Evaluation of Lung Magnetic Resonance Imaging of Patients Followed Up With Bronchopulmonary Dysplasia

Bronkopulmoner Displazi Tanısı ile İzlenen Hastaların Akciğer Manyetik Rezonans Görüntülemelerinin Değerlendirilmesi

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ABSTRACT

Objective: Bronchopulmonary dysplasia is a common long-term complication of preterm birth. The evaluation of patients with advanced radiologic methods at early ages is essential in terms of determining the severity of the disease and follow-up. As a non-ionizing modality, magnetic resonance imaging is particularly appropriate for the repeated radiological assessment of pulmonary pathologies associated with bronchopulmonary dysplasia.

Material and Methods: Patients who were followed up with the diagnosis of bronchopulmonary dysplasia and underwent lung magnetic resonance imaging between August 2017 and August 2019 were evaluated retrospectively. Coronal and axial T2-weighted magnetic resonance imaging was performed (TR/TE: 4500-5300/90-106 msec). A pediatric radiologist evaluated magnetic resonance imaging findings. Pulmonary structural findings and their distribution were determined (fibrotic bands, distortion). The findings were compared with bronchopulmonary dysplasia patients' severity, clinical and demographic characteristics. The imaging was performed during the patient's sleep time without sedation or by giving chlorhydrate.

Results: A total of 7 patients were included in the study. Three patients were female, and 4 were male. According to bronchopulmonary dysplasia classification, 1 patient was mild, 3 patients were moderate, and 3 were severe bronchopulmonary dysplasia. The median gestational week was 26.2. In mild bronchopulmonary dysplasia patients, fibrotic bands were seen in <3 segment, and there was no parenchymal distortion. Bronchovascular distortion was observed in moderate and severe bronchopulmonary dysplasia patients.

Conclusion: Pulmonary magnetic resonance imaging can reveal structural abnormalities in patients with bronchopulmonary dysplasia, and can be used as an imaging method in the follow-up of patients.

Key Words: Bronchopulmonary dysplasia, Magnetic Resonance imaging, Prematurity

ÖZ

Amaç: Bronkopulmoner displazi erken doğumun sık görülen uzun vadeli bir komplikasyonudur. Hastaların erken dönemde en yeni radyolojik teknikler kullanılarak değerlendirilmesi, hastalığın şiddetinin değerlendirilmesi ve takip

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planının yapılması açısından çok önemlidir. İyonize olmayan bir modalite olan manyetik rezonans görüntüleme, bronkopulmoner displazi ile ilgili akciğer patolojilerin radyolojik değerlendirmesi ve izleminde yol gösterici olabilir.

Gereç ve Yöntemler: Ağustos 2017-Ağustos 2019 tarihleri arasında bronkopulmoner displazi tanısı ile takip edilen ve akciğer manyetik rezonans görüntülemesi yapılan hastalar retrospektif olarak değerlendirildi. Koronal ve aksiyel T2 ağırlıklı magnetik rezonans görüntüleri incelendi (TR/TE: 4500-5300/90-106 msn). Manyetik rezonans görüntüleme bulguları bir pediatrik radyolog tarafından değerlendirildi. Akciğerlerin yapısal durumu ve patolojik bulguları değerlendirildi (fibrotik bantlar, distrosiyon). Bulgular, BPD hastalarının şiddeti, klinik ve demografik özellikleri ile karşılaştırıldı. Görüntüleme sedasyon yapılmadan veya kloralhidrat verilmeksizin hastanın uyku süresinde yapıldı.

Bulgular: Toplamda yedi hasta araştırmaya dahil edildi. Hastaların dördü erkek, üçü kızdı. Bonkopulmoner displazi sınıflamasına göre 1 hastanın hafif, 3 hastanın orta düzeyde ve 4 hastanın şiddetli bronkopulmoner displazisi vardı. Ortalama gebelik haftası 26.2 haftaydı. Hafif bronkopulmoner displazi hastalarında <3 segmentte fibrotik bantlar görüldü ve parankimal distorsiyon saptanmadı. Orta ve şiddetli bronkopulmoner displazi hastalarında bronkovasküler distorsiyon gözlendi.

