MEDICAL SCIENCE MONITOR

CLINICAL RESEARCH

e-ISSN 1643-3750
© Med Sci Monit, 2018; 24: 7375-7381
DOI: 10.12659/MSM.911749

Received: 2018.06.21
Accepted: 2018.09.12
Published: 2018.10.15

Diagnostic Value of Multi-Slice Spiral Computed Tomography for Bronchial Dysplasia in Premature Infants

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Manuscript Preparation E
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Source of support: This work was supported by the 2016 Shenzhen Science and Technology Development Foundation (JCYJ20160429090648512)

Background: The aim of this study was to investigate the diagnostic value of multi-slice spiral computed tomography (MSCT) for bronchial dysplasia in premature infants.

Material/Methods: A retrospective analysis of 248 premature infants who were highly suspected to have bronchial dysplasia and were admitted to our hospital from 2015 onwards was conducted. We observed bronchus morphologies, sizes, and tissue characteristics using fiberoptic bronchoscopy (FB) as the criterion standard for diagnosis. We calculated the sensitivity, specificity, and diagnostic compliance of MSCT in the diagnosis of bronchial dysplasia.

Results: Thoracic computed tomography mainly revealed capsular bubbles. The translucency of the 2 lungs was reduced, and extensive and local ground-glass changes were observed. Imaging findings mostly included strip or honeycomb-like shadows. Pleural thickening and pleural effusion were rare. MSCT was able to establish a diagnosis in 92 cases (37.10%) of bronchopulmonary cysts, 69 cases (27.82%) of congenital pulmonary emphysema, 31 cases (12.50%) of bronchial atresia, 1 case (0.40%) of congenital cystadenoma malformation, and 3 cases (1.21%) of giant tracheal bronchitis. Another 52 children (20.97%) were found to have conventional pulmonary inflammation. The sensitivity of MSCT in the diagnosis of bronchial dysplasia was 88.21%, the specificity was 75.00%, and the diagnostic compliance was 86.29%. There was a significant difference between the MSCT and FB findings in the diagnosis of bronchial hypoplasia ($P<0.001$).

Conclusions: MSCT has great utility in the diagnosis of bronchial dysplasia in premature infants and may become an excellent method for diagnosing bronchial dysplasia in the future.

MeSH Keywords: Bronchi • Bronchoscopes • Infant, Premature

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/911749

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Background

Bronchial dysplasia is a chronic lung disease caused by respiratory distress syndrome [1], usually owing to immature lung development and high concentrations of oxygen, which are very common in premature infants [2]. According to Bush et al. [3], about 72% of premature infants develop bronchial dysplasia. The incidence of bronchial dysplasia has increased by about 10 times over the past 10 years [4]. Additionally, more and more studies [5–7] have shown that bronchial dysplasia does not always begin in infancy, but may also occur in some premature neonates within 10 months of maternal delivery.

The large number of cesarean section applications is one of the contributing factors, and the deteriorating environmental conditions are also important factors affecting newborn development [8]. The prognosis of children with bronchial dysplasia is extremely poor. According to Trittmann et al. [9], the survival rate of children with severe bronchial dysplasia is less than 70%. Due to the irreversible mucosal epithelium damage caused by bronchial dysplasia and pulmonary fibrosis, even if the treatment is completed, it will have a serious negative impact on these children's future growth and development [10]. Recent research has shown that although the large number of glucocorticoids that are used in clinical applications and the use of limited mechanical ventilation have increased the survival rate of premature infants, bronchial dysplasia has also increased [11]. For children with bronchial dysplasia, early detection and early treatment are advocated in the clinic, but the diagnosis of bronchial dysplasia is still based on fiberoptic bronchoscopy [12]. The application of fiberoptic bronchoscopy is difficult, and the damage to children is extremely serious [13]. Therefore, in clinical practice, we are trying to find a method that can effectively reduce the damage to children and achieve a more accurate diagnosis of bronchial dysplasia.

With the recent development and application of multi-slice spiral CT (MSCT), significant breakthroughs have been achieved in the techniques for various obstetrics and gynecology examinations. As a non-invasive examination, MSCT has a high spatial resolution. It also has excellent display capabilities for examining cardiovascular and cerebrovascular blood vessels in neonates and also has obvious chest examination advantages [14]. Compared with traditional single-layer CT, MSCT uses a completely different scanning and imaging mode. Through axial helical scanning and non-helical scanning, the spatial range of scanning can be expanded without reducing the spatial resolution. Currently, its application in isotropic imaging, muscle, vascular, and organ examination is far superior to single-layer CT [15,16]. However, the application of MSCT for diagnosing bronchial dysplasia in premature infants has not been demonstrated locally or internationally, and its utility has not yet been proved.

