Observational Study

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Distribution of lung blood on modified bilateral Glenn shunt evaluated by Tc-99m-MAA lung perfusion scintigraphy

A retrospective study

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Abstract

The aim of the present study was to determine the distribution of lung blood in a modified bilateral Glenn procedure designed in our institute with lung perfusion scintigraphy. Sixteen consecutive patients who underwent modified bilateral Glenn operation from 2011 to 2014 were enrolled in the study. The control group consisted of 7 patients who underwent bidirectional Glenn shunt. Radionuclide lung perfusion scintigraphy was performed using Tc-99m-macro aggregated albumin (MAA) in all patients. For the patients in modified bilateral Glenn group, the time at which the radioactivity accumulation peaked did not differ significantly between the right and left lung field ($t=0.608$, $P=0.554$). The incidence of perfusion abnormality in each lung lobe also did not differ significantly ($P=0.426$ by Fisher exact test). The radioactive counts were higher in the right lung than in the left lung, but the difference was not statistically significant ($t=1.502$, $P=0.157$). Radioactive perfusion in the lower lung field was significantly greater than that in the upper field ($t=4.368$, $P<0.001$). Compared with that in the bidirectional Glenn group, the ratio of radioactivity in the right lung to that in left lung was significantly lower in the modified bilateral Glenn group ($t=3.686$, $P=0.002$). Lung perfusion scintigraphy confirmed the benefit of the modified bilateral Glenn shunt with regard to more balanced blood perfusion in both lungs.

Abbreviation: MAA = macro aggregated albumin.

Keywords: congenital, Glenn procedure, heart defects, operative, pulmonary perfusion scintigraphy, surgery

1. Introduction

The Fontan procedure is widely adopted in vascular surgery to treat patients with a single functional ventricle.[1] Sudden hemodynamic changes due to reconstruction of the vascular anatomy can cause ventricular volume overload and increase venous pressure. Many late complications, such as arrhythmia, thromboembolism, ascites, hepatic dysfunction, and protein-losing enteropathy, may occur in Fontan patients.[2]

Staging the Fontan operation has been shown to decrease postoperative risk.[3,4] The bidirectional Glenn shunt is one of the important intermediate operations in Fontan anastomosis. In some cases, it can serve as final palliation for high-risk patients with univentricular physiology.[5] However, the preferential blood flow from the superior vena cava to one side of the lung occurs inevitably because of the characteristic anatomic reformulation in the bidirectional Glenn operation.[6,7] To correct this discrepancy in perfusion between the sides of the lung, a modified bilateral Glenn shunt was applied in our institute, in which the innominate vein and superior vena cava were anastomosed with the left and right pulmonary artery, respectively. We hypothesized that a balanced lung blood distribution in the bilateral lung vessel bed should be obtained. In the present study, the effect of this procedure on pulmonary blood perfusion was investigated by Tc-99m lung perfusion scintigraphy.

2. Materials and methods

2.1. Participants

The study was approved by the Internal Research Ethics Board Committee of the General Hospital of Jinan Military Region, and all participants signed an informed consent form. From 2011 to 2014, 16 consecutive patients (7 males and 9 females; age, 2.0–14.0 years) who underwent the modified bilateral Glenn shunt were enrolled in the modified bilateral Glenn group. To compare the ratio of radioactivity in the right lung to that in left lung with bidirectional Glenn groups, 7 consecutive patients (3 males and 4 females; age, 2.5–7.0 years) who all undergone traditional Glenn operation from 2008 to 2012 were enrolled in the control group. Lung perfusion scintigraphy was performed on all the patients during follow-up, and a retrospective analysis on the data was carried out. The general patient information is listed in Table 1.

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Table 1

General characteristics of patients.

