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Ventilation/perfusion SPECT/CT in patients with severe and rigid scoliosis: An evaluation by relationship to spinal deformity and lung function☆

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ABSTRACT

Objective: Structural changes of the spine and chest wall associated with SRS result in poor cardiopulmonary function. Comprehensive assessment of pulmonary function is extremely important for patients with SRS before a correction operation. We explore the changes of distribution of lung ventilation and perfusion function in patients with SRS using SPECT/CT and describe the relation between these changes with Cobb angle and FVC%.
Patients and methods: From March 2015 to August 2016, 16 consecutive SRS patients with a mean age of 20.1 years(range 11–36 years) were included in the study. Scoliotic parameters on radiographs were analyzed. FVC% were obtained by spirometry test. Lungs ventilation/perfusion single photon emission computed tomography scans was performed preoperatively in all patients to explore pulmonary ventilation and perfusion function changes. These changes were measured as the deviation form the normal perfusion and ventilation function distribution in right and left lung and correlated with the Cobb angle of main curve and FVC%.
Results: The regional lung ventilation and perfusion function defects were not found in all SRS patients. Ventilation function deviation was a mean 5.7%(range, −3.6% to 10.1%), significantly less than perfusion function deviation of 8.2%(range, −0.3% to 22.2%) ($P = 0.015$, $t = -2.732$). Lung ventilation and/or perfusion function deviation did not correlated with Cobb angle and FVC%, respectively. There was significant correlation between lungs ventilation and perfusion function deviation($P = 0.001$, $r = 0.753$).
Conclusion: The ventilation and perfusion function distribution were favourable in convex and concave side lung of SRS. Deformity bring about greater lungs perfusion function changes than ventilation function. The measurement of lung ventilation and perfusion function changes may represents an additional functional feature to assess pulmonary function of SRS more comprehensively.

1. Introduction

Severe and rigid scoliosis (SRS) is defined as a spinal Cobb angle larger than 90° and curve flexibility less than 30% [1,2]. Structural changes of the spine and chest wall associated with SRS include thoracic scoliosis and kyphosis, spinal rotation, spinal intrusion into the thorax, chest wall distortion, and rib hump. These deformities squeeze the lungs and heart, resulting in poor cardiopulmonary function [3]. Surgical treatments are the main methods for correcting deformity of SRS. Various correction methods, such as posterior instrumentation combined with an anterior release, halo traction after anterior release, anterior release with internal distraction, vertebral column resection, and vertebral decancellation, have been sequentially developed to greatly improve the curve correction rate in recent years [1,2,4–6]. However, management of SRS remains a large challenge to spinal surgeons because of neurological and pulmonary complications. Furthermore, anterior release through the chest with thoracotomy or a thoracoscopic has often been recently used to achieve better correction of spinal deformity [1,2,4,7]. These invasive anterior procedures with the addition of poor cardiopulmonary function of SRS patients may cause an increased incidence rate of pulmonary complications, including hemothorax, hemopneumothorax, pneumothorax, pneumonia, dyspnea, and respiratory failure [8,9]. Severe pulmonary complications can increase hospitalization costs and suffering, and even threaten life.

☆ The study was approved by the Ethics Committee of West China Hospital. Written informed consent was obtained from both patients.

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Therefore, comprehensive assessment of pulmonary function (PF, including ventilation and perfusion function) is extremely important for patients with SRS before a correction operation.

Spirometry currently represents the standard of reference to evaluate PF. Forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV1) can accurately measure the degree of impairment of PF [10,11]. Spirometry test results are used to predict the incidence of postoperative pulmonary complications for patients with SRS as well [12]. However, according to the anatomical structure of the lungs, complete respiratory function is composed of pulmonary ventilation and perfusion. A spirometry test only reflects part of pulmonary ventilation function, and might not completely represent PF.

