Relevance of location of defect and pulmonary vascular resistance to the intracardiac pattern of left-to-right shunt flow in dogs with experimental ventricular septal defect


ABSTRACT Left-to-right (L-R) shunting across a ventricular septal defect (VSD) often involves a direct VSD–pulmonary arterial component (jet) that surges from the VSD immediately into the pulmonary artery. We used the thermodilution technique in dogs with acute experimental VSD to quantify this component. In dogs with supracristal VSD (n = 7), the direct component represented 76 ± 4% (mean ± SE) of the total L-R shunt on average, vs 39 ± 7% (p < .001) of the total in dogs with infracristal VSD and the same level of L-R shunting (n = 6). The direct component can be expected to impose additional hyperkinetic forces on the pulmonary artery since it is driven by the left ventricular pressure. Although not yet clinically proven, we speculate therefore that patients with supracristal VSD may be at greater risk of becoming jeopardized by late-onset pulmonary vascular obstructive disease. Since a part of the total shunt other than the direct component dropped into the right ventricle, the right ventricle bore only 24% of the total shunt in supracristal VSD, but 61% in infracristal VSD. We also found that the amount of direct component was decreased, and therefore another part must have increased, as the pulmonary vascular resistance was artificially raised. As a second speculation, therefore, we suggest that patients with supracristal VSD may have less enlargement of the right ventricle than those with infracristal VSD before pulmonary hypertension develops.

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IT IS a common finding in routine cineangiographic examinations of patients with ventricular septal defect (VSD; figure 1) that part of the left-to-right (L-R) shunted blood surges from the defect immediately into the pulmonary artery without being trapped in the right ventricle. The remainder of the shunted blood drops into the body of the right ventricle, and is then delivered to the pulmonary artery. In this report, the former portion is referred to as the direct VSD-PA component, with a flow f_{dp}, and the latter as the VSD-RV-PA component, with a flow f_{dr}. Clinically, the direct VSD-PA component is often termed a jet. The present study was undertaken to investigate the pathophysiologic significance and characterize the hemodynamic nature of such an intracardiac pattern of shunt flow.

Pulmonary vascular obstructive disease is known to represent one of the most serious clinical problems in treating patients suffering from congenital heart disease with shunt.\(^1\) It has been theorized that hyperkinetic hemodynamic forces imposed on the pulmonary arterial wall are major factors in the genesis of vascular disease.\(^2\)\(^-\)\(^6\) Elevation of the pulmonary arterial pressure, wide pulse pressure, and/or an increase in flow may certainly contribute to the extra hemodynamic forces.\(^3\)\(^-\)\(^6\)

Our group has suggested in a preceding report\(^7\) that in patients with VSD, one possible additional putative hemodynamic factor, which if not a major causative factor is at least an accelerating one, is the presence of the direct VSD-PA component. In that study, we quantified the component in dogs with experimental VSD produced for a short period at the entrance of the outflow tract of the right ventricle and found that it occu-
FIGURE 1. Schematic drawing of the intracardiac flow pattern of a L-R shunt across a VSD. The total L-R shunt flow \( f_d \) consists of two components: a direct VSD-PA component \( f_{dp} \), which surges from the defect immediately into the pulmonary artery (PA), and a VSD-RV-PA component with flow \( f_d \), which is once trapped in the right ventricle (RV) and then delivered in parts to the PA during subsequent heart cycles. \( f_p \) = total pulmonary flow; \( LV \) = left ventricle; \( RA \) = right atrium.

Pieced 23% of the total pulmonary flow on average and, in an extreme case, 43%. This finding led us to favor the hypothesis, although not yet clinically established, that the direct VSD-PA component tends to regulate one of the mechanisms conducive to pulmonary vascular obstructive disease.

Another characteristic feature of patients with VSD was found by Graham et al.\(^8\) \(^9\) to be a lesser degree of enlargement of the right ventricle than of the left ventricle. They described the pathophysiologic mechanism leading to this clinical manifestation as follows:\(^8\)

"Since normally the major shunting occurs during ventricular systole and is ejected into the outflow tract of the right ventricle, the right ventricle does not enlarge to the same extent as the left ventricle." Our group\(^7\) has supported their interpretation, based on the finding that on average 43%, and as little as 15% in an extreme case, of the total L-R shunted blood dropped into the right ventricle as the VSD-RV-PA component, whereas the left ventricle bore the entire amount of the total shunt.

