Le scanner thoracique dans la dysplasie bronchopulmonaire: corrélations cliniques et radiologiques

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LE SCANNER THORACIQUE DANS LA DYSPLASIE BRONCHOPULMONAIRE : CORRELATIONS CLINIQUES ET RADIOLOGIQUES

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Résumé

La bronchodysplasie pulmonaire (BPD) est la principale complication pulmonaire de la prématurité. Les enfants qui en souffrent peuvent être évalués d'une part à l'aide des fonctions pulmonaires et d'autre part à l'aide de l'imagerie, le scanner étant reconnu comme plus sensible que la radiographie standard pour visualiser les lésions pulmonaires. Peu d'études ont cependant analysé l'utilité des résultats d'imagerie dans l'évaluation de la BPD. Dans ce travail, nous avons analysé la corrélation entre les lésions pulmonaires retrouvées au scanner thoracique dans le cadre de la BPD et les données cliniques principales de cette maladie. Pour ce faire, nous avons utilisé un score radiologique simple validé, et gradué sur une échelle de 0 à 36 comprenant les 6 lésions pulmonaires principales décrites dans la BPD pouvant être présentes sur une échelle de 0 à 6 lobes maximum (lingula incluse) .

Les dossiers médicaux de 19 enfants prématurés avec diagnostic de BPD nés à l'Hôpital Universitaire de Genève entre 1998 et 2007 et ayant bénéficié d'au moins un CT pulmonaire ont été revus.

Cette étude montre qu'il existe une corrélation entre le degré de sévérité de la BPD et les zones d'atténuation radiologiques. Elle démontre également qu'un score radiologique simple est réalisable et qu'il peut s'avérer utile pour évaluer la sévérité de la BPD.

Abréviations utilisées

Texte français :

BPD :	bronchodysplasie pulmonaire
SA :	semaine(s) d'aménorrhée

Texte anglais :

BPD :	Bronchopulmonary Dysplasia
PMA :	Postmenstrual Age
CT :	Computed Tomography
DRL :	Diagnostic Reference Levels
GA :	Gestational Age
BW :	Birth Weight
NEC :	Necrotizing Enterocolitis
HMD :	Hyaline Membrane Disease
PDA :	Patent Ductus Arteriosus
CPAP :	Continuous Positive Airway Pressure
MV :	Mechanical Ventilation
CF :	Cystic Fibrosis
HRCT :	High Resolution Computed Tomography
CLDI :	Chronic Lung Disease of Infancy

I. INTRODUCTION

1.1 LA DYSPLASIE BRONCHOPULMONAIRE

Définition

La dysplasie bronchopulmonaire (BPD) est une maladie pulmonaire chronique représentant l'une des complications les plus fréquentes de la prématurité. La première description de la BPD par Northway remonte à 1967 chez des prématurés avec syndrome de détresse respiratoire résultant de la toxicité de l'oxygène et de la ventilation mécanique agressive. Grâce aux progrès dans la prise en charge des prématurés suite à l'introduction de nouvelles thérapies (corticothérapie anténatale, surfactant et ventilation mécanique moins agressive limitant les facteurs de distension pulmonaire), la forme classique de BPD a été progressivement remplacée par une forme plus modérée affectant des prématurés de plus faible poids de naissance, et à un stade de développement pulmonaire plus précoce qu'autrefois. Cette modification du profil de la maladie met ainsi l'immaturité pulmonaire et les facteurs inflammatoires au premier plan, et non plus les traumatismes de la ventilation mécanique et de l'oxygénothérapie.

Selon le NICHD (National Institute of Child and Human Development), la définition de la BPD repose sur une dépendance à l'oxygène pendant 28 jours, et sa sévérité est évaluée à 36 semaines d'aménorrhée en fonction de la persistance ou non d'une oxygénothérapie et/ou d'un soutien ventilatoire par pression positive (Table 1)[1]. A noter que l'oxygénodépendance ne survient pas forcément dès la naissance mais peut débuter après une période de durée variable appelée « lune de miel » lors de laquelle l'état respiratoire du nouveau né s'améliore transitoirement suite à l'administration de surfactant de synthèse, puis se détériore suite à une infection, une surcharge volumique ou un canal artériel perméable[2]. Selon M. C. Walch, cette définition servirait à uniformiser le diagnostic de BPD, à la fois comme critère de qualité des soins médicaux et aussi comme outil de mesure dans la recherche clinique[3].

Le diagnostic de la BPD se fait donc sur une base clinique. La présentation classique initiale étant celle d'un enfant prématuré qui développe un syndrome de détresse respiratoire et bénéficie d'une ventilation mécanique avec oxygénothérapie. L'amélioration clinique est suivie par une détérioration correspondant au développement de la BPD.

Tableau 1 : Classification de la BPD à 36 semaines d'âge gestationnel pour les enfants nés < 32 SA, ou à 56 jours de vie pour les enfants nés à ≥ 32 SA *(adapté selon Jobe AH, Bancalari E : American Journal of Respiratory and Clinical Care Medicine 163(7) : 1723-1729, 2001[1])*

1. Légère	FiO_2 0.21%
2. Modérée	FiO_2 0.22-0.29%
3. Sévère	$Fi0_2 \geq$ 0.30% ou ventilation mécanique

Epidémiologie

Malgré les progrès considérables effectués dans la réanimation néonatale et le contrôle optimal des différents facteurs de risque identifiés, l'incidence de la BPD a atteint un plateau depuis quelques années après avoir initialement diminué[4]. Actuellement, la BPD survient approximativement chez un tiers des prématurés ayant un poids de naissance <1000g et contribue à une importante morbidité dans cette population[5].

L'étude de Berger qui rassemble tous les cas sortis des services de néonatologie en Suisse de 1986 à 1990, de 1993 à 1994 et de 2000 à 2001, estime l'incidence totale de la BPD à 19% dans les années 2000, contre 26% avant l'apparition du surfactant, molécule de synthèse permettant de remplacer le surfactant endogène déficient chez les prématurés de moins de 32 SA[6] . Une autre étude multicentrique suisse portant sur toutes les naissances d'enfants de très bas poids de naissance (VLBW, 550-1500g) en 1996 et 2000 a mesuré un taux de BPD de 16.7% et 13.2% respectivement, taux comparables avec les données de plusieurs pays industrialisés[7].

Le taux de mortalité chez les prématurés de très bas poids de naissance en Suisse a également nettement diminué puisqu'il était estimé à 7% dans les années 2000, contre 30% avant l'apparition du surfactant entre 1986 et 1990[6].

Physiopathologie

Le développement pulmonaire embryonnaire est divisé en 5 phases : embryonnaire (0-7 SA), pseudoglandulaire (7-17 SA), canaliculaire (17-27 SA), sacculaire (28-36 SA) et alvéolaire (36 SA-2 ans post natal)[8]. Les structures acineuses comprenant bronchioles, canaux alvéolaires et alvéoles primitives sont formées durant la phase canaliculaire. Quant au surfactant, substance possédant des capacités tensio-actives permettant d'éviter le collapsus alvéolaire, sa sécrétion débute dès la 21ème SA et sa production augmente jusqu'à la fin de la grossesse.

Actuellement, les enfants les plus à risque de développer une BPD naissent à un stade très précoce de leur développement pulmonaire entre 24 et 26 SA durant la phase canaliculaire où la multiplication alvéolaire et la croissance micro-vasculaire distale sont à peine débutées[9].

De plus, une naissance très prématurée interrompt le développement pulmonaire distal normal, aboutissant aux aspects histologiques caractéristiques de la BPD.

L'étude de Coalson réalisée sur des autopsies pulmonaires d'enfants nés avant 30 SA démontre que les lésions histopathologiques de la « nouvelle » BPD sont caractérisées par un trouble du développement pulmonaire périphérique incluant une diminution du nombre et de la complexité alvéolaire avec un réseau capillaire dysmorphique. En revanche, avant l'ère du surfactant, la forme « classique » était caractérisée par une atteinte sévère des voies aériennes, avec alternance de lésions d'emphysème et de fibrose liées aux effets de la ventilation mécanique agressive et à la toxicité de l'oxygène[10]. On constate que depuis l'utilisation du surfactant exogène, les lésions des voies aériennes et de fibrose ont disparu, la « nouvelle » BPD étant principalement caractérisée par un arrêt du développement alvéolaire.