In this study we determined the diagnostic value of MSCT for bronchial dysplasia in premature infants, and thus provide an effective reference for future clinical diagnosis and treatment of children with bronchial dysplasia.

Material and Methods

Case information

A retrospective analysis of 248 premature infants who were highly suspected to have bronchial dysplasia and were admitted to the Women's and Children's Health Institute Futian, University of South China was conducted. The inclusion criteria were as follows: pregnancy duration less than 10 months; suspicious inflammation in the lungs; visible foreign body in the bronchus; repeated infection of the lower respiratory tract; different degrees of dyspnea and cyanosis; and low partial pressure of oxygen. After confirmation of bronchial dysplasia by initial MSCT followed by fiberoptic bronchoscopy, 324 patients were initially included in this study. Exclusion criteria were: a family history of genetic disease; congenital tumors; severe cardiopulmonary insufficiency; congenital cardiovascular and cerebrovascular disease; children with abnormalities; and children transferred from another medical facility. After application of the exclusion criteria, 248 patients were included in this study. The gestational age was 30.15±6.24 weeks and the birth weight was 1724.65±426.83 g. For details of the study participants, see Table 1. All children's relatives signed informed consent forms.

Methods

After having been initially diagnosed by a respiratory physician in our hospital, children with bronchial dysplasia then underwent MSCT. General chest scanning was performed using a GE Light Speed 128-slice spiral CT. Children were treated with 10% water and 0.5–1.0 ml/kg chloral solution as a tranquilizer. See Table 2 for MSCT parameter settings. The scans included areas ranging from the apex pulmonis to the basis plumonis. We used standard algorithms to reconstruct the original image data, including surface masking (SSD), maximum intensity projection (MIP), minimum projection density (Min-IP), virtual endoscope (VB), and volume reproduction (VR). All imaging results were reviewed by 3 senior imaging physicians in our hospital, with a double-blind method, strictly according to the 2015 bronchial dysplasia diagnosis manual [17] as the evaluation basis. The final result was determined based on unanimous agreement. We observed bronchial morphology, size, and organization characteristics. Two weeks after the MSCT examination, a fiberoptic bronchoscopy was performed, strictly according to the 2015 fiberoptic bronchoscopy manual [18]. We used fiberoptic bronchoscopy as the criterion standard for diagnoses, and calculated the sensitivity, specificity, and diagnostic

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Table 1. Clinical data of the children [n (%)].

Project	n=248	n (%)
Gestational age (week)	<30	194 (78.23)
	≥30	54 (21.77)
Birth quality (g)	<1724	172 (69.35)
	≥1724	76 (30.65)
Is it the first child?	Yes	84 (33.87)
	No	164 (66.13)
Mother's age (year old)	<28	62 (25.00)
	≥28	186 (75.00)
Family home	City	113 (45.56)
	Rural	135 (54.44)
WBC($\times 10^9$)[a]	≤20	64 (25.81)
	>20	184 (74.19)
RBC($\times 10^{12}$)[b]	≤5	164 (66.13)
	>5	84 (33.87)
PLT($\times 10^9$)[c]	≤300	92 (37.10)
	>300	156 (62.90)
LYMPH% (%)[d]	≤40	98 (39.52)
	>40	150 (60.48)
Clinical manifestation	Difficulty breathing	176 (70.97)
	Wheezing	62 (25.00)
	Repeated infection	6 (2.42)
	Congenital malformation	4 (1.61)

Table 2. MSCT parameter settings.

Project	Value
Scan parameters	0.625 mm×128
Pitch	1.4
Tube voltage	80 kV
Tube current	90 mAs
Thickness	7 mm
Reconstruction thickness	0.5 mm
Children's vision	14~36 cm
Matrix	512×512 mm

Table 3. Chest CT features [n (%)].

Features	Number of cases (n=248)
Capsule bubble	159 (64.11)
Glass sample	148 (59.68)
Strips	132 (53.23)
Honeycomb	94 (37.90)
Pleural thickening	22 (8.87)
Pleural effusion	16 (6.45)

accuracy of MSCT for diagnosing bronchial dysplasia as follows: sensitivity=number of true positive patients/number of criterion standard-positive patients ×100%; specificity=number of true-negative patients/number of criterion standard-negative patients ×100%; diagnostic compliance=(number of true-positive patients+number of true-negative patients)/total number ×100%.