In relation to the above two pathophysiologic processes, the major question examined in the present study was which location of the defect on the ventricular septum gives rise to the greater degree of flow of the direct VSD-PA component. In addition, an attempt was made to evaluate the influence of an artificially elevated pulmonary vascular resistance on the magnitude of the direct component. Finally, we examined the accuracy of another method in which the standard oxygen content technique for quantifying the direct component is used.

**Methods**

**Determination of hemodynamic variables.** Our method for evaluating the intracardiac pattern of shunt flow used the thermodilution technique in dogs with experimental VSD. The details of the principle have been fully discussed in a preceding report.\(^7\) In brief, the tracer injected into the left atrium drains into the left ventricle and forms a dilution curve there. Part of the tracer in the left ventricle is then transported to the pulmonary artery through the direct VSD-PA and the VSD-RV-PA components (figure 1). Thus, the dilution curve developing at the root of the pulmonary artery should represent the intracardiac pattern of the L-R shunt. This assessment was expressed quantitatively in equations 1 and 3 in our previous report. We assumed absent right-to-left (R-L) shunt across the VSD.

In practice, we observed a simultaneous pair of thermodilution curves at the roots of the aorta and pulmonary artery after a bolus injection of tracer, i.e., cold saline, into the left atrium. The dilution curve at the aorta should be a precise copy of that in the left ventricle, although the latter preceded the former in time by one heart cycle. Values of the dilution curves were sampled at each ventricular end-diastole when the tracer was known to be mixed well with the blood in these major vessels and before the tracer recirculated via the systemic circulation to reenter the pulmonary artery. The right ventricular ejection fraction (RVEF) was determined by observing another dilution curve at the pulmonary artery obtained by a separate bolus injection of the tracer into the right ventricle.\(^10\) The RVEF was necessary to assess the behavior of the tracer in the right ventricle on its way to the pulmonary artery through the VSD-RV-PA component.

A discretized form of convolution integral (equations 3 and 13 in our previous report) permitted us to establish the relationship between these dilution curves, RVEF, and the fractional flows, \( f_{dp}/f_p \) and \( f_{dr}/f_p \), where \( f_p \) represents the total L-R shunt flow and \( f_p \) the total pulmonary flow (equations 4 through 8 in previous report). The numerical computation for these fractional flows depended on a stable one-pass deconvolution with simultaneous introduction of multiple regression analysis.\(^11\) Another fractional expression of the direct component \( f_{dp}/f_p \) was obtained as the product of the above two fractional flows.

The \( f_p \) (liters/min) was calculated with a modified Stewart-Hamilton formula\(^12\) from the thermodilution curve at the aorta obtained after injection of cold saline into the left atrium. The systemic flow, \( f_s \) (liters/min), and the total pulmonary resistance, TPR (in units of mm Hg min liter\(^-1\)), were calculated as follows: \( f_s = f_p (1 - f_{dp}/f_p) \) and TPR = mean pulmonary arterial pressure/fdp, respectively.

The fractional flow of the direct VSD-PA component, \( f_{dp}/f_p \), was also determined by the standard oxygen content technique. The fraction was calculated from the equation \( f_{dp}/f_p = (C_P - C_A)/(C_P - C_R) \), where \( C_A \), \( C_P \), and \( C_R \) represent the oxygen contents of blood sampled from the aorta, pulmonary artery, and body of the right ventricle, respectively. The equation was introduced since \( C_P = C_R(f_s) + C_A(f_d) + C_{AO}f_{dr} \), \( f_s = f_p - f_d \), and \( f_d = f_{dp} - f_{dr} \).

**Experimental procedures.** Thirteen mongrel dogs of both sexes weighing 8 to 14 kg were anesthetized with pentobarbital sodium (30 mg/kg iv; Abbott Laboratories, North Chicago) and ventilated with a respirator (Mark 8; Bird Corp., Palm Springs) with room air. The femoral artery and vein were cannulated to monitor blood pressure with a transducer (P23ID, Gould Inc., North Chica...
Statham Instruments Division, Oxnard, CA) and to administer fluids or supplemental doses (5 to 8 mg/kg) of anesthetic.

