Doppler flow evaluation can anticipate abnormal left lung perfusion after transcatheter closure of patent ductus arteriosus

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Aims Coil protrusion into the left pulmonary artery (LPA) has been described after transcatheter closure of the patent ductus arteriosus (PDA). The possible impact of such a finding in lung perfusion has not been completely clarified. We evaluated Doppler flow velocities and lung perfusion in patients submitted to that procedure.

Methods After transcatheter closure of PDA with coils, 70 patients (mean age 8.6 ± 3.4 years) were followed for a period of 3.6 ± 0.9 years (range 2.1–5.9) and compared to 22 controls. Peak flow velocities and coil protrusion were assessed by Doppler echocardiography. A Doppler velocity index (DVI) was calculated by the difference between the LPA and right pulmonary artery (RPA) peak flow velocities relative to the pulmonary trunk (PT) expressed in percentage, as follows: DVI = (LPA velocity/RPA velocity/PT velocity) × 100. Lung scintigraphy was performed using 99mTc-labelled macro-aggregated albumin.

Results Device protrusion was observed in 94% of the patients, 10% of whom presented abnormal left lung perfusion. Peak LPA velocity and DVI were significantly greater in patients (p = 0.001) and correlated negatively with left lung perfusion values ($R^2 = 0.21$ and $R^2 = 0.65$, respectively). A cut-off value of 50% for the DVI showed high sensitivity and specificity for reduced lung perfusion.

Conclusion Impaired left lung perfusion may appear following transcatheter closure of PDA with coils and the determination of DVI may anticipate such alteration.
Introduction

Transcatheter closure of patent ductus arteriosus (PDA) has been widely performed and its excellent immediate results are well-known, while long-term studies are relatively few and are mainly devoted to the description of prevalence of residual shunts. Mechanical distortions of the adjacent vessels, particularly the left pulmonary artery (LPA), have been described after use of some types of prosthesis. Protrusion towards the lumen of the LPA has been reported after coil occlusion of PDA, but the potential consequences of flow distribution to the lungs have not been completely evaluated and the current literature demonstrates contradictory findings relating coil protrusion to flow disturbances.

In order to evaluate the prevalence of coil protrusion to the LPA and its possible impact on the vessel diameters, flow disturbances and left lung perfusion, we studied prospectively, by echocardiography and radionuclide lung scintigraphy, a large group of patients submitted to transcatheter closure of PDA with coils.

Patients and methods

Seventy patients (53 female, 17 male, mean age 8.6 ± 3.4 years, range 2.2–17.3 years) submitted to transcatheter closure of PDA at the Heart Institute (InCor), University of São Paulo Medical School, were followed for a mean period of 3.6 ± 0.9 years (range 2.1–5.9).

Ten (14.3%) patients presented other associated congenital cardiac defects. Four of them had been previously operated on (one ventricular septal defect, one atrial septal defect, two sub-aortic stenoses) and submitted at the same operation to PDA closure, but showed recanalization in the post-operative evolution and were considered for transcatheter closure. Five other patients had minimal ventricular septal defects, all showing a Qp:Qs < 1.2:1. The remaining patient had mild pulmonary valve thickening, without stenosis (peak flow velocity in the pulmonary trunk = 1.3 m/s).

Eight patients (11.4%) were diagnosed as having congenital rubella syndrome but none of them presented stenosis of the pulmonary arterial branches.

Control group

The control group consisted of 22 children and adolescents (11 female, 11 male, mean age 9.37 ± 4.2 years, range 3.7–19), 15 were normal and seven had minimal cardiac lesions (five small ventricular septal defects and one secundum atrial septal defect, all of them presenting Qp:Qs ≤ 1.1:1, and one non-stenotic bicuspid aortic valve).

This study was approved by the Institution’s Ethics and Research Committee and an informed consent was obtained before all procedures for patients and controls.

Coil occlusion procedure

Left lateral aortograms were used to define the ductal angiographic type, according to Kirichenko et al. Coil occlusion of PDA was performed in a retrograde fashion, via the femoral artery, using the methods of coil selection and implantation described in previous reports. Implantation was attempted using the Gianturco coils (Cook Inc., Bloomington, IN, USA) in 62 patients (88.6%) or Cook detachable coils (William Cook Europe, Bjaeverskov, Denmark) in eight patients.

Echocardiographic examinations

Transthoracic echocardiographic studies were performed using HDI 5000 equipment (Philips Medical Systems, Bothell, WA). Images were stored on 0.5 in. VHS format and were available for off-line analysis.

Measurements of the PDA minimal diameter and length were obtained prior to the transcatheter closure from the high left parasternal view.