Malgré la disponibilité des traitements récents (corticoïdes prénataux, surfactant) et des méthodes de ventilation moins agressive, l'exposition à des soins intensifs durant les stades très précoces du développement pulmonaire semble mener d'une part à une présentation clinique différente et d'autre part à une altération des fonctions pulmonaires à long terme[11].

La BPD résulte d'un processus dynamique impliquant successivement inflammation, lésion,

réparation et maturation, et les enfants souffrant de BPD continueraient à avoir des séquelles pulmonaires significatives durant l'adolescence et l'âge adulte[12].

Facteurs de risque

Le développement de la BPD est un processus multifactoriel et les facteurs de risque impliqués sont nombreux tant dans la période prénatale immédiate que postnatale.

La prématurité constitue le facteur de risque déterminant avec une forte corrélation positive entre l'incidence de la BPD et le degré de prématurité[13].

De plus, le faible poids de naissance joue un rôle majeur dans l'établissement de la BPD[13]. La chorioamnionite maternelle, en induisant un stimulus inflammatoire anténatal, semble également en augmenter le risque[14].

En ce qui concerne les facteurs environnementaux, les baro- et volutraumatismes liés à la ventilation mécanique et le stress oxydatif induit par l'oxygénothérapie sont souvent incriminés[13]. Certains facteurs postnataux semblent également impliqués tels l'entérocolite nécrosante, la maladie des membranes hyaline, le sepsis néonatal et la persistance du canal artériel.

Les facteurs de risque cités ci-dessus sont ceux que nous avons choisi d'étudier dans notre travail. Il existe cependant d'autres facteurs de risque génétiques qui semblent également contribuer à augmenter la susceptibilité d'un individu à développer une BPD. Le sexe masculin est associé à un risque plus élevé de BPD[15].

Certains polymorphismes de gènes intervenant dans la régulation de la différenciation alvéolaire, de la croissance vasculaire et des voies aériennes semblent également intervenir[16].

L'étude récente de Hadchouel publiée en 2011 a d'ailleurs permis d'identifier une association entre le gène SPOCK2 impliqué dans le développement alvéolaire et la susceptibilité de l'hôte à développer une BPD[17].

1.2 COMMENT EVALUER LES SEQUELLES DE LA BPD EN CLINIQUE ?

Fonctions pulmonaires

L'impact de la prématurité et de la BPD sur la fonction respiratoire peut être évalué à l'aide de fonctions pulmonaires à travers les mesures, entre autre, de la capacité résiduelle fonctionnelle, du débit expiratoire maximal et des résistances. Chez les enfants jeunes, ces examens nécessitent une sédation et ne peuvent se pratiquer que dans un laboratoire d'explorations fonctionnelles équipé, ce qui limite leur utilisation à des centres spécialisés. Chez les enfants plus grands, en général dès 5 à 6 ans, la coopération est plus facile à obtenir et ces mesures peuvent être réalisées dans tous les laboratoires d'explorations fonctionnelles ayant l'habitude de la pédiatrie.

Les nouveau-nés qui développent une BPD présentent déjà des fonctions pulmonaires altérées en période néonatale, en lien direct avec la sévérité de leur BPD. Il est surtout décrit une diminution de la capacité résiduelle fonctionnelle et de la compliance du système respiratoire, ainsi qu'une augmentation de la résistance des voies aériennes. Des études longitudinales ont démontré que ces altérations durant les premiers mois de vie avaient tendance à s'améliorer progressivement à l'âge de 2-3 ans[18,19].

D'autres études effectuées chez des enfants d'âge scolaires ont démontré que les patients ayant souffert de BPD avec un très faible poids de naissance présentaient de plus faibles volumes expiratoires, un cloisonnement gazeux et une hyperréactivité bronchique plus importante comparativement aux enfants du même âge nés à terme[20-22].

En d'autres termes, les épreuves fonctionnelles respiratoires mettent en évidence l'association d'un syndrome restrictif et obstructif d'intensité variable ayant tendance à s'améliorer progressivement avec le temps[23].

Cependant, à plus long terme, de récentes études ont démontré que les enfants ayant soufferts de BPD avaient un volume de réserve respiratoire plus limité et une probabilité plus élevée de développer par la suite une broncho-pneumopathie chronique obstructive (BPCO)[24].

Sur le plan thérapeutique, ces examens permettent de mettre en place un traitement adapté avec par exemple introduction d'un traitement bronchodilatateur dans un contexte d'hyperréactivité bronchique. En ce qui concerne le suivi, cela implique que les enfants ayant souffert de BPD avec un poids de naissance très faible devraient pouvoir bénéficier d'un suivi régulier des fonctions pulmonaires à long terme.

Imagerie

L'imagerie thoracique du nourrisson et du petit enfant est une méthode facile à réaliser dans les centres pédiatriques.

La radiographie standard tendrait à sous-estimer les lésions pulmonaires. En effet, plusieurs auteurs ont constaté une importante discordance entre les lésions radiologiques et les symptômes pulmonaires[25-27]. En revanche, le scanner thoracique a été démontré comme étant nettement plus sensible que la radiographie standard[25] et il tient ainsi un rôle essentiel dans l'évaluation de l'atteinte pulmonaire lésionnelle liée à la BPD.

La première description systématique des lésions pulmonaires de la BPD retrouvées au scanner thoracique fut celle d'Oppenheim en 1994. L'étude décrivait l'analyse de scanner thoraciques de 23 enfants âgés en moyenne de 4 ans et présentant des dysfonctions pulmonaires chroniques. Elle mettait en évidence les lésions caractéristiques de la BPD, soit des zones d'atténuation, des opacités linéaires et des opacités sub-pleurales triangulaires[25]. La plus importante série publiée fut celle d'Aukland en 2005, qui analysait les scanners de 72 enfants nés à 28 SA ou moins. Dans cette étude aussi, les lésions les plus fréquemment retrouvées étaient les opacités linéaires (72%) et les opacités subpleurales (58%). Les zones d'atténuation et d'air trapping n'étaient décrites respectivement que dans 14% et 26 % des cas[28].

Le scanner thoracique est donc un excellent moyen d'établir l'étendue et le type de lésions liés à la BPD, et il permet également de calculer un score de sévérité déjà utilisé dans d'autres pathologies pulmonaires telle la mucoviscidose[29]. Selon Brody, l'utilisation d'un système de score permettant de convertir les images radiologiques en données numériques est un facteur essentiel pour l'interprétation des résultats d'un scanner. Utiliser des données chiffrées comme langage de référence permet en effet à la fois une lecture simplifiée et une meilleure compréhension des images par le clinicien.

Dans le cadre de la BPD, différents systèmes de score ont été investigués et certains ont même été récemment validés[30]. Tel que décrit entre autres par Oppenheim 1994, Howling 2000 et Mahut 2007, nous nous sommes servis des 6 lésions caractéristiques de la BPD

rapportées dans la littérature (zones d'atténuation, emphysème, épaississement bronchique, opacités linéaires, opacités sous-pleurales et bronchiectasies) pour le calcul du score de sévérité.

Cependant, peu d'études se sont intéressées à investiguer l'existence d'une association entre les facteurs néonataux et les lésions pulmonaires retrouvées au scanner[31,32].

II. BUT DU TRAVAIL

Le but de notre travail était d'une part de décrire et d'étudier les anomalies pulmonaires retrouvées au scanner thoracique dans la BPD, et dans la mesure du possible leur évolution. D'autre part, l'objectif était d'intégrer les données cliniques aux résultats des scanners thoraciques à l'aide d'un score pour établir l'existence ou non de corrélations entre la sévérité de la BPD, ses facteurs de risque, le mode de ventilation mécanique, avec le type de lésions pulmonaires, leur fréquence et leur sévérité. Il s'agit d'une étude rétrospective permettant de mettre en évidence l'utilité potentielle d'un score radiologique dans l'évaluation de la BPD.

Chest CT in bronchopulmonary dysplasia: clinical and radiological correlations

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Abstract

Chest CT is very sensitive in assessing pulmonary damage in bronchopulmonary dysplasia (BPD) and radiological findings in BPD are well described. Validated CT scores are available to asses BPD, as available in other pulmonary diseases such as cystic fibrosis.

