Aims The purpose of this study is to determine the possible influence of a left to right atrial shunt over the pulmonary venous flow pattern in children with ostium secundum atrial septal defect (ASD).

Methods and results Complete two-dimensional, spectral Doppler and colour flow Doppler examination were undertaken to examine the pulmonary vein flow pattern in 74 patients with ASD. This group was compared with a control group of 49 non-cardiological patients of similar ages and gender. Ultimately, pulmonary venous flow patterns changed. Pulmonary vein systolic velocities were significantly increased and diastolic velocities decreased in the ASD patient group compared with the control group. The right ventricular (RV) systolic function, evaluated by tricuspid annular displacement and tricuspid annular systolic velocity, was increased in patients with ASD. No left ventricular dysfunction was detected in the patient study group.

Conclusion Patients with ASD show changes in the pattern of pulmonary venous flow with an increase in systolic velocity and a decrease in diastolic velocities. This could be caused by an increase in the RV systolic function, which creates a vacuum effect against not only blood from the superior and inferior vena cavae, but also blood from the pulmonary vein through the ASD.
probe for routine echocardiography and a 2.5-MHz probe for Doppler tissue imaging (DTI). Data were recorded on videotape for later playback and analysis. A display speed of 100 mm/s was used. Continuous single-lead electrocardiogram monitoring was maintained during the study.

Right ventricular (RV) and left ventricular (LV) end-diastolic diameters and pulmonary flow/systemic flow (Qp/Qs) index were calculated according to standard technique. RV and LV end-diastolic diameters were divided by body surface area. LV systolic function was evaluated by M-mode-derived shortening fraction (LVSF) and ejection fraction (LVEF). M-mode echocardiography was used to study mitral and tricuspid annular motion, according to standard technique.

Echocardiographic data were obtained from mitral inflow Doppler (mitral peak E- and A-wave velocities and E-wave deceleration time), LV outflow tract Doppler (isovolumic relaxation time, IVRT), pulmonary venous Doppler (S- and D-wave peak velocities and pulmonary vein atrial reversal (PVAR) wave), and colour M-mode velocity of propagation (Vp) of the mitral inflow.

Pulmonary vein Doppler signals were acquired in the apical 4-chamber view by interrogating the right upper pulmonary vein. Colour flow imaging was used to align the beam parallel to pulmonary vein flow. A sample volume was placed 1 cm into the pulmonary vein, and at least five satisfactory signals were recorded. A division in the pulmonary vein forward flow signal was made at the point where the flow velocity curve changed slope. Systolic flows occurred before the slope change, and diastolic flows occurred after. If no change in slope occurred (because faster heart rate), the signal was considered to be fused, and the patient was excluded for this study.

Pulsed wave Doppler tissue (DTI) velocities were obtained at the cardiac base in the apical 4-chamber orientation from three locations: the lateral mitral annulus, the interventricular septum, and the lateral tricuspid annulus. DTI measurements from each of these myocardial segments included peak systolic annular velocity (S'), peak early diastolic annular velocity (E'), and peak late diastolic annular velocity (A') waves. From these measurements, the E/A, S/D, E/E', and E/Vp ratios were calculated.

Statistical analysis

All values are expressed as mean ± SEM. Normality of distribution was assessed through the use of the Kolmogorov-Smirnov test. Differences in measurements between groups were compared using the unpaired two-sided Student’s t-test and Mann-Whitney U test. A P < 0.05 was considered to be significant.

Results

As shown in Table 1, there was a statistically significant lower body surface area in Group 1, because patients with ASD weighed less than age-matched normal children. The heart rate was similar in both groups. According to the echocardiogram, there was a statistically significant difference in the LV end-diastolic diameter normalized by body surface area in Group 1 with respect to Group 2. LVFS and LVEF were similar to control group. RV end-diastolic diameter and Qp/Qs index were significantly increased in Group 1.

There were statistically significant higher pulmonary venous systolic velocities (0.72 ± 0.01 vs. 0.46 ± 0.01 m/s; P < 0.0001) and lower pulmonary venous diastolic velocities (0.56 ± 0.01 vs. 0.62 ± 0.01 m/s; P = 0.01) in Group 1 with respect to Group 2, as well as a higher ratio of pulmonary venous systolic velocity to diastolic velocity (S/D ratio) (1.28 ± 0.02 vs. 0.74 ± 0.02; P < 0.0001) (Figures 1 and 2).