In the follow-up period, the prevalence of residual shunt was evaluated by colour and pulsed wave Doppler, as well as the position of the coils and the presence of protrusion into the lumen of the LPA from high left and short axis parasternal views. The diameters of both pulmonary arteries were measured from the suprasternal views, at end-systole, and indexed by body surface area as shown in Figs. 1 and 2.

We also measured the peak flow velocities by pulsed wave Doppler at the pulmonary trunk (PT), immediately above the valve, from the parasternal short-axis view, at the LPA, below the coil protrusion and at the proximal segment of the right pulmonary artery (RPA) from the high parasternal short-axis view. A Doppler velocity index (DVI) was calculated by the difference between the left and right pulmonary arteries peak flow velocities in relation to the PT, expressed in percentage, as follows:

\[
DVI = \frac{\text{LPA velocity} - \text{RPA velocity}}{\text{PT velocity}} \times 100
\]

All examinations were performed by the same investigator without knowledge of either the clinical data or the lung scintigraphy results.

Lung perfusion scintigraphy

Lung perfusion scans were performed using a peripheral intravenous injection of 100,000 to 150,000 particles (10 and 90 lm) of \(^{99m}\text{Tc}\)-labelled macroaggregated albumin, at a dose of 0.03 mCi/kg. Two views were obtained in the anterior and posterior positions to evaluate the blood flow distribution between the lungs. The percentage of perfusion in both lungs was calculated by dividing the mean radioactivity obtained in both positions.

Predictors of decreased left lung perfusion

Several variables were examined in an attempt to predict which patients might be at increased risk for reduced left lung perfusion: age and weight during occlusion, other congenital cardiac defect or rubella syndrome associated, angiographic ductal type, PDA minimal diameter and length, amount and type of the coils, residual shunt, LPA diameter, coil protrusion into the LPA, peak LPA velocity and DVI.

Statistical analysis

Comparisons of means were performed by the paired or non-paired Student’s t-test or the analysis of variance (ANOVA), according to the kind of data and number of tested groups. Correlation between continuous variables was evaluated by the Pearson product–moment correlation coefficient. The ROC curve was used to select an optimal decision regarding the cut-off value of the DVI to predict abnormal lung perfusion. Results are expressed as means ± standard deviation and range p-value was set at 0.05 to achieve statistical significance.
Results

In 47 patients (67.1%), the PDA was diagnosed by angiography as type A, in 4 (5.7%) type B, in 3 (4.3%) type C, in 8 (11.4%) type D, and 8 (11.4%) type E. In most procedures (65.7%) only one coil was implanted. Two coils were implanted in 31.4% and three coils in 2.9% of the cases. The most common type of device was the Gianturco coil in 62 patients (88.6%).

The mean PDA minimal diameter obtained by echocardiography was 2.9 ± 0.75 mm (range, 1.2–5.0 mm) and by angiography 2.1 ± 0.8 mm (range, 0.7–4.1 mm). The mean lengths were, respectively, 7.9 ± 2.7 mm (range, 4–16 mm), and 8.3 ± 3.2 mm (range, 2.6–17.2 mm).
mm). The prevalence of residual shunt at the latest follow-up evaluation was 8.6%.

During the PDA occlusion procedure, coil embolization to the pulmonary artery was observed in three patients (2.1%), all of them being successfully retrieved. No embolic episode was noticed at the aorta.

**Coil protrusion and pulmonary flow velocities**

Sixty-six patients (94.3%) showed protrusion of the device. While the LPA mean peak velocity was significantly higher than in the RPA and the pulmonary trunk ($p = 0.001$), there were no differences between the regional mean peak flow velocities in the control group ($p = 0.68$, Fig. 3). Additionally, the peak LPA velocities and DVI were significantly greater in patients compared to controls ($p = 0.001$) (DVI: $21.6 \pm 25.8\%$ versus $1.7 \pm 7.3\%$).

**Radionuclide lung scintigraphy**

There was a significant difference between right and left lung perfusion in both controls ($53.2 \pm 2.4\%$ versus $46.8 \pm 2.4\%; 95\%$ CI: $41.6$–$52.0\%$) and patients ($54.4 \pm 2.9\%$ versus $45.6 \pm 2.9\%$), respectively ($p = 0.001$).

**Correlation between left lung perfusion and LPA velocity and DVI**

The mean time interval between the lung scintigraphy and the late echocardiographic study was $81 \pm 73.4$ days ($0$–$287$). Seven patients with abnormal left lung perfusion (mean $39 \pm 2.6\%$) presented mean LPA velocity and DVI greater than those with normal left lung perfusion (mean LPA velocity $= 1.59 \pm 0.33$ m/s versus $1.09 \pm 0.26$ m/s; mean DVI $= 55.5 \pm 32.96\%$ versus $12.3 \pm 11.9\%$) (Table 1). Maximal LPA velocity and DVI showed significant negative correlations with left lung perfusion ($p = 0.001$). However, the coefficient was stronger for the DVI ($R^2 = 0.65$) than for maximal LPA velocity ($R^2 = 0.21$) (Fig. 4). A regression equation was determined as follows: Left lung perfusion (%) $= 47.797 \div C0.0923 \times DVI$.