The thoracic cage of each dog was opened widely by making a sternal splitting incision, and a pericardial cradle was constructed. The distal pulmonary artery of approximately 3 mm in diameter was cannulated for recording the pulmonary arterial pressure with another Gould-Statham transducer (P23ID). Each dog was then given heparin (400 units/kg iv; Novo Research Institute, Bagsvaerd, Denmark). A patch of muscle in the ventricular septum was excised with a boring device of 8 mm in diameter to produce an experimental VSD. The device was introduced through the midpoint of a purse-string suture placed in the anterior wall of the right ventricle. The defect was positioned in the subpulmonic portion as a supracristal VSD. In the anterior wall of the right ventricle. Another catheter-tip thermistor was placed at the root of the ascending aorta via an incision made in the apex of the left ventricle. These thermistor-tipped Teflon catheters were as thin as 1.2 mm in diameter and flexible. We therefore believe that any regurgitation across the pulmonary or aortic valve caused by them was, if present, minimal.

Two thin-walled polyethylene cannulas (2.0 mm in diameter), both with blind tips and lateral openings, were used for injection of tracer. They were advanced through the left atrial appendage and through the external jugular vein so that their tips were located in the left atrium and the body of the right ventricle, respectively. Signals from the thermistors were fed into a multichannel pen recorder (Biophysiology 140 System, San-ei Sokki Co., Tokyo, Japan) via a Wheatstone bridge. Calibration of the recording system for absolute values of temperature was performed before the experiments. Intravenous low molecular weight dextran (50 to 100 ml) with or without epinephrine (Dai-Ichi Pharmaceutical Co., Tokyo, Japan) was used to combat hypotension due to hemorrhage or the introduction of lycopodium spores (see below). The blood gas tensions and pH were monitored with a gas analyzer (IL1303; IL Inc., Lexington, MA). The oxygen content was measured with an oximeter (IL282 CO-Oxymeter; IL Inc.) that was coupled with the IL1303 and adjusted for dog blood. The animals were maintained in a homeothermic state with a servocontrolled rectal thermistor probe and a heating pad.

We used cooled (0° C) normal saline (0.8 to 1.5 ml) as the tracer. Tracer injections were repeated several times to allow pairs of thermodilution curves at the aorta and pulmonary artery to be obtained. Another bolus of tracer injected into the right ventricle yielded a thermodilution curve at the PA, permitting determination of RVEF. The data were fed manually into a computer to calculate the fractional flows, \( f_{dp} / f_p \) and \( f_d / f_p \) (equations 4 through 8 in our previous report). Blood was then sampled from the aorta, pulmonary artery, and body of the right ventricle for oxymetric determination of \( f_{dp} / f_p \).

Subsequent to these experimental runs, we introduced a suspension of lycopodium spores (30 \( \mu m \) in diameter) in normal saline into the right ventricle to produce pulmonary embolism and hence increase pulmonary vascular resistance. Experimental runs similar to those in the preceding study were then carried out. At the end of each experiment, the animal was killed with an intravenous overdose of pentobarbital. Postmortem examination was carried out to confirm the location of the VSD.

**Statistical treatment.** The results were calculated as mean ± SE. The significance of differences in the mean values was evaluated by the Student paired or unpaired t test, or one-way analysis of variance followed by the Bonferroni test, as appropriate. The data were processed with a computer (PDP 11/44; Digital Equipment Corp., Marlboro, MA).

We recalculated the dilution curve at the pulmonary artery by use of the computed flow fractions, RVEF, and time interval of the single heart cycle, according to equation 3 of our previous paper. Differences between the curves so recalculated and the observed dilution curves were tested for their significance with use of the correlation coefficient and the t test for one mean. Data resulting in \( r < .90 \) and/or \( p < .2 \) were abandoned. Additional tests for autocorrelation might need to be performed to obtain information concerning whether or not the differences were systematically generated. However, the number of observations performed in each pair of dilution curves obtained at the aorta and pulmonary artery was limited to five to eight because of reentry of the tracer into the pulmonary artery through the systemic circulation. The number of observations was thus too small to allow use of the test for autocorrelation, which requires more than 15 observations.