No.	Sex	Age, y	Time after operation, mo	Predominant disease	Blood oxygen saturation, %
Modified Glenn					
1	Male	6.7	30/30	PA/IVS	83.6
2	Female	4.3	14/30	SV (B)	88.9
3	Male	4.3	190/30	SV (A), Dextroversion	93.2
4	Female	9	138/30	TA	86.0
5	Female	3	98/30	TA	82.0
6	Female	3	104/30	SV (A), Dextrocardia	83.3
7	Male	5	103/30	PA, LVI	94.0
8	Female	14	106/30	LVI	93.8
9	Female	2	43/30	SV (B), CA	94.4
10	Male	4	103/30	SV (B), CA	92.4
11	Male	14	105/30	SV (C)	83.7
12	Female	4.8	248/30	SV (B)	88.9
13	Female	9	168/30	SV (L)	99.4
14	Male	8	172/30	Taussig–Bing	84.6
15	Female	4.8	127/30	TA	88.7
16	Male	6	297/30	LVI, Dextrocardia	90.1
Bidirectional Glenn					
a	Male	6	12	SV (A)	80.1
b	Male	3.5	37	SV (C)	82.4
c	Male	2.5	23	SV (A)	81.2
d	Female	5	60	SV (A), Dextrocardia	N/A
e	Female	6	60	SV (B)	79.8
f	Female	5	59	SV (B)	83.1
g	Female	7	48	SV (B)	91.6

CA = coronary anomalies, LVI = left ventricular insufficiency, N/A = not available, PA/IVS = pulmonary artery atresia with intact ventricular septum, SA = single atrium, SV (A) = single ventricle (A type), SV (B) = single ventricle (B type), SV (C) = single ventricle (C type), TA = tricuspid atresia.

2.2. Operation design

In the bidirectional Glenn operation, the superior vena cava was cut down from the right atria and connected with the right pulmonary artery with or without occlusion of the main pulmonary artery. To improve the distribution of pulmonary blood, a modified bilateral Glenn procedure was designed in our center. The main techniques included: fully liberating the superior vena cava, innominate vein, and pulmonary artery away from the associated tissue; transversely incising and completely separating the innominate vein from the superior vena cava; anastomosing the innominate vein and superior vena cava with the left and right pulmonary artery, respectively; reforming the pulmonary valve through which an appropriate pulsatile forward flow was maintained; widening the stenosis of the pulmonary artery if necessary; and repairing the atrioventricular valve, avoiding regurgitation (Fig. 1).

2.3. Lung perfusion scintigraphy

On a SPECT scanner of Millennium VG (GE, Milwaukee, WI), lung perfusion scintigraphy was performed using technetium-99m-labeled macro aggregated albumin (MAA), which was

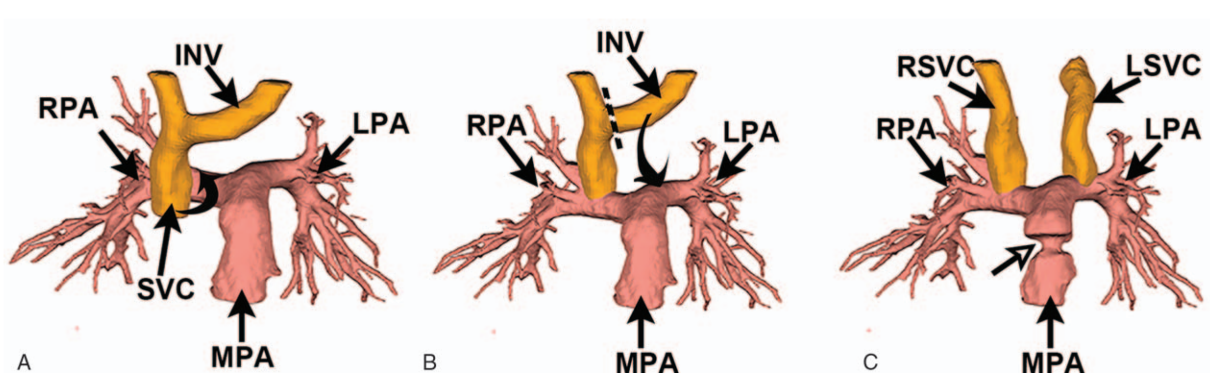

Figure 1. A diagram illustrating the design of the modified bilateral Glenn procedure. (A) Anastomosing the SVC with the RPA (curved arrow). (B) Cutting down the INV from the SVC (dash line) and anastomosing the INV with LPA (curved arrow). (C) Reforming the pulmonary valve (hollow arrow) through which appropriate pulsatile forward flow was maintained. INV = innominate vein, LPA = left pulmonary artery, LSVC = left superior vena cava, MPA = main pulmonary artery, RPA = right pulmonary artery, RSVC = right superior vena cava, SVC = superior vena cava.