**Diameter of the pulmonary arteries**

The mean LPA diameters were significantly smaller when compared to the RPA diameters in patients. Moreover, LPA diameters were significantly smaller in patients with DVI $\geq 50\%$ when compared to patients with DVI $< 50\%$ and to the control group (Table 2).

**DVI as a predictor of abnormal left lung perfusion**

Among all variables examined, DVI was the only one to show an excellent association with decreased left lung perfusion ($p = 0.001$). A cut-off value of 50% for the DVI was determined, with 100% sensitivity and 98% specificity for the left lung perfusion deficits. From 8 patients (11.4%) that showed DVI $\geq 50\%$ (Table 3), 7 had decreased left lung perfusion. Two coils had been deployed in four of such patients and one coil in the remaining four. Only one of them had undergone previous surgical closure of the PDA. Fig. 5 illustrates a patient with increased DVI and reduced left lung perfusion.

**Fig. 3** Box plot of flow velocities (m/s) at the pulmonary arteries in patients and controls. LPA, left pulmonary artery; PT, pulmonary trunk and RPA, right pulmonary artery.

**Fig. 4** Scatter diagram of left lung perfusion (%) and DVI (%) for patients (circles) and controls (triangles). The regression line for patients is also shown ($R^2 = 0.65$).

**Table 1** Individual values of peak LPA velocity and DVI in the seven patients with abnormal left lung perfusion

| LPA vel (m/s) | 1.6 | 2 | 2 | 1.36 | 1.3 | 1.2 | 1.7 |
| DVI (%)     | 75 | 85 | 110 | 51 | 116 | 83 | 106 |
Discussion

The immediate and medium-term results of the transcatheter closure of PDA show unquestionable efficacy and safety. On the other hand, the long-term consequences of lung perfusion disturbances are still unknown.

The use of Gianturco coils to occlude the ductus is largely employed in developing countries, due to their low cost, easy manipulation and, above all, efficacy and safety. In the present series, Gianturco coils were used more frequently than Cook coils. The main difference between these two devices is the possibility of release control in the Cook model. Moreover, during the procedure implantation, some degree of protrusion into the pulmonary artery is normal, because in order to anchor the device, the first half of the first loop of the coil is positioned inside the pulmonary artery. This can be minimized by the mechanism of retrievability of the Cook coils. Consequently, Gianturco coils present higher rates of protrusion to the LPA when compared to other coils. While Stromber et al., described a 90% prevalence of Gianturco coil protrusion in a series of 31 patients, in the present study it was even higher (94.7%).

An alternative explanation for the high protrusion rate would be the greater thrombogenicity of Gianturco coils because of the presence of Dacron wool fibres. Cheung et al., comparing different types of coils, found that the reduction of residual shunt with time tended to be greater when Gianturco coils were used.

When we studied the mean peak velocity in the LPA, we found a higher value than that observed in the RPA and in the PT (p = 0.01). However, before trying to correlate such values to lung perfusion results, we tried to avoid possible sources of error, by establishing the DVI, which takes into account not only the LPA velocity, but also the velocities obtained in the pulmonary trunk and in the RPA. We believe that it is difficult to ascertain whether the absolute value of the velocity is normal or not in a specific segment of the pulmonary tree, as it may be influenced by factors such as the heart rate, ventricular function, volemia, etc. Therefore, the use of the proposed DVI may overcome these problems. Moreover, the evaluation of flow velocities in both right and left pulmonary arteries depends on the adequate alignment of the Doppler cursor with the long axis of the vessel, therefore compromising the calculation of the DVI. However, identical procedures were carried out for the control group, which showed a DVI close to zero.

Dessy et al. evaluated 49 patients submitted to transcatheter closure of PDA with the Rashkind prosthesis and detected device protrusion into the LPA in 10% of the cases. They also found a strong correlation between device protrusion and increased peak velocity, but a weak correlation with decreased lung perfusion values (they arbitrarily chose the value <40% as abnormal). Sreeram et al., also studied lung perfusion after the utilization of Cook detachable coils. In their series of 35 patients, 40% showed device protrusion into the LPA, with a significant correlation with mean peak velocity evaluated by Doppler. Although patients with coil protrusion showed a tendency to have lower values of lung perfusion, no significant difference could be detected when compared to the ones without protrusion. Additionally, no significant association was detected between low lung perfusion values and number of coils used or increased flow velocity in the LPA.