Lung scintigraphy visualizes the distribution of ventilation and perfusion in the lungs. Lung scintigraphy is used to detect lung embolism, pneumonia, chronic obstructive pulmonary disease, and congestive heart failure [13–15]. Three-dimensional ventilation/perfusion single photon emission computed tomography (V/P SPECT) has improved the accuracy in diagnosis of lung embolism and facilitated recognition of other cardiopulmonary diseases [16,17]. Additionally, V/P SPECT and CT fusion imaging can provide morphological and functional information of the lungs. However, lung ventilation and perfusion scans are rarely used to assess changes in PF in scoliosis. Only a few studies have investigated the relative contribution of each hemithorax to breathing, the asymmetry of lung function, or the changes in distribution of lung function after correction surgery through lung scintigraphy for early-onset scoliosis [18,19].

To the best of our knowledge, no studies have shown changes in PF for SRS based on V/P SPECT/CT of the lungs. Therefore, this study aimed to examine changes in distribution of ventilation and perfusion function in the right and left lungs in SRS, and to describe the relationship between these changes with the Cobb angle and FVC%.

2. Patients and methods

Our study was approved by the ethics committee of our hospital, and written informed consent was obtained from all of the patients. Inclusion criteria were preparing for a correction operation for scoliosis, curves with a Cobb angle of at least 90°, and a flexibility of less than 30% on bending radiographs. Exclusion criteria were neuromuscular scoliosis, the combination of an intraspinal tumor and tethered cord, heart or lung disease, including pulmonary tuberculosis, bronchial asthma, and congenital heart disease, and a previous history of a spinal operation. From March 2015 to August 2016, 16 consecutive patients with a mean age of 20.1 years (range, 11–36 years) were included in the study. There were 7 males and 9 females. The thorax and lungs of all patients were pressed and obviously distorted.

2.1. Radiographic assessment

Whole spinal posteroanterior and lateral radiographs were obtained preoperatively to measure the Cobb angle of the main curve, apical vertebral translation, and thoracic kyphosis. Apical vertebral translation (AVT) for thoracic curves was measured as the distance between the C7 plumb line and the center of the apical vertebral body or disc. Thoracic kyphosis (TK) was measured by the Cobb method from the superior endplate of T5 to the lower endplate of T12. Flexibility of the curves was calculated according to the Cobb angle, which was obtained from bending radiographs (Fig. 1).

2.2. Spirometry test

A spirometry test was performed for all patients after admission. The parameters are expressed as a percentage of the predicted value, and included FVC%, FEV1%, FEV1/FVC, total lung capacity (TLC%), vital capacity (VC%), and single-breath diffusing capacity of the lungs for carbon monoxide (DLco SB%). Deformity of the spine and thorax were often the result of limitation of chest movement, which caused restrictive ventilatory dysfunction. Therefore, FVC% was the main parameter used for assessing PF in patients with SRS. According to the American Thoracic Society guidelines [11], patients with an FVC% greater than 80% were considered to have no pulmonary impairment, FVC% values between 65% and 80% indicated mild impairment, FVC% values between 50% and 65% indicated moderate impairment, and severe impairment corresponded to FVC% values of 50% or less.

2.3. V/P SPECT/CT protocol

Technegas was prepared and inhaled with clamping of the nostrils for patients with SRS in the supine position. Ventilation tomography was performed when radioactivity in the front of chest was 100 uSv. A total of 5 mCi of 99mTc-radiolabeled macroaggregates of human albumin was slowly injected intravenously with the patient not moving and in the supine position. Perfusion tomography (Discovery NM/CT 670, General Electric Co., Connecticut, USA) was then performed. Low-dose chest CT was preformed immediately after perfusion tomography in the same position without any movement. The total data acquisition time was approximately 20 min, which was well tolerated by all of the patients with SRS. Finally, lung V/P SPECT/CT fusion images were obtained by data reconstruction (Xeleris Functional Imaging Workstation, Version 3.1). These reconstructive images were prepared for blinded review by an independent nuclear medicine physician. The proportion of radioactivity in each lung was also measured by the same physician.