Sonuç: Akciğerlerin manyetik rezonans görüntüleme ile değerlendirilmesi bronkopulmoner displazili hastalarda yapısal anormallikleri gösterebilir ve hastaların takibinde görüntüleme yöntemi olarak kullanılabilir.

Anahtar Sözcükler: Bronkopulmoner displazi, Manyetik rezonans görüntüleme, Prematürite

INTRODUCTION

In premature infants, bronchopulmonary dysplasia (BPD), a chronic lung condition, frequently develops as a result of oxygen and mechanical ventilation during the early neonatal period (1). Fifty years ago, it was first described as chronic lung disease in newborns who had been intubated after being given a diagnosis of respiratory distress syndrome (2). The prevalence of BPD remains high despite improvements in clinical care, such as the use of prenatal steroids and postnatal surfactants, because severely premature newborns are now more likely to survive (3). The survival rates of preterm neonates, especially those born at an exceptionally low gestational age, have increased significantly in recent decades due to significant advancements in neonatal intensive care and the creation of novel treatments. Even though the course of this illness has probably improved, the burden of BPD has remained constant (4). Although the actual cause of BPD is unknown, it is believed to be complex (5). Prematurity, low birth weight, duration of mechanical breathing, oxygen toxicity, infection, patent ductus arteriosus, and genetic factors are the main variables influencing the etiology of BPD (6-8). The definition of the BPD diagnosis is a contentious matter that has evolved throughout time (9, 10). The severity of the disease is defined and categorized using a variety of clinical data. The current consensus definition of BPD, a severity-based scale for infants born younger than 32 weeks who require supplemental oxygen at 36 weeks postmenstrual or at least 28 days prior to the assessment of continued oxygen demand at discharge, was first proposed by the National Institutes of Health in 2000 (9). The scope of this definition's impartiality is restricted to variations in oxygen delivery between institutions (11). As a result, definitions of BPD lack prognostic information and do not consider problems. Effective biomarkers are required for BPD follow-up to identify the disorder's severity and nature, anticipate how it will progress, and assess each patient's response to treatment. BPD is also a long-lasting disease with effects that last into adulthood, and preterm birth should be recognized as a chronic condition that requires long-term follow-up for the prevention and treatment of potential health sequelae into mid-adulthood. Lung function typically increases progressively throughout development and adolescence, plateauing at about age 23-25. It is now known that those who enter adulthood with a lung function that is below average have a higher risk of subsequently getting the chronic obstructive pulmonary disease (12). It is crucial to prevent early infant lung injury because of this. BPD and preterm birth are two glaring instances of how damage might be connected to health problems that last throughout adulthood.

The radiographic evaluation of BPD has begun to play a new role in diagnosing and treating the disease as the diagnostic criteria for BPD have evolved. In cases of severe BPD, findings on standard chest X-rays that suggest fibrosis and hyperinflation are visible and correlate with the severity of BPD. With its excellent resolution and ability to identify structural abnormalities, computed tomography (CT) is a highly effective tool for monitoring BPD patients (13, 14). Given the total amount of ionizing radiation that patients are exposed to, it is not suitable for monitoring disease progression. Modern developments in radiological imaging, particularly magnetic resonance imaging (MRI), can help assess lung structures and may direct therapeutic care techniques for disorders like BPD that develop early in infancy and require regular follow-up. By noninvasively detecting the pulmonary structural alterations early on, initiating treatment sooner, and avoiding problems by assessing the present course of therapy, the morbidity and mortality of these individuals can be decreased. The chosen imaging modalities should be simple, radiation-free, and sensitive to show pulmonary abnormalities. Radiological examination of BPD has taken on a new significance in diagnosing and managing the condition as the diagnostic criteria for BPD continue to change. Due to image opacities, lucensiles, and ventilation heterogenity, radiographic phenotypes on chest X-rays including fibrosis and hyperinflation have been postulated. Patients with severe BPD can see this phenotype on routine chest radiographs, and the severity of BPD is correlated with this phenotype (1). The traditional gold standard of chest imaging, CT, has been given a qualitative scoring system that considers hyperinflation, emphysema, fibrosis, and radiologists' personal opinions.