The lack of association in their study could be explained by the fact that they considered flow velocity absolute values. Several findings of their study may be pointed out as different from the present investigation: the type of coil, a smaller prevalence of protrusion and lower incidence of decreased lung perfusion. We speculate that radionuclide lung scintigraphy being performed in the early post-procedural period could have minimized the perfusional alterations that could appear along the time. In this context, Hijazi et al., demonstrated a decrease of 7% in left lung perfusion values based on scintographies performed immediately and 13 months after transcatheter closure of PDA.

Differently from Dessy et al., who considered Doppler as a non-reliable method to evaluate possible alterations of lung perfusion, the proposed DVI was an excellent predictor of perfusional abnormalities. Based on the determination of normal values for lung perfusion, we verified that from eight patients presenting DVI < 50%, seven had reduced left lung perfusion. Although we could also detect a negative correlation between peak LPA flow velocity and left lung perfusion, the coefficient was much lower than that obtained with the DVI. Furthermore, some apparently normal values of LPA velocities showed abnormal DVI (Table 1), which reinforces the concept of taking into account not only the LPA velocity but also the velocities in the pulmonary trunk and in the RPA.

The diameters of the pulmonary arteries should also be pointed out. This is a subject of some concern, as it has been argued that the closure procedure could impair

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<tr>
<th>Table 2</th>
<th>Mean right and left diameters of the pulmonary arteries in the control group and in the patients with DVI &lt; 50% and ≥ 50%</th>
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<tbody>
<tr>
<td>DVI</td>
<td>Mean RPA (mm/m²)</td>
</tr>
<tr>
<td>Control group (n = 22)</td>
<td>13.19 ± 2.32*</td>
</tr>
<tr>
<td>DVI &lt; 50% (n = 62)</td>
<td>13.45 ± 2.28*</td>
</tr>
<tr>
<td>DVI ≥ 50% (n = 8)</td>
<td>13.11 ± 3.02*</td>
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</tbody>
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Comparisons: (+) paired t-test, p = ns; (Δ) and (0) paired t-test p = 0.04; (*) ANCOVA p = 0.001.

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<th>Table 3</th>
<th>Distribution of patients according to the DVI and lung perfusion</th>
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<tr>
<td>DVI</td>
<td>Left lung perfusion</td>
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<tr>
<td></td>
<td>Normal</td>
</tr>
<tr>
<td>&lt;50%</td>
<td>62</td>
</tr>
<tr>
<td>≥ 50%</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>63</td>
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the normal growth of such vessels. Our results depicted a
difference between the right and left pulmonary artery
diameters in patients, and even lower values for the left
artery in the group showing an elevated DVI. These find-
ings are in accordance with the hypothesis that the pro-
cedure can affect growth. However, we cannot
completely rule out the possibility of it being related
to a congenital abnormality or even if it is present due
to an open-chest PDA closure.

Limitations of the study

Some limitations of this study must be considered. The
comparison of flow velocities in the pulmonary arteries
could not be performed between the pre and post-pro-
cedural periods, since before the PDA closure the pul-
monary flow pattern was already abnormal. Finally,
and perhaps the major limitation of our study, was

that we could not quantify the degree of coil protrusion
into the LPA. We only detected qualitatively the
presence or absence of protrusion. We do not rule
out the possibility that if we had devised a way to
quantify the protrusion, we could have achieved a bet-
ter correlation with abnormal values of pulmonary
velocity and perfusion.

Perspectives

In our opinion, it would be of great clinical relevance
to perform similar echocardiographic and scintigraphic
evaluations in patients submitted to surgical closure
of a PDA or to the implantation of other types of de-
vice, in order to clarify the nature and importance of
our findings. It may be that not only the presence of
the prosthesis, but mainly retraction and fibrosis
occurring after closure, and also some extension of
ductal tissue into the LPA, lead to abnormalities in local flow velocities. Troise and Arciprete\textsuperscript{11} suggested recently that ductal “invasion” into the LPA is determined by the amount of ductal tissue present in each case. Maroto et al.,\textsuperscript{12} speculated that ductal closure could be the aetiology of a transitory stenosis of the LPA. Guntheroth\textsuperscript{13} compared premature infants with PDA to those with spontaneously closed ductus, showing significantly higher LPA flow velocity values in the second group.

The utilization of the DVI may also be devised for other clinical situations where the presence of pulmonary arterial stenosis may be technically difficult to be confirmed, such as in the post-operative evaluation of the central pulmonary arteries in Fallot’s tetralogy, Rastelli operation and arterial switch operation.\textsuperscript{14}

Finally, the real long-term clinical relevance of left lung perfusion values lower than 39% detected in this study needs clarification which we believe may appear in the follow-up course of the affected patients.

References