More Accurate Quantification of Pulmonary Blood Flow by Magnetic Resonance Imaging Than by Lung Perfusion Scintigraphy in Patients With Fontan Circulation

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Background—Quantitative evaluation of pulmonary perfusion using lung perfusion scintigraphy in patients with atrio pulmonary anastomosis (APA) or total cavopulmonary connection (TCPC) or partial cavopulmonary connection (PCPC) is difficult because of preferential draining of the venae cavae to one lung. Scintigraphy is the gold standard. Phase-velocity MRI (PV-MRI) is a new technique for determining pulmonary perfusion. The aim of this study was therefore to determine whether PV-MRI is more accurate than scintigraphy for quantitative evaluation of pulmonary perfusion ratios in patients with APA, TCPC, or PCPC.

Methods and Results—We studied 15 patients with APA, TCPC, or PCPC (16±7 years old, 4 female). Twelve patients (15±8 years old, 3 female) with a single pulmonary blood source supplied by a subpulmonary ventricle, ensuring complete mixing of the radioactive tracer before entering the pulmonary circulation, served as controls. Pulmonary scintigraphy and PV-MRI were performed in all patients. Bland-Altman analysis showed a clinically unacceptable difference of 7.1% right pulmonary blood flow (27.2% upper and −13.0% lower limit of agreement) between the two methods in the study group. The two methods agreed excellently in the control group (difference, 1.6%; 4.0% upper and −7.2% lower limit of agreement), showing that the bad agreement in the study group was caused by the problems encountered using pulmonary scintigraphy in patients with APA, TCPC, or PCPC.

Conclusions—Because of preferential caval flow into either lung, PV-MRI is more accurate for evaluating pulmonary perfusion ratios than lung perfusion scintigraphy in patients with Fontan-like circulation. (Circulation. 2002;106:1510-1513.)

Key Words: Fontan procedure ■ magnetic resonance imaging ■ scintigraphy ■ lung

A t present, 99mTc lung perfusion scintigraphy is considered the gold standard for evaluating quantitative pulmonary perfusion in patients with congenital heart disease.1,2 Pulmonary perfusion abnormalities in patients with a Fontan-like circulation are clinically of particular interest and may have substantial consequences. Patients with atrio pulmonary anastomosis (APA),3 total cavopulmonary connection (TCPC),4 or partial cavopulmonary connection (PCPC) have been studied using lung perfusion scintigraphy.2,5,6 However, because of the preferential drainage of the caval blood into the right or left pulmonary arteries in these patients, lung perfusion scintigraphy does not optimally reflect the genuine perfusion ratio in this setting.7,8 Recently, in this patient group, pulmonary flow dynamics have been studied by phase-velocity MRI (PV-MRI).9-11 By PV-MRI, stroke volumes into each lung can be assessed. Thus, in principle, this method provides all the necessary information for evaluation of the lung perfusion ratio. The aim of this study was therefore to determine whether PV-MRI is more accurate than lung perfusion scintigraphy for quantitative evaluation of pulmonary perfusion ratios in patients after modified Fontan procedure.

Methods

Study Group
Fifteen patients with APA (n=9), TCPC (n=4), or PCPC (n=2) formed the study group. These patients were concurrently studied by PV-MRI and lung perfusion scintigraphy, which was part of a routine clinical follow-up. Four patients were female. The mean age was 16.0±7.4 years (Table). The time interval between the last cardiac intervention and the MRI study was 7.3±4.2 years. Informed consent was obtained in all patients. None of the patients had a baffle fenestration.

Control Group
All patients undergoing routine diagnostic lung perfusion scintigraphy at our center were screened for the underlying diagnosis.

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Patients with a single pulmonary blood source supplied by a subpulmonary ventricle were asked to enter the study as controls. This control group was chosen because its hemodynamic situation ensures complete mixing of the radioactive tracer in the subpulmonary ventricle before entering the pulmonary circulation. Preferential blood flow from the venae cavae into the pulmonary arteries does not have to be suspected in this situation, and therefore no consideration has to be made regarding the injection site of the radioactive tracer. Informed consent was obtained in all patients. Demographic characteristics are depicted in the Table.