Axial, sagittal, and coronal fusion images of lung V/P SPECT/CT were reconstructed. This was performed to evaluate the distribution of radiolabeled material in the right and left lungs, reflecting the distribution of functional alveoli pulmonis and pulmonary vasculature. Defects and a reduction in regional ventilation and perfusion function were also reviewed. The presence of regionally reduced ventilation and perfusion function were described as matched (reduction in ventilation = reduction in perfusion), mismatched (perfusion < ventilation), or reverse mismatched (ventilation < perfusion) [15]. The amount of radioactivity in the right, left, or total lungs was measured by the imaging workstation. Calculation of relative right and left lung ventilation and perfusion function was derived from the relative proportion of radiolabeled material for each lung quantified by right or left / total (%). In accordance with previous reports, the normal distribution of lung function in children was considered to be 55% on the right and 45% on the left [20]. A variation of greater than 5% beyond this value was considered as abnormal [20,21]. Therefore, The normal range of lung ventilation and perfusion distribution was defined as 55% ± 5% in the right and 45% ± 5% in the left in current study. The variation of lung ventilation and perfusion function was defined as the predicted normal value (55% right /45% left) minus the measured value in the convex side lung or the measured value of the concave side lung minus the predicted value.

2.4. Statistical analysis

The variation of lung ventilation and perfusion function was correlated with the Cobb angle, FVC%, and FEV1% using the Pearson correlation coefficient. The variation of lung ventilation function was correlated with that of perfusion function using the Pearson correlation coefficient. The paired Student's *t*-test was applied to compare the difference in variation of lung ventilation and perfusion function. Data were analyzed using descriptive statistics. All analyses were performed using the SPSS 19.0 (SPSS Inc., Chicago, IL). The null hypothesis was rejected when $P < 0.05$.

3. Results

Demographic and imaging data are shown in Table 1. Fourteen

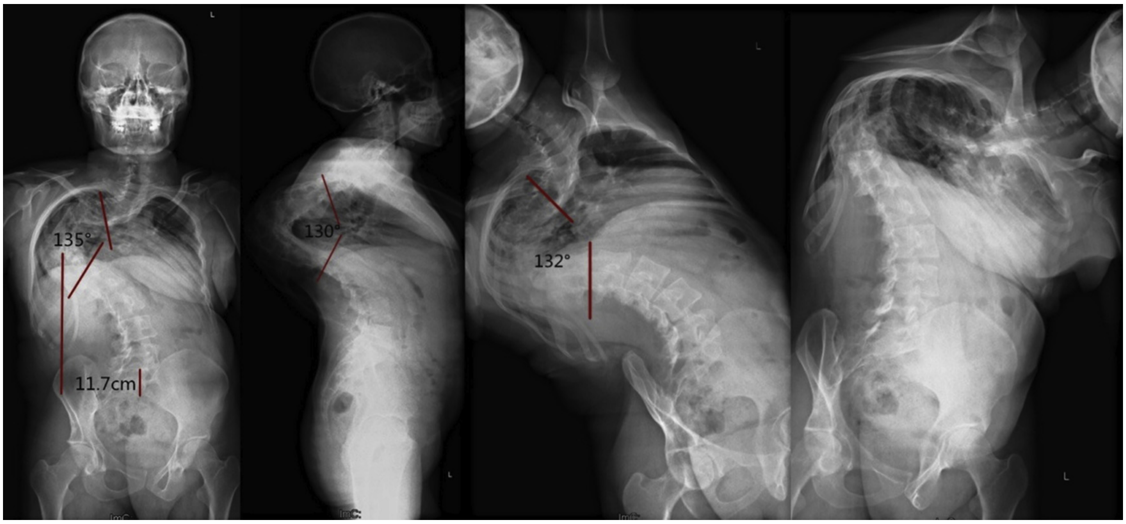

Fig. 1. This is the patient of No.2 who is a 36 years old male with severe and rigid idiopathic scoliosis. He had a 135°coronal plane deformity and 130°of thoracic kyphosis measured on whole spinal posteroanterior and lateral radiographs. The curve flexibility was 2.2% on side-bending radiographs. The apical vertebral translation was 11.7 cm. The convex side of major curve was right, and right lung was pressed and distorted apparently.

