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Review

Role of artificial intelligence in earlier diagnosis of bronchopulmonary dysplasia

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Abstract

Bronchopulmonary dysplasia (BPD) affects premature infants and causes long-term breathing problems. Along with respiratory complications, BPD can also lead to developmental delays, poor growth, pulmonary hypertension, heart failure, and hearing impairment. To avoid these dangerous complications, it is necessary to diagnose and treat BPD in a timely manner. Early diagnosis of BPD primarily relies on monitoring a premature baby's oxygen needs, using tools like pulse oximetry, alongside chest X-rays to visualize lung changes, blood tests to assess oxygen levels, and sometimes an echocardiogram to rule out heart defects as a contributing factor; a diagnosis is usually made if a baby requires supplemental oxygen for an extended period after birth, particularly beyond 28 days, and shows characteristic lung changes on imaging.

Artificial intelligence (AI) is becoming an integral part of healthcare. AI technologies can be used to study chest X-ray images to improve the diagnostic accuracy of BPD in preterm infants. A deep learning component can be used for lung segmentation of preterm chest radiographs to build a BPD prediction model by focusing on lung anatomy.

This article explains the criteria used for BPD diagnosis and compares them with AI-based algorithms, especially for accuracy, applicability, and efficiency. The article also highlights the pros and cons of using AI-based algorithms in patients with BPD.

Keywords

Bronchopulmonary dysplasia, artificial intelligence, hyaline membrane disease, machine learning, oxygen.

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Background and introduction

With a growing focus on artificial intelligence (AI), there has been an increasing interest in AI in the medical landscape. Particularly in machine learning (ML), where computers can formulate algorithms and connections without specific guidance, there may be greater applications in earlier predictions of pediatric outcomes [1, 2]. In premature infants, there has been a concern with limited pulmonary maturation, resulting in hyaline membrane disease (HMD) [3]. Further investigation resulted in assisted ventilation for premature infants and improved mortality rates [4]. However, an unintended consequence was bronchopulmonary dysplasia (BPD) from prolonged exposure to high inspired oxygen with mechanical ventilation [5].

The criteria of BPD have been revised multiple times as new patterns and discoveries are made, resulting in difficulty in determining specific models or algorithms for prediction [6]. Subsequent predictive models have incorporated genetic biomarkers, nutrition, blood gas values, and more invasive metrics in order to determine whether a neonate would develop BPD [7, 8]. Recently, there have been more attempts to use AI to form an algorithm utilizing non-invasive methods and integrating a wide range of previously uncombined factors [9, 10]. Notably, the predictive performance of these algorithms is comparable to that of the National Institute of Child Health and Human Development (NICHD) criteria [11]. However, there is room for improvement in terms of accuracy and also the concern of possible consequences such as missed diagnosis or false results if the proposed predictions fail to encompass all possible outcomes [12, 13].

This article highlights the importance of the use of AI in earlier diagnosis of BPD.

Review

Methodology

For the review, electronic PubMed/Medline and Google Scholar databases were searched to find peer-reviewed articles that addressed AI use in the diagnosis of BPD. The keywords used were "artificial intelligence," "bronchopulmonary dysplasia," "hyaline membrane disease," "machine learning," and "oxygen." AND and OR operators were applied to narrow the search. Two authors separately conducted the search utilizing the search method. We also found additional articles by looking at the reference lists of the retrieved articles. As a result, a total of 60 articles were identified. The papers were evaluated based on their titles, abstracts, and complete texts, with the primary inclusion criteria being the description of AI use and BPD. The most important exclusion criterion was that the article addressed diseases other than AI use and BPD. Papers that were not written in the English language were also excluded. The review included 23 articles after the final evaluation.

Discussion

Bronchopulmonary dysplasia in premature infants

BPD is a chronic lung disease that affects premature infants. It occurs when the lungs do not develop properly after birth, leading to inflammation and scarring of the lung tissue. Premature birth, low birth weight, respiratory distress syndrome and use of mechanical ventilation and oxygen therapy in the newborn period are some of the predisposing causes of BPD. Infants may present mainly with respiratory symptoms such as cough, rapid breathing, wheezing, increased work of breathing, and tiredness [14].

