Assessment of aortopulmonary collateral flow and pulmonary vascular growth using a 3.0 T magnetic resonance imaging system in patients who underwent bidirectional Glenn shunting

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Abstract

OBJECTIVES: To explore the feasibility of evaluating the aortopulmonary collateral flow (APCF) and pulmonary vascular growth of patients who underwent bidirectional Glenn shunting (BGS) using phase-contrast magnetic resonance imaging (PC-MRI) and contrast-enhanced magnetic resonance imaging (CE-MRI).

METHODS: Blood flow measurements of the great vessels of the body were recorded in 22 post-BGS patients using 3.0 T PC-MRI. Right and left pulmonary blood flow (Qs), stroke volume (SV) of the ascending aorta (Qa), blood flow of descending aorta (Qd) and venous return of the superior and inferior venae cavae (Qv) per minute were calculated using the Report Card software. APCF was equal to the difference between Qs and Qv. The parameters for pulmonary vascular growth were assessed using CE-MRI. The relationship between pulmonary vascular growth and APCF was evaluated using correlation analysis. A comparative analysis was conducted between the MRI results and the results of five cases who underwent cardiac catheterization and 10 cases who underwent angiography.

RESULTS: Estimated APCF ranged from 0.23 to 1.63 l/(min/m²), accounting for 5–44% of Qs. Morphologic abnormalities such as pulmonary stenosis, dilatation and thrombosis were clearly visualized through CE-MRI. Significant differences in individual pulmonary artery growth were observed. A significant negative correlation was found between APCF and the pulmonary artery index (PAI; r = -0.461, P = 0.031) when the McGoon rate was 2.04 ± 0.59 and the PAI was 253.27 ± 85.86 mm²/m². Good consistency or relativity was found between cardiac catheterization, angiography and MRI.

CONCLUSIONS: Assessing the APCF and parameters for pulmonary vascular growth in patients who underwent BGS is feasible using 3.0 T PC-MRI integrated with CE-MRI, which may play an important role in clinical and therapeutic decision-making and prognostic evaluation.

Keywords: Magnetic resonance imaging • Congenital heart defects • Bidirectional Glenn shunt • Aortopulmonary collateral flow

INTRODUCTION

Bidirectional Glenn shunt (BGS) is a type of palliative surgery commonly used in patients who have a complex congenital heart disease with inadequate pulmonary blood supply [1–3]. In post-bidirectional Glenn patients, aortopulmonary collateral flow (APCF) increases pulmonary artery pressure and pulmonary vascular resistance, thus resulting in a systemic flow redistribution from the upper body to the lower body [4]. APCF also increases the collateral flow from the superior vena cava to the inferior vena cava [intercaval collateral flow (ICCF)]. Decreased blood flow to the upper compartment of the body may jeopardize the normal development of the central nervous system. To conduct a second Fontan surgery, conditions of pulmonary vascular growth, collateral vessels and so on should be understood after BGS. The amount of APCF and its influence on the cavopulmonary connection have always required attention because APCF is essentially an ineffective circulation [4, 5].

In recent years, some scholars have reported that APCF could be measured through catheterization with pulmonary perfusion scintigraphy [6]. Although the non-invasive measurement of APCF has been reported in other countries [7, 8], there has been no such report in China. In this study, 22 post-BGS patients underwent great vessel blood flow measurements of the lung and the body, as well as angiography, using 3.0 T phase-contrast magnetic resonance imaging (PC-MRI) and contrast-enhanced magnetic resonance imaging (CE-MRI). Then, the pulmonary vascular growth indices and APCF were calculated. Furthermore, a comparison between the calculated results and some cases of cardiac catheterization and angiocardiography was made in order to determine the correlation between APCF and pulmonary vascular growth and its clinical significance.
MATERIALS AND METHODS