patients had idiopathic scoliosis and the remaining 2 patients had congenital scoliosis. The average Cobb angle of the major curves in the coronal plane was 105.5° (range, 91°–135°). The mean curve rigidity was 13.1% (range, 2.2%–27.8%). The apical vertebrae was located in the thoracic vertebrae in all patients. The convex side of the major curve was on the right in 75% (12/16) of the patients and on the left in 25% (4/16) of the patients. The median value of the AVT was 8.03 cm (range, −10.80 to 11.70 cm). The median value of the TK was 60° (range, 25°–130°).

The parameters of the spirometry test are shown in Table 2. A total of 75% of patients had impaired PF. Among them, 1 patient had severe pulmonary impairment, 6 had moderate impairment, and 5 had mild impairment according to the classification of FVC%. The remaining 4 patients with normal PF were all male. The value of FEV1/FVC for all of the patients was normal (range, 80.6%–98.8%). The average lung volume parameters of TLC% and VC% were 83.3% (range, 57.3%–108.5%) and 72.2% (range, 47.9%–106.9%), respectively. The TLC% in 37.5% of patients and VC% in 75% of patients were less than the normal value (80%). Mean DLco SB% was 99.4% (range, 64.1%–156.3%) and 81.3% patients had normal values.

Reconstruction images showed that lung ventilation and perfusion function was uniformly distributed in the axial, sagittal, and coronal planes in all patients with SRS. Defects and a reduction in regional ventilation and perfusion function were not found. Hot spots on lung perfusion images were more dense than those on ventilation images. The fusion images of lung V/P SPECT/CT of all patients showed that lung morphological images based on CT were almost matched with

Table 2
The parameters of spirometry test.

Case	FVC%	FEV1%	FEV1/FVC	TLC%	VC%	DLCO SB%
1	83.2	85.5	85.5	86.3	82.2	103.4
2	49.6	47.2	81.3	57.3	47.9	109.1
3	108.5	115.9	89.0	108.5	106.9	156.3
4	59.6	58.2	84.1	78.5	60.6	88.7
5	98.0	106.0	90.0	100.0	99.3	139.3
6	64.8	64.4	85.2	77.9	62.5	74.1
7	64.4	69.3	93.5	66.4	64.4	89.3
8	70.6	71.8	88.0	81.2	66.8	101.4
9	59.2	55.3	80.6	85.4	62.4	93.2
10	65.7	70.3	83.4	82.7	67.2	101.3
11	64.1	56.2	94.3	61.5	63.1	72.6
12	65.4	70.7	94.1	78.7	65.2	82.6
13	87.0	92.0	91.2	94.2	101.2	112.6
14	67.4	59.8	87.7	93.8	73.4	111.0
15	60.2	54.4	91.4	87.2	62.6	64.1
16	69.1	78.8	98.8	92.4	69.4	92.0

Table 1
Patient characteristics.

Case	Gender	Age	Scoliosis type	Convex side	Apical vertebral	Cobb angle	Flexibility (%)	TK(°)	AVT(cm)
1	M	16	2A+	R	T10	103	13.6	54	9.59
2	M	36	4B+	R	T6	135	2.2	130	11.70
3	M	17	CS	L	T11	100	7	75	−8.64
4	F	13	4C+	R	T9	95	17.9	60	6.51
5	M	18	4C+	R	T9	97	27.8	68	6.15
6	F	11	4CN	R	T8-9	102	27.5	43	8.01
7	F	23	CS	R	T9	105	21	45	9.21
8	F	16.5	5A+	R	T10	91	6.6	53	8.49
9	F	23	4B+	L	T9	116	5.2	109	−10.32
10	F	24	2A+	R	T9	115	24.3	108	11.6
11	M	25	1AN	L	T7	119	7.6	39	−10.80
12	F	17	4A+	R	T9	110	9.1	60	8.63
13	M	24.6	4B+	L	T7	95	8.4	40	−8.72
14	M	17.3	2AN	R	T9	105	14.3	60	8.04
15	F	15	4BN	R	T8	95	6.3	25	7.86
16	F	25	4A+	R	T10	105	11.4	85	8.52

