Drug Discovery and Molecular Docking (DDMD)
ISSN: 3107-6688 | Vol. 02, Issue-02, May-Aug., 2026 | pp. 21-38

Oxygen Homeostasis and Dysregulation: Alveolar Failure, Etiology, Pathophysiology, AI & ML Models, 3D Fingerprinting, Epidermology, Computational Frameworks in Hypoxemia, Hypoxia, and Oxygen Toxicity

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Abstract:

Maintaining oxygen homeostasis is crucial to the proper functioning of the body, which depends on the integrated control of pulmonary ventilation, alveolar gas exchange, oxygen transport via circulation, and cellular-level metabolism. Any disturbance in this regard results in hypoxemia, hypoxia, alveolar dysfunction, and oxygen toxicity, among others, which lead to the development of several conditions. This review provides an overview of the physiological fundamentals of oxygen homeostasis, the causes and pathophysiology of oxygen imbalance, and its main clinical presentations like acute hypoxemic respiratory failure, chronic hypoxia, and oxygen toxicity. The latest breakthroughs in Artificial Intelligence (AI), Machine Learning (ML), computational physiology, digital twins, and three-dimensional (3D) physiological fingerprints for oxygen diseases are also discussed in this review. The emerging computational models show significant promise in helping detect respiratory degradation at an early stage, improving oxygen therapy, and enabling accurate clinical decision-making. Model validation, data standardization, explainability, and clinical translation have been key challenges discussed in the review. In general, combining physiological insight and intelligent computational techniques is a promising approach toward precision respiratory medicine.

Keywords: Oxygen homeostasis; Hypoxemia; Hypoxia; Artificial intelligence; Digital twins; Precision respiratory medicine.

Received: May 12, 2026 **Revised: June 05, 2026** **Accepted: July 18 ,2026** **Published: August 10, 2026**

DOI: https://doi.org/10.64474/3107-6688.Vol2.Issue2.2

https://ddmd.nknpub.com/1/issue/archive

1. INTRODUCTION

Oxygen homeostasis is an important physiological phenomenon that involves the maintenance of equilibrium among oxygen intake, oxygen transportation, and its utilization within the cells, which allows for proper metabolism and functioning of organs[1]. It is possible due to effective breathing through the lungs, oxygen exchange in the alveoli, oxygen delivery by the circulatory system, and cell-level oxygen sensing processes. In physiological conditions, all these systems cooperate to satisfy the needs of the tissues for oxygen, while disruptions in oxygen balance may lead to hypoxemia, tissue hypoxia, or even oxygen toxicity[2]. Such problems are related to different diseases, such as acute respiratory distress syndrome, chronic obstructive pulmonary disease, pulmonary fibrosis, cardiovascular disease, sepsis, and neurological diseases.

Advancements in recent times in the field of artificial intelligence, machine learning, computational physiology, and digital health technologies have brought about new possibilities to enhance the understanding and treatment of oxygen disorders. Models such as predictive models, digital twins, and three-dimensional computational models can be used to incorporate physiological, clinical, and imaging information for purposes of early detection and personalized oxygen treatment as well as decision making in a clinical setting. Present research is fragmented in fields like physiology, molecular biology, respiratory medicine, and computational sciences, necessitating a comprehensive review of the same[3].

1.1 Background and Context

The maintenance of oxygen homeostasis is crucial for sustaining normal cell physiology and physiological balance. Optimal oxygenation depends on proper alveolar structure, appropriate matching of ventilation to perfusion, efficient diffusion, and transport via the circulatory system. Any malfunction in any of these systems caused by respiratory, cardiovascular, infection or systemic disease may result in failure in oxygen delivery and triggering pathways such as oxidative stress and inflammation[4]. In addition, recent advancements in computational medicine and intelligent analysis have opened up new avenues to study oxygen dysregulation.

1.2 Objectives of the Review

This review aims to:

- To understand the physiological control of oxygen regulation and alveolar gas exchange.
- To outline the causes and underlying pathophysiology of hypoxemia, hypoxia, and oxygen toxicity.
- To describe the clinical and epidemiological features of oxygen dysfunction in diseases.

- To explore new insights in the fields of artificial intelligence, machine learning, digital twins, three-dimensional fingerprinting, and computation related to oxygen disorders.
- To determine knowledge gaps and opportunities for future precision respiratory medicine.