Statistical methods

SPSS22.0 statistical software was used to analyze and process the data. All data are expressed in the form of rates. The results were compared using the chi-square test. $P<0.05$ was considered statistically significant.

Results

MSCT image characteristics

The thoracic CT mainly showed capsular bubbles. The translucency of the 2 lungs was reduced, and extensive or local ground-glass changes were observed. Imaging findings mostly included strip or honeycomb-like shadows. Pleural thickening and pleural effusion were rare, and the cysts were mostly located in the upper right lobe of the trachea and in the adjacent carina. The diameter of the capsule wall was about 1~2 mm. There were many round, oval block shadows with uniform density, uniform thickness, and sharp edges. Bilateral hilar cysts were rare, and the gas-liquid in the cysts was flat with blurred edges and tissue exudation. The gas content in the large lobe increased significantly, and the lung texture, trachea, and heart leftward showed significant shifts. After the enhanced scan, the visible blood vessels were significantly sparser and smaller than those observed in the normal population (Table 3).

Diagnostic results obtained using MSCT

Among the 248 children who were highly suspected to have bronchial dysplasia and had been diagnosed by MSCT, bronchial

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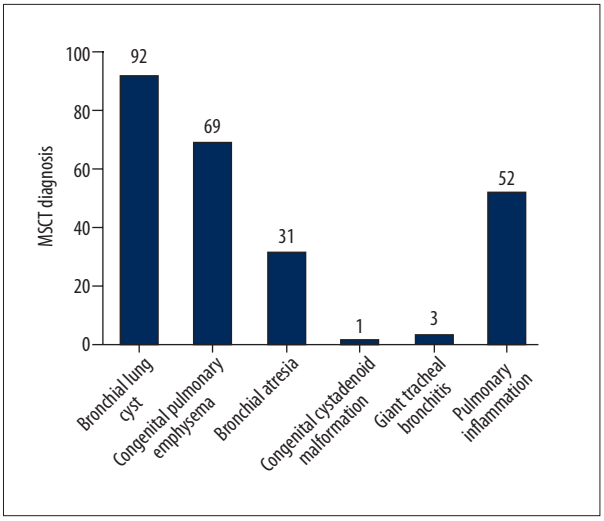

Figure 1. Diagnosis of bronchial dysplasia using MSCT. Diagnosis was achieved in 92 cases of bronchial lung cysts, 69 cases of congenital pulmonary emphysema, 31 cases of bronchial atresia, 1 case of congenital cystadenoma-like malformation, 3 cases of giant tracheal bronchitis, and 52 cases of conventional pulmonary inflammation such as in bronchial pneumonia.

cysts were present in 37.10% (92 cases) of the patients, congenital pulmonary emphysema in 27.82% (69 cases), bronchial atresia in 12.50% (31 cases), congenital cystadenoma malformations in 0.40% (1 case), and giant tracheal bronchitis in 1.21% (3 cases). Another 20.97% (52 cases) of children were found to have conventional pulmonary inflammation, such as in bronchial pneumonia (Figure 1).

The efficacy of MSCT in the diagnosis of bronchial dysplasia

After fiberoptic bronchoscopy examinations, 212 patients were diagnosed with bronchial dysplasia and another 36 patients were diagnosed with conventional pulmonary inflammation. We compared the recorded the numbers of true-positives, false-positives, true-negatives, and false-negatives cases between the 2 methods. The sensitivity of MSCT for bronchial dysplasia diagnosis was 88.21%, the specificity was 75.00%, and the diagnostic compliance was 86.29% (Tables 4, 5).

MSCT diagnosis of bronchial hypoplasia

Of the 212 confirmed cases, 188 were diagnosed with primary bronchial hypoplasia and 24 were diagnosed with bronchial hypoplasia caused by external pressure. Of the 196 patients diagnosed with MSCT, 108 were diagnosed as primary bronchial hypoplasia, another 88 cases were diagnosed as bronchial hypoplasia caused by external pressure, and there were significant differences in determining the types of the bronchial hypoplasia between 2 methods (P<0.001). There were no differences

Table 4. Comparison of the diagnoses made using MSCT and fiberscopy (n=248).

	Fibroscopies confirmed	Fibroscopies not diagnosed	n
MSCT confirmed	187	9	196
MSCT not diagnosed	25	27	52
n	212	36	

Table 5. MSCT diagnosis of bronchial dysplasia.