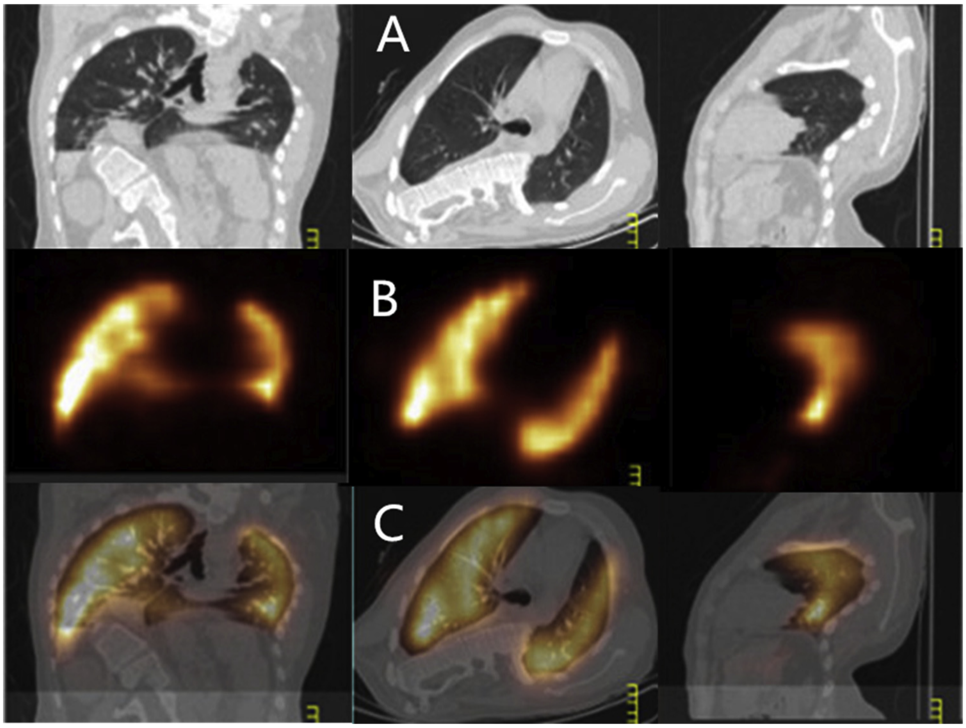

Fig. 2. These are lungs 3-dimensional CT image **(A)**, reconstructed perfusion function image **(B)** and their fusion image **(C)** in axial, sagittal and coronal plane for the patient of No.2. The reconstruction images show that right and left lungs perfusion function were distributed uniform. Distorted lungs present favourable perfusion function and no defects were found. The distribution of perfusion function in right lung is 41.9% and in left lung was 57.4%.