1.3 Importance of the Topic

Dysregulation of oxygen metabolism continues to be a leading cause of respiratory failure, critical illness, and multiorgan dysfunction around the world. Early detection of oxygen dysmetabolism and appropriate medical treatment are necessary in order to enhance patient prognosis and avoid any adverse effects from either too much or not enough oxygen exposure. The combination of knowledge in physiology with artificial intelligence, modeling, and digital twins creates new opportunities in terms of predictive diagnostics and personalized medicine in respiratory care. Therefore, a multidisciplinary approach to oxygen metabolism is crucial for future development in medicine[5].

2. OXYGEN HOMEOSTASIS, ALVEOLAR PHYSIOLOGY, AND DYSREGULATION

Control of oxygen balance is achieved via the synchronized action of systems such as respiratory, cardiovascular, hematology, and cellular ones that provide steady supply of oxygen to metabolically active tissues. In physiological conditions, oxygen enters from the environment to alveoli, then diffuses through the alveolar-capillary barrier, binds to hemoglobin, and is delivered to peripheral tissues where aerobic metabolism takes place[6]. This chain of processes is constantly controlled by the systems of pulmonary physiology, cardiovascular system physiology, and cellular oxygen sensing to rapidly adjust to any metabolic needs. Any disruption in these pathways can disrupt tissue oxygenation and result in such conditions as hypoxemia, hypoxia, respiratory failure, and oxygen intoxication, which makes understanding of these pathways crucial for diagnostic, therapeutic, and mathematical purposes[7].

2.1 Physiology of Oxygen Homeostasis and Alveolar Gas Exchange

The maintenance of oxygen homeostasis starts from effective pulmonary ventilation wherein the inspired air gets to the alveoli due to the actions of the respiratory muscles. There are a provision of an extensive surface area and a short diffusion distance in the alveolar-capillary membrane, which enables fast diffusion of gases[8]. Oxygen diffusion obeys Fick's Law and is dependent on membrane thickness, diffusion capacity, surface area, and pressure gradient. Normal alveolar structure and pulmonary microcirculation are hence vital for arterial oxygenation.

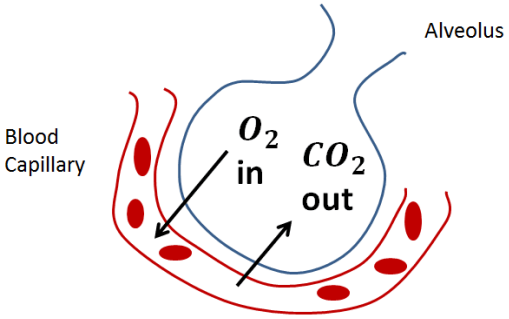

Figure 1. Physiological Mechanism of Alveolar Gas Exchange.

Post diffusion in the lungs, oxygen is mostly carried by hemoglobin molecules in erythrocytes while a small amount is carried in solution in the plasma. Oxygen transport is facilitated by various physiological factors such as arterial oxygen saturation, cardiac output, concentration of hemoglobin, tissue perfusion, and metabolic activity. In exercise, hypoxia, or physiological stress, coordinated control of respiration, cardiovascular system, vasoconstriction, and erythropoiesis ensure that there is proper oxygen balance[9].

Oxygen homeostasis at the cellular level is achieved by well-conserved oxygen-sensing systems. Hypoxia inducible factors play a crucial role in regulating oxygen homeostasis by turning on genes that regulate various processes such as angiogenesis, erythropoiesis, glucose utilization, and cell adaptation under conditions of low oxygen availability. Mitochondria, on the other hand, regulate both oxidative phosphorylation and generation of reactive oxygen species[10].

2.2 Etiology of Oxygen Dysregulation and Alveolar Failure

Oxygen dysregulation occurs whenever there is a malfunction in oxygen supply, oxygen delivery, or oxygen use within the body. Alveolar dysfunction is one of the major causes of oxygen dysregulation, and can result from abnormalities in ventilation, pulmonary diffusion, ventilation/perfusion mismatching, or pulmonary blood flow. Respiratory conditions such as pneumonia, acute respiratory distress syndrome (ARDS), chronic obstructive pulmonary disease (COPD), pulmonary fibrosis, pulmonary edema, and severe asthma affect the function of the alveoli, causing poor gas exchange[11].

There are multiple mechanisms involved in the dysfunction of alveoli. The mismatch of ventilation and perfusion involves a failure of oxygenation despite the normal supply of pulmonary blood flow. On the other hand, diffusion impairment involves the delay in the passage of oxygen into the alveoli through the alveolar capillary membrane. The intrapulmonary shunt mechanism involves the passage of deoxygenated blood around well-ventilated alveoli. Alveolar hypoventilation is caused by low ventilation due to obstruction of airways or central respiratory depression[12].