provided by Peking Atomic Energy High-Tech Application Ltd Co. In the modified bilateral Glenn group, Tc-99m-MAA was administered intravenously into both the left and right upper limbs at the same time via median the cubital vein for 14 patients, and into the upper limbs one at a time for 2 patients (Patients 15 and 16). For each limb, 74 MBq (2 mCi) of radionuclide agent followed by 3 mL of additional saline were administered. In the bidirectional Glenn group, the same total dose was applied but only through right median cubital vein. The administration lasted for about 5 seconds with a steady injection rate.

To evaluate the distribution of pulmonary blood, dynamic and planar perfusion imaging was performed. The acquisition matrix was 256×256, and acquisition was trigged in 3 seconds immediately after the start of the injection. Imaging data were acquired for 60 seconds for dynamic imaging at 2 frames per second. A total of 8 projected views of planar perfusion imaging were obtained, stepped by 45°. Data were acquired for 90 seconds in each projected view.

Visualized dynamic imaging was performed over the entire perfusion process. The time–activity perfusion curves were generated to evaluate the perfusion rates in both sides of the lung. Quantification was performed by delineating the regions of interest for the major lobes of the lung and obtaining the relative ratio of radioactivity counts in different regions.[8] Experienced physicians identified the lung segment with a perfusion abnormality, where the presence of a reduction in radioactivity counts or a perfusion defect was observed, and to quantitate the degree of the perfusion deficit further. A positive diagnosis was established if 1 or 2 lung segments concurrently exhibited perfusion abnormity.

The ratio of radioactive counts in the right lung to that in the left lung is referred to as the *right-to-left ratio*; the ratio of the activity in the upper lung field to that in lower lung field is referred to as the *upper-to-lower ratio*; and the time at which the maximum radioactivity accumulation in a specified region was reached is referred to as the *peak time*.

2.4. Statistical analysis

Statistical analysis was carried out in SPSS 19.0 (SPSS, Chicago, IL). Data are expressed as mean ± standard deviation. A paired experimental design was applied to compare the radioactivity distribution in the left/right as well as the upper/lower lung field, and significant differences between groups were determined by paired t tests. Independent samples t test was employed to compare the differences in the right-to-left ratio between the modified bilateral Glenn and bidirectional Glenn groups. Counted data for comparison of the incidence of a lung perfusion defect in various lung lobes were included in an $R \times C$ contingency table, and then Fisher exact test was performed. The sample size was decided by the number of existing cases. Missing data were excluded when performing the statistical analysis. P values less than 0.05 were considered statistically significant.

3. Results

Radioactivity data in the regions of interest in the 2 study groups were obtained (Table 2). Based on these data, the ratio of radioactive counts in different lung lobes was calculated to quantify the distribution of lung blood flow. The peak time was determined to evaluate the lung perfusion rate in the regions of interest.

3.1. Outcomes in the modified bilateral Glenn group

3.1.1. Lung perfusion rate. The peak time in the right lung field was not significantly different from that in left lung field (t= 0.608, P=0.554; Table 3, also see an example in Fig. 2A). In 7 patients, the lung perfusion rate in the right lung was slightly faster than that in the left lung, and in 2 other patients, the peak times in the right and left lungs were significantly different (Patient 2, 22.2 seconds vs 1.2 seconds; Patient 5, 44.2 seconds vs 7.2 seconds).

3.1.2. Lung perfusion discrepancy. Dynamic perfusion imaging showed that the radionuclide agent, which came from 27 regions in a total of 32 upper limbs of 16 patients, drained mostly into the ipsilateral single lung (Fig. 2B). Only 2 patients had obvious central pulmonary convergence. In 1 single upper limb, the destination of blood flow mixed with nuclide agent was obscured.

3.1.3. Perfusion abnormality. Sixteen lung segments with a perfusion abnormality were observed among a total 84 lung segments of 14 patients. Figure 2C illustrates that the radioactive perfusion defect was observed in the right upper lung field in 8 projected views. However, the incidence of perfusion abnormality in each lung lobe showed no statistical difference between the 2 groups (P=0.426 by Fisher exact test; Table 4). Overall, scintigraphy of multiposition planar imaging depicted balanced lung perfusion in the modified bilateral Glenn group.