### PV-MRI

Patients <6 years of age were sedated by chloralhydrate (60 to 100 mg/kg body weight) or chlorpromazine (1 mg/kg body weight). Retrospective ECG-gated MRI was performed with a 1.5-T MRI scanner (Philips ACS-NT). A conventional phase-sensitive gradient echo sequence was used in a double-oblique plane perpendicular to the dominant flow direction in the right and left pulmonary artery to measure antegrade, retrograde, and total flow volumes. The following acquisition parameters were used for PV-MRI: TR/TE, 25/6 ms; slice thickness, 6 mm; flip angle, 30 degrees; receiver bandwidth, 31.25 kHz; rectangular field of view, 260 to 400 mm; matrix, 256×256; and number of excitations, 2. At the beginning of each study, a velocity encoding (VENC), according to our experience, was chosen. Usually it was 1.5 m/sec for biventricular circulation and 1.0 m/sec for Fontan circulation. A higher VENC was used if an anatomic stenosis of the right or left pulmonary artery was detected in the pilot scans. After the first flow maps were acquired, they were checked for aliasing. If aliasing was detected, the scan was repeated using a higher VENC. This approach resulted in VENCs between 1.5 and 4.0 m/sec. Respiratory and flow compensation was used in subjects to minimize ghosting artifacts. Data were reconstructed to provide 25 to 33 magnitude (anatomic) and phase (velocity-mapped) images per cardiac cycle. Data analysis was performed offline using commercially available software (Flow®, MEDIS Inc). The resulting stroke volumes into the two pulmonary arteries were set in relation to each other, receiving a percent right pulmonary blood flow.

### Lung Perfusion Scintigraphy

Lung perfusion scintigraphy was performed using 99mTc-labeled human albumin macroaggregates and a gamma camera (Siemens). After intravenous injection, the 99mTc-labeled macroaggregate particles (15 to 40 μm) are homogeneously distributed in the lungs, enabling the study of pulmonary radioactivity distributions that reflect the pulmonary blood flow. The number of particles and the amount of radioactivity administered were adjusted according to the guidelines of the European Association of Nuclear Medicine.12 The lung scintigrams were obtained from anterior and posterior directions by collecting 200 000 counts per view. The percentage of perfusion of the lungs measured from anterior and posterior views (by the mean counts of both views) divided by two. Patients with a TCPC received an injection into the upper and lower limb on 2 days within 1 week. The total percent right pulmonary blood flow was calculated by subtracting the result of the two studies and dividing the result by two. Using an upper to lower ratio of 3:2 or 2:1 did not change the resulting total percent right pulmonary blood flow significantly. The percent left pulmonary blood flow was calculated by subtracting the percent right pulmonary blood flow from 100.

### Statistics

All data are presented as mean±SD or as medians and ranges. Linear regression analysis was used to determine the correlation between the percent right pulmonary blood flows assessed with PV-MRI and lung perfusion scintigraphy. In addition, a Bland and Altman analysis13 was performed to determine the agreement between the two methods measuring the same quantity.

### Results

The mean time span between the lung perfusion scintigraphy and the PV-MRI examination was 121±254 days in the study group and 120±289 days in the control group. All PV-MRI measurements were completed within 30 to 40 minutes. The
lung perfusion scintigraphy study time was about 15 minutes. The diagnosis, demographic data, and results of the two examinations of all patients are summarized in the Table. Bland-Altman analysis showed a difference of $7.1 \pm 10.1\%$ right pulmonary blood flow between the two methods in the study group. Upper and lower limits of agreement were $27.2\%$ and $-13.0\%$, respectively, and are therefore clinically unacceptable (Figure 1).

In the control group, the agreement of the measurements by lung perfusion scintigraphy and PV-MRI to assess the percent right pulmonary blood flow was excellent. We found a negligible difference of $-1.6 \pm 2.8\%$ between the two methods in the control group. Upper and lower limits of agreement were $4.0\%$ and $-7.2\%$, respectively (Figure 2). Thus, both methods may differ by $4.0\%$ above and $-7.2\%$ below in $95\%$ of the cases. One patient (Table, No. 17) had bilateral stenosis of the pulmonary arteries, which was not detected by lung perfusion scintigraphy.

One control patient (Table, No. 28) was excluded from the study. The pulmonary artery of this infant, who had multiple ventricular septal defects, had been banded when he was 1 month old. A follow-up lung perfusion scintigraphy and an MRI scan according to the study protocol were carried out when the infant was 23 months old. Flow volume into the right pulmonary artery could not be quantified by PV-MRI because of turbulent flow caused by the pulmonary band.