BPD is mainly diagnosed by physical exams, chest X-ray findings, and pulmonary function tests. Oxygen therapy is the mainstay of treatment. Other measures, such as the use of bronchodilators and corticosteroids, are used. Severe cases may need lung transplantation. The severity of the disease and the child's overall health determine the prognosis of the disease. With proper treatment, many children with BPD can live full and active lives. However, some children may experience long-term respiratory problems and other health issues [15, 16].

Complications of bronchopulmonary dysplasia

BPD is a chronic lung disease that can lead to many complications, including respiratory infections, heart diseases, and developmental problems. Patients with BPD are more likely to get respiratory infections, which can require hospitalization, such as pneumonia, bronchiolitis, pulmonary hypertension, reactive airway disease and asthma. In severe cases, BPD can lead to heart failure. Babies with BPD may have vision and hearing problems and developmental delays, especially speech. In later childhood, they may encounter learning difficulties. Other complications may include trouble feeding, gastroesophageal reflux disease, and increased susceptibility to infections [17].

Diagnosis and management of bronchopulmonary dysplasia

NICHD defined BPD in 2001 using two main criteria: gestational age and the need for supplemental oxygen. The NICHD revised its definition in 2018 to include new methods of ventilation and radiographic evidence. Please refer to **Tab. 1** for the summary of diagnostic criteria for BPD [18, 19].

With a combination of breathing support, nutrition, and medications, the goal of the management is to help the baby's lungs grow and function well.

Use of modern technology and use of artificial intelligence in the management of bronchopulmonary dysplasia

New medications and technologies are being used for early diagnosis and management of BPD. Since use of AI is becoming an integral part of healthcare, it is also getting attention in the use of BPD. Currently, there is a greater push towards smart and automated applications of AI due to several benefits such as early diagnosis with accuracy. Particularly ML, where computers can learn patterns and make predictions from data without explicit programming and identify patterns and relationships in data with minimal human intervention [1].

ML is currently divided into four categories based on utilizing input data: supervised, unsupervised, semi-supervised, and reinforcement [1, 2]. Supervised ML typically learns mapping from inputs to outputs based on labeled data rather than associations or groupings. This requires human involvement in specifying and labeling data for the ML to evaluate, and then the system will classify and fit the data into a model. Supervised learning can be applied to a wide range of models like linear regression and neural networks [2]. Meanwhile, unsupervised ML has the least human interference as AI interprets the input data and identifies significant trends, groupings, and clustering or anomaly detection in datasets without specific goals in mind. Semisupervised combines aspects of both supervised and unsupervised in order to find meaningful relationships between labeled and unlabeled data. Lastly, reinforcement takes a known algorithm and finds ways to make the process more efficient.

ML can be used to determine the ideal timing and dosage of insulin for diabetic patients, given the patient's past glucose levels and responses [2]. Depending on the desired purpose, ML may extract insights or patterns from input data that was not previously considered in a quicker manner. Particularly in the pediatric healthcare setting, ML can potentially find new ways for prediction, diagnosis, and intervention [2].

In the early 1960s, HMD was recognized as the most prominent cause of acute lung injury and mortality in newborns [3]. At that time, neonates were evaluated clinically, and the expected presentation involved prematurity, cyanosis unresolved with oxygen support, slow respiratory

Table 1. Summary of criteria for the diagnosis of bronchopulmonary dysplasia (BPD) [18,19].

	NICHD 2001 criteria	NICHD 2018 criteria
Main criteria	Oxygen requirement Gestational age	Addition of type of respiratory support Must have radiographic evidence of parenchymal lung disease The infant must require respiratory support for at least 3 consecutive days at 36 weeks' PMA
Classification	Mild: breathing room air at 36 weeks' PMA Moderate: need for < 30% oxygen at 36 weeks' PMA Severe: need for ≥ 30% oxygen and/or positive pressure at 36 weeks' PMA	Grade I: mild BPD, which includes oxygen levels < 1 L/min with an FiO_2 of 0.22-0.7 Grade II: moderate BPD, which includes nasal cannula flow < 1 L/min with an FiO_2 > 0.7 Grade III: severe BPD, which includes invasive mechanical ventilation > 21 days or nasal cannula > 3 L/min > 30 days Grade III A: severe BPD defined as early death between 14 days postnatal age and 36 weeks postmenstrual age due to persistent parenchymal lung disease and respiratory failure that is not attributable to other neonatal morbidities