To investigate whether there is a correlation between radiological pulmonary lesions and relevant BPD clinical data (gestational age, type and duration of mechanical ventilation and severity of BPD) and assess the usefulness of a CT score in evaluating clinical severity, predicting complications of BPD and improving middle term caring of patients suffering from BPD.

Materials and method: Retrospective study of 19 premature infants with BPD born between 1998 and 2007 who underwent at least one chest CT during their first year of life. A total of 29 CT were blindly evaluated by two radiologists for the presence or absence of pulmonary parenchymal abnormalities described in BPD (areas of decreased attenuation, presence of bullae/emphysema, bronchial wall thickening, bronchiectasis, linear and subpleural opacities). This score was then compared with the most relevant clinical data and the long term evolution of these patients.

Results: All CT scans showed abnormalities. The most frequent lesion was bronchial wall thickening observed in all patients, followed by linear (89.5%) and subpleural (89.5%) opacities. Areas of decreased attenuation were found in 68.4%. Bullae/emphysema and bronchiectasis were the less frequent item described (26.3% and 21.1% respectively). The presence of areas of decreased attenuation significantly correlated with BPD severity (P=0.03). However, there was no significant correlation between the CT score and clinical data or middle term clinical evolution.

This study demonstrates the potential usefulness of chest CT score to assess the severity of BPD. Areas of decreased attenuation seem the most sensitive item to predict BPD severity. More patients are needed to validate this approach and to evaluate the long term usefulness of CT scan.

Keywords Bronchopulmonary dysplasia. Computed tomography (CT). Scoring system.

Introduction

Bronchopulmonary dysplasia (BPD), a well known consequence of prematurity, is associated with a high morbidity and is considered the main cause of chronic lung disease in infancy. Its incidence is inversely related to gestational age and birth weight [2]. In Switzerland, recent data reported the incidence of BPD to be 13 to 17 % of all preterm births [7]. Initially related to the effects of aggressive mechanical ventilation and oxygen toxicity on the lungs, BPD is a multifactorial process and is now partly attributed to a disruption or an arrest in lung development [2,33]. Since initially described, its incidence has remained stable due to an increase in the survival of extremely premature infants of very low birth weight [34]. Because of the change in BPD clinical presentation, the National Institute of Child and Human Development (NICHD) proposed a new definition based solely on oxygen use [35]; BPD is now defined as oxygen dependency for at least 28 days after birth, and the severity is graded according to the need for oxygen or ventilatory support at 36 weeks postmenstrual age (PMA). Therefore, the definition is mostly clinical.

Functional evaluation of children suffering from BPD can be performed in specialized research laboratories [18], whereas radiological evaluation are available in most paediatric centres. Chest CT has been shown to be a more sensitive tool than chest x-ray in assessing pulmonary damage following premature birth, providing an objective evidence of lung injury [25]. Pulmonary parenchymal abnormalities found in BPD are well described and include multifocal hyperlucent area, linear and subpleural opacities, bronchial wall thickening, bullae and bronchiectasis [25,36]. Multiple scoring systems that analyse some [31,32], or all items [28,30], are available to assess chest CT scan in BPD. Some of these scores have been thoroughly validated [28,30]. Even though most studies show a correlation between clinical severity and radiological scores, there are no radiological prognostic factors usable in the clinical management of BPD.

In this retrospective study, we used a validated chest CT score [30] to describe pulmonary parenchymal abnormalities found in BPD as to correlate radiological findings to disease severity and clinical characteristics, and to determine the potential usefulness of HRCT findings in the evaluation of BPD.

Material and methods

Patients

We retrospectively studied preterm infants born between 1998 and 2007 at the Geneva University Hospital. Study selection criteria were a diagnosis of moderate to severe BPD, and at least one chest CT performed either routinely or because of a protracted clinical course. BPD was defined following the NIH recommendations as "supplemental oxygen use for at least 28 days", and severity was graded according to the need for oxygen or ventilatory support at 36 weeks PMA [35]. The study was approved by the human research ethics committee of the University Hospital of Geneva.

CT Protocol

Children were sedated with halogenated sevoflurane gas to maintain spontaneous breathing. If required, they were assisted by facial mask ventilation. Apnea was induced with intravenous Propofol or Alfentanyl. High-resolution CT scans were performed with a Siemens Sensation 64, a GE medical systems highspeed CT or a Philips MX 800 CT obtaining 1-mm section at 10 mm intervals from the apex to the diaphragm. Full inspiration was obtained with positive pressure, and expiration without respiratory support. Lung window settings were used for the display.

CT radiation doses were determined according to age-based Diagnostic Reference Levels (DRL) in Switzerland proposed by Verdun et al [37].

CT images were evaluated for the presence of pulmonary abnormalities described in bronchopulmonary dysplasia [25,38] using Fleishner's glossary of terms [39]. Areas of decreased attenuation were defined as diminished lung density resulting from hypoperfusion, bullous emphysema as bullous destruction of the lung parenchyma, bronchial wall thickening as bronchovascular interstitial thickening, subpleural opacities as small triangles with a pleural base and an internal apex, linear opacities as continuous thickening of peribronchial area, and finally bronchiectasis as bronchial dilatation with respect to the accompanying artery, lack of tapering of bronchi, or identification of bronchi within 1 cm of the pleura surface.

CT scans were evaluated for the number of affected lobes for each pulmonary abnormality. The absence of lesions was scored 0 and their presence was graded from 1 to 6 according to the number of affected lobes (lingula included). The CT scores ranged from 0 (no abnormalities) to 36 (each abnormality in all 6 lobes), such that a higher score reflected more severe disease. According to Aukland et al [30], the option to base the scores on findings in the

different lung lobes instead of lung segments makes the scoring process less complex, reducing the risk of inaccuracies. The CT scans were blindly reviewed by two radiologists, first independently, then by consensus in case of discrepancy. We report only the consensus scores.

Neonatal data

Neonatal data was obtained from the medical records of the neonatal intensive care unit. Variables such as gestational age (GA), birth weight (BW), type/duration of mechanical ventilation and oxygen supplementation were analysed.

Other potential contributing factors known to increase the risk of BPD such as chorioamnionitis, necrotizing enterocolitis (NEC), hyaline membrane disease (HMD), patent ductus arteriosus (PDA) and neonatal sepsis were also recorded [7,40]. Medical interventions (surfactant, ante-postnatal steroids and diuretics) and two significant clinical parameters, pCO_2 and respiratory rate at 28 days and 36 weeks PMA, respectively, were also analyzed. Finally, two outcomes (readmission due to reactive airway disorders and death) were recorded.

Statistical analysis

The clinical characteristics, the clinical data and the CT findings were described by percentage or median (with range). The radiological items (scored on a scale 0-6) were compared to the binary clinical data (BPD severity, surfactant, corticosteroids, complications including readmission and death) using a Fisher exact test. The median number of affected lobes according to BPD severity was analysed using a Mann-Withney test. Associations between the radiological items and the quantitative clinical data (GA, BW, duration of CPAP, duration of O_2, respiratory rate and pCO_2 at 28 days and 36 weeks PMA) were explored using linear regression models. Comparisons between subgroups were performed using Fisher exact tests or Mann-Whitney's tests.

The radiological items were binarised into categories: absent (score of 0), or present (score of 1 or more). The positive predictive value of each radiological item in the prediction of BPD severity was assessed (proportion of severe patients among the patients with a score greater than 0). The confidence intervals (95%) were obtained by the Clopper-Pearson method.

The global agreement of CT findings between the 2 readers was assessed by the Cohen's Kappa coefficient interpreted on the Landis and Koch scale: the agreement is almost perfect

for a Kappa statistic beyond 0.80, substantial between 0.60 and 0.80, moderate between 0.40 and 0.60, fair between 0.20 and 0.40, and slight below 0.2.