However, CT is not well suited for longitudinal disease progression monitoring, particularly in pediatric patients, due to the risk of ionizing radiation. BPD is a chronic lung condition that requires breathing assistance at 36 postmenstrual weeks, but structural complications like lung hyperinflation are frequently immeasurable. Without sedation, MRI allows for tomographic determination of lung volumes and densities during quiet breathing (silent breathing).

In this study, the long-term follow-up of BPD patients in our pediatric pulmonology clinic was examined with the pulmonary MRI characteristics. In addition, by identifying these patients' demographic, clinical, laboratory, and radiological traits, it was hoped to assess the value of pulmonary MRI in the long-term follow-up of patients.

MATERIALS and METHODS

Retrospective analysis of the lung MRI findings of the patients who received a BPD diagnosis and were followed up at the Health Sciences University of Ankara Pediatrics Hematology Oncology Training and Research Hospital Pediatric Chest Diseases Clinic was done between August 2017 and August 2019. The patients' MRI results were compared to their demographic information and most recent chest X-ray results. Medical records were used to acquire patients' demographic, clinical, laboratory, and radiological information. Without using intravenous contrast material, MRI imaging was carried out in two sequences (axial and coronal T2-weighted, average 7 minutes), with pictures corresponding with breathing. MRI was performed with or without superficial anesthesia while the patient was asleep (chlorohydrate). Coronal and axial T2-weighted MRI imaging was performed (TR/TE: 4500-5300/90-106 msec) without giving sedation or by giving chlorhydrate, and the average imaging time was 6-7 minutes. The descriptive statistics of the study were shown as a number, percentage, median and interquartile range (IQR). Statistical analysis was evaluated in SPSS 23 package program.

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Clinical Research Ethics Committee, Ankara Child Health and Diseases Hematology Oncology Training and Research Hospital (24.05.2019 – 2019-186).

RESULTS

The study comprised seven patients with the diagnosis of bronchopulmonary dysplasia who were being monitored. Four of the patients (57.1%) were male. The patients' median age was 19.4 months (11-34). The patients' median corrected age was 16 months. The patients had all previously undergone hospitalization in the neonatal intensive care unit. The average stay was 92.5 (28-214) days. Four of the patients (57.1%) required positive pressure ventilation (PPV). All except one of the patients received surfactant treatment. During the neonatal era, all patients required oxygen for longer than 28 days, and one patient was still receiving it. All patients had continuous positive airway pressure (CPAP) during the postnatal period, with a mean time of 9.1 (1-20) days. In the newborn phase, mechanical breathing was required in five individuals (71.4%). None of the patients had Respiratory Syncytial Virus (RSV) infection, and all patients received RSV prophylaxis. Pulmonary hypertension was not seen in any of the patients throughout the newborn phase echocardiographic assessments. Five patients (71.4%) in the newborn critical care unit had a history of sepsis. Three patients received oxygen after they were transferred out of the Neonatal intensive care unit (NICU). Table I provides an overview of patients' demographic and clinical characteristics.

Table I: Demographic and clinical results of the study group.

Age (month)	19.4 (IQR:7)*
Corrected age (month)	16 (IQR:7.25)*
Sex (Male/Female)	57.1 / 42.9†
Gestational age (week)	26.2 (IQR:2)*
Neonatal intensive care unit length of stay (day)	92.5 (IQR:85)*
Surfactant	85.7†
Medical history of pneumonia	57.1†
Medical history of bronchiolitis	28.5†
Gestational age (week)	26.2 (IQR:2)*

*****The median and interquartile range were shown by IQR (interquartile range), **†**(%)

Three patients exhibited retardation compared to their contemporaries, even though the developmental evaluation of 4 patients was commensurate with that of their peers. According to their medical histories, four patients had pneumonia, six had bronchiolitis, and four had recurrent bronchiolitis. When the severity of BPD was assessed, 3 patients had severe BPD, 3 patients had moderate BPD, and 1 patient had mild BPD. The mean age at the time of lung MRI of the patients was 17.8 (11-34) months.