Subjects

Twenty-two post-BGS patients at >1 year after surgery who were undergoing a second Fontan surgery were selected successively from March 2008 to February 2009. Among them, 14 were males and eight were females. The median age was 10 years (range: 3–25 years), post-BGS duration was 3.09 ± 1.50 years and the body surface area (BSA) was 1.01 ± 0.29 m². All cases in this group had pulmonary artery outlet obstruction, including five cases of pulmonary atresia (one case of right ventricular infundibular atresia, one case of pulmonary valve atresia, two cases of lower pulmonary artery atresia, one case of whole pulmonary artery atresia with right and left pulmonary artery confluence) and 17 cases of pulmonary stenosis. Among the 22 patients, 13 cases had single functional ventricles, and nine cases had two ventricles (with a relatively balanced development). Fourteen cases had unilateral superior vena cava, and eight cases had bilateral superior vena cava. Ten of the patients underwent arteriography, and five underwent cardiac catheterization.

Fast Cine phase-contrast sequence

Triple inversion recovery sequence axial scans and coronal scans were first conducted, followed by the long axis of the pulmonary artery. The main parameters were as follows: repetition time (TR) = 1000 ms, echo time (TE) = 22.4 ms, inversion time = 448 ms, echo chain length = 16; bandwidth = 62.5 kHz; thickness = 4 mm; spacing = 1 mm; field of view (FOV) = 35 cm × 35 cm and matrix = 256 × 256. The obtained anatomical structure was used for the positioning of the blood flow measurements. The right and left pulmonary arteries were vertically positioned 1–2 cm away from the lateral side of the cavopulmonary connection at the right and left pulmonary artery levels of the axis. The ascending aorta, descending aorta, superior and inferior venae cavae were vertically positioned 2 cm away from the coronary aortic valve, diaphragm level and 2 cm away from the cavopulmonary connection at the superior and inferior venae cavae levels (Fig. 1). Blood flow was measured using the Fast Cine PC sequence. The main parameters were as follows: TR/TE = automatically select the minimum TR/min full; flip angle: 20°; bandwidth: 31.25 kHz; FOV: 40 cm × 40 cm; matrix: 256 × 128; thickness of the scanning slice: 5 mm; excitation frequency: 1; the velocity encoding value of the artery: 150 cm/s; the velocity encoding value of the vein: 80 cm/s; and the encoding direction was Slice. Thirty-phase non-breath-holding scans of the Fast Cine PC sequence were successively conducted at the right and left pulmonary arteries, the ascending aorta, the descending aorta and the superior and inferior venae cavae perpendicular to the long axis of the blood vessel using the retrospective electrocardiogram gating triggering sectional K-space imaging. This sequence was performed on the patients with continuous main pulmonary artery at ~2 cm away from the pulmonary valve on the long axis of the pulmonary artery.

Contrast-enhanced magnetic resonance imaging sequence

Pulmonary vascular growth was evaluated using the 3D TRICKS (CE-MRI) sequence. Gadolinium-diethylenetriaminepentaacetic acid was used as a contrast agent to enhance the scan with a dosage of 0.2 mmol/kg of the body weight. The contrast agent was injected into the body through the forearm vein at a flow rate of 3 ml/s. Saline (20 ml) was subsequently injected at the same flow rate, and scanning was started 5 s after the contrast agent was injected. Respiratory training was given to patients who could co-operate by holding their breath before the scan, instructing them to keep the same breath-holding amplitude as much as possible during the examination. As for the patients who could not hold their breath, they were given 10% chloral hydrate 0.5–0.7 ml/kg as a sedative before the examination, and non-breath-holding scans were conducted continuously.

Blood flow measurements and calculation method

Image data were sent to a AW4.3 MR Workstation, and the blood flow parameters of the PC-MRI sequence were measured using the Report Card software. The dots were drawn manually with a certain interval at the margin where the amplitude image was present along the blood vessel of the target area. The vascular area of the target area could automatically be drawn using the software with an automatic tracing of 30-phase target area for one cardiac cycle, which could completely copy the position of the target area to the corresponding phase plot (Fig. 1E and F). After the automatic calculation using the software, the forward peak velocity, negative peak velocity, average blood flow of every stroke, average positive flow (APF), average negative flow (ANF) and time-flow curve of one cardiac cycle were obtained (Fig. 2). The corresponding regurgitant fraction was calculated as (ANF/APF) × 100%.