Results

Study patients

According to Geneva's Maternity Hospital database, a total of 3717 preterm infants (under 37 weeks GA) were born between 1998 and 2007, representing 10.4% of all births. Among these, 88 (2.4%) developed moderate or severe BPD according to the NICHD definition [35]. Nineteen premature infants (10 boys, 9 girls) who underwent at least one chest CT were included in the study group. Median gestational age (GA) at birth was 26.1 weeks (range 24.3-33.3) and median birth weight (BW) was 740 grams (range 510-1370). Six patients (31.6%) were classified as moderate BPD (supplemental oxygen use ≥ 28 days and oxygen < 30% at 36 weeks PMA or discharge) and 13 patients (68.4%) as severe BPD (supplemental oxygen use ≥ 28 days and oxygen > 30% and/or CPAP at 36 weeks PMA or discharge). Median age at the first CT was 14.6 months (range 1.5-53.7). Patient characteristics are summarized in Table 1. Four of the 19 patients died and 9 were readmitted.

Table 1 Clinical characteristics

	N = 19
Sex, M/F	10/9
GA, weeks	26.1 (24.3-33.3)
BW, grams	740 (510-1370)
BPD severity:	
- moderate	6
- severe	13
Age at 1st CT scan, months	14.6 (1.5-53.7)

Data are presented as median (range). GA gestational age, BW birth weight

CT findings

Nineteen patients underwent at least one chest CT at the median age of 14.6 months (1.5-53.7). Four patients had 2 or 3 imaging studies performed at the median age of 19.5 months (3.9-63.7) for the second one and 80 months (24-99) for the third one.

All CT scans showed abnormalities. The most frequent abnormality was bronchial wall thickening in all patients (100%) (Fig.1a). Linear and subpleural opacities were observed in 17 cases (90%). Areas of decreased attenuations were detected in more than half of the patients (69%) (Fig.1b), and only 5 patients (26 %) presented emphysema. Bronchiectasis was visible in only 4 cases (21.1%).

The presence of bronchial wall thickening affected at least 4 lobes for all patients, whereas the presence of all other items was more variable. For the lesions including bronchial wall thickening, linear opacities, subpleural opacities and emphysema/bullae, the proportion of patients who had at least 1 lobe affected was similar between severe and moderate BPD (p = 1).

In the 4 patients who had more than one chest CT (between 10.6 and 43.2 months later), the lesions remained fairly stable over time, with poor improvement and no further evolution.

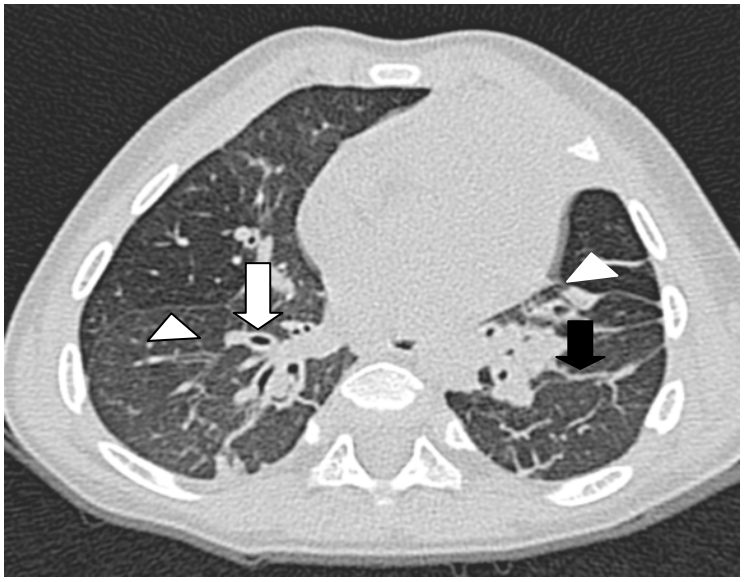


Figure 1a: 13 months-old boy with severe BPD. Inspiratory axial CT showing regions of attenuation (arrowheads), parenchymal linear opacities (black arrow), bronchial wall thickening and bronchiectasis (white arrow).

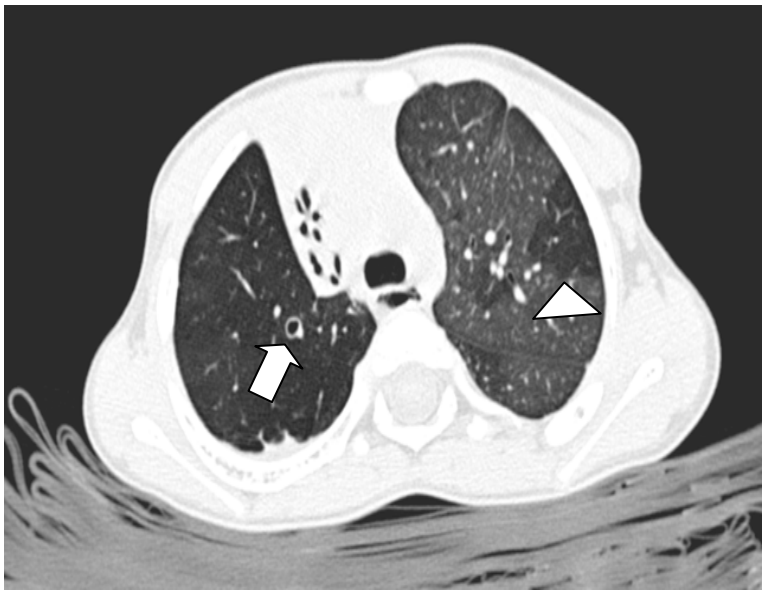


Figure 1b: 3 years-old girl with severe BPD. Inspiratory axial CT showing regional attenuations (arrowheads). The pulmonary vessels caliber in those areas are smaller. Bronchiectasis (white arrows) are also noted.

Interobserver reproducibility

Agreement of CT findings among the 2 reviewers was further evaluated using the Cohen's kappa indice. Bronchial wall thickening, bronchiectasis and subpleural opacities showed high concordance (Cohen's kappa ranged from 0.79 for bronchial wall thickening to 0.99 for emphysema/bullae). Concordance was inferior but still substantial for the items attenuation (Cohen's kappa = 0.62) and linear opacities (Cohen's kappa = 0.71).

Correlation between CT findings and clinical data

There was no significant correlation for the comparison of each radiological item from the baseline CT, individually and as a total score, to the clinical data. However, when comparing the radiological items to BPD severity, there were significantly more areas of decreased attenuation in severe BPD compared to moderate ($p = 0.046$) [Figure 2]. Furthermore, there were significantly more lobes showing decreased attenuation according to BPD severity ($p = 0.03$). Differences in other parenchymal abnormalities and median composite score were not statistically different between moderate and severe BPD [Table 2].

The positive predictive value of each radiological item assessed by binary categorisation was good to excellent to predict BPD severity: subpleural and linear opacities: 70.6% (44.1-89.7),

bronchectasis: 100.0% (39.8-100.0), emphysema: 80.0% (28.4-99.5) and attenuation: 84.6% (54.6-98.1).

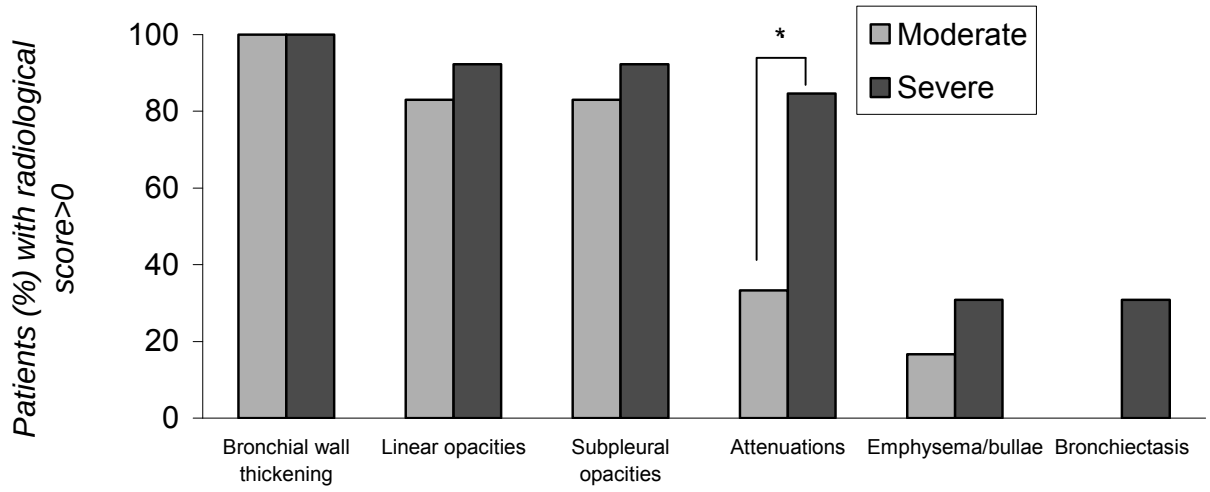
Table 2 Number of affected lobes according to BPD severity