3.1.4. Distribution of radioactivity. The mean lung radioactivity count in the right lung appeared to be higher than that in the left lung (199.1 ± 19.6 Kc vs 171.7 ± 13.9 Kc), but the difference was not statistically significant (t=1.502, P=0.157; Table 3). In 2 patients who were given the agent in a unilateral upper limb separately, the right-to-left ratio was sharply distinct from that observed after injection into both upper limbs simultaneously (Patient 15, 0.374 from left limb vs 17.018 from right limb; Patient 16, 0.573 from left limb vs 6.614 from right limb). Activity in the lower lung field was higher than that in the upper field based on single lung segment analysis, and the difference was statistically significant (t=4.368, P < 0.001; Table 3).

The regions of interesting for the major lung lobes are delineated as examples in Figure 2D.

3.1.5. Comparison of modified bilateral Glenn group with bidirectional Glenn group. The ratio of radioactivity in the right lung to that in the left lung was significant higher in the bidirectional Glenn group than in the modified bilateral Glenn group (t=3.686, P=0.002). The right-to-left ratio was 1.2 ± 0.4 in the modified bilateral Glenn group (95% confidence interval, 0.984–1.432) and 1.9 ± 0.4 in the bidirectional Glenn group (Table 3).

4. Discussion

A key modification of the modified bidirectional Glenn procedure was the anastomosis of the innominate vein with the left pulmonary artery. Thus, the hemodynamics of this connection will present characteristic changes according to the change in anatomy. The blood flow derived from one side of the superior vena cava would be drained into the ipsilateral pulmonary vessel. Consequently, a balanced blood distribution in both sides of lung was hypothesized to result from this Glenn connection.

From the visualized cine imaging in the study, the whole process of the agent draining into the pulmonary system could be

Table 2

Distribution of radioactivity in segments of lungs.

	Ratio of radioactivity			Perfusion index						Peak time of activity, s	
No.	RL/LL	RUL/RLL	LUL/LLL	RL/(RL+LL)	LL/(RL+LL)	RUL/RL	RLL/RL	LUL/LL	LLL/LL	Right lung	Left lung
Modified Glenn											
1	1.304	0.590	1.007	0.586	0.414	0.371	0.629	0.502	0.498	59.8	51.8
2	0.789	0.603	0.990	0.441	0.559	0.376	0.624	0.497	0.503	22.2	1.2
3	1.103	0.688	0.797	0.503	0.497	0.408	0.592	0.443	0.557	35.2	25.9
4	1.056	0.595	0.813	0.514	0.486	0.373	0.627	0.448	0.552	50.2	50.2
5	1.570	0.669	2.662	0.611	0.389	0.401	0.599	0.727	0.273	44.2	7.2
6	2.083	0.531	0.997	0.676	0.324	0.347	0.653	0.499	0.501	40.8	41.2
7	0.867	0.472	0.683	0.464	0.536	0.321	0.679	0.406	0.594	38.2	54.8
8	1.567	0.522	0.952	0.610	0.390	0.343	0.657	0.488	0.512	28.2	42.8
9	1.028	0.748	0.796	0.507	0.493	0.428	0.572	0.443	0.557	36.8	32.2
10	0.909	0.599	0.976	0.476	0.524	0.374	0.626	0.494	0.506	21.8	37.8
11	1.043	0.615	0.854	0.510	0.490	0.381	0.619	0.461	0.539	53.8	46.8
12	1.161	0.805	0.921	0.537	0.463	0.446	0.554	0.480	0.520	53	57
13	1.610	0.653	0.964	0.617	0.383	0.395	0.605	0.491	0.509	56.8	58.8
14	0.714	0.510	0.474	0.417	0.583	0.338	0.662	0.322	0.678	57.8	58.2
15-1*	0.374	0.578	1.074	0.272	0.728	0.366	0.634	0.518	0.482	N/A	N/A
15-2†	17.018	0.560	—	0.945	0.055	0.347	0.620	0.000	0.000	34.2	15.8
16-1*	0.573	0.700	0.662	0.364	0.636	0.412	0.588	0.398	0.602	37.8	48.2
16-2†	6.614	0.786	0.546	0.869	0.131	0.440	0.560	0.353	0.647	51.8	58.2
Bidirectional Glenn											
a	1.638	0.443	0.545	0.621	0.379	0.307	0.693	0.353	0.647	7.800	10.200
b	1.985	0.795	0.824	0.665	0.335	0.443	0.557	0.452	0.548	22.800	17.200
c	2.492	0.554	0.570	0.714	0.286	0.356	0.644	0.363	0.637	53.200	39.800
d	0.710	0.811	0.716	0.415	0.585	0.448	0.552	0.417	0.583	10.200	8.800
e	0.437	0.613	0.724	0.304	0.696	0.380	0.620	0.420	0.580	21.200	40.200
f	1.743	0.453	0.810	0.635	0.365	0.312	0.688	0.447	0.553	43.800	11.200
g	2.174	0.517	0.914	0.685	0.315	0.341	0.659	0.478	0.522	55.800	9.800

