SQUARE ROOT SIGN OF LEFT VENTRICULAR DIASTOLIC PRESSURE CURVE IN ATRIAL SEPTAL DEFECT

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The square root (dip and plateau) sign was observed in 7 of 21 adult patients with atrial septal defect (ASD). This study evaluated left ventricular (LV) diastolic filling dynamics and hemodynamic findings in 7 patients (Group 1) with, and 14 patients (Group 2) without the square root sign; 10 normal subjects (Group 3) served as controls. No significant differences were observed in LV end-diastolic and end-systolic volumes, ejection fraction, or left to right shunt. In Group 1, 77% of LV filling was completed in the first half of diastole; this percentage was 49% and 53% in Groups 2 and 3, respectively (both p<0.01 versus Group 1). Early diastolic filling velocity (at 20% of diastole) in Group 1 was significantly greater, and late diastolic filling velocity (at 80% and 90% of diastole) was reduced in Group 1 compared to those in Groups 2 and 3 (all p<0.05). The average values for right and left ventricular end-diastolic pressures were significantly higher in Group 1 (11±2 and 10±4 mmHg, p<0.05) than Group 2 (7±2 and 7±2 mmHg, p<0.05). It is suggested that a constrictive pathophysiology due to 4 chambers interaction or right ventricular constraint may play a role in the genesis of the square root sign in ASD.

THE square root (dip and plateau) sign of the left ventricular (LV) diastolic pressure curve has been considered to be characteristic of, but not specific for, constrictive pericarditis. This pattern is related to a rapid early diastolic filling followed by an abrupt termination of filling in mid-diastole by the thickened pericardium! During the diagnostic catheterization, we noticed the square root sign in some patients with atrial septal defect (ASD) when LV pressure was recorded with a high fidelity tip-manometer system. To study the clinical significance of this observation, hemodynamic and clinical data were analysed in patients with and without the square root sign, and compared to those of normal subjects.

METHODS

Patients (Table I): Twenty-one adult patients with ostium secundum ASD seen from January 1979 to April 1985 were the subjects of this study: 8 males and 13 females aged 17 to 65 years (mean 40.1). Preoperative cardiac catheterization was performed with a high fidelity tip-manometer system in all patients. Seven patients had the square root sign in the LV pressure tracing (Group 1), and 14 patients did not (Group 2). One patient in Group 1 and 4 patients in Group 2

Key words:
Atrial septal defect
Square root sign
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Normal Subjects (n = 10)

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a: Group 1 vs 2 p < 0.05, b: Group 1 vs 3 p < 0.05, c: Group 2 vs 3 p < 0.05
1', 21': patients after surgery

Abbreviations: Af = atrial fibrillation; ed = end-diastolic; EDVI = end-diastolic volume index; EF = ejection fraction; ESVI = end-systolic volume index; HR = heart rate; LV = left ventricular; Mn = mean; NSR = normal sinus rhythm; PAm = mean pulmonary arterial; PCM = mean pulmonary capillary; peak(−) = peak negative; Qp/Qs = ratio of pulmonary to systemic flow; RA = mean right atrial; RV = right ventricular; s = systolic; SD = standard deviation; T = time constant of isovolumic left ventricular pressure fall.
were excluded from the LV filling study because cineangiograms were not good enough for the frame by frame analysis. The data were compared with those of 10 age-matched control subjects without significant heart disease (Group 3). The square root sign was defined as a deep negative deflection ("dip") in early diastole followed by a plateau of the pressure curve in middle to late diastole (Fig. 1).

Study procedure: Cardiac catheterization was performed by the brachial approach in the fasting state under mild sedation. Right heart pressures were recorded with a fluid-filled system. In all cases left heart pressures were recorded by a Mikro-tip® angiocatheter (model PC-471 or 481, Millar Instruments). Zero level was calibrated electrically by a transducer control unit (model TCB-100, Millar Instruments) before the insertion of the catheter. Zero drift, when present, was adjusted at the mid-chest position through the fluid-filled system of the same catheter. Five consecutive complexes in patients with normal sinus rhythm and 10 in those with atrial fibrillation were averaged for the determination of pressure and the data derived from pressure tracings. The time constant of the LV pressure fall was calculated from the high-speed (100 mm/sec) recordings of LV pressure and $\frac{dP}{dt}$ by the method of Weiss et al. LV cine-angiography was performed simultaneously with LV pressure recording with the same catheter in a 30° right anterior oblique projection. Twenty-five to 40 ml of contrast material (Angioconray®) were injected in 3 seconds with a power injector. Films were exposed at a rate of 60 frames per sec with a 35 mm cine camera (Arritechno 35) mounted on a 25 cm image intensifier (Cardioscope U, Siemens).

