact that the LV stroke volume is markedly larger than that of RV.

Unlike the PDA cases, the values of R(amp) in VSD cases were distributed mainly within the normal range, with no significant difference from normal values demonstrable even in cases with a large L-to-R shunt (Subgroup 3b). This lack of change in R(amp) from Group 1 to Group 3 might occur because in VSD patients the RV has to eject, in addition to the blood from the right atrium, the blood forced across the VSD by the LV. Consequently, the R(amp), which reflects stroke-

volume ratio (RV/LV), will not differ much from its normal range, unlike that in PDA patients.

Finally, Figs. 2 and 7 emphasize that D(phase) and R(amp) can usually distinguish a large PDA (Subgroup 2b) from a large L-to-R shunt through a VSD (Subgroup 3b). This differentiating ability is of practical value in the diagnosis of these lesions in young infants, because it is often difficult, if not impossible, to differentiate the one from the other without resort to invasive diagnostic procedures such as cardiac catheterization or contrast angiocardiography.

In conclusion, the temporal Fourier analysis of multigated cardiac blood-pool data is valuable for pathophysiologic investigation of ventricular emptying patterns in congenital heart disease with L-to-R shunt, and can be of help in noninvasive differential diagnosis between VSD and PDA.

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