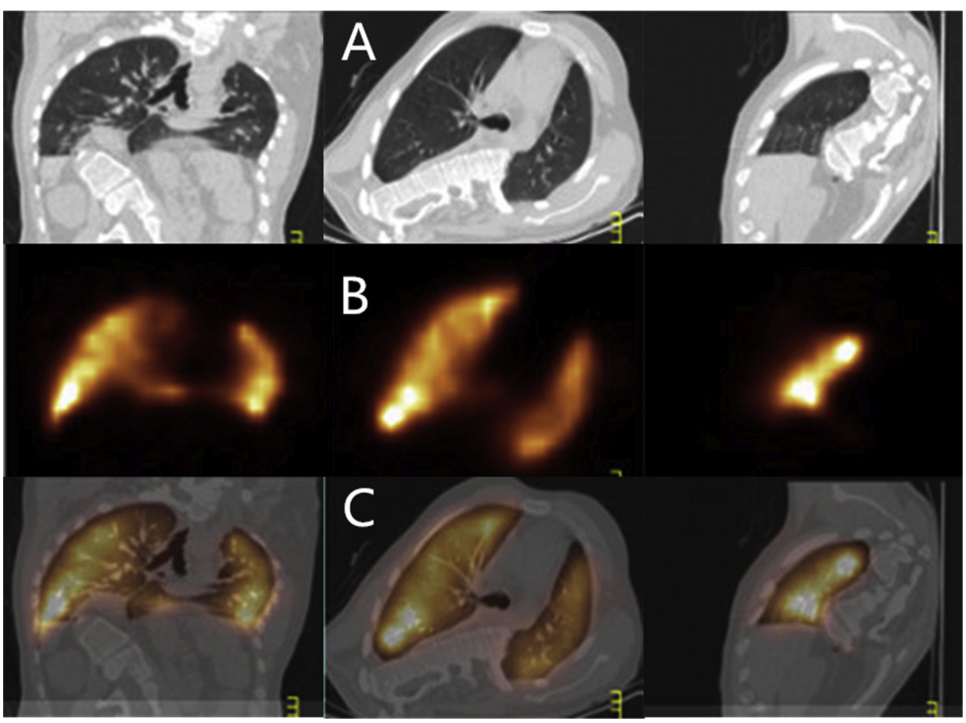

Fig. 3. These are lungs 3-dimensional CT image **(A)**, reconstructed ventilation function image **(B)** and their fusion image **(C)** in axial, sagittal and coronal plane for the patient of No.2. The reconstruction images show that right and left lungs ventilation function were also distributed uniform. Distorted lungs present favourable ventilation function and no defects were found. The distribution of ventilation function in right lung is 44.9% and in left lung was 55.1%.

ventilation and perfusion functional images (Figs. 2 and 3). This finding indicated that whole pressed and distorted lung tissue of patients with SRS showed favorable ventilation and perfusion function. Lung ventilation function appeared to be well matched with perfusion function on reconstructive images. However, the mean variation of ventilation function was 5.7% (range, −3.6%–10.1%), which was significantly less than that of perfusion function (8.2%; range, −0.3%–22.2%; $P = 0.015$, $t = -2.732$). Fourteen of 16 patients with variation of lung ventilation function had reduced function in the convex side and 2 had reduced function in the concave side. Fifteen of 16 patients with variation of lung perfusion function had reduced function in the convex side and 1 had reduced function in the concave side. Ventilation function variation in 68.8% of the patients and perfusion function variation in 62.5% of the patients were greater than 5%. Additionally, all of the patients with variation of lung function greater than 5% had reduced function in the convex side. There was no correlation between variation of ventilation function and the Cobb angle ($P = 0.066$, $r = 0.470$) or FVC% ($P = 0.734$, $r = 0.089$). No correlation was found between variation of perfusion function and the Cobb angle ($P = 0.206$, $r = 0.334$) or FVC% ($P = 0.770$, $r = -0.079$). There was a significant correlation between variation of lung ventilation and perfusion function ($P = 0.001$, $r = 0.753$). The distribution of ventilation and

Table 3
The distribution of ventilation and perfusion function in right and left lungs.

Case	Ventilation		variation (%)	Perfusion		variation (%)
	L(%)	R(%)		L(%)	R(%)	
1	50.8	49.2	5.8	56.5	43.5	11.5
2	55.1	44.9	10.1	57.4	41.9	12.4
3	40.7	59.3	4.3	41.8	58.2	3.2
4	47.4	52.6	2.4	47.3	52.7	2.3
5	54.6	45.4	9.6	55.4	44.6	10.4
6	53.5	46.5	8.5	67.2	32.8	22.2
7	54.6	45.4	9.6	55.5	44.5	10.5
8	42.9	57.1	−2.1	45.7	54.3	0.7
9	40.2	69.8	4.8	37.6	63.2	8.2
10	51.4	48.6	6.4	58.3	41.7	13.3
11	39.6	60.4	5.4	41.2	58.8	3.8
12	52.2	47.8	7.2	54.4	45.6	9.4
13	37.5	62.5	7.5	36.3	63.7	8.7
14	50.6	49.4	5.6	49.8	50.2	4.8
15	41.4	58.6	−3.6	44.7	55.3	−0.3
16	53.9	46.1	8.9	55.4	44.6	10.4

perfusion function in the right and left lungs is shown in Table 3.