	Moderate BPD N = 6 lobes	**Severe BPD N = 6 lobes**	**P°**
Bronchial wall thickening	6 (6-6)	6 (4-6)	0.32
Linear opacities	5 (0-6)	3 (0-6)	0.85
Subpleural opacities	3 (0-6)	4 (0-6)	0.56
Attenuations	0 (0-5)	2 (0-6)	0.03
Bullae	0 (0-4)	0 (0-6)	0.5
Bronchiectasis	0 (0-0)	0 (0-4)	0.14
Median composite score*	12 (9-27)	18 (8-24)	0.28

°Mann-Withney test. Data are presented as median (range)

*Median composite score on 6 lobes x 6 radiological items = total score of 36

Figure 2 Distribution of parenchymal abnormalities according to BPD severity



*=P < 0.05

Risk factors and medical interventions

The highest risk factor for severe BPD was the presence of hyaline membrane disease (p = 0.004). The presence of PDA, clinical sepsis, NEC and chorioamnionitis were not significantly relevant.

The most important drug therapies used in the prevention and management of BPD were analysed. To the exception of surfactant used more often in patients with severe BPD (p = 0.02), there was no significant difference in the administration of diuretics between moderate and severe BPD (used in all children, 100%), or steroids (prenatal p = 0.52, postnatal p = 0.62).

Respiratory support

All patients with moderate and severe BPD required oxygen supplementation and CPAP during their neonatal period, while 79 % were mechanically ventilated. Mechanical ventilation (MV) was more frequent in severe BPD, but median duration of MV was similar between severe and moderate BPD (21.5 vs. 26 days, respectively). The use of CPAP was longer in severe BPD. There was no difference in the mean duration of oxygen therapy.

Prognosis data

Median pCO_2 was significantly higher at 36 weeks PMA when BPD severity was assessed for severe BPD patients compared to moderate (7.9 kPa vs. 6.27, p = 0.03), but not at 28 days PMA when BPD was diagnosed (7.4 kPa vs. 7.29, respectively).

Median respiratory rate was comparable in the two groups (49/minute at 28 days and 50 at 36 weeks PMA for moderate BPD vs. 44/minute and 55 respectively for severe BPD).

Discussion

In this retrospective study, we used a validated chest CT score [30] to describe pulmonary parenchymal abnormalities found in BPD, and we correlated radiological findings to disease severity and clinical characteristics. We assessed the score's usefulness in predicting the severity of BPD.

Thoracic CT is a minimally invasive way to assess lung morphology, and a very sensitive method to detect and quantify lung disease. For example in cystic fibrosis (CF), CT imaging is known to correlate with clinical assessment of disease severity and to correspond to pathological findings [29]. In BPD, previous studies have shown that all survivors born before the mid 90's had abnormalities on CT scanning, whether they still presented pulmonary signs or symptoms [25] or not [36,41]. Nowadays, the CT scores of BPD patients compared with those of healthy control subjects are significantly higher in children with persistent chronic lung disease of infancy, and correlate significantly with the number of days of supplemental oxygen [42], reflecting more severe disease. Likewise, in a prospective study evaluating infants with BPD with a more complex CT analysis grid, there was a significant correlation between CT scores and the duration of oxygen supplementation, but not with the duration of mechanical ventilation [32].

The most frequent abnormal CT findings described in BPD are well defined linear opacities, areas of decreased lung attenuation and triangular subpleural opacities. Associated pathologic features are strands of atelectasis extending to the pleura for linear opacities, and small airway obstruction leading to obstructive emphysema for reduced attenuation [25,43]. We found the same abnormalities in our patient population where the most frequent finding was bronchial wall thickening. This suggests that, added to the dysregulation of lung morphologic maturation with an arrest at the canalicular phase of lung development and simplified alveolar septation [10], there might be airway changes with peribronchial and peribronchiolar fibrosis. Thus, BPD is a chronic disease involving lung parenchyma and airways.

Interestingly, bronchiectasis was only rarely found in our population and did not predict any clinical outcome. However, the presence of bronchiectasis was associated with BPD severity even more significantly when combined with areas of attenuation.

In our retrospective analysis, the single item which correlates significantly with BPD severity was the presence of areas of decreased attenuation. Similarly, in the first study looking at correlations between CT and clinical findings [31], only the extent of hyperaeration correlated to clinical severity, even if the clinical items evaluated are not part of the BPD grading system now in use. Thus, hyperaeration possibly reflects a decreased number of functional alveoli,

consequently playing an important role in the impairment of pulmonary function and BPD severity. Therefore, the item attenuation could be most useful to predict the severity of BPD.

Chest x-rays abnormalities found in BPD gradually improve in the long term [40]. On the contrary, we have shown no further degradation or improvement in chest CT abnormalities on repeated exams, suggesting that radiological scores do not strictly follow clinical amelioration in BPD. Therefore, CT patterns might reflect fixed parenchymal abnormalities. This result is interesting as it raises the question about the usefulness of repeated chest CT in children. Furthermore, the risks of irradiation during CT should not be underestimated despite using automatic exposure systems and age-based Diagnostic Reference Levels (DRL) as advocated by Verdun [37,44].

The comparison of chest CT findings and pulmonary function tests in BPD survivors has shown conflicting results. Aukland and al found a significant association between decreased maximal expiratory flow rates and HRCT scores [30]. On the contrary, Sarria and al [42] found that CT score was more accurate in discriminating between the patients with CLDI (Chronic Lung Disease in Infancy) and the controls, even if BPD survivors had lower forced expiratory flows. CT imaging, with an appropriate evaluation grid, is certainly complementary to pulmonary function testing in the evaluation of BPD patients and both methods offer different assessments of the lungs.

The major drawbacks of this study come from its retrospective nature and the small sample size, limiting significant correlations with clinical data and outcomes such as rehospitalisation or death.

In conclusion, the reading and interpretation of pulmonary CT findings in BPD according to a validated score is easily feasible. It can be useful in assessing the severity of this disorder, and areas of decreased attenuation seem to be the most sensitive radiological item to predict BPD severity. As CT requires sedation and provides the child with radiation exposure, we suggest the acquisition of further prospective data to better evaluate the impact on treatment and outcome of BPD patients before implementing routine chest CT in their management.

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IV. TABLEAUX SUPPLEMENTAIRES

Table 3. BPD risk factors

	Moderate BPD N=6 n (%)	**Severe BPD N=13 n (%)**	**P value****
PDA	4 (66.7)	9 (69.2)	1
Chorioamnionitis *	1 (16.7)	3 (23.1)	1
Clinical sepsis	1 (16.7)	8 (61.5)	0.14
NEC	2 (33.3)	4 (30.8)	1
HMD	2 (33.3)	13 (100.0)	0.004

Main risk factors contributing to increase the risk of bronchopulmonary dysplasia and their repartition between moderate and severe patients. The highest risk factor for severe BPD was the presence of HMD. The presence of PDA, chorioamnionitis, clinical sepsis and NEC were not significantly relevant.