No statistically significant differences were observed for PVAR-wave velocity (Table 2).
Tricuspid annular displacement normalized by body surface area (3.00 ± 0.15 vs. 2.16 ± 0.13 cm; \( P < 0.0001 \)) and tricuspid annular systolic velocity (16.45 ± 0.38 vs. 14.95 ± 0.48 cm/s; \( P = 0.016 \)) were statistically higher in Group 1 than in Group 2. Mitral annular displacement normalized by body area and mitral annular systolic velocity registered at the lateral side did not show significant differences between Group 1 and Group 2 (Table 3), but systolic velocities registered with DTI at the tricuspid annulus were higher than the corresponding velocities measured at the mitral annulus (14.95 ± 0.48 vs. 14.53 ± 2.26 cm/s; \( P < 0.01 \)) in normal children.

Diastolic ventricular performance was assessed by analysis of mitral inflow Doppler tracing (E- and A-waves; E/A ratio, and E-wave deceleration time). No significant differences were observed in either group. IVRT lengthened significantly in Group 1 vs. Group 2 (53.30 ± 1.64 vs. 45.56 ± 1.46 ms, \( P < 0.001 \)) (Table 4).

Early diastolic septal and lateral mitral annular velocities (\( E_0^{MS} \) and \( E_0^{ML} \) wave) were significantly decreased in Group 1 (14.26 ± 0.80 vs. 15.41 ± 0.42 cm/s, \( P < 0.01 \) and 18.22 ± 0.63 vs. 21.84 ± 0.59 cm/s; \( P < 0.0001 \)). There was a significant increase in the \( E/E_0^{ML} \) ratio in Group 1 vs. Group 2 (5.77 ± 0.30 vs. 4.81 ± 0.20; \( P < 0.05 \)). No statistically significant differences were observed for the late diastolic velocity (\( A_0 \)-wave) at the lateral mitral annulus, but it was significantly increased at the septal mitral annulus (8.9 ± 1.27 vs. 6.51 ± 0.26 cm/s; \( P < 0.05 \)) and at the lateral tricuspid annulus in patients with ASD (13.79 ± 0.53 vs. 11.20 ± 0.56 cm/s; \( P = 0.0015 \)) (Table 5).

The mean \( V_p \) was 54.83 ± 2.80 cm/s in Group 1 and 64.25 ± 4.77 cm/s in Group 2 (\( P = 0.0765 \), and the \( E/V_p \) ratio was 1.86 ± 0.14 in Group 1 and 1.71 ± 0.10 in Group 2 (\( P = 0.057 \)). The ASD systolic velocities were statistically higher than the diastolic velocities (1.14 ± 0.02 vs. 0.70 ± 0.02 m/s; \( P < 0.0001 \)).

**Discussion**

In normal children, the pulmonary venous flow shows two components (systolic and diastolic) with diastolic predominance and \( S/D \) ratio < 1. In our control group, the results are consistent with previously published data, but in patients with significant ASD, the pulmonary venous flow pattern was quite different, with \( S/D \) ratio > 1.

The most common vein accessible from the transthoracic apical view is the right upper pulmonary vein and this view was used in this study. Transesophageal echocardiography is superior to transthoracic echocardiography in the visualization of the left upper and the left lower pulmonary vein, but

---

### Table 2

<table>
<thead>
<tr>
<th></th>
<th>S-wave, m/s</th>
<th>D-wave, m/s</th>
<th>PVAR-wave, m/s</th>
<th>S/D ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (ASD)</td>
<td>0.72 ± 0.01</td>
<td>0.56 ± 0.01</td>
<td>0.30 ± 0.01</td>
<td>1.28 ± 0.02</td>
</tr>
<tr>
<td>Group 2 (control)</td>
<td>0.46 ± 0.01</td>
<td>0.62 ± 0.01</td>
<td>0.28 ± 0.01</td>
<td>0.74 ± 0.02</td>
</tr>
<tr>
<td>( P )-value</td>
<td>0.0001</td>
<td>0.0101</td>
<td>0.001</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Data are given as mean ± SEM.