4. Discussion

PF of patients with scoliosis has been assessed in many previous studies. There are several aspects that reflect the condition of PF, including the spirometry test, arterial blood gas analysis, lung volume reconstructed by CT, and the distribution of lung ventilation and perfusion function [11,18,22,23]. Most studies attempted to identify a certain predictive indicator for postoperative pulmonary complications. However, because of the 3-dimensional deformities of the spine and chest wall, identifying a certain indicator to represent PF or predicting pulmonary complications is difficult, especially in patients with SRS. Reding et al. [19] reported that the Cobb angle was poorly correlated with FVC preoperatively in early-onset scoliosis. Liu et al. [23] also found that there was no significant correlation between the results of preoperative arterial blood gas tests and postoperative pulmonary complications in patients with scoliosis and pulmonary dysfunction. Additionally, several studies showed that FVC% and FEV1% of patients with scoliosis after a corrective operation had even declined and did not return to the preoperative baseline value for a long time [24,25]. Therefore, comprehensive evaluation of PF in patients with SRS should be performed.

Lung ventilation and perfusion scans are rarely used to assess PF in patients with scoliosis. Reding et al. [18] first used these scans to describe the asymmetry of lung ventilation and perfusion function in congenital and infantile scoliosis. In the current study, we used the V/P SPECT and CT fusion technique to examine anatomical and functional information of the lungs for evaluating PF in patients with SRS. Our study showed that the distribution of lung ventilation and perfusion function in patients with SRS was uniform. No regional ventilation and perfusion functional defects were found (Figs. 2B, 3 B). We consider that the reason for this finding could be because the average age of patients with SRS was 20.1 years in our study. Accelerated progress of spinal deformity may occur at a later time of adolescence. The lung tissues of these patients showed normal development before aggravation of the spinal curve. Therefore, pulmonary alveoli and capillary of distorted lung tissue were functional or had potential functions. Because lung V/P SPECT images cannot provide information of anatomy, V/P SPECT and CT fusion images were used to show anatomical and functional information of the lungs clearly and simultaneously (Figs. 2C, 3 C). Fusion images showed that pressed and distorted lung tissue observed on CT had favorable ventilation and perfusion function.

In our study, fusion images showed uniform distribution of ventilation and perfusion in the lungs, but we found abnormal ventilation and perfusion asymmetry in the right and left lungs in patients with SRS. The distribution of normal lung function is generally considered as 55% right/45% left [20]. However, no studies have reported the standard variations of distribution of PF in the right and left lungs by ventilation and perfusion scan measurements in normal children. Majoral et al. [26] measured the distribution of lung ventilation function with a mean ratio (left/right) of 0.87 ± 0.1 standard variation in 11 healthy human volunteers. This finding indicated that the distribution of variation in lung ventilation function was 1%–2%. Blickman et al. [21] reported that standard variations of the distribution of ventilation and perfusion function in the right and left lungs of children with pectus excavatum deformities were 4.3% and 3.6%, respectively. Therefore, as assumed by Redding et al. [18], we considered that a standard variation of ± 5% was the normal range of lung function distribution. In the current study, lung ventilation variation in 87.5% of the patients and perfusion variation in 93.8% of the patients were positive. This finding indicates that a reduced lung function distribution mostly occurs in a convex lung according to the definition of variation of lung ventilation and perfusion function. This finding was different to that of Redding et al. [18] who reported that there was no difference in reduction of lung function between convex and concave lungs in children with congenital and infantile scoliosis. We consider that lung tissue is underdeveloped in infants or small children and changes in distribution of lung function in these patients are probably affected by various factors. However, lung tissue of patients with SRS with an average age of 20.1 years was fully developed. Therefore, consistent results of reduced distribution of lung function in a convex lung suggest that regional PF based on concavity or convexity of the lungs, as detected by a spinal radiograph, could be predicted in patients with SRS and an older age.