**Discussion**

The gold standard to evaluate quantitative pulmonary perfusion is lung perfusion scintigraphy. However, because of the preferential drainage of the caval blood into the right or left pulmonary arteries, lung perfusion scintigraphy does not optimally reflect the genuine perfusion ratio of patients with APA, TCPC, or PCPC. Although reliable information about the lung perfusion in this patient group in the perioperative and long-term follow-up is of particular clinical importance, to date no alternative imaging technique for evaluating this problem has been developed. The results of our study show that PV-MRI offers a solution to this unsatisfactory situation. We show that in control patients (with a single pulmonary blood source supplied by a subpulmonary ventricle), PV-MRI identified the same percent right pulmonary blood flow as lung perfusion scintigraphy (Figure 2). In this group, complete mixing of the radioactive tracer in the subpulmonary ventricle is ensured, because no preferen-
tial blood flow from the veina cava into the pulmonary arteries has to be suspected. This complete mixing assures that the measurements by lung perfusion scintigraphy reflect the genuine perfusion patterns. On the other hand, determination of percent right pulmonary blood flow in patients with APA, TCPC, or PCPC (study group) did not agree with the two methods (Figure 1). Considering the fact of preferential drainage of the caval blood into the right or left pulmonary arteries in these patients and the excellent agreement of the measurements in the control group (Figure 2), we conclude that PV-MRI is more accurate than lung perfusion scintigraphy for evaluating quantitative pulmonary perfusion in patients after APA, TCPC, or PCPC.

PV-MRI for quantitative evaluation of pulmonary blood flow in patients with APA, TCPC, or PCPC offers several additional advantages compared with lung perfusion scintigraphy. First, an injection of a radioactive tracer or a contrast agent is not needed. Second, in TCPC patients, PV-MRI evaluates the pulmonary blood flow patterns in a single investigation, whereas lung perfusion scintigraphy needs two consecutive studies. Another benefit of MRI is its ability to quantify flow and depict the anatomy in one session. To date, only complementary lung perfusion scintigraphy and pulmonary angiography can yield this information. Finally, as seen in one of the control patients, another advantage of PV-MRI lies in the possibility of detecting bilateral pulmonary artery stenosis, which was missed by lung perfusion scintigraphy.

Limitations

Some general limitations of PV-MRI and some specific limitations of our study need to be mentioned. Two general limitations of MRI are that it is contraindicated in patients with pacemakers and that in small children sedation is needed. In our study, patients younger than 6 years of age were sedated without complications. Another general limitation of PV-MRI is that turbulent flow may limit the accuracy of PV-MRI, as seen in one of our control patients. High-grade stenosis may therefore be difficult to quantify. Furthermore, PV-MRI may be limited by early branching of the distal pulmonary arteries. A double-oblique plane perpendicular to the course of the artery without cutting the branches may be difficult or impossible to obtain in all phases. Moving slice velocity mapping, as recently shown by Kozerke et al., may contribute to solving this problem.

A limitation of our study is the small sample size, both in the control and in the study group. However, the excellent agreement of the two methods in the control group does not justify a larger sample size in this group. On the other hand, a larger sample size in the study group would make the clinically important comparison of the inaccuracy of lung scintigraphy in the APA and TCPC subgroups possible. The small sample size of the study group is attributable to the difficulty in recruiting these patients, because all lung scintigraphies were solely clinically indicated. It would be unethical to increase radiation to patients, family members, and staff to achieve a larger sample size.

Another potential limitation of our study is the long interval between PV-MRI and lung scintigraphy. However, we do not think this interval caused any kind of bias. Because all APA and TCPC patients were taking anticoagulant medication throughout the study, short-term changes in the hemodynamics of these patients attributable to thrombus formation in the systemic venous pathway are very unlikely. Additionally, clinical changes were not observed in any of the subjects during the time interval between PV-MRI and lung scintigraphy.

Conclusions

This study provides data that in patients after a modified Fontan procedure, PV-MRI is more accurate for evaluating pulmonary perfusion ratios than is lung perfusion scintigraphy. This greater accuracy is attributable to an error of lung scintigraphy caused by preferential flow of the caval veins to one lung and the need for repetitive injection of the radioactive tracer.

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References

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