### Table 3

<table>
<thead>
<tr>
<th></th>
<th>Tricuspid annular systolic movement (cm)</th>
<th>Mitral annular systolic movement (cm)</th>
<th>DTI mitral (cm/s) (( S_0 ) wave)</th>
<th>DTI tricuspid (cm/s) (( S_T ) wave)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (ASD)</td>
<td>3.00 ± 0.15</td>
<td>1.72 ± 0.09</td>
<td>12.74 ± 0.43</td>
<td>16.45 ± 0.38</td>
</tr>
<tr>
<td>Group 2 (control)</td>
<td>2.16 ± 0.13</td>
<td>1.68 ± 0.09</td>
<td>14.53 ± 2.26</td>
<td>14.95 ± 0.48</td>
</tr>
<tr>
<td>( P )-value</td>
<td>0.0001*</td>
<td>0.71</td>
<td>0.53</td>
<td>0.016</td>
</tr>
</tbody>
</table>

Data are given as mean ± SEM.

*Statistically significant from group 2.
Pulmonary venous flow in ostium secundum ASD patients

Table 4 Diastolic ventricular function indexes

<table>
<thead>
<tr>
<th></th>
<th>Peak E (m/s)</th>
<th>Peak A (m/s)</th>
<th>E/A ratio</th>
<th>E-DT (ms)</th>
<th>IVRT (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (ASD)</td>
<td>0.97 ± 0.02</td>
<td>0.56 ± 0.01</td>
<td>1.82 ± 0.06</td>
<td>128.81 ± 3.60</td>
<td>53.30 ± 1.64</td>
</tr>
<tr>
<td>Group 2 (control)</td>
<td>1.00 ± 0.02</td>
<td>0.53 ± 0.01</td>
<td>1.97 ± 0.08</td>
<td>135.86 ± 5.47</td>
<td>45.56 ± 1.46</td>
</tr>
<tr>
<td>P-value</td>
<td>0.29</td>
<td>0.23</td>
<td>0.15</td>
<td>0.26</td>
<td>0.0025</td>
</tr>
</tbody>
</table>

Data are given as mean ± SEM.
Peak E, early transmirtal flow velocities; Peak A, late transmirtal flow velocities; E-DT, E-wave deceleration time; IVRT, isovolumic relaxation time.

Table 5 Diastolic ventricular function indexes

<table>
<thead>
<tr>
<th></th>
<th>DTI: EML (cm/s)</th>
<th>DTI: ELS (cm/s)</th>
<th>DTI: ETL (cm/s)</th>
<th>DTI: AML (cm/s)</th>
<th>DTI: ALS (cm/s)</th>
<th>DTI: AEL (cm/s)</th>
<th>E/EML ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (ASD)</td>
<td>18.22 ± 0.63</td>
<td>14.26 ± 0.80</td>
<td>18.33 ± 0.70</td>
<td>9.13 ± 0.51</td>
<td>8.90 ± 1.27</td>
<td>13.79 ± 0.53</td>
<td>5.77 ± 0.30</td>
</tr>
<tr>
<td>Group 2 (control)</td>
<td>21.84 ± 0.59</td>
<td>15.41 ± 0.42</td>
<td>17.48 ± 0.60</td>
<td>8.26 ± 0.44</td>
<td>6.51 ± 0.26</td>
<td>11.20 ± 0.56</td>
<td>4.81 ± 0.20</td>
</tr>
<tr>
<td>P-value</td>
<td>0.0001</td>
<td>0.0039</td>
<td>0.6179</td>
<td>0.4028</td>
<td>0.0479</td>
<td>0.0015</td>
<td>P = 0.0179</td>
</tr>
</tbody>
</table>

Data are given as mean ± SEM.
DTI, Doppler tissue imaging; EML, early diastolic peak velocity at the lateral mitral annulus; ELS, early diastolic peak velocity at the septal mitral annulus; ETL, early diastolic peak velocity at the lateral tricuspid annulus; AML, late diastolic peak velocity at the lateral mitral annulus; ALS, late diastolic peak velocity at the lateral tricuspid annulus; AEL, late diastolic peak velocity at the septal mitral annulus.