Ventilation and perfusion function were evenly distributed in convex and concave sides of the lungs according to lung V/P SPECT images. We found that lung ventilation appeared to be matched with perfusion function. However, we found that variation in ventilation function was significantly less than that of perfusion function ($P = 0.015$, $t = -2.732$). This finding suggests that spinal deformity leads to greater changes in perfusion than ventilation of the lungs in patients with SRS. The difference in reduced ventilation and perfusion function in the convex side of the lungs could be regarded as a mismatch of lung Ventilation and perfusion function in patients with SRS. This could be one of the potential factors that aggravate pulmonary dysfunction in patients with SRS. We also found that there was significant correlation between variation of lung ventilation and perfusion. This finding suggests that changes in lung perfusion function could replace ventilation function for assessing PF in patients with poor compliance of breathing exercises, such as small children or patients with SRS postoperatively [18].

In the current study, we attempted to identify a related radiographic indicator to predict changes in lung ventilation and perfusion function in patients with SRS. However, there was no correlation between the Cobb angle and variation in lung ventilation and perfusion function. The reason for this lack of finding could be because the Cobb angle alone does not accurately reflect the 3-dimensional deformities of the spine and chest wall in patients with SRS. Other changes, including kyphosis and spinal rotation, also affect lung function collectively [18,19]. Additionally, we did not find a correlation between FVC% or FEV1% and variation of lung function. We consider that FEV1 measures the degree of airflow limitation, but provides no information on the underlying pathophysiology [27]. FVC is a dynamic PF parameter for reflecting the degree of restrictive ventilatory dysfunction. Acquisition of a high-quality FVC value depends on good compliance of the patient [28]. Therefore, using FVC% and FEV1% based on respiratory tests to examine and explain the complex changes in pulmonary consequences of SRS is insufficient. Lung ventilation and perfusion function scans need to be supplemented. We preliminarily analyze the relationship between the scoliotic curve and ventilation and perfusion images of SRS by Pearson correlation coefficient. However, because of the limited sample size, regression analysis can not be used to control various confounding individual factors for affecting respiratory function in scoliosis in current study. It limits the strength of evidence for our results. Moreover, because of the consideration of economic conditions and surgical risk, 3 patients in our study gave up the corrective surgical treatment. The other 2 patients were loss to follow-up. We think that the lower sample size made it difficult to decide the effective relationship between clinical outcomes and preoperative scintigraphic images. Therefore, the follow up data were not involved in current study. A larger sample size is needed to further evaluate the relationship between imaging findings and clinical outcomes.

This study showed useful functional pulmonary results of SRS. We described a new method to determine lung functional and radiographic consequences in patients with SRS. This method could help surgeons to acquire more complete information on respiratory function of SRS and to choose the criteria for intervening surgically. However, the current study has several limitations. There was a limited number of patients in this prospective study. A larger sample size is required to verify the changes in ventilation and perfusion function of SRS and the relation of these changes with the Cobb angle and FVC%. Furthermore, lung ventilation and perfusion function scans only use relative values of right and left lung function ratio to assess changes in lung ventilation and perfusion [18,26]. The absolute values of changes in lung ventilation and perfusion function in SRS cannot be accurately measured by the present methods. Therefore, similar to spirometric data, a quantitative index should be provided by developing a new measurement technique to accurately show changes in lung ventilation and perfusion function in SRS. Moreover, we only showed the preoperative data of SRS. Postoperative clinical outcome data were not involved in current study and need to be further evaluated. Finally, changes in the distribution of lung ventilation and perfusion function after corrective surgery need further evaluation.

5. Conclusions

Ventilation and perfusion function is evenly distributed in the convex and concave sides of the lungs in SRS. Deformity leads to greater changes in lung perfusion function than ventilation function in patients with SRS. Measurement of changes in ventilation and perfusion function in the lungs may represent an additional functional feature to assess PF of SRS more comprehensively.

Conflicts of interest

The authors have no conflicts of interest to declare.

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