* Administration from left upper limb.

† Administration from right upper limb.

LL = left lung activity, LL/(RL + LL) = perfusion index of the left lung, LLL = left lower lung activity, LLL/LL = perfusion index of left lower lung, LUL/LL = perfusion index of left upper lung, LUL = left upper lung activity, N/A = not available, RL = right lung activity, RL/(RL + LL) = perfusion index of the right lung, RLL = right lower lung activity, RLL/RL = perfusion index of the right lower lung, RUL = right upper lung activity, RUL/RL = perfusion index of the right upper lung.

traced dynamically. The peak times for both sides of the lungs were similar, and the blood in the vena cava flowed into the ipsilateral lung. The sharp differences in the right-to-left ratio between by 2 methods of administration verified the findings further. Statistical analysis also showed no significant differences in radioactive counts in both sides of the lungs. In addition, the right-to-left ratio was more reasonable in the modified bilateral Glenn connection compared with the bidirectional Glenn connection. All these findings suggest that a balanced distribution of lung blood, which corresponds well to the normal physiological state, was achieved through the improvement of the operation technique.

Previous research suggests that asymmetry of lung perfusion is one of the risk factors for follow-up outcome and exercise capacity.[7,9–12] We therefore deduced that a balanced distribution should contribute to a satisfactory postoperative outcome. Indeed, the reasonable pressure and resistance in the pulmonary circulation, according to our clinical examination results, also prompted us to believe that the modified bilateral Glenn may be a definitive procedure of choice for treating patients with a

Table 3

Statistical analysis results for radioactivity distribution.

Radioactivity counts, Kc				Right-to-left ratio		Peak time, s	
Left lung (n=14)	Right lung (n=14)	Upper lung (n=28)	Lower lung (n=28)	Modified Glenn group (n=14)	Bidirectional Glenn group (n=7)	Left lung (n=14)	Right lung (n=14)
171.7±13.9	199.1±19.6	77.0±27.7	106.0±46.5	1.2±0.4	1.9±0.4	40.4±18.3	42.7±13.0
t=1.502, P=0.157		t=4.368, P=0.000*		t=3.686, P=0.002†		t=0.608, P=0.554	

Left column: statistical analysis results for radioactivity counts in regions of interest. Median column: statistical analysis results for the ratio of radioactive counts in the right lung to that in the left lung. Right column: statistical analysis of the average peak time when the peak value of radioactivity reached the lung.

Data are expressed by means ± standard deviation. The paired t test was applied to compare the radioactivity counts in the left/right as well as the upper/lower lung field, and the independent samples t test was employed to compare the differences in the right-to-left ratio between the modified bilateral Glenn and the bidirectional Glenn group.

* $P<0.05$ represents the presence of a significant difference in activity counts between the upper lung field compared with the lower one.

† $P<0.05$ represents the presence of a significant difference in the ratio of radioactive counts between the right lung and the left lung.