Saric et al. found no significant difference in the pulmonary venous flow velocity pattern in left vs. right or superior vs. inferior pulmonary veins.

Gomez et al. have reported significant changes in pulmonary venous flow pattern after the closure of ASD with a decrease in S/D ratio. These features suggest that ASD not only produces chronic RV volume overload, but changes in pulmonary venous flow pattern are evident as well.

Pulsed Doppler signal in the ASD (right atrium) shows systolic flow disturbance beginning midway through systole and continuing almost up to the wave of atrial contraction with S/D ratio >1. This systolic and diastolic pattern flow through the ASD is similar to the pattern of pulmonary venous flow in patients with ASD. Moreover, the superior and inferior vena cava venous flow pattern is also biphasic with systolic dominance, which is due to the displacement of the annular tricuspid plane during RV systole. It yielded a drastic decrease in right atrial pressure, which in turn, produced a vacuum effect on the blood from the superior and inferior vena cavae during systole.

If there is a correlation among pulmonary, superior and inferior vena cavae, and ASD flow patterns, the rationale may be that RV contraction is increased due to RV volume overload (Frank-Starling law), in principle due to longitudinal myocardial fibre contraction. Moreover, these fibres are the major cause of apical systolic movement of the tricuspid annular plane. This systolic movement of the tricuspid annulus produces a significant decrease in the right atrial pressure that could produce a sucking effect not only on the systemic venous blood return (via inferior and superior vena cavae), but also on the blood coming from the left atrium and pulmonary veins through the ASD.

The RV has a shape and inflow very different than that of the left ventricle, with great compensatory capacity for volume overload. RV function is difficult to assess with conventional Doppler echocardiography due to failure of mathematical equations to reconstruct its complex geometric shape. The assessment of RV function has previously involved M-mode scanning through the lateral end of the tricuspid annulus. The rate of tricuspid valve annular descent and the degree of long-axis ventricular shortening have demonstrated sensitivity to echocardiographic indices of ventricular function.

DTI velocities quantify longitudinal shortening that represents the main mechanism of RV function. The measurement of the velocity through the tricuspid annulus recorded by DTI reflex is the main factor for RV function, even though the rotation and translation movements are also factored.

Eidem et al. established reference values for DTI velocities in healthy children, and Frommelt et al. concluded that RV systolic and diastolic function could be assessed non-invasively using DTI analysis of tricuspid annular motion.

In a normal setting, the right ventricle shows greater systolic longitudinal shortening than the left ventricle. Similar to the previous results of other authors, the tricuspid annular velocity was significantly higher than the mitral annular velocity in our control group. Pauliks et al. reported higher myocardial systolic velocities, generated from the tricuspid annulus in patients suffering from ASD, to support the hypothesis that patients with ASD have an increase in the RV function.

RV systolic function was valued through systolic movement (M-mode) and the systolic velocity of the tricuspid annulus (DTI). The significant increase in RV systolic function observed in Group 1 (ASD patients) compared with patients from the control group, support the hypothesis that RV volume overload ultimately increases RV systolic performance due to the Frank-Starling law. In our ASD group, this energetic RV systole would cause a significant displacement of the tricuspid annular plane. In order to verify this hypothesis, the systolic movement of the tricuspid annular plane was significantly increased in our patients with ASD, according to data obtained from the M-mode echocardiogram.
In patients with ASD, where the contractile function of the right ventricle and displacement of the tricuspid annular plane are increased, the systolic suction also could increase, and in turn have its effect not only on the flow of both vena cavae, but also on the pulmonary venous flow through the ASD.

It is well known that the pulmonary vein flow pattern changes when there is diastolic LV dysfunction. Nevertheless, the observed changes in the pulmonary venous flow in patients with ASD do not seem like an outcome of the LV systolic or diastolic function.