Patients’ height and weight were determined during scanning. BSA was calculated using the software according to the following formula: BSA (m²) = 0.0061 × height (cm) + 0.0128 × weight (kg) – 0.1529. The corresponding output per minute was calculated according to the average stroke volume and the average heart rate of the great vessels. Then, pulmonary blood flow (Qp) was equal to the sum of left and right pulmonary blood flow. Vena caval blood flow (Qv) was equal to the sum of superior and inferior venae cavea blood flow (QsVC and QIVC). The stroke volume of the ascending aorta (Qa) and the descending aorta (Qd) was also calculated. Then, APCF was obtained using the formula APCF = Qs/ Qv. The ratio of blood flow to the upper compartment of the body was obtained using the formula Qu = Qs – APCF × Qd. The ratio of blood flow to the upper compartment of the body was calculated from Rv = Qu/ Qs × 100%. Similarly, ICCF was calculated as ICCF = Qp – QsVC and the ICCF ratio as Rv = ICCF/Qu × 100%. The values for APFC and Qd, which were standardized through the BSA and the pulmonary artery index (PAI), were analysed. Using the simplified Bernoulli’s equation ∆P = 4V² max, the pressure difference in pulmonary regurgitation was obtained (where V max is the negative peak velocity).

Evaluation methods for pulmonary vascular growth

On the AW4.3 MR Workstation, the vessels were recombined through the 3D TRICKS sequence, and the maximum intensity projection (MIP) recombinant was conducted at the phase when
the pulmonary artery was in a good condition, which could help determine whether stenosis or dilatation occurred in the great vessels, thrombosis and so on. The long-axis image of the left and right pulmonary arteries was recombined by paralleling the left and right pulmonary arteries at the axis of the left and right pulmonary artery levels. The diameters of the left and right pulmonary arteries were measured to be 1-2 cm away from the bifurcation of the long-axis image \(D_{LPA}, D_{RPA}\). The cross-sectional area of the pulmonary artery \(A_{LPA}, A_{RPA}\) was obtained through a recombinant that was perpendicular to the long-axis image at the corresponding measurement area. The McGoon ratio and PAI were calculated according to the following formula: McGoon ratio = \((D_{RPA} + D_{LPA}) \text{ mm}/D_{AD} \text{ mm}\) and PAI = \((A_{RPA} + A_{LPA}) \text{ mm}^2/\text{BSA} \text{ m}^2\), where \(D_{AD}\) is the diaphragm diameter of the descending aorta.

**Statistical analysis**

Statistical analysis was conducted using the SPSS 13.0 software, and the quantitative data were expressed as mean ± SD. The
correlation between APCF, \( R_U \) and \( R_{IVCF} \) and that between APCF and pulmonary vascular growth indices was analysed using correlation analysis. Comparative analysis was conducted between the MRI results and that of the catheter examination in five cases and angiocardiography in 10 cases. A P-value of <0.05 was considered significant.

RESULTS

Aortopulmonary collateral blood flow

The APCF ranged from 0.23 to 1.63 l/(min/m\(^2\)), with an average of 0.88 l/(min/m\(^2\)), which accounted for 5–44% of the \( Q_S \) and averaged 24% of aortal stroke volume. APCF was consistent with the amount or the thickness of collateral vessels observed under CE-MRI (Figs 3 and 4). \( Q_U \) ranged from 0.54 to 1.19 l/min, with an average of 0.95 l/min. The mean \( R_U \) was 26.03 ± 4.67% (range: 17.14–33.33%). The ICCF ranged from 0.03 to 0.15 l/min, with an average of 0.09 l/min. \( R_{IVCF} \) was 10.14 ± 5.32% (range: 3.36%–20.37%). APCF significantly inversely correlate with \( R_U (r = -0.856, P = 0.000) \) and positively correlate with \( R_{IVCF} (r = 0.838, P = 0.000) \).