**Results**

Figure 2 gives a comparison of values obtained by oxymetry for the fractional flow of the direct VSD-PA component, \( f_{dp} / f_p \), with those obtained by the thermodilution method. Although a statistically significant correlation was observed, the discrepancy between the values obtained by these two techniques was considerable. Unrealistic negative values were given by the oxymetry technique. We therefore used the results obtained by the thermodilution technique for the quantitative evaluation of the intracardiac pattern of L-R shunting in this study.

Figure 3 illustrates the 13 positions of the experimental defects placed in the right ventricular septum.

![FIGURE 2. Comparison of values for the fractional flow through the direct VSD-PA component, \( f_{dp} / f_p \), calculated by the standard oxymetry and thermodilution techniques.](http://circ.ahajournals.org/doi/fig/10.1161/01.LAB.73.4.777)
Supracristal VSD than in that of infracristal VSD. In relation to these findings, it should be emphasized that when the component exists, the left ventricle delivers the tracer to the aorta across the aortic valve, as well as to the pulmonary artery simultaneously through the direct VSD-PA component. For this reason, the dilution curve at the pulmonary artery resembles the curve at the aorta when the direct component occupies a larger proportion of the L-R shunt. These findings indicate that the direct VSD-PA component existed in both cases, but its flow occupied a much greater proportion of the total L-R shunt in the dogs with supracristal VSD than in those with infracristal VSD. When the tracer was injected into the body of the right ventricle for the determination of RVEF, the aortic dilution curve did not develop before the sixth to ninth heart cycles in every animal. This finding indicates absence of R-L shunting across the VSD.

Table 1 summarizes the experimental data and calculated results. Most of the major hemodynamic variables as well as the amount of the total L-R shunting in dogs with supracristal and infracristal VSD were remarkably similar, indicating that the basal hemodynamic conditions of the two groups of dogs were identical. The RVEF was considerably low in both groups. This may represent right ventricular dysfunction due to myocardial injury after ventriculotomy and ventricular enlargement in the face of an acute volume and pressure overload. Nevertheless, we believe that our animal preparation in the present short-term study is broadly comparable to a human patient in phase I of disease (according to Dammann and Ferencz) with a medium-sized VSD and approximately normal pulmonary vascular resistance and moderately high pulmonary arterial pressure. The proportion occupied by the direct VSD-PA component \( f_{p} = f_{d}/f_{p} \) was found to be considerably greater in the supracristal VSD group than in the infracristal VSD group.

The data in table 2 show the effect of artificially increased pulmonary vascular resistance due to lycopodium-induced pulmonary embolism on the hemodynamic parameters. The pulmonary artery revealed an increase in pressure and resistance as the dose of lycopodium was increased. Acute pressure overload imposed on the right ventricle caused systemic hypertension and a decreased RVEF. Continuous intravenous infusion of epinephrine (0.2 to 6 \( \mu \)g/min) restored the arterial blood pressure to the control level, but did not do so for the RVEF. \( f_{p} \) and \( f_{d}/f_{p} \) did not undergo any significant changes. The fractional shunt flow of the direct VSD-PA component, \( f_{d}/f_{p} \) (table 2 and figure 5) or \( f_{d}/f_{p} \) (table 2), decreased markedly as the total pul-

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**FIGURE 3.** Location of the experimental VSD on the ventricular septum (indicated by arabic numerals) viewed from the right ventricular aspect. The defects numbered 1 to 7 represent supracristal VSD, and those numbered 8 to 13, infracristal VSD. AO = aorta; CSV = crista supraventricularis; MRPM = main right papillary muscle; PV = pulmonary valve; TV = tricuspid valve.

Seven defects were found to be located at the outflow tract of the right ventricle below the pulmonary valve, and six defects were situated in the perimembranous muscular portion of the ventricular septum. It is reasonable therefore to refer to the former as supracristal VSD, and to the latter as infracristal VSD. The axial direction of the defect was always approximately perpendicular to the surface of the septum. Abscession of the major chordae tendineae of the tricuspid valve was not observed.