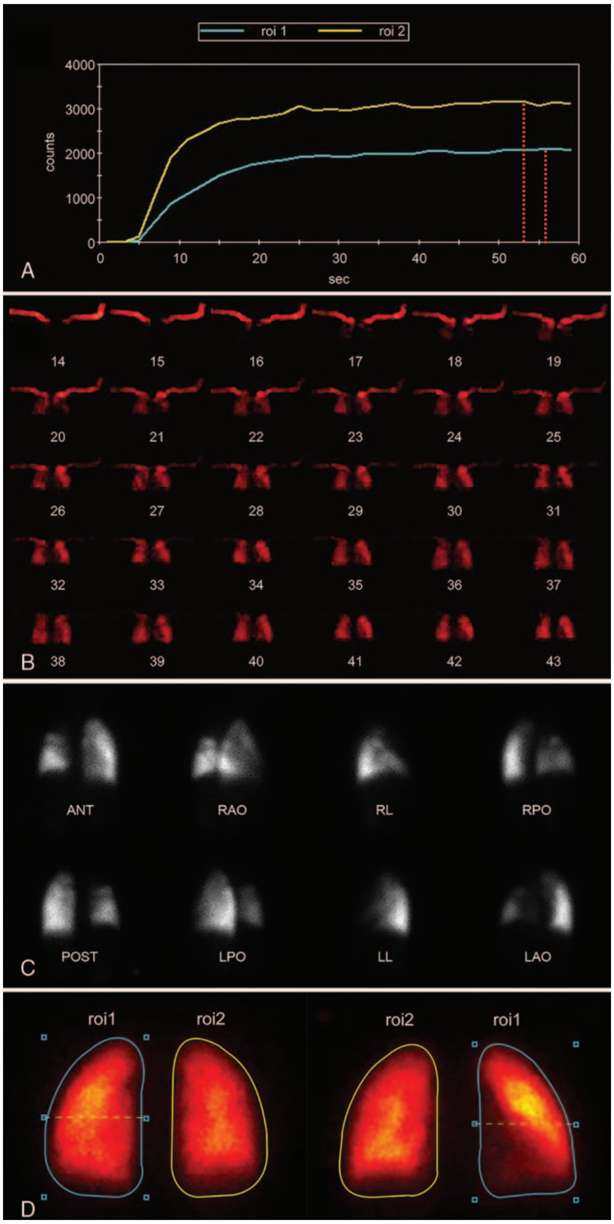

Figure 2. Representative images from lung perfusion scintigraphy. The images from left-to-right are as follows: (A) The peak time, when maximum radioactivity accumulation was reached, was obtained from dynamic perfusion curves to evaluate the speed of lung perfusion in different regions. The peak time was 53.0 seconds in the upper curve, and 56.8 seconds in the lower one. (B) Dynamic perfusion imaging of radioactivity in both sides of the lung. The perfusion image from the 14th to 43rd frame revealed the fact that the scintigraphy agent was preferentially drained into the ipsilateral single lung most of the same time. (C) Lung perfusion abnormality. The radioactive perfusion defect in the right upper lung field was clearly observed on 8 projected views of planar perfusion imaging. (D) Regions of interest of the lung lobes outlined in order to obtain the ratio of radioactivity counts in these regions of interest. ANT = anterior, LAO = left anterior oblique, LL = left lateral, LPO = left posterior oblique, POST = posterior, RAO = right anterior oblique, RL = right lateral, RPO = right posterior oblique.

functional single ventricle who are not suited for undergoing the Fontan procedure.

Previous research has shown that patients who undergo conventional bidirectional Glenn shunt are subject to hypostatic pulmonary congestion, which is presumably related to the occurrence of pulmonary arteriovenous fistula.[13] The present study confirmed the preferential distribution of radioactivity to the lower lung lobe in the modified bilateral Glenn procedure, but the incidence of perfusion abnormality in each lung lobe showed no significant difference on statistical analysis. Reductions in the radioactive counts were observed in the 4 lower lobes of 3 cases. Notably, the lack of low pulsatile pulmonary blood flow after Glenn procedure would be increased by blood perfusion to the lower lung lobes.[13,14] In the modified bilateral Glenn connection, the maintaining additional pulmonary blood flow would result in pulsatile pulmonary blood flow in the lungs and reasonable blood oxygen saturation. Thus, we can speculate that possible blood flow redistribution due to low pulsatile flow would occur slowly after the operation. Moreover, theoretically, the modified bilateral Glenn connection can be beneficial to lower pulmonary static pressure, because the blood from the upper body is partially led into the left lung through the left superior vena cava. We, therefore, supposed that the incidence of hypostatic lung blood distribution would decrease during follow-up.