Dysregulation of oxygen is not confined only to lung diseases. Cardiac conditions result in reduced delivery of oxygen by limiting cardiac output, while anemia affects the oxygen-carrying capacity of blood. Sepsis, metabolic abnormalities, and mitochondrial failure interfere with oxygen use in cells even when there is sufficient oxygen content in arteries. External factors such as exposure to high altitudes and toxic inhalants can affect oxygen availability. Thus, dysregulation of oxygen is a multi-faceted phenomenon with various inter-related systems being affected.

2.3 Molecular Pathophysiology of Hypoxemia, Hypoxia, and Oxygen Toxicity

Hypoxemia involves low levels of oxygen in the arterial blood, while hypoxia involves low oxygen delivery to cells or tissues. While hypoxemia and hypoxia may be similar, these two may happen independently based on tissue perfusion, hemoglobin levels, and oxygen consumption. The process of adaptation by cells to low oxygen is mainly regulated through the hypoxia-inducible factors that affect angiogenesis, erythropoiesis, glucose metabolism, and vascular remodeling in order to ensure tissue survival in low oxygen conditions[13].

Oxidative stress is a key factor contributing to the development of oxygen disorders. Under hypoxia and subsequent re-oxygenation, reactive oxygen species are produced leading to damage to the cell membranes, proteins, and DNA along with the processes of inflammation, endothelial dysfunction, and mitochondrial dysfunction. This is how oxidative stress contributes to the development of acute respiratory distress syndrome, ischemia-reperfusion injury, organ dysfunction caused by sepsis and other respiratory disorders[14].

On the other hand, sustained exposure to abnormally high levels of oxygen can give rise to oxygen toxicity via the mechanism of uncontrolled oxidative stress which overpowers intrinsic antioxidant defense mechanisms of the body. Hyperoxia-related damage targets the cells of the lung epithelium, vasculature, retina, and nervous tissues, thus causing problems such as pulmonary fibrosis and neurological deficits. Hence, achieving a proper balance between treating hypoxemia and avoiding hyperoxia is an essential goal of contemporary respiratory medicine and the basis of precision medicine facilitated by artificial intelligence[15].

Table 1. Physiological and Pathophysiological Characteristics of Oxygen Dysregulation

Component	Normal Physiology	Dysregulation	Clinical Consequence
Pulmonary Ventilation	Adequate airflow	Hypoventilation	Hypoxemia

Alveolar Gas Exchange	Efficient diffusion	Diffusion limitation	Reduced PaO_2
Ventilation–Perfusion Matching	Balanced V/Q ratio	V/Q mismatch	Respiratory failure
Oxygen Transport	Hemoglobin-mediated transport	Anemia, reduced cardiac output	Tissue hypoxia
Cellular Oxygen Utilization	Normal mitochondrial respiration	Mitochondrial dysfunction	Metabolic failure
Oxygen Sensing	HIF regulation	Persistent HIF activation	Chronic hypoxia
Oxidative Balance	Controlled ROS production	Excess ROS	Oxygen toxicity

3. CLINICAL MANIFESTATIONS AND ORGAN-SPECIFIC ADVANCES

The clinical presentation of oxygen dysregulation depends greatly on its severity, duration, and origin of dysfunction in the delivery of oxygen to the tissues[16]. The acute presentation of dysfunctional oxygen supply manifests itself in hypoxic respiratory failure, whereas the chronic condition develops as structural and functional adaptation processes in various organs and systems. On the other hand, the excessive provision of oxygen may lead to its toxicity due to oxidative damage to tissues[17]. The knowledge about the wide variety of such clinical manifestations is very important in order to develop treatment approaches and create algorithms for the prediction of disease dynamics. Moreover, advances in precision medicine give an opportunity to apply such techniques to clinical practice.

3.1 Acute Hypoxemic Respiratory Failure

Acute Hypoxemic Respiratory Failure (AHRF) refers to poor oxygenation in the arteries due to dysfunctional gas exchange in the lungs despite normal or lowered CO2 concentrations. This condition is one of the commonest reasons for the ICU admission of patients and is known to cause considerable morbidity and mortality rates[18]. AHRF may be caused by ARDS, pneumonia, sepsis, pulmonary edema, aspiration, and viral respiratory infections. These factors impair the function of the alveoli, affect the Ventilation/Perfusion matching, and hinder oxygen transfer through the alveolar capillary membrane.