Figure 4 shows typical records of the systemic arterial pressure and pairs of dilution curves observed at the roots of the aorta and pulmonary artery after injection of tracer into the left atrium. The left panel illustrates records obtained from a dog with supracristal VSD, and the right, those from a dog with infracristal VSD. The dilution curve in the pulmonary artery developed simultaneously with that in the aorta during the first heart cycle in both dogs. The time courses of the coupled dilution curves in the aorta and pulmonary artery were far more similar to each other in the case of

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monary resistance was increased. In most of these experimental runs, a R-L shunt did not develop, as judged by observation of the aortic dilution curve after the tracer injection into the right ventricle. When a R-L shunt did develop, it was minimal, and the data were discarded.

Discussion

Assessment of methodology and baseline values for hemodynamic parameters. In the present study, the RVEF was low in almost all cases. We believe that this represents right ventricular dysfunction due to myocardial injury inflicted by ventriculotomy and a ventricular enlargement in the face of an acute pressure and volume overload. Tricuspid regurgitation, if present, could also have contributed to the low RVEF, and might have been caused by either the intracardiac catheterization across the valve for tracer injection or volume overload of the right ventricle. Such ventricular dysfunction and regurgitation might lead to poor mixing of tracer in the right ventricle and give rise to inaccurate determination of RVEF. However, the only prerequisite of our principle is that a bolus of tracer that has entered the body of the right ventricle be ejected in parts into the pulmonary artery at a uniform rate during consecutive heart cycles. The dilution curve so formed in the pulmonary artery would thus show a geometric progression toward zero concentration. This prerequisite has been discussed and demonstrated to be realistic, as shown in figure 4 of our previous report. In addition, inaccurate determination of RVEF would not create a serious problem, since we also demonstrated in our previous report that the value of RVEF was not extremely important in the calculation of the direct VSD-PA component.

The possibility of right ventricular dysfunction raised another question: whether or not the dysfunction itself affected the size of the direct VSD-PA component. With approximately normal pulmonary vascular resistance, as in our animal preparation, the driving force of the direct component, i.e., the left ventricular systolic pressure, should be overwhelmingly greater than the right ventricular or pulmonary arterial systolic pressure, irrespective of the state of the right ventricular performance. Indeed, in a long-term study with experimental VSD, in which right ventricular function was recovered after the operation, the pulmonary arterial peak pressure was reported to range from 16 to 37.
mm Hg, very similar to that in our study (20 to 38 mm Hg). We therefore conclude that in our animal preparation, the size of the direct component would not be considerably influenced by the dysfunction of the right ventricle.

Our results for the TPR (6.6 or 7.8 U on average) in dogs with acute experimental VSD are comparable to those in a previously reported study16 (6 U) in which this value was higher than that found in another study (3 U; calculated from data presented in Mesel17). Infusion of epinephrine might have modified the vascular resistance in our study, since the pulmonary artery is known to constrict in response to α-adrenergceptor agonists (see Grover et al.18 for references), so increasing its resistance. However, between the groups with supracristal and infracristal VSD, we found no remarkable differences in any of the major hemodynamic variables, including the TPR. It seems reasonable to conclude therefore that the substantial difference in size of the direct VSD-PA components in these two groups depended specifically on the difference in location of the VSD.

As mentioned, unrealistic negative values for the direct VSD-PA component were given by the oxytome try technique. Application of this technique requires perfect mixing of oxygenated blood in the right ventricle, and in our study, this requirement was not entirely met in the face of acute enlargement of the right ventricle. Additionally, inappropriate positioning of the tip of the sampling catheter in the right ventricle might cause withdrawal of highly oxygenated blood from the blood stream of the direct VSD-PA component on its way to the pulmonary artery. Careful selection of sampling position within the body of the right ventricle under x-ray fluoroscopic monitoring, and timed sampling triggered by the electrocardiogram at each ventricular end-diastole, if possible, might improve the results. In contrast, our thermodilution method is free of such problems of mixing in the right ventricle, as explained above.