Pulmonary vascular growth

A marked variability in individual pulmonary vascular growth was observed. Measured under CE-MRI angiography, the McGoon ratio was 2.04 ± 0.59 and PAI was 253.27 ± 85.86 mm\(^2\)/m\(^2\). Under MIP angiography, one case was found to have local stenosis at the right pulmonary artery (Fig. 5A); one case of local dilatation in the right pulmonary artery (Fig. 5B); two cases of thrombosis in the right pulmonary artery, one of which had combined thrombosis in the superior and inferior venae cavae (Fig. 6); one case of local stenosis in the left upper vena cava; and one case of anomalous pulmonary venous drainage. Among the 22 cases, 20 MIP angiography cases showed that the central pulmonary artery was proportional in size to the peripheral branches and two cases showed that the central pulmonary artery was significantly broadened, which was asymmetrical with peripheral branches of the pulmonary artery (Fig. 7).

![Figure 3](image-url) Pulmonary atresia with blood supply by collateral vessels. MIP shows that more aortal collateral vessels (arrows) are involved in supplying blood for both lungs (A). APCF measured by PC-MRI accounts for 44% of the aortal stroke volume. Aortography shows that the conditions of collateral vessels are similar to those showed in A (B).

![Figure 4](image-url) Pulmonary stenosis with blood supply by collateral vessels. MIP shows that more aortal collateral vessels (arrows) are involved in supplying blood for both lungs (A). APCF measured by PC-MRI accounts for 17% of the aortal stroke volume. Aortography shows that the conditions of collateral vessels are similar to what MIP displays (B).
Correlation of aortopulmonary collateral flow and lung vascular growth indices

Exploratory analysis of APCF, McGoon ratio and PAI was performed, all of which showed normal distributions. APCF had a remarkable negative correlation with the PAI ($r = -0.461$, $P = 0.031$) and a weak negative correlation with the McGoon ratio without any significance ($r = -0.395$, $P = 0.069$).

Relationship between magnetic resonance imaging and cardiac catheterization, and angiocardiography

Five patients underwent cardiac catheterization, and the results of the lung and body blood flow measurements using PC-MRI and cardiac catheterization are shown in Table 1.

The value of $Q_p$, $Q_S$ and $Q_p/Q_S$ obtained through PC-MRI and cardiac catheterization was consistent, and had a good correlation between the regurgitant fraction that was measured using PC-MRI and the total resistance of pulmonary circulation that was measured using cardiac catheterization. The pressure difference of pulmonary regurgitation measured using PC-MRI and the pressure of main pulmonary artery measured using cardiac catheterization also showed a good consistency. Ten cases underwent pulmonary angiography and aortography. The consistency in the central pulmonary artery branches was displayed by MIP angiography and pulmonary angiography. Collateral vessels of different degrees were seen in the MIP images of all cases. The collateral vessels of the patients with pulmonary atresia were significantly more numerous and thicker than those with pulmonary stenosis, which were inoculated with those shown by aortography (Figs 3 and 4).
DISCUSSION

The accuracy and repeatability of speed and flow quantity measured using PC-MRI had been verified through many model tests and also through in vivo blood flow measurements [9–13]. Considering the standard positioning and fixed parameters for blood flow measurements, a few human factors will affect the results. The pulmonary vascular growth and the conditions of collateral vessels must be determined before the second Fontan surgery after BGS in a complex congenital heart disease. Patients have developmental delays because of hypoperfusion of vital organs such as the cerebral system and the kidneys, resulting from a large amount of collateral vessel shunts. Although collateral vessels have been discovered through aortography for several decades, quantitative measurement of APCF has been reported just recently [6, 8].