Data analysis: Frame by frame measurements of LV volume were obtained from end-systole (minimum LV volume) to end-diastole (maximum LV volume) by the area-length method of Dodge et al with the use of a semicomputerized system (Cardias GP2000, NAC). In cases of atrial fibrillation, the duration of 5 consecutive beats was averaged, and a standard well-opacified one was selected for the calculation. The volumes were smoothed with the use of a

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Fig. 2. Composite percentile LV filling curves of 6 patients with ASD with (solid line, open circles, Group 1), 10 patients without (broken line, open triangles, Group 2) square root sign and 10 normal subjects (broken line, open squares, Group 3).

While the filling curve of Group 2 was similar to that of Group 3, the filling curve of Group 1 showed early diastolic augmentation and late stasis. A significant difference was observed in the percentile volumes through 40 to 70% of diastole between Groups 1 and 2 (*: p < 0.05, **: p < 0.01). Data are expressed as mean ± standard error of the mean.

Fig. 3. Comparison of LV filling curves before (closed circles) and after (open circles) closure of ASD with reference to that of constrictive pericarditis (open squares). The filling curve of a patient with the square root sign (Case No.1) is similar to that of a patient with constrictive pericarditis. The configuration returned to normal post-operatively.

ability was less than 0.05 (p < 0.05).

RESULTS

Of the 21 patients with ASD, 7 (33.3%) had the square root sign in LV diastolic pressure tracings (Group 1). The hemodynamic data of the 3 groups are presented in Table I. Biventricular filling pressures (right and left ventricular end-diastolic pressures, mean right atrial and pulmonary capillary wedge pressures) were significantly higher in Group 1 than in Group 2. No significant differences were observed in mean pulmonary arterial pressure, LV end-diastolic or end-systolic volume, ejection fraction, left to right intracardiac shunt, peak negative dP/dt or the time constant of LV pressure fall between Groups 1 and 2. One ASD patient with (case 1) and one without the square root sign (case 21) were evaluated pre- and post-operatively. In case 1 biventricular filling pressures fell and LV volume increased postoperatively.

Percentile LV filling curves shown in Fig. 2, were obtained by the method of Tyberg et
Fig. 4. Composite instantaneous LV filling velocity curves (dV/dt/V) in Group 1 (solid line, open circles), Group 2 (broken line, open triangles) and Group 3 (broken line, open squares). At 20% of diastole instantaneous LV filling velocity in Group 1 was greater than in Groups 2 and 3, whereas at 80 and 90% of diastole it was significantly lower in Group 1 than in Groups 2 and 3 (*: p < 0.05). Data are expressed as mean ± standard error of the mean.

Fig. 5. Composite instantaneous LV filling velocity curve (dV/dt/V) in 4 patients with normal sinus rhythm (solid lines, closed circles) and in 2 patients with atrial fibrillation (broken lines, open circles) in Group 1. The figure shows no substantial difference of the filling velocities between the cases with normal sinus rhythm and atrial fibrillation in Group 1 at 80 to 90% of diastole which are coincident with the timing of atrial contraction. Data are expressed as mean ± standard error of the mean.

There was a statistically significant difference between Groups 1 and 2 during 40 to 70% of diastole (at 40%, p < 0.05; at 50 to 70%, p < 0.01), but not between Groups 2 and 3. The composite diastolic filling curves of Groups 2 and 3 showed rapid filling in the interval from 10 to 30% of diastole and a late increment due to atrial contraction at 80 and 90% of diastole. The curve of Group 1 had an upward convex configuration which
patient with the square root sign the LV filling curve (Fig. 3) became normal.

Normalized instantaneous LV filling velocity curves are shown in Fig. 4. The early filling velocity in Group 1 was significantly greater at 20% of diastole and lower at 80 and 90% of diastole than in Groups 2 and 3 (p<0.05). This filling velocity curve differed from that of normal subjects, which had 2 peaks, one in early and another in late diastole. At 20% of diastole instantaneous filling velocity was 5.20±1.04 sec⁻¹ in Group 1, 2.00±0.78 sec⁻¹ in Group 2, and 3.22±0.93 sec⁻¹ in Group 3, and at 80% of diastole, it was 0.85±0.48 sec⁻¹, 2.10±0.64 sec⁻¹ and 2.97±0.59 sec⁻¹ in Groups 1, 2 and 3, respectively. Fig. 5 shows normalized instantaneous LV filling velocity curves of 4 patients with normal sinus rhythm and 2 with atrial fibrillation in Group 1. No significant differences were present between these curves throughout diastole. Even in patients with normal sinus rhythm in Group 1, early filling velocity was augmented and later acceleration due to atrial contraction was reduced.

Pressure-volume loop of the patient with the square root sign (Fig. 6-A) revealed that stroke volume increased and diastolic curves shifted to the right and downward with disappearance of this sign postoperatively (Fig. 7). On the other hand, in the patient without the square root sign, it was not changed by the closure of the defect (Fig. 6-B).