**Pathophysiologic significance of the intracardiac pattern of L-R shunt flow.** As early as the 1950s, it was widely recognized in patients suffering from congenital heart disease with shunt that the pulmonary vascular bed often underwent pathologic changes, thereby seriously affecting the hemodynamic features of the pulmonary circulation, the intracardiac pattern of shunt flow, and clinical signs and symptoms.1, 19-21 Dammann and Ferencz1 and Heath and Edwards22 classified such pulmonary vascular lesions into several grades depending on the progression of the lesions from reversible medial hypertrophy and cellular intimal proliferation to progressive medial hypertrophy, irreversible occlusion by intimal fibrosis and fibroelastosis, and finally necrotizing arteritis and dilatation lesions. Such vascular lesions develop most prominently in the smaller muscu-

### TABLE 1

Summary of results

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<th>Pulmonary arterial pressure (mm Hg)</th>
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Values are mean ± SE.

*Difference from mean in supracristal VSD is significant (p < .01, unpaired t test); b p < .001; c not significant.
lar pulmonary arteries and arterioles, with diameters ranging from 300 μm down to 100 μm or less.22

Direct evidence has yet to be obtained establishing the mechanisms conducive to these pathologic vascular lesions,8 although hyperkinetic hemodynamic forces imposed on the pulmonary arteries seem to be of potential importance.2-4 Evaluation of the O2 saturation or hematocrit is considered to be a minor factor, if it is a factor at all.4,6

As observed in peripheral arteries,23 hyperkinetic hemodynamic forces, i.e., pulmonary hypertension or wide pulse pressure, may tend to stimulate the pulmonary vascular smooth muscle to counteract abnormal distension, thereby resulting in medial hypertrophy.2,3 Additional intimal damage and subsequent proliferation and fibrosis further narrow the lumen of the muscular pulmonary arteries. Rudolph6 and Hoffman et al.3 theorized that one finding in the isolated aorta24 of endothelial damage caused by increased shearing forces due to a high flow velocity may also be a mechanism conducive to such intimal lesions.

Our group has suggested in a previous report7 that the presence of the direct VSD-PA component of the shunt may be one of the pathogenetic factors, which if not a major causative factor is at least an accelerating one, conducive to pulmonary vascular obstructive disease. Since the flow of the direct VSD-PA component is driven by the left ventricular pressure, this component may have a high flow velocity and result in a more powerful impact of pressure on the pulmonary vessel wall.

Bhattacharya and colleagues25,26 have reported that the pressure drop between the pulmonary lobular artery and the arterioles of 30 to 50 μm in diameter was only 1.8% of the lobular arterial pressure. In their experiments on isolated dog lung perfused with nonpulsatile flow, they demonstrated that artificially induced subtle undulations of lobular arterial pressure were, indeed, conducted down to the capillary without significant deformation of the pressure wave.26 It seems highly likely, therefore, that the hyperkinetic hemodynamic forces yielded by the direct VSD-PA component are conducted all the way through the pulmonary arterial vasculature. Target vessels for pulmonary vascular obstructive disease may then suffer from mechanical stress of considerable magnitude when the component occupies the total pulmonary flow in a greater proportion.

In the present study, we characterized the intracardiac hemodynamic behavior of shunted blood flow. The major finding was that supracristal VSD delivered an approximately two times greater amount of the direct VSD-PA component than did infracristal VSD with the same level of L-R shunting. The logical conclusion to be drawn from the above discussion and our findings is that the patient with supracristal VSD is at a greater risk of becoming jeopardized by pulmonary vascular obstructive disease than the patient with infracristal VSD when the sizes of the defects are comparable.