When a normal person is relaxed, the aortal stroke blood returns to the superior and inferior venae cavae after circulating from body organs, entering the left side of the heart system through the pulmonary vein after pulmonary circulation. Blood flow involves the exchange of blood and oxygen during both the systemic circulation and pulmonary circulation, and the total blood flow remains stable. Therefore, the values of $Q_R$, $Q_P$, and $Q_V$ in normal people should be equal or approximately equal, which have been verified in some studies. Pulmonary outlet obstruction occurred in patients before BGS. To compensate for the insufficient blood supply in the lungs, collateral vessels are often involved in the pulmonary blood supply in varying degrees. Collateral vessels are involved in pulmonary blood supply alone or in connection with vessels under the interlobar artery through the aorta and its main branches. Thus, the blood volume returned in the pulmonary vein is more than the sum of the blood flow in the left and right pulmonary arteries. A part of the aortal stroke blood develops into an ineffective circulation through collateral vessels $\rightarrow$ lung $\rightarrow$ heart $\rightarrow$ aorta, and the rest returns to the venae cavae after body circulation. Based on this result, two methods were used to calculate the APCF: (1) blood flow of the bilateral pulmonary vein minus blood flow of the bilateral pulmonary artery and (2) aortal stroke blood flow minus reflux volume of the venae cavae. Recently, some scholars have reported the calculation of APCF using PC-MRI. Grosser-Wortmann et al. [7] applied the first method to calculate the APCF of one group with 16 post-BGS cases and the result was $0.58–3.83 \text{l/}(\text{min}/\text{m}^2)$. Whitehead et al. [8] applied the two methods simultaneously to measure the APCF of 13 post-BGS patients and four post-Fontan patients, which verified that there was no statistical difference between the results obtained using the two methods. The second method was adopted to calculate the APCF in the present study because the pulmonary vein is relatively small and not easy to detect with four or five blood vessels to be measured. APCF in the present group of patients was $0.23–1.63 \text{l/}(\text{min}/\text{m}^2)$, which is lower than the two groups reported above. The reason may be due to the individual differences and post-BGS time difference.

The quantitative measurement of APCF and its influences on cavopulmonary connection have always been a problem which requires attention in clinical settings. The present study demonstrates that APCF influences systemic flow redistribution. It inversely correlates with the blood flow ratio to the upper compartment of the body and positively correlates with the blood flow ratio of ICCF. A large number of studies indicate that APCF is a negative factor for postoperative chest exudate, heart failure and poor prognosis and that a direct proportion between post-second Fontan complications and the conditions of collateral vessels (the amount of blood flow) exist [5, 14–19]. Given the large number of small collateral vessels, quantitative measurement is hard to conduct. Inuzuka et al. [6] reported that APCF can be measured using the Tremie casting method combined with pulmonary perfusion scintiphotography until recent years, but it is invasive with a lot of influencing factors. Noninvasive assessment of APCF can be conducted through PC-MRI, which only measures five great vessels. The measurement of APCF with PC-MRI is not influenced by pulmonary stenosis or atresia. Simultaneously, it obtains information about blood flow, flow velocity, the regurgitant fraction and so on, which provides reliable evidence for choosing clinical therapeutic schemes and evaluating prognosis.

Apart from the McGoon ratio and the PAI, indices for the pulmonary vascular growth also include the ratio between the pulmonary artery and the aorta (PA/AO) and the pulmonary vein index (PVI). The normal value of PA/AO is 1:1, which can be preliminarily used to assess the conditions of the pulmonary vascular growth. However, it is not suitable for patients with pulmonary stenosis or atresia and, is therefore, not applicable for post-BGS evaluation. The sum of the cross-sectional area of four pulmonary veins divided by the BSA is the PVI. Significant differences in the measured values in different places are observed because of the significant morphological variations among patients with a