Lung MRI of the patient with mild BPD had fibrotic band changes in 2 segments. All patients with moderate BPD (n=3) had fibrotic band changes and areas of distortion. While 1 of the patients (n=3) with severe BPD had fibrotic band changes, the other two had both fibrotic band changes and areas of distortion. The patient with mild BPD had a reticular appearance and bilateral hyperaeration areas in the right lung on the chest X-ray. Patients with moderate BPD (n=3) had bilateral hyperaeration areas in one patient, bilateral peribronchial thickenings in one patient, and bilateral hyperaeration areas and bilateral peribronchial thickening in one patient. While all patients with severe BPD (n=3) had bilateral areas of hyperaeration, one patient had additional bilateral peribronchial thickenings. Table II compares

Table II: Patient characteristics and results of imaging modalities.

Cases	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Gestational age (week)	27	25	27	24	26	27	28
Birth weight (gram)	1080	845	975	705	780	1230	950
APGAR 1 minute	7	5	6	5	6	6	6
APGAR 5 minute	8	6	7	6	7	7	8
BPD severity*	mild	severe	moderate	severe	severe	moderate	moderate
Respiratory support as discharge	oxigene	oxigene	none	none	none	oxigene	none
Age at lung MRI (month)	16	15	22	13	22	18	30
Lung MRI findings	band=2 segments	band=3 segments	band=5 segments, distortion: 3 lobes	band=6 segments, distortion: 3 lobes	band=2 segments, distortion:2 lobes	band=6 segments, distortion: 4 lobes	band=2 segments, distortion: 1 lobes
Chest X-Ray findings	reticular appearance on the right lung, bilaterally hyperaeration	bilaterally hyperaeration	bilateral peribronchial thickening, bilaterally hyperaeration	bilateral peribronchial thickening, bilaterally hyperaeration	bilaterally hyperaeration	bilateral peribronchial thickening	bilaterally hyperaeration

**assessed 36 weeks postmenstruel age or discharge*

the results of the patients' chest X-rays and MRIs taken during the same time period.

DISCUSSION

In this retrospective study, a total of 7 patients underwent lung MRI. None of the patients had newly developed respiratory complaints during lung MRI. Again, none of the patients had any newly developed pathological findings in the chest X-ray. Chest radiography is a simple, quick, and common technique used for imaging patients or control purposes. However, it is not sufficient to follow the lung structure in terms of sequelae and development in the follow-up of the disease (15). Chest radiography, the most used imaging technique in premature infants, enables the assessment of the pulmonary parenchyma status. Interstitial thickness, localized or generalized hyperexpansion, and atelectasis are chest X-ray characteristics of BPD (16). In our study, patients' simultaneous chest radiographs tended to show bilateral hyperaeration and hyperexpansion. In addition, reticular appearance and chronic changes were noted, albeit these assessments are unrelated to the patients' BPD severity (Table II). None of the patients had thorax CT. Routine thorax CT is not performed in the follow-up of BPD patients in our clinic, but it is requested when necessary. The abnormalities seen on chest CT in patients with BPD, such as reduced attenuation, emphysematous changes, linear and subpleural opacities, and thickening of the bronchial wall, are more easily detected on CT. Additionally, it has been demonstrated that the clinical severity of BPD correlates with the amount of structural abnormality on CT (17).