BPD: bronchopulmonary dysplasia; NICHD: National Institute of Child Health and Human Development; PMA: postmenstrual age.

rates, and umbilical arterial PO_2 less than 100 mm or pH less than 7.20 [3]. As HMD became better documented, factors of tachypnea, retractions, grunting, negative gastric aspirate shake test, and post-mortem atelectasis in unaerated areas and eosinophilic hyaline membranes in aerated areas joined the list of potential considerations for HMD diagnosis [4]. In response, there was the development of assisted ventilation in order to increase survivability. However, in the late 1960s, it was noted that neonates that underwent prolonged exposure to high inspired oxygen concentrations resulted in lung injury termed BPD [4, 5].

Classically, BPD requires that the infant be premature, exposed to high inspired oxygen concentrations for prolonged periods due to HMD, and showing radiographic signs of overinflation such as interspersed fibrotic strands or pathologic signs of airway or parenchymal damage [5]. However, this definition has been frequently revised over the years to involve other requirements while specifying or eliminating other qualifiers. According to a 2000 criteria revision, BPD also included infants who received high FiO_2, lower concentrations of inspired oxygen, and use of ventilation for apnea unrelated to HMD [6]. The previous requirement of radiographic findings of "multiple cystic areas with linear densities interpreted as fibrotic strands" was found to be unnecessary as the progression into chronic lung disease could occur without the presence of cysts on chest radiographs. Currently, BPD is considered to be due to the disruption of alveolar and pulmonary vascular development, hence the predominance incidence in premature neonates [7].

Besides the traditional considerations, sepsis, endotoxin exposure, nutrition, fetal growth restriction, and genetic makeup have joined the ever-growing list of contributing factors for BPD development. Moving away from risk prediction based on clinical presentation, recent studies have begun to dive into the involvement of endothelial immune activation with toll-like receptors 4, lipopolysaccharides, and pattern recognition receptors [7]. As of 2016, risk factors of BPD include fibrosis or interstitial presence on chest radiographs, pulmonary structural damage on chest computed tomography scans, pulmonary hypertension, gestational age, ventilatory index, cytokine levels, angiogenic growth factors, epithelial and fibrotic pulmonary markers, oxidant injury markers, surfactant substrates, urinary bombesin-like peptide, exhaled breath condensates, and genomic markers [8]. While an extensive list of risk factors has been noted, lung pathology and presentation remain difficult to predict and present variably in different ethnicities. Research continues to contribute to the directory of predictive risk factors, but the practicality and implementation remain burdensome [8].

Past clinical prediction models have had variable areas under the receiver operating characteristic curve (AUROC). Notably, a 2013 review of 26 clinical prediction models for BPD had AUROCs that ranged from 0.50 to 0.76, with only 4 models having any external validation and 0 models with calibration of predictive value. This wide range of variability could be related to potential challenges in generalizing these models in diverse populations and clinical environments, which may require further research to explore the possible causes [9]. A later 2015 multifactorial model that considered body weight, gestational age, sex, significant patent ductus arteriosus, hypotension, respiratory distress within 72 hours of life, and intraventricular hemorrhage showed greater predictability with an AUROC of 0.930 [9]. However, this study also noted that while there was great discernment of BPD with all the factors, it was difficult to apply such a model in a clinical setting. Nevertheless, a model that considers more variables may have greater accuracy in predicting BPD development. The possible reasons for the limitations to apply in clinical practice could be the complexity of the model, the need for extensive data collection, and the input of data, which may need further research [9].

As previous risk models included mostly clinical factors, there has been a greater push toward formulating a model that also considers genetic factors. A 2021 study created a predictive model using ML to evaluate risk gene sets (RGS) commonly found in neonates with BPD and the correlation of subsequent BPD and severe BPD (sBPD) developed. To find the risk genes, exome sequencing and a gene burden test was performed. Risk genes were found with loss-of-function mutations or missense mutations over-represented in BPD and sBPD patients. 31 clinical features for BPD were selected based on antenatal and birth history, first-week morbidities, early treatment after birth, morbidities during hospitalization, and 37 features for sBPD prediction added 6 more features from morbidities during hospitalization, and treatment [9].

Based on RGS data alone, there was an AUROC of 0.814 and 0.826 for BPD and sBPD, respectively. Notably, when the model was combined with 31 clinical features for BPD and 37 for sBPD, the AUROC increased to 0.915 and 0.826. ML was specifically used to create these predictive models, especially when analyzing multiple sets and genes. Interestingly, a prediction model involving deleterious gene variants failed to indicate AUROC improvement with clinical features. This notable outlier suggests that ML may be beneficial in detection of under-investigated factors that influence the phenotype of BPD. Notably, this study required exome sequencing, and results took 2 weeks to complete, suggesting that the earliest interventions would require this time buffer [9].

Also using ML, a 2020 study formed an algorithm that combined spectral data of gastric aspirate samples at birth with clinical data for BPD prediction [10]. The algorithm was able to detect BPD with 88% sensitivity and 91% specificity with birth weight, surfactant treatment, gestational age, and gastric aspirate spectroscopy. Notably, the gastric aspirate was taken during routine procedures such as feeding tubes or suction catheters while establishing continuous positive nasal airway pressure, minimizing the number of factors and tests taken from the neonate [10]. While this study addressed that there are other possible predictive factors, they aimed to establish an ML-based algorithm that could be used soon after birth while highlighting the factors that seemingly had the most influence on predictability. Although the use of predictive values could not be all-encompassing for all neonates, there may still be some benefit of having a predictive algorithm at such an early stage as opposed to the traditional 28 days. This algorithm was compared to the 2001 and 2018 NICHD criteria. The 2018 NICHD definition had an AUROC of 0.893 and the 2001 NICHD definition of 0.746 [11]. The current NICHD criteria consider body weight, gestational age, male sex, intrauterine growth restriction, low Apgar scores, intubation in the delivery room, and surfactant doses. While the AUROC ranges have been similar to those of other criteria, ML algorithms have the advantage of producing earlier estimations [11].

However, there have been concerns about the lack of calibration for these models. Although the ML consistently recalibrates by reestimating the intercept, there has been no other specified method to calibrate the ML itself. Notably, the comparison of 9 ML-based random forest algorithms had only an AUROC of 0.884 compared to 0.856 of logistic regression [12]. However, that is not to say that ML was not useful when enabling sensitivity, specificity, or predictive values. Perhaps sensitivity would be a better metric of consideration for earlier models, as clinical treatment aims to address as many at-risk infants as possible. Additionally, the calibration only accounted for maternal factors (e.g., premature rupture of membranes, antenatal steroids, hypertension, mode of delivery), neonatal factors (e.g., gestational age, SNAPPE-II score, sex, small for gestational age, inborn status), interventions (e.g., resuscitation with intubation, surfactant, IPPV, CPAP, inotropes, nitric oxide) [12]. Possibly in the future, calibration can also provide insight into ML performance compared to logistic regression for the recent considerations of genetic biomarkers and pulmonary markers [12].

Diagnostic errors in pediatrics have not been extensively studied, but the few studies that are present note that errors may be as common as 1-2 times per month [13]. Given the frequency of human errors, it could be also one of concern when using an ML-generated algorithm when pediatric outliers or extenuating circumstances are present. An analysis of 1985-2005 pediatric malpractice claims revealed that most claims were involved with care within the hospital [13]. Perhaps taking inspiration from adult medicine, an implementation of a tool such as Safer Dx Instrument can be established. Such tools identified possible undesirable diagnostic events, especially for high-risk conditions in pediatric settings, which may be sepsis and congenital anomalies. Additionally, ML can provide an unbiased mathematical parameter on how providers can stage and treat BPD patients by analyzing large, diverse data and can identify patterns that might otherwise be missed. They can offer more individualized care. However, risks like algorithmic bias can arise if data represents certain group only, which can be addressed by a broader range of inputs without relying on prior assumptions or readily available information [13]. By having updated clinical models, cognitive bias and human fallibility in inpatient settings are minimized.

Lastly, ML diagnostic models should not replace human involvement with clinical reasoning. The simple inclusion of diagnostic checklists showed little influence on diagnostic error rates in adult settings when used alone, but only when several applied tools were used in addition to clinical reasoning did they show improvement. Over-reliance, whether conscious or unconscious, can lead to harmful patient outcomes due to flawed health decisions, overdiagnosis, overtreatment, and defensive medicine. Concern has also been raised about the incremental replacement of human beings with AI systems [13].

The use of AI can help in BPD with early detection, predictive analytics, improved accuracy, and personalized treatment. It can support and help improve patient outcomes by tracking at-risk infants and intervene early. Despite its promise, AI's limitations include potential issues with accuracy, especially if trained on insufficient or biased datasets, and its reliance on high-quality data. Reliance on AI may raise the risk of ignoring clinical judgment. Cost, unavailability of AI everywhere, diverse settings, limited available data, and ethical and privacy concerns may make the use of AI difficult. Please refer to **Tab. 2** for a summary of the benefits and challenges of the use of AI in early diagnosis of BPD [20].

Findings

AI, particularly ML algorithms, can assist in the diagnosis of BPD by analyzing medical data. Postnatal monitoring of breathing patterns and oxygen saturation may help to predict BPD development even before clinical signs become apparent. Deep learning models can help in the analysis of abnormal lung texture and air trapping that can help in the precise assessment of lung development on X-ray results [21].

Along with radiological features, AI tools can analyze clinical parameters, especially gestational age and birth weight of preterm infants, to predict the development of BPD by identifying patterns in the data, which may not be apparent to clinicians with more accuracy, complementing the traditional methods. Prediction of the risk of the development of BPD can allow for proactive monitoring and early intervention. By analyzing a patient's unique data, AI can help clinicians develop personalized treatment plans tailored to the specific needs of each infant with BPD [10].

Future directions

Further research may help for directions especially to address the challenges in the use of AI tools. Rigorous validation of AI models may be necessary on diverse groups of neonatal and infant preterm populations to define the generalized use of

Table 2. Summary of benefits and challenges of the use of artificial intelligence (AI) in early diagnosis of bronchopulmonary dysplasia (BPD).

	Benefits	Challenges
Flexibility	Can be used across different healthcare settings and geographic areas	May not be adapted to diverse clinical environments, especially in low-resource settings
Continuous monitoring	Tracking of at-risk infants continuously to provide real-time alert and intervention recommendations	Concerns about data privacy
Cost-effectiveness	Faster decision Reduced workload of staff Lowered healthcare cost	Costly initial investment May not be cost-effective in low resource settings, lack of infrastructure
Individualized plan	Based on individual risk profiles can get personalized plans	May lack clinical validation, leading to over- or under-treatment
Supportive role	Assist clinicians in interpreting complex images Reduced diagnostic time	Undermine the role of clinicians May require continuous updates
Accuracy	Analyze large volumes of data with greater consistency Integration of complex clinical variables for a comprehensive analysis of BPD	Data-dependent accuracy Risk of low accuracy where data is sparse or unrepresentative
Prediction	Prediction of BPD based on multiple factors	Models may not account for all clinical variables Reduced generalizability
Early diagnosis	Analysis of large data Identification of subtle BPD patterns	Risk of false results occurs if the AI model has not been sufficiently trained on diverse data, leading to misdiagnosis

AI: artificial intelligence; BPD: bronchopulmonary dysplasia.

AI tools in the management of BPD. The use of AI tools depends on the feeding of data. High quality and accurate feeding of data should be ensured to avoid errors in the use. It may be difficult to incorporate the use of AI tools into the daily practice of clinicians [22].

Training of health care professionals and continuous educational activity may help to keep everyone updated with the AI technology used in health care. High cost, unavailability, ethical concerns, and bias issues may need to be addressed before it is implemented everywhere. The use of AI tools in underserved areas of the patient population may need the involvement of community participation and policymakers. Training of health care professionals may help clinicians understand the limitations of AI models and interpret the results in the context of the patient's overall clinical picture so that AI tools can be used as complementary models instead of replacing the clinicians [23].

Conclusion

BPD leads to severe respiratory and other systemic complications. Early diagnosis and management can help prevent these complications. There are several past and current criteria available for early diagnosis of BPD. The use of AI can help to aid in the early diagnosis of BPD. Further research may help to learn the benefits, limitations, and challenges of using AI in the early diagnosis of BPD.

Declaration of interest

The Authors declare that there is no conflict of interest. Financial support disclosure: none.

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