In cineangiographic examinations of patients with supracristal VSD, however, the amount of the direct

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<td>0.46 ± 0.02</td>
<td>0.48 ± 0.01</td>
<td>0.22 ± 0.01</td>
<td>6.0 ± 0.2</td>
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<td>0.55</td>
<td>0.46</td>
<td>0.25</td>
<td>10.6</td>
</tr>
<tr>
<td>0.52 ± 0.02</td>
<td>0.50 ± 0.05</td>
<td>0.26 ± 0.03</td>
<td>5.5 ± 0.2</td>
</tr>
<tr>
<td>0.52 ± 0.01</td>
<td>0.51 ± 0.02</td>
<td>0.26 ± 0.01</td>
<td>5.7 ± 0.2</td>
</tr>
<tr>
<td>0.72 ± 0.02</td>
<td>0.16 ± 0.01</td>
<td>0.12 ± 0.01</td>
<td>7.5 ± 0.2</td>
</tr>
<tr>
<td>0.75 ± 0.01</td>
<td>0.20 ± 0.02</td>
<td>0.15 ± 0.02</td>
<td>11.7 ± 0.4</td>
</tr>
<tr>
<td>0.59 ± 0.05</td>
<td>0.39 ± 0.07</td>
<td>0.21 ± 0.02</td>
<td>7.8 ± 1.1</td>
</tr>
</tbody>
</table>

**FIGURE 5.** Inverse relationship between f_d/f_a (% of control) and change in TPR (ΔTPR in units, U). The TPR was raised by injection of a suspension of lycopodium spores into the right ventricle. Numbers of observations are shown in parentheses. *Difference in f_d/f_a from control was significant (p < .01, one-way analysis of variance); **p < .001; #not significant (p > .05).
VSD-PA component (jet) is not always greater. We speculate that such patients may already have developed an elevated pulmonary vascular resistance. Such a hemodynamic change severely reduces the amount of the jet flow, as was evident in the present study in dogs with experimental pulmonary hypertension. No clinical data have yet been presented that support our speculation that the incidence of pulmonary vascular obstructive disease may be high in patients with supracristal VSD. To prove our speculation, more elaborate clinical investigations are needed. For such a study, it is of major importance that we select patients with supracristal and infracristal VSDs of the same size and that the patients be age matched.

In an attempt to demonstrate greater hyperkinetic hemodynamic forces imposed on the pulmonary vessels when a larger direct VSD-PA component exists, we monitored pulmonary arterial systolic, pulse, and mean pressures. None of these parameters in dogs with supracristal VSD with a greater direct component were significantly different from those in dogs with infracristal VSD. We therefore conclude that the hemodynamic forces exerted by the direct component may be more sensitively reflected in moment-to-moment subtle changes in the pulmonary arterial pressure or flow. The first time derivative of the pulmonary pressure (dP/dt) or the flow velocity may thus be a more appropriate indicator for evaluation of the mechanical stress than its integral, the pressure or mean flow.

In a preliminary study in dogs 3 and 5 through 13, we observed the maximum dP/dt of the ascending portion of the pulmonary arterial pressure. In the four dogs with supracristal VSD, this value was significantly larger than in the six dogs with infracristal VSD (553 ± 98 vs 306 ± 48 mm Hg/sec; p < .05, unpaired t test). Such results, however, should be interpreted with some caution since we used a water-filled cannula to conduct the pulmonary arterial pressure to the transducer and determined the dP/dt by visual inspection. Further experiments are needed, employing a catheter-
tip pressure transducer coupled with an electronic analogue computer for the determination of dP/dt.

A lesser degree of enlargement of the right ventricle than of the left ventricle is also one of the clinical manifestations related to the direct VSD-PA component4,9 (see Introduction). In the present study, it was found in dogs with supracristal VSD that, on average, 24% of the total L-R shunt flow, and as little as 11% in an extreme case, contributed to the end-diastolic volume of the right ventricle, whereas in dogs with infracristal VSD, the value was 61% on average, and as large as 84% in an extreme case.

In summary, supracristal VSD gave rise to an approximately two times greater direct VSD-PA component than did infracristal VSD with the same level of L-R shunting. Such an intracardiac pattern of shunting suggests that patients with supracristal VSD may have less enlargement of the right ventricle in earlier stages of disease. Although clinical evidence has yet to be provided, it is speculated that patients with a greater direct component may be at greater risk of becoming jeopardized by late-onset pulmonary vascular obstructive disease than patients with infracristal VSD with the same size of defect. At the later stage of disease, the direct component that has been distinctively large in supracristal VSD may become smaller as the pulmonary vascular resistance is raised, thereby resulting in an equal degree of enlargement of the right ventricle and left ventricle.

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S Okubo, M Nakai and T Tomino

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