In our patients, there were no differences between the LV systolic function in the circumferential plane (determined by the ejection and shortening fraction) and also in the longitudinal plane. The paradoxical motion of the ventricular septum in ASD is a well-known phenomenon. Measurements of internal LV dimensions and functional data derived from them have been considered to be unrepresentative in patients with abnormal septal motion. Although septal motion was abnormal in 82%, the systolic mitral annular movement (obtained by M-mode) and the systolic velocities of the mitral annulus obtained by DTI did not show a difference between the patients with ostium secundum ASD and the control group.

Sutton et al. believed that regional and cavity function of the left ventricle in patients with secundum ASD is normal regardless of age and the type of septal motion. When reversed septal motion is present, its smaller-than-normal contribution to LV cavity filling and emptying are compensated for by enhanced septal and posterior wall thickening.

Regarding diastolic function of the left ventricle, our patients with ASD showed no significant differences in mitral peak E- and A-wave velocities, and E-wave deceleration time compared with the control group. However, the difference was significant when we compared the IVRT, which can be explained by the geometric shape disturbance of the ventricle and not so much due to changes in diastolic LV function.

There was no difference in the transmitral E-wave between Group 1 and Group 2. However, there was a significant decrease in the diastolic pulmonary venous flow velocities between Group 1 and Group 2. The transmitral E-wave velocity might be also decreased in Group 1, but multiple interacting factors determine the pattern of transmital blood flow and include left atrial pressure and compliance, LV pressure and compliance, dynamic change in the size of the mitral annulus, ventricular relaxation rate, and heart rate.

Nagueh et al. and Abaci et al. considered that the premature diastolic E-waves were ventricular preload dependent. In our ASD patients, the E’ velocities of the mitral annulus (free wall and septal level) obtained by DTI were slower than in the control group (P < 0.0001). It is possible that there is a decrement in the left atrium preload due to the shunt between the atria. For this reason, both the mitral annular and septal E’-wave, and the ratio of E/E’, could be influenced by the LV preload reduction as a result of the shunting. Other LV diastolic function indices did not show major differences between both groups, i.e. the propagation velocity by colour M-mode (Vp), the relationship between the peak velocity of the early mitral diastolic filling (E-wave), and the propagation velocity of flow obtained by the Dopper colour M-mode (E/Vp ratio). Because these indices are independent of the LV preload, these results support the statement that the LV diastolic function of ASD patients is similar to those patients without it.

Late diastolic velocity (A’-wave) measured at the level of septal mitral annulus and tricuspid annulus was significantly increased in patients with ASD, probably due to energetic atrial contraction as the result of increased right atrium preload.

### Study limitations

Effect of respiration: during inspiration, the LV stroke volume decreases. The mechanisms proposed for this include: (i) an increase in venous capacitance of the pulmonary vessels; (ii) an increased heart rate and therefore a shorter diastolic filling time; (iii) an increase in systemic afterload secondary to negative pleural pressure, and (iv) increased LV diastolic pressure due to a shift in the position of the interventricular septum, following augmentation of RV filling with inspiration.

Riggs et al. show changes in spectral Doppler echocardiogram obtained from the mitral valve and recorded simultaneously with the electrocardiogram and respiration. The peak E velocity is maximal at end-expiration and minimal at end-inspiration. There is a change in peak E velocity but no change in the pattern of mitral inflow.

Similarly, Appleton showed a basic pattern of lowest pulmonary venous flow velocity components on inspiration and highest on expiration, that was always present, but without changes in the pattern of pulmonary venous flow (S/D ratio).

These findings have implications for the interpretation of the pattern of pulmonary venous flow by current Doppler echocardiographic techniques that require further clinical investigation.

### Conclusion

The presence of a significant ostium secundum ASD modifies the pulmonary venous flow during childhood and adolescence, transforming it into a pattern of systolic predominance.

This pathology changes the normal relationship between systolic and diastolic flow velocities (S/D) <1 into a relationship (S/D) >1. RV systolic function could be increased due to the volume overload secondary to the atrial shunting, and it could be responsible for the change of the pulmonary venous flow pattern, by suctioning not only the systemic venous return coming from the superior and inferior vena cavae during systole, but also the left atrial flow and pulmonary veins through the ASD. These changes would not be due to subclinical diastolic dysfunction of the left ventricle.

### Conflict of interest: none declared.

### References

Pulmonary venous flow in ostium secundum ASD patients