**DISCUSSION**

In 33% of adult patients with ASD, the square root sign was noted when the LV pressure was recorded with a high fidelity catheter tipped-manometer system. There were distinct differences in the LV filling dynamics of those with and without the square root sign. In patients with the square root sign we found a more rapid early filling and less filling from mid to late diastole; in addition right and left ventricular filling pressures were elevated.

It is generally believed that the square root sign is characteristic of constrictive pericarditis and restrictive cardiomyopathy. Hirota et al. and Chew and coworkers, however, reported that a typical square root sign was not present in patients with restric-

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Constrictive cardiomyopathy when LV pressure was recorded with a tip-manometer system. For the genesis of this sign, constrictive pericarditis has a peculiar pathophysiology characterized by: 1) elevated and equal left and right diastolic pressures, 2) normal isovolumic relaxation, and 3) normal chamber compliance during early diastole until the ventricles are constricted by the stiff pericardium. As is shown in Fig. 3, the filling curves from a patient with constrictive pericarditis and case 1 were very similar; there was markedly increased filling in early diastole and reduced filling in late diastole. In patients with ASD and the square root sign, relaxation was subnormal and biventricular filling pressures were elevated and equal. Postoperative data of the patient with the square root sign showed that restriction of the left ventricle was abolished by the closure of the defect. These diastolic properties suggest that the pathophysiology of the square root sign in ASD is similar to that in constrictive pericarditis.

In adult patients with ASD, LV failure develops clinically although volume overload is only on the right atrium and ventricle. The causes and mechanisms of LV dysfunction in ASD remain unclear. As LV diastolic failure develops, biventricular filling pressures increase, and there is an associated decrease in exercise tolerance. However, systolic function are reported to be normal. Distensibility of the left ventricle has been thought to be decreased, but precise diastolic properties are not well studied. Tikoff et al. observed that the incidence of heart failure increased with age, and elevated right atrial pressure was a common finding in adults with large ASD. They considered that elevation of right atrial pressure might be a sign of biventricular failure because the elevated right or common atrial pressure was regarded as an increase in LV filling pressure to maintain systemic output.

LV filling is determined by the dynamic interaction of the atrium and ventricle, and LV constraints such as the right ventricle, pericardium and intrathoracic pressure. Early rapid filling is affected by ventricular relaxation, elastic recoil created during systole and left atrial driving pressure after mitral valve opening. Increased left atrial pressure, LV chamber stiffness and the contractile state of the left atrium are the determinants of late filling. In patients with the square root sign, right ventricular filling pressures and pulmonary capillary wedge pressures were elevated. Therefore, augmented early diastolic filling in these patients...
patients may depend mainly on the elevated left atrial driving pressure. Hung et al. showed by radionuclide ventriculography that the peak filling rate of the left ventricle was normal in 11 adult patients with ASD. The reason for the difference in results remains unexplained, but it is probably due to the fact that they did not divide their patients into groups with and without elevated filling pressures.

In experimental studies Bemis et al. demonstrated that the alterations in the right ventricular filling pressure affected the LV geometry and pressure. An increment of 5 mmHg in right ventricular end-diastolic pressure raises LV end-diastolic pressure 2.3 mmHg, decreases the septum-to-free wall distance, and increases the anterior-to-posterior dimension of the left ventricle. In experimental animal models as well as typical clinical cases of acute right ventricular infarction, hemodynamic characteristics were very similar to those of constrictive pericarditis. This abnormality was reported to be reversible by the removal of the pericardium in experimental animals. Under these conditions, the LV passive pressure-volume curve was displaced to the left and upward and intrapericardial pressure was elevated by the enlarged right heart chambers in the relatively stiff pericardium. The same mechanisms may be the genesis of the square root sign and congestive heart failure in ASD. More research is required to investigate the relation between square root sign and congestive heart failure in ASD.

Rare cases of combined constrictive pericarditis and ASD were previously reported. Such cases had clinical features of ASD but did not have characteristic Kussmaul sign and pulsus paradoxus except for severe right heart failure. Our patients have no evidence for pericardial disease at the time of surgery.

We used the right anterior oblique angiographic projection for the analysis of LV volumes. In this view one cannot evaluate the paradoxical movement of the interventricular septum. The septum becomes flattened and displaced toward the left ventricle during late diastole and the left ventricle becomes oval or bow shaped. During systole it bulges anteriorly toward the right ventricle, and the left ventricle resumes its normal curvature. Therefore, this projection should provide an accurate measure of LV volume during early to mid diastole while it may produce an overestimation of volume during late diastole. Applying these facts to the filling curve, we believe that our findings are not exaggerated in this method of volume analysis.

Patients with the square root sign had a higher incidence of atrial fibrillation than those without the square root sign. Instantaneous filling velocity curves, however, did not show a difference between normal sinus rhythm and atrial fibrillation during the entire period of diastole (Fig. 5).

Acknowledgments

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