PDA: patent ductus arteriosus; NEC : necrotizing enterocolitis ; HMD: hyaline membrane disease

** postnatal infection defined as positive blood culture or clinical deterioration, not explained by ductus arteriosus or necrotizing enterocolitis, necessitating empirical antibiotherapy*

*** Fischer's exact test*

Table 4. Respiratory support

	Moderate BPD N=6		Severe BPD N=13	
	N (%)	**Duration***	**N (%)**	**Duration***
Oxygen therapy	6 (100.0)	89.5 [55-679]	13 (100.0)	144 [43-465]
- discharge home on oxygen	1 (16.7)	308 [308-308]	5 (38.5)	211 [164-322]
Mechanical ventilation	3 (50.0)	26 [12-112]	12 (92.3)	21.5 [2- 84]
- HFO only	2 (33.3)	26 [12- 68]	4 (30.8)	21 [12- 43]
- Conventional only	0	/	2 (15.4)	9.5 [2-17]
- HFO + conventional	1 (16.7)	112 [112-112]	6 (46.2)	32 [6- 84]
CPAP	6 (100.0)	43 [14- 53]	13 (100.0)	54 [15-188]
- and mechanical ventilation	3 (50.0)	48 [25- 52]	12 (92.3)	55 [15-188]

Type and duration of mechanical ventilation and oxygen supplementation between moderate and severe BPD patients. All patients with moderate and severe BPD required oxygen supplementation and CPAP during their neonatal period. Mechanical ventilation was more frequent in severe BPD but median duration of MV was similar between severe and moderate BPD (21.5 vs. 26 days, respectively). The use of CPAP was longer in severe BPD. There was no difference in the mean duration of oxygen therapy.

HFO: high-frequency oscillatory ventilation; CPAP: continuous positive airway pressure

**Median [range] in days*

Table 5. Outcomes

	Moderate BPD N=6 n (%)	**Severe BPD N=13 n (%)**
Number of readmissions	2 (33.3)	7 (53.8)
none	3 (50.0)	3 (23.1)
1	1 (16.7)	5 (38.5)
2	0	1 (7.7)
3	1 (16.7)	0
4	0	1 (7.7)
Death	1 (16.7)	3 (23.1)
Readmission +/- death	3 (50.0)	10 (76.9)

Record of the two main outcomes including number of readmission due to reactive airway disorders and death. Number of readmissions and deaths was higher in severe BPD patients.

V. PERSPECTIVES :

Cette étude rétrospective a montré que le scanner thoracique tenait une place importante dans l'évaluation de la BPD. Elle a également permis de souligner l'utilité d'un score radiologique simple pour permettre aux cliniciens d'effectuer une évaluation plus précise des complications de la BPD.

En dépit du fait que notre étude n'avait pas comme but d'étudier les facteurs de risque et les conséquences de la BPD, nous avons été surpris de constater que les enfants qui recevaient du surfactant appartenaient tous au groupe BPD sévère. Ce résultat suggère que le surfactant pourrait être considéré comme un facteur de risque de la BPD, comme l'a démontré l'étude de Hentschel qui a mis en évidence une augmentation de BPD chez les patients recevant du surfactant[7], et plus récemment une étude multicentrique observationnelle en Norvège[45]. A l'inverse, cette constatation pourrait aussi être le résultat d'une détresse respiratoire initiale plus sévère justifiant l'utilisation de surfactant, qui pourrait ne pas avoir la même efficacité chez les grands prématurés dont le développement pulmonaire est encore au stade canaliculaire plutôt que sacculaire.
Une autre observation intéressante est la corrélation objectivée entre la valeur de pCO_2 à 36 SA et la sévérité de la BPD. Bien que ce paramètre clinique ne soit pas inclus dans les critères diagnostiques actuellement utilisés pour la BPD[1], ce résultat soutient l'idée que la pCO_2 pourrait être un paramètre supplémentaire utilisé pour juger de la sévérité de l'atteinte et guider les suites de traitement.

L'imagerie soulève en revanche encore bien des craintes concernant les risques liés à l'irradiation. Il existe peu de données sur les effets radiologiques à long terme d'imageries répétées, à l'exception de l'oncologie. Cependant, les progrès récents effectués dans les techniques d'imagerie ainsi que les protocoles tendant à réduire l'exposition aux radiations[37] permettront à l'avenir d'utiliser plus librement le scanner thoracique comme outil d'évaluation des changements structurels pulmonaires à long terme, en complément aux fonctions pulmonaires. La place de cet examen devrait être largement discutée en l'absence d'évolution favorable ou en cas de complications secondaires car il permet d'avoir une bonne vision des séquelles de la BPD. Cependant, il est à noter que la nécessité d'effectuer une anesthésie générale chez les jeunes enfants reste un facteur limitant significatif à prendre en compte.

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Chest CT in Bronchopulmonary Dysplasia: Clinical and Radiological Correlations

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Summary. Background: Chest CT is very sensitive in assessing pulmonary damage in bronchopulmonary dysplasia (BPD) and radiological findings in BPD are well described. Validated CT scores are available to assess BPD, as available in other pulmonary diseases such as cystic fibrosis. Aim: To investigate whether there is a correlation between radiological pulmonary lesions and relevant BPD clinical data (gestational age, type and duration of mechanical ventilation, and severity of BPD) and assess the usefulness of a CT score in evaluating clinical severity. Materials and Methods: Retrospective study of 19 premature infants with BPD born between 1998 and 2007 who underwent at least one chest CT during their first year of life. A total of 29 CT were blindly evaluated by two radiologists for the presence or absence of pulmonary parenchymal abnormalities described in BPD (areas of decreased attenuation, presence of bullae/emphysema, bronchial wall thickening, bronchiectasis, linear, and subpleural opacities). This score was then compared with the most relevant clinical data. Results: All CT scans showed abnormalities. The most frequent lesion was bronchial wall thickening observed in all patients, followed by linear (89.5%) and subpleural (89.5%) opacities. Areas of decreased attenuation were found in 68.4%. Bullae/emphysema and bronchiectasis were the less frequent item described (26.3% and 21.1%, respectively). The presence of areas of decreased attenuation significantly correlated with BPD severity ($P = 0.03$). However, there was no significant correlation between the CT score and clinical data. Conclusions: This study demonstrates the potential usefulness of chest CT score to assess the severity of BPD. Areas of decreased attenuation seem the most sensitive item to predict BPD severity. More patients are needed to validate this approach and to evaluate the long-term usefulness of CT scan. **Pediatr Pulmonol.** © 2012 Wiley Periodicals, Inc.

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INTRODUCTION

Bronchopulmonary dysplasia (BPD), a well-known consequence of prematurity, is associated with a high morbidity and is considered the main cause of chronic lung disease in infancy. Its incidence is inversely related to gestational age (GA) and birth weight (BW).[1] In Switzerland, recent data reported the incidence of BPD to be 13–17% of all preterm births.[2] Initially related to the effects of aggressive mechanical ventilation and oxygen toxicity on the lungs, BPD is a multifactorial process and is now partly attributed to a disruption or an arrest in lung development.[1,3] Since initially described, its incidence has remained stable due to an increase in the survival of extremely premature infants of very low BW.[4] Because of the change in BPD clinical presentation, the National Institute of Child and Human Development (NICHD) proposed a new definition based solely on oxygen use[5]; BPD is now defined as oxygen dependency for at least 28 days after birth, and the severity is graded according to the need for oxygen or

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Conflict of interest: None.

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ventilatory support at 36 weeks postmenstrual age (PMA). Therefore, the definition is mostly clinical.

Functional evaluation of children suffering from BPD can be performed in specialized research laboratories,[6] whereas radiological evaluation is available in most pediatric centers. Chest CT has been shown to be a more sensitive tool than chest X-ray in assessing pulmonary damage following premature birth, providing an objective evidence of lung injury.[7] Pulmonary parenchymal abnormalities found in BPD are well described and include multifocal hyperlucent area, linear and subpleural opacities, bronchial wall thickening, bullae, and bronchiectasis.[7,8] Multiple scoring systems that analyze some,[9,10] or all items,[11,12] are available to assess chest CT scan in BPD. Some of these scores have been thoroughly validated.[11,12] Even though most studies show a correlation between clinical severity and radiological scores, there are no radiological prognostic factors usable in the clinical management of BPD.

We hypothesize that clinical data correlated with radiological score. We aimed to evaluate pulmonary parenchymal abnormalities found in BPD by using a validated chest CT score,[11] to correlate radiological findings with disease severity and clinical characteristics, and to determine the potential usefulness of HRCT findings in the evaluation of BPD.

MATERIALS AND METHODS

Patients

We retrospectively studied preterm infants born between 1998 and 2007 at the Geneva University Hospital. Study selection criteria were a diagnosis of moderate to severe BPD, and at least one chest CT performed either routinely or because of a protracted clinical course. BPD was defined following the NIH recommendations as "supplemental oxygen use for at least 28 days," and severity was graded according to the need for oxygen or ventilatory support at 36 weeks PMA.[5] The study was approved by the human research ethics committee of the University Hospital of Geneva. Because this study was retrospective and involved only medical charts and imaging review, the ethics committee of the Institution did not require parental consent but only the study approval.