BPD still carries a heavy burden of morbidity and mortality in survivors of extreme prematurity, and it causes significant health expenditures. The radiographic assessment of the lungs is crucial for determining the severity and consequences of the disease in both historical and modern medicine (18). Therefore, it is crucial to assess imaging methods for identifying lung anomalies in BPD patients. Although the roles of chest radiography and CT in BPD are well understood, technological advancement and ongoing imaging modality development have opened the door to pulmonary structural assessment using lung MRI and functional assessment using breathing. Knowing more about recent technology advancements and the possibilities of new techniques is becoming increasingly crucial. Chest imaging plays an essential role in the diagnosis and evaluation of potential complications of BPD (19). Imaging abnormalities may persist into adolescence and adulthood. In our study, patients with chest radiographs that remained unchanged from earlier chest radiographs and who were in a stable clinical state were assessed using MRI. While clinically stable lung MRI had the distortion in one or more lobes in all moderate and severe BPD patients, no distortion was found in the patient with mild BPD. There were bilateral hyperaeration

areas in the simultaneous chest X-ray of 6 patients. Three patients had bilateral peribronchial thickening, but chest X-ray findings were not associated with BPD severity. Due to the small sample size, no correlation was found between chest X-ray findings and MRI findings. MRI appears to be the ideal modality for cross-sectional imaging in the pediatric population because it is an imaging technique that does not require exposure to ionizing radiation. However, conventional MRI's significant inherent limitations severely restrict its application in pediatric thoracic imaging. The lung parenchyma has a low proton density and numerous natural air-tissue contacts. As a result, it produces a rapidly degrading signal at very low intensities, leading to images of the lung parenchyma with very low resolution (14). Lung architectural distortion detected in the patients in our study may be a distinctive feature of any pulmonary fibrosis process. Parenchymal bands also often extend from the visceral pleural surface and pass through the lung parenchyma. They can develop in various ways and are often accompanied by lung architecture deformation (20). In the follow-up of BPD patients, pulmonary MRI findings can be followed sequentially from these aspects in the follow-up of stable patients. With the advancement of technology, there are new developments in imaging techniques. These improvements in MRI technology make it possible to detect fibrosis and hyperinflation in young children using sensitive tomographic imaging without the need of ionizing radiation. As a new technique, ultrashort echo time (UTE) MRI, which better visualizes proton density in parenchymal tissue, where the MR signal typically displays rapid T*2 relaxation, provides higher image quality. Additionally, UTE MRI is less susceptible to motion inaccuracies than conventional MR sequences (14, 21, 22). Although it has limitations due to the low proton density of the lung, short T2*, high magnetic susceptibility at various air-tissue interfaces, and motion artifacts from the heart and lungs, magnetic resonance imaging (MRI) may be a better option (23).

The relatively small sample size of our study is one of its critical limitations. Additionally, the BPD patients included in the study could be regarded as "survivors" of the condition due to their numerous potential comorbidities and the possibility of recurring respiratory issues in early infancy. As a result, our patient group may contain individuals with more severe diseases. Further research into the pathophysiology of the illness, especially studies of younger children and infants who develop BPD, may be beneficial. Given the small sample size of this study, it is difficult to determine the benefit of pulmonary MRI imaging in the further follow-up of BPD. MRI has the potential as a tool for the longitudinal assessment of BPD. However, widespread clinical use will require more effective validation in a larger patient population and greater automation of the techniques used. Several cross-sectional studies have looked at school-aged and older BPD survivors and revealed airway blockages, although we lack the proper technology to evaluate lung function in newborns (24, 25). Both "old" and "new" BPD survivors have been described as having reduced lung function, which has been linked to an increase in respiratory symptoms and aberrant chest imaging results (26).

Additionally, longitudinal investigations of preterm and BPD survivors have found a decline in lung function during childhood and adolescence. According to the Padova BPD study (27), adult lung function does not reach its peak in the presence of severe airway obstruction in infancy and remains until age 24. In addition, since patients with BPD are a group that should be followed up until adulthood in terms of the respiratory system, it is very important to determine the appropriate method for longitudinal follow-up in these patients.

CONCLUSION

In terms of imaging the lungs in the long-term follow-up of BPD patients, MRI is a non-ionizing technique, unlike other imaging modalities; this is particularly important for imaging children who are more vulnerable to the harms of radiation exposure and is important for chronic disease cases where longitudinal monitoring is desired. With larger studies, MRI may become the gold standard.

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