<table>
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<th>Case</th>
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$Q_R$: blood flow of right and left pulmonary arteries; $Q_S$: blood flow of the ascending aorta; $Q_V/Q_S$: the ratio of blood flow of right and left pulmonary arteries divided by blood flow of the ascending aorta; $R_P$: pulmonary vascular resistance; $P_{MPR}$: pressure of the main pulmonary artery; CC: cardiac catheter; PC-MRI: phase-contrast magnetic resonance imaging; $R$: resistance of pulmonary vascular; RF: regurgitant fraction; MP: mean pulmonary pressure; GP: gradient pressure. $R$ and $MP$ measured with cardiac catheter; RF and GP measured with PC-MRI.
complex congenital heart disease [20]. Consequently, the PVI is not commonly used. Based on these results, the more practical indices for pulmonary vascular growth after BGS are the McGoon ratio and PAI. The McGoon ratio should be >1.5 and the PAI should be >250 mm²/m² (the normal value is 300±30 mm²/m²), with a minimum of 200 mm²/m² [21] during the Fontan surgery. The McGoon ratio and the PAI should be in the normal range during the evaluation of pulmonary vascular growth. Larger values for the McGoon ratio and the PAI may not be considered good. Although no current normal upper limit for the McGoon ratio exists, one patient, with a McGoon ratio of 3.8 and a PAI of 505 mm²/m² in the present study group, had obstructive pulmonary hypertension. His central pulmonary artery was obviously dilated, and his peripheral pulmonary artery became thinner. Furthermore, abnormal morphological changes such as pulmonary stenosis, dilation and thrombosis, as well as the conditions of the pulmonary vein, venae cavae, aorta and collateral vessels can be determined when CE-MRI is used to measure the indices for pulmonary vascular growth.

In the present study group, APCF was correlated with the thickness and the amount of collateral vessels, and a significant negative correlation was observed between the APCF and the PAI (r = -0.461, P = 0.031), which indicated that the thicker or more numerous collateral vessels, and the larger the APCF, the poorer the development of the pulmonary artery (with a smaller PAI). The reason for the slightly negative correlation between the APCF and the McGoon ratio without significance (r = -0.395, P = 0.069) may be that the central pulmonary artery was broadened (the McGoon ratio was increased) and the right-to-left shunt was increased in few patients with pulmonary hypertension. In patients with normal pulmonary arterial pressures, pulmonary artery development is poor with increasing APCF (with a smaller McGoon ratio). In addition, the APCF and the PAI were standardized with respect to the BSA. The McGoon ratio is the ratio between the sum of the diameters of the right and left pulmonary arteries and the descending aorta, which is not standardized with respect to the BSA.

Five patients in the present study underwent cardiac catheterization 2 weeks before or after the MRI examination. A good consistency was observed between the pulmonary and the body blood flows measured using PC-MRI and cardiac catheterization as well as a good correlation was observed between the PC-MRI-measured RF, gradient pressure and the cardiac catheterization-measured total resistance of pulmonary circulation, and the pulmonary artery pressure. Some scholars [22, 23] established a regression equation after the regression analysis between the reflux volume and the ratio between pulmonary and body blood flow was measured using PC-MRI and between the pulmonary artery pressure and resistance was measured using cardiac catheterization. Therefore, the pulmonary artery pressure and resistance can be calculated according to the pulmonary reflux volume and the ratio between pulmonary and body blood flows. The statistical analysis was not conducted because of the small sample sizes. Ten patients in the present study group underwent pulmonary angiography and aortography. The amount and the thickness of the collateral vessels in the main pulmonary artery branches and aorta were identical with the results of the MIP angiography.

The limitations of the present study are as follows: the number of samples was small. Although some patients underwent cardiac catheterization and angiography, the number of patients was small and insufficient for standardization. The influence of APCF on post-BGS should be studied with a long-term follow-up. Preliminary studies show that the blood flow of the great vessels of the body after BGS can be correctly measured using 3.0 T PC-MRI, and APCF can be calculated. CE-MRI can correctly measure the indices for pulmonary vascular growth and it can display the morphological abnormalities of the pulmonary artery and collateral vessel conditions, which coincided with the angiography, thereby emphasizing the less invasiveness and sensitivity of the MRI.

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