CT Protocol

Children were sedated with halogenated sevoflurane gas to maintain spontaneous breathing. If required, they were assisted by facial mask ventilation. Apnea was induced with intravenous Propofol or Alfentanyl. High-resolution CT scans were performed with a Siemens Sensation 64, a GE medical systems highspeed CT or a Philips MX 800 CT obtaining 1-mm section at 5- or 10-mm intervals from the apex to the diaphragm. This dataset is generally used for CT scan when performed to assess chronic lung disease in order to minimize the radiation dose. Full inspiration was obtained with positive pressure, and expiration without respiratory support. Lung window settings were used for the display. Scan parameters used were between 80 and 140 for kV (median 120) and between 50 and 200 for mAs (median 100). Before 2008, there was a great dispersion between the different centers in the product dose length (PDL) delivered to the patients. First recommendations were made according to Verdun survey in 2008[13] and Swiss official recommendations were published by OFSP (Office fédéral de la santé publique) in 2010. CT images were evaluated for the presence of pulmonary abnormalities described in BPD[7,14] using Fleishner's glossary of terms.[15] Areas of decreased attenuation were defined as diminished lung density resulting from hypoperfusion, bullous emphysema as bullous destruction of the lung parenchyma, bronchial wall thickening as bronchovascular interstitial thickening, subpleural opacities as small triangles with a pleural base and an internal apex, linear opacities as continuous thickening of peribronchial area, and finally bronchiectasis as bronchial dilatation with respect to the accompanying artery, lack of tapering of bronchi, or identification of bronchi within 1 cm of the pleural surface.

CT scans were evaluated for the number of affected lobes for each pulmonary abnormality. The absence of lesions was scored zero and their presence was graded from one to six according to the number of affected lobes (lingula included). The CT scores ranged from 0 (no abnormalities) to 36 (each abnormality in all 6 lobes), such that a higher score reflected more severe disease. According to Aukland et al.,[11] the option to base the scores on findings in the different lung lobes instead of lung segments makes the scoring process less complex, reducing the risk of inaccuracies. The CT scans were blindly reviewed by two radiologists, first independently, then by consensus in case of discrepancy. We report only the consensus scores.

Neonatal Data

Neonatal data was obtained from the medical records of the neonatal intensive care unit. Variables such as GA, BW, type/duration of mechanical ventilation, and oxygen supplementation were analyzed.

Other potential contributing factors known to increase the risk of BPD such as chorioamnionitis, necrotizing enterocolitis (NEC), hyaline membrane disease (HMD), patent ductus arteriosus (PDA), and neonatal sepsis were also recorded.[2,16] Medical interventions (surfactant, ante-postnatal steroids, and diuretics) and

two significant clinical parameters, pCO_2 and respiratory rate at 28 days and 36 weeks PMA, respectively, were also analyzed.

Statistical Analysis

The clinical characteristics, the clinical data and the CT findings were described by percentage or median (with range). The radiological items (scored on a scale 0–6) were compared to the binary clinical data (BPD severity, surfactant, corticosteroids using a Fisher exact test. The median number of affected lobes according to BPD severity was analyzed using a Mann–Whitney *U*-test. Associations between the radiological items and the quantitative clinical data (GA, BW, duration of CPAP, duration of O_2, respiratory rate, and pCO_2 at 28 days and 36 weeks PMA) were explored using linear regression models. Comparisons between subgroups were performed using Fisher exact tests or Mann–Whitney's *U*-tests.

The radiological items were binarized into categories: absent (score of zero), or present (score of one or more). The positive predictive value of each radiological item in the prediction of BPD severity was assessed (proportion of severe patients among the patients with a score >0). The confidence intervals (95%) were obtained by the Clopper–Pearson method.

The global agreement of CT findings between the two readers was assessed by the Cohen's Kappa coefficient interpreted on the Landis and Koch scale: the agreement is almost perfect for a Kappa statistic beyond 0.80, substantial between 0.60 and 0.80, moderate between 0.40 and 0.60, fair between 0.20 and 0.40, and slight below 0.2.

RESULTS

Study Patients

According to Geneva's Maternity Hospital database, a total of 3,717 preterm infants (under 37 weeks GA) were born between 1998 and 2007, representing 10.4% of all births. Among these, 88 (2.4%) developed moderate or severe BPD according to the NICHD definition.[5]

Nineteen premature infants (10 boys, 9 girls) who underwent at least one chest CT were included in the study group. Median GA at birth was 26.1 weeks (range, 24.3–33.3) and median BW was 740 g (range, 510–1,370). Six patients (31.6%) were classified as moderate BPD (supplemental oxygen use $\geq$28 days and oxygen $<$30% at 36 weeks PMA or discharge) and 13 patients (68.4%) as severe BPD (supplemental oxygen use $\geq$28 days and oxygen $>$30% and/or CPAP at 36 weeks PMA or discharge). Median age at the first CT was 14.6 months (range, 1.5–53.7). Patient characteristics are summarized in Table 1.

CT Findings

Nineteen patients underwent at least one chest CT at the median age of 14.6 months (1.5–53.7). Four patients had two or three imaging studies performed at the median age of 19.5 months (3.9–63.7) for the second one and 80 months (24–99) for the third one.

All CT scans showed abnormalities. The most frequent abnormality was bronchial wall thickening in all patients (100%; Fig. 1a). Linear and subpleural opacities were observed in 17 cases (90%). Areas of decreased attenuations were detected in more than half of the patients (69%; Fig. 1b), and only five patients (26%) presented emphysema. Bronchiectasis was visible in only four cases (21.1%).

The presence of bronchial wall thickening affected at least four lobes for all patients, whereas the presence of all other items was more variable. For the lesions including bronchial wall thickening, linear opacities, subpleural opacities, and emphysema/bullae, the proportion of patients who had at least one lobe affected was similar between severe and moderate BPD ($P = 1$).

In the four patients who had more than one chest CT (between 10.6 and 43.2 months later), the lesions remained fairly stable over time, with poor improvement, and no further evolution.

Interobserver Reproducibility

Agreement of CT findings between the two reviewers was further evaluated using the Cohen's kappa indice. Bronchial wall thickening, bronchiectasis, and subpleural opacities showed high concordance (Cohen's kappa ranged from 0.79 for bronchial wall thickening to 0.99 for emphysema/bullae). Concordance was inferior but still substantial for the items attenuation (Cohen's kappa = 0.62) and linear opacities (Cohen's kappa = 0.71).

Correlation Between CT Findings and Clinical Data

There was no significant correlation for the comparison of each radiological item from the baseline CT,

TABLE 1—Clinical Characteristics

	N = 19
Sex (M/F)	10/9
GA (weeks)	26.1 (24.3–33.3)
BW (g)	740 (510–1,370)
BPD severity	
Moderate	6
Severe	13
Age at 1st CT scan (months)	14.6 (1.5–53.7)

GA, gestational age; BW, birth weight.
Data are presented as median (range).

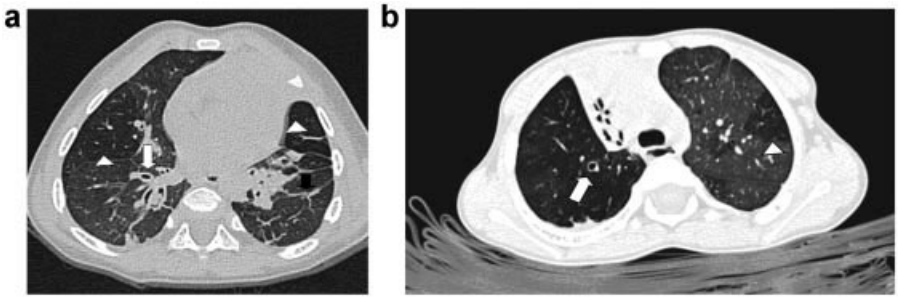

Fig. 1. a: 13 months old boy with severe BPD. Inspiratory axial CT showing regions of attenuation (arrowheads), parenchymal linear opacities (black arrow), bronchial wall thickening, and bronchiectasis (white arrow). b: 3 years old girl with severe BPD. Inspiratory axial CT showing regional attenuations (arrowheads). The pulmonary vessels caliber in those areas are smaller. Bronchiectasis (white arrows) is also noted.

individually and as a total score, to the clinical data. However, when comparing the radiological items to BPD severity, there were significantly more areas of decreased attenuation in severe BPD compared to moderate ($P = 0.046$; Fig. 2). Furthermore, there were significantly more lobes showing decreased attenuation according to BPD severity ($P = 0.03$). Differences in other parenchymal abnormalities and median composite score were not statistically different between moderate and severe BPD (Table 2).