Table 4

The frequency distribution of occurrence of perfusion abnormality in pulmonary lobes.

Lobes	With radioactivity reduction or defect (times)	Normal (times)	Total (times)
Right upper lobe	4	10	14
Middle lobe	1	13	14
Right lower lobe	2	12	14
Left upper lobe	2	12	14
Lingual lobe	5	9	14
Left lower lobe	2	12	14
Total	16	68	84

Despite this, arteriovenous shunting was observed in 2 cases in the study. The peak times in the right and left lung of 2 cases were different significantly (22.2 seconds vs 1.2 seconds, and 44.2 seconds vs 7.2 seconds). The time–activity perfusion curves for the left lung region in Patient #5 exhibited a decreasing tendency. We consequently speculated that microcirculatory arteriovenous shunting would occur in these 2 patients. In further nuclide scintigraphy with an enlarged field of view, the light radionuclide imaging in the brain and kidney confirmed the presence of arteriovenous shunting. Pulmonary vascular remodeling due to oxygen deficiency after operation could account for this phenomenon. Yin et al[12] reported that arterial venolization eventually causes the arteriovenous shunt of the pulmonary capillary net. However, further research is needed to illustrate the exact mechanism of arteriovenous shunting in the modified bilateral Glenn shunt in the future.

The contribution of blood volume from the upper body to the pulmonary circulation varies with age among the general population.[15] Disturbingly, the present study did not rule out the confounding effects caused by age. Blood flow perfusion may be easily influenced by the postural change, which was not considered in this study. The exact impact of the modified bilateral Glenn shunt on the circulatory physiology of patients remains to be elucidated. It is imperative to enlarge the sample size and to prolong the follow-up time in order to obtain reliable results in the future. Moreover, the technique to reduce the radiation needs to be improved further in young patients.

Many techniques can be used to obtain information regarding your blood flow rate in the pulmonary artery. Phase contrast magnetic resonance imaging served as a traditional option to acquire the blood velocity in the clinic. However, due to the presence of metal in the suture line, this technique was not available for evaluating hemodynamics after heart operation. Sedation was a difficult topic during examination for young patients. Another method to measure the flow rate is Doppler ultrasonography, which has been applied widely in vascular surgery. However, it is difficult to obtain the precise blood velocity in our pulmonary artery, because ultrasonic waves were subject to obstruction by the air in both sides of lung. The application of pulmonary perfusion scintigraphy to evaluate lung function and the development of lung vessels has been documented in many studies.[8,16–18] It is widely available for clinical practice and fundamental research with unique advantages. First, lung perfusion scintigraphy was hardly affected by the tracer injection pressure. The Tc-99m-MAA remains trapped in the pulmonary capillary bed in a natural way, and radioactivity is distributed in the lung segments in proportion to the relative blood flow.[16] Secondly, this method provides an alternative to the quantitative and hemi-quantitative methods to evaluate the physiology information regarding pulmonary microcirculation with relatively higher sensitivity, specificity, and accuracy. Moreover, it was easy to perform, and the results were easy to interpret.[19] Thus, this may be an effective clinical tool of choice for evaluating the hemodynamic significance of pulmonary blood flow. However, a previous study revealed the preferential drainage of the vena cava into 1 lung due to insufficient mixing of the radioactive tracer in superior vena cava.[10] Therefore, it is vital to maintain a smooth front by injecting a tracer in the vena cava during administration of Tc-99m-MAA. According to our policy, the agent was administered for about 5 seconds with a steady injection rate to improve this technical imperfection.

In conclusion, the optimized lung flood distribution in the modified bilateral Glenn connection was verified by radionuclide scan. The modified bilateral Glenn procedure may be a promising alternative for patients with a functional single ventricle who cannot endure the Fontan operation due to high-risk factors. Lung perfusion scintigraphy can be conveniently performed to evaluate the lung blood perfusion after a modified bilateral Glenn shunt. It can be regarded as an effective clinical tool to determine the hemodynamic characteristics of complex congenital heart defects.

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