Project	Value (%)
Sensitivity	88.21
Specificity	75.00
Diagnostic compliance	86.29

between FB and MSCT in the diagnosis of airway stenosis, bronchial opening variation, tracheal diverticulum, and tracheal sinus when dealing with primary bronchial hypoplasia (P>0.050). There was a significant difference in the diagnosis of tracheobronchomalacia, laryngeal dysplasia, pulmonary cysts, emphysema, pulmonary bullae, pulmonary sequestration, loss of lung lobe, and increased lobes (P<0.050). In the diagnosis of bronchial hypoplasia caused by external pressure, there were no significant difference between FB and MSCT in the diagnosis of tracheal esophageal fistula, occupying lesion in thoracic cavity, esophageal hernia, and cardiac compression (P>0.050). Significant differences were observed in the diagnosis of esophageal compression and vascular compression (P<0.050) (Tables 6, 7).

Discussion

Bronchial dysplasia is a developmental retardation that commonly occurs during the growth and development stages in newborn children [19]. The respiratory system, including the bronchus, larynx, and lungs, begins to develop during the fourth week of pregnancy [20]. Under normal circumstances, the airway appears in the embryonic endoderm. One end of the trachea gradually splits into 2 parts, namely, the left and right trachea. The branches continue to develop into the bronchi of the lung, forming multiple branches that comprise the trachea tree [21,22]. However, abnormalities can occur at certain stages during trachea development. This can cause diseases such as bronchial bridge and tracheal bronchi, which result in an incomplete respiratory system, and children with these diseases experience poor breathing, suffocation,

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Table 6. MSCT diagnosis of primary bronchial hypoplasia [n(%)].

	Fiberscope mirror (n=188)		MSCT (n=108)		χ^2	P
Airway narrowing	81	(43.09)	52	(48.15)	0.711	0.399
Tracheobronchial softening	69	(36.70)	0	(0.00)	51.692	<0.001
Bronchial opening variation	26	(13.83)	16	(14.81)	0.055	0.815
Laryngeal cartilage hypoplasia	9	(4.79)	0	(0.00)	5.332	0.021
Tracheal diverticulum	1	(0.53)	0	(0.00)	0.576	0.448
Tracheal sinus	2	(1.06)	3	(2.78)	1.213	0.271
Pulmonary cyst	0	(0.00)	8	(7.41)	14.312	0.002
Emphysema	0	(0.00)	6	(5.56)	10.663	0.001
Lung bubble	0	(0.00)	8	(7.41)	14.312	0.002
Pulmonary isolation	0	(0.00)	4	(3.70)	7.058	0.008
Lung leaf missing	0	(0.00)	5	(4.63)	8.853	0.003
Increased lung lobes	0	(0.00)	6	(5.56)	10.663	0.001

Table 7. MSCT diagnosis of external pressure bronchial hypoplasia [n(%)].

	Fiberscope mirror (n=24)		MSCT (n=88)		χ^2	P
Esophageal compression	9	(37.50)	12	(14.29)	7.049	0.008
Tracheal esophageal fistula	1	(4.17)	16	(19.05)	2.877	0.090
Thoracic cavity	1	(4.17)	5	(5.95)	0.085	0.770
Esophageal hiatus	0	(0.00)	7	(8.33)	2.036	0.154
Cardiac compression	12	(50.00)	26	(30.95)	3.519	0.061
Vascular compression	1	(4.17)	21	(25.00)	4.635	0.031

and even death [23]. There is no obvious specific presentation of bronchial dysplasia at early stages, and this condition is often overlooked by parents who lack medical knowledge.

The earliest use of X-ray examination in the clinical diagnosis of bronchial dysplasia used dynamic pulmonary hyperinflation and texture blur as the diagnosis standard [24]. However, the X-ray examination results are generally only apparent at 1 to 2 months after the child presents obvious signs of bronchial dysplasia. By this time, irreversible damage has occurred during the bronchial development of children's lungs. This causes a serious negative impact on treatment and prognosis [25].

In the 1990s, clinical trials began to use computed tomography (CT) for the diagnosis of bronchial dysplasia. CT has higher resolution for tissue imaging and provides better imaging results for some blood vessels and tissues throughout the body than do X-ray methods [26]. However, due to the limitations in technology, imaging neonatal micro-bronchi is still difficult, and significant breakthroughs in the diagnosis of bronchial dysplasia have not been achieved. With the advancement of science and technology, the development and application of MSCT has achieved higher spatial resolution than with traditional CT, and the presentation of some small blood vessels has become even more pronounced. Combined with CT volumetric technology and data acquisition technology, the bronchus and the entire lungs of children can be observed in multiple orientations and angles, reducing the artifacts that are caused by breathing and allowing the best imaging results to be obtained [27]. To date, no relevant local or international study has provided evidence for the use of MSCT for diagnosing bronchial dysplasia in premature infants. Therefore, we retrospectively analyzed the imaging results of premature infants with bronchial dysplasia who were diagnosed by MSCT in our hospital. We compared MSCT procedures with fiberoptic bronchoscopy findings, determined the value of MSCT in diagnosing bronchial dysplasia, and provided guidance for clinical practice.