The clinical manifestations of AHRF include dyspnea, tachypnea, work of breathing, cyanosis, and decreased peripheral oxygen saturation. With further decrease in oxygen levels, the heart rate and cardiac output increase due to compensatory cardiovascular changes, but long-term hypoxemia leads to ischemia of tissues, metabolic acidosis, neurologic complications, and multi-organ dysfunction. Early detection with blood gases, pulse oximetry, and chest imaging is important in order to prevent organ damage[19].

Present management techniques center on maintaining adequate oxygenation without causing any damage to the lungs from ventilation. Normal oxygen therapy, high flow nasal cannula (HFNC), non-invasive ventilation (NIV), invasive mechanical ventilation, and extracorporeal membrane oxygenation (ECMO) techniques are chosen based on the severity of the disease and physiological response. With advancements in technology, AI algorithms have been introduced in critical care settings to anticipate respiratory failure, ventilatory management, and advanced respiratory support.

3.2 Chronic Hypoxia and Systemic Oxygen Dysregulation

Unlike the acute respiratory failure, chronic hypoxia is developed slowly and triggers some physiological adaptations that help maintain oxygen supply to various body organs. Chronic oxygen deprivation is common in conditions such as chronic obstructive pulmonary disease, interstitial lung disease, pulmonary hypertension, congenital heart disease, obstructive sleep apnea, and even high-altitude exposure. Despite the fact that the physiological adaptations help maintain oxygenation, chronic hypoxia ultimately leads to organ dysfunction[20].

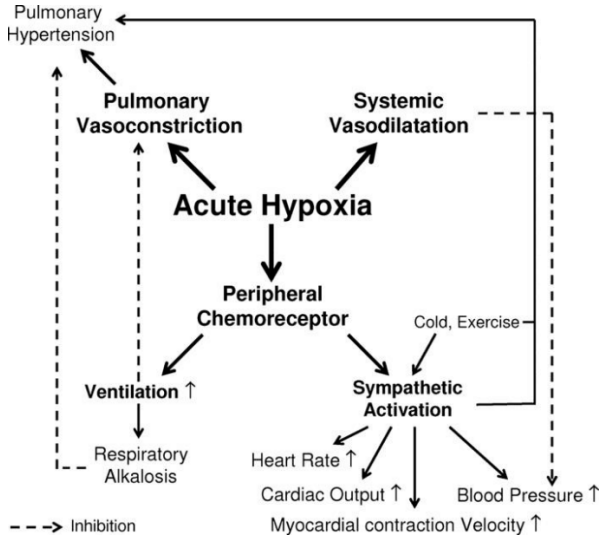

Figure 2. Physiological Responses to Acute Hypoxia.

Systemically speaking, oxygen deprivation results in stimulation of erythropoiesis, vasoconstriction of the lungs, angiogenesis, metabolic reprogramming, and activation of hypoxia-inducible signal transduction pathways. Although all of these adaptations enhance oxygen delivery, persistent activation of such reactions is known to result in pulmonary vascular remodeling, right ventricular hypertrophy, endothelial dysfunction, inflammation, and oxidative stress, all of which lead to impaired exercise capacity, cognitive problems, and other complications[21].

Prolonged hypoxia also affects several other organs that do not belong to the respiratory system. In terms of cardiovascular problems, there can be hypertension, arrhythmias, and heart failure. As for neurological issues, there are disorders related to cognition, neurodegeneration, and decreased blood flow to the brain[22]. The examples of renal problems, metabolic issues, and hormonal imbalances can also demonstrate the systemic effects of prolonged hypoxia.

3.3 Oxygen Toxicity Across Organ Systems

While additional oxygen is absolutely necessary in treating hypoxemia, too much oxygen exposure can be detrimental due to the adverse effects associated with oxidative stress from hyperoxia[23]. Oxygen toxicity involves the formation of reactive oxygen species in amounts that are beyond the body's antioxidant capacity, causing tissue damage and derangement of physiological processes. The level of toxicity is influenced by oxygen levels, length of exposure, age, and underlying pathology[24].

The lungs are especially susceptible to hyperoxic insult. High levels of oxygen cause injury to alveolar epithelial cells, vascular endothelial cells, and type II pneumocytes responsible for producing surfactants, causing atelectasis, inflammation, edema, and fibrosis[25]. Therefore, hyperoxia may further damage lung tissues in mechanically ventilated patients, if oxygen is not administered properly.

Aside from damaging the lungs, oxygen toxicity targets several organ systems. In relation to the CNS, oxygen overload could lead to neural damage, seizures, and cognitive impairment, but retinal damage remains a serious problem among premature babies that are exposed to oxygen for a long time. The cardiovascular consequences of oxygen toxicity involve endothelial dysfunction, coronary vasoconstriction, and poor microvascular perfusion, whereas oxidative stress can increase renal dysfunction and inflammation[26].