The positive predictive value of each radiological item assessed by binary categorization was good to excellent to predict BPD severity: subpleural and linear opacities: 70.6% (44.1–89.7), bronchectasis: 100.0% (39.8–100.0), emphysema: 80.0% (28.4–99.5), and attenuation: 84.6% (54.6–98.1).

Risk Factors and Medical Interventions

The highest risk factor for severe BPD was the presence of HMD ($P = 0.004$). 13/19 patients had PDA. The ratio of PDA in severe (9/13) and moderate BPD (4/6) was not different and the number of clinical sepsis, NEC and chorioamnionitis were not significantly relevant.

The most important drug therapies used in the prevention and management of BPD were analyzed. To the exception of surfactant used more often in patients with severe BPD ($P = 0.02$), there was no significant difference in the administration of diuretics between moderate and severe BPD (used in all children, 100%), or steroids (prenatal $P = 0.52$, postnatal $P = 0.62$).

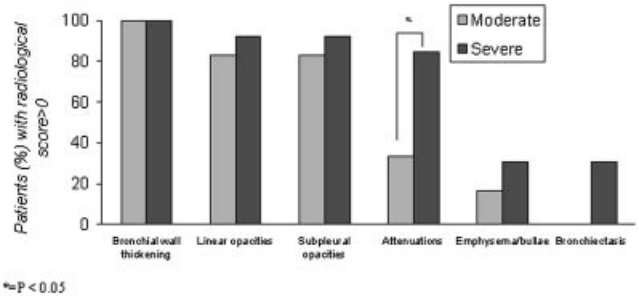

Fig. 2. Distribution of parenchymal abnormalities according to BPD severity.

Respiratory Support

All patients with moderate and severe BPD required oxygen supplementation and CPAP during their neonatal period, while 79% were mechanically ventilated. Mechanical ventilation (MV) was more frequent in severe BPD, but median duration of MV was similar between severe and moderate BPD (21.5 days vs. 26 days, respectively). The use of CPAP was longer in severe BPD. There was no difference in the mean duration of oxygen therapy.

Prognosis Data

Median pCO_2 was significantly higher at 36 weeks PMA for severe BPD patients compared to moderate (7.9 kPa vs. 6.27 kPa, $P = 0.03$), but not at 28 days PMA when BPD was diagnosed (7.4 kPa vs. 7.29 kPa, respectively).

TABLE 2— Number of Affected Lobes According to BPD Severity

	Moderate BPD, N = 6 lobes	Severe BPD, N = 6 lobes	P^1
Bronchial wall thickening	6 (6–6)	6 (4–6)	0.32
Linear opacities	5 (0–6)	3 (0–6)	0.85
Subpleural opacities	3 (0–6)	4 (0–6)	0.56
Attenuations	0 (0–5)	2 (0–6)	0.03
Bullae	0 (0–4)	0 (0–6)	0.5
Bronchiectasis	0 (0–0)	0 (0–4)	0.14
Median composite score[2]	12 (9–27)	18 (8–24)	0.28

[1]Mann–Whitney *U*-test. Data are presented as median (range).
[2]Median composite score on 6 lobes × 6 radiological items = total score of 36.

Median respiratory rate was comparable in the two groups (49/min at 28 days and 50 at 36 weeks PMA for moderate BPD vs. 44 and 55/min, respectively for severe BPD).

DISCUSSION

In this retrospective study, we used a validated chest CT score[11] to describe pulmonary parenchymal abnormalities found in BPD, and we correlated radiological findings to disease severity and clinical characteristics. We assessed the score's usefulness in predicting the severity of BPD.

Thoracic CT allows good assessment of lung morphology. Moreover, it is a very sensitive method to detect and quantify lung disease. Indeed, in cystic fibrosis (CF), CT imaging is known to correlate with clinical measures of disease severity and to correspond to pathological findings.[17] In BPD, previous studies have shown that all survivors born before the mid-1990s had abnormalities on CT scanning, whether they still presented pulmonary signs or symptoms[7] or not.[8,18] Nowadays, the CT scores of BPD patients compared with those of healthy control subjects are significantly higher in children with persistent chronic lung disease of infancy, and correlate significantly with the number of days of supplemental oxygen,[19] reflecting more severe disease. Likewise, in a prospective study evaluating infants with BPD with a more complex CT analysis grid, there was a significant correlation between CT scores and the duration of oxygen supplementation, but not with the duration of mechanical ventilation.[10]

The most frequent abnormal CT findings described in BPD are well-defined linear opacities, areas of decreased lung attenuation, and triangular subpleural opacities. Associated pathologic features are strands of atelectasis extending to the pleura for linear opacities, and small airway obstruction leading to obstructive emphysema for reduced attenuation.[7,20] In our patient population, the most frequent abnormality was bronchial wall thickening, suggesting that there might be airway changes with peribronchial and peribronchiolar fibrosis, added to the dysregulation of lung morphologic maturation with an arrest at the canalicular phase of lung development and simplified alveolar septation.[21] Thus, BPD is a chronic disease involving lung parenchyma and airways.

Interestingly, bronchiectasis was only rarely found in our population and did not predict any clinical outcome. However, the presence of bronchiectasis was associated with BPD severity even more significantly when combined with areas of attenuation.

In our retrospective analysis, the single item which correlates significantly with BPD severity was the presence of areas of decreased attenuation. Similarly, in the first study looking at correlations between CT and clinical findings,[9] only the extent of hyperaeration correlated to clinical severity, even if the clinical items evaluated are not part of the BPD grading system now in use. Thus, hyperaeration possibly reflects a decreased number of functional alveoli, consequently playing an important role in the impairment of pulmonary function and BPD severity. Therefore, the item attenuation could be most useful to predict the severity of BPD.

Chest X-rays abnormalities found in BPD are known to gradually improve in the long term.[16] Little is known about the evolution of CT scan abnormalities. Although follow up of radiological lesions was not the purpose of this retrospective study, in the four patients who had repeated chest CT in a relatively short time, the lesions remained stable with poor improvement and no further degradation. Indeed, according to Aquino et al.,[18] abnormal findings on high resolution CT scans were described in 92% of children and adolescents with a past history of BPD. The correlation between CT scan and functional evolution should be addressed in further prospective studies.

Moreover, the risks of irradiation during CT should not be underestimated despite using automatic exposure systems and age-based Diagnostic Reference Levels (DRL) as advocated by Verdun.[22]

The comparison of chest CT findings and pulmonary function tests in BPD survivors has shown conflicting results. Aukland et al.[11] found a significant association between decreased maximal expiratory flow rates and HRCT scores. On the contrary, Sarria et al.[19] found that CT score was more accurate in discriminating between the patients with CLDI and the controls, even if BPD survivors had lower forced expiratory flows. CT imaging, with an appropriate evaluation grid, is certainly complementary to pulmonary function testing in the evaluation of BPD patients and both methods offer different assessments of the lungs.

The major drawbacks of this study come from its retrospective nature and the small sample size, limiting significant correlations with clinical data and outcomes such as rehospitalization or death.

In conclusion, the reading and interpretation of pulmonary CT findings in BPD according to a validated score is easily feasible. It can be useful in assessing the severity of this disorder, and areas of decreased attenuation seem to be the most sensitive radiological item to predict BPD severity. However, this cannot be used at the present time to predict BPD evolution. As CT requires sedation and provides the child with radiation exposure, this exam should be performed when CT findings are expected to have direct impact on clinical management. We suggest the acquisition of further prospective data to better evaluate the impact on treatment and outcome of BPD patients before implementing routine chest CT in their management.

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