The results of this experiment showed that, by MSCT examination, bronchial cysts were more common in children,

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concentrated in the upper right lobe trachea and adjacent tissue, mainly with round shadow, uniform density, and sharp edges. The imaging results showed that the gas content of the large lobe and lobe brightness were significantly greater in these patients than in normal individuals. Both the overall texture of the lungs and the trachea were shifted to the left, which generated pressure on the normal lung tissue. In addition, some patients experienced bronchial atresia. The clinical manifestations were dyspnea and cough, mainly due to bronchial atresia or stenosis [28]. There were no significant differences between these infants and normal infants observed on routine examinations. However, CT images showed that the number of alveoli was remarkably lower, and the lung tissue was abnormally difficult to ventilate. There was obvious emphysema and swelling, and the airway mucus was in a state of long-term secretion. Bronchiectasis and a large quantity of mucus were seen.

MSCT has excellent imaging effects on surrounding emphysema and mucous plugs. A large number of dendritic structures were present, and the mucus plugs mainly had a watery appearance. Congenital cystadenoma malformations and bronchial bronchitis are rare in children with bronchial dysplasia. MSCT examinations reveal a clear solid mass in the thin-walled cavities, whereas giant tracheal bronchitis shows significant tracheal dilatation and internal diameter increase. Furthermore, patients with bronchial dysplasia are susceptible to concurrent infections. The high resolution of MSCT, combined with thin-layer reconstruction, provides strong control for small radiation doses and excellent imaging results that can differentiate between the fine structure of the lungs and lung mesenchyme. In this study, the sensitivity of MSCT in diagnosing bronchial dysplasia in premature infants was 88.21%, the specificity was 75.00%, and the diagnostic compliance was 86.29%, which are of high utility. This is also consistent with the study of Wang et al. [29], which corroborate the results of this experiment. Compared with fiberoptic bronchoscopy, MSCT will provide a more effective means for diagnosing bronchial dysplasia in the future, with less damage and faster diagnosis.

In the diagnosis of primary and external pressure-type bronchial hypoplasia, more patients with bronchial hypoplasia caused by external pressure were diagnosed with MSCT than with FB. The main reason may be that this type of bronchial hypoplasia results from conditions such as cardiovascular development abnormalities and chest or esophageal compression [30]. For the MSCT examination, the entire chest of the child was inspected and a more objective judgment could be obtained. However, in the diagnosis of tracheal stenosis, there is no significant difference between the 2 methods, suggesting that the diagnostic sensitivity and specificity of MSCT for bronchial hypoplasia are better, but special cases could not be excluded.

Most patients were diagnosed with bronchial hypoplasia combined with pulmonary infection [31], and MSCT and FB examination cannot determine whether there is inflammatory stenosis or congenital dysplasia. In the meantime, pulmonary infection may cause edema and mucus embolism in the lung tissue which interfere with the results of MSCT, making it impossible judge whether there is local stenosis. For the abnormal structural lesions of the whole lung tissue, the diagnosis rate of MSCT is significantly higher than that of FB because MSCT is excellent for imaging tissue details, and the lung tissue of the distal airway can be clearly observed. FB only has a good imaging effect on the III~IV bronchus, so the diagnostic value of MSCT on bronchial hypoplasia with structural abnormalities is better than with FB.

Due to the limited experimental conditions, there are certain deficiencies in this study. For example, our study included few research subjects, the population was relatively unique, and there was no breakthrough in bronchial dysplasia pathogenesis. In addition, the results of MSCT examination in premature infants can be greatly affected by the dysplasia of premature infants. We plan to conduct a long-term follow-up on the subjects of this study. In the future, we will continue to improve our experiments and conduct more thorough and deeper studies on bronchial dysplasia in order to achieve the best experimental results.

Conclusions

MSCT has high utility for diagnosing bronchial dysplasia in premature infants and is expected to become an excellent method for diagnosing bronchial dysplasia in the future.

Conflict of interest

None.

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