3.4 Precision Medicine, Computational Physiology, and Clinical Translation

The proliferation of systems that allow for physiological monitoring, imaging technologies, biosensors, and EHRs has propelled the move towards precision medicine in the field of respiratory care. Instead of basing clinical practice only on standard protocols, modern medical practice has

placed more stress on the personalized evaluation of oxygen delivery, pulmonary physiology, perfusion, and metabolic requirements. This approach allows clinicians to tailor oxygen therapy and avoid risks arising from both hypoxemia and hyperoxia.

Computational physiology has become an essential part of the ongoing revolution by bringing together mathematical modeling, systems biology, and physiological simulation in order to use it for clinical decision-making support[27]. Technologies of digital twins make it possible to create virtual models of patients that have the capability to simulate their respiratory functions, predict their disease development, assess their therapies, and plan individual ventilation strategies. Likewise, computational fluid dynamics and three-dimensional physiological modeling contribute to improved understanding of how air is distributed and exchanged in healthy and pathological lungs.

AI and ML make the translation of the described above computational methods into clinical practice even more efficient. Predictive algorithms are able to process continuous physiological information, results of laboratory and imaging studies, and clinical data to calculate the probability of hypoxemia development, detect early signs of respiratory failure, and make optimal treatment decisions[28]. However, successful application of such technologies in clinical practice presupposes standardization of datasets, validation, explainability of the model, regulation, and multi-professional cooperation.

4. AI-DRIVEN COMPUTATIONAL FRAMEWORKS, DIGITAL TWINS, AND 3D FINGERPRINTING

Advances in the fields of artificial intelligence, machine learning, computational physiology, and biomedical engineering have made remarkable contributions to the study and management of oxygen homeostasis and respiratory conditions. While traditional statistical analysis relies solely on clinical features, the AI-based approaches combine physiological, biochemical, medical imaging, pulmonary functional, and wearable sensor data along with patient health records to forecast the development of oxygen imbalance and related diseases[29]. These approaches are aimed at continuous patient monitoring, early diagnosis of respiratory decompensation, personalized therapeutic management, and timely decisions on patient management. Furthermore, the implementation of the technology of digital twins, computational simulations, and 3D physiological fingerprints opens the way towards a new approach to precision respiratory medicine.

4.1 AI and Machine Learning Models for Oxygen Homeostasis Prediction

AI has gained considerable significance as a means of detecting any disruption in oxygen homeostasis through analyzing sophisticated sets of physiological and clinical data. Using ML

methods, such changes are detected before the development of evident clinical symptoms. Combining demographic data, arterial blood gas analysis, pulse oximetry, respiratory rate, radiologic signs, and laboratory markers, these methods yield a number of useful diagnostic insights to help in treating patients in time[30].

Several methods of supervised machine learning, such as Random Forest (RF), Support Vector Machine (SVM), Extreme Gradient Boosting (XGBoost), Decision Trees (DT), and Logistic Regression, have shown themselves as very efficient in the prediction of hypoxemia, respiratory failure, and the severity of illness. These methods enable the analysis of different types of clinical variables while providing high predictive ability and sufficient computation speed.

The deep learning approach has even bettered prediction through automatic feature extraction from the multi-dimensional clinical datasets in hierarchical manner. The use of Convolutional Neural Network (CNN) is common in chest radiograph and CT image analysis. The Long Short-Term Memory (LSTM) and Bi-LSTM networks perform well in the physiological time-series data processing for early prediction of hypoxemia[31]. However, the transformers have been found to perform well in predicting the respiratory decompensation using the longitudinal data from the electronic medical records.

4.2 Digital Twins, Computational Modeling, and Clinical Decision Support

The digital twin concept has become one of the most important innovations in computational medicine since it helps create virtual copies of each individual patient based on up-to-date physiological and clinical data. In the field of respiratory medicine, the use of digital twins involves consideration of lung function, circulatory system dynamics, oxygenation, imaging studies, biomarkers, and medical history of the patient to predict the course of the disease and treatment response.

The field of computational physiology compliments that of the digital twin through the creation of mathematical models for simulating pulmonary ventilation, alveolar gas exchange, oxygen diffusion, perfusion, and cellular oxygen consumption[32]. This aids in gaining insights into respiratory physiology in normal and pathological situations such as acute respiratory distress syndrome, chronic obstructive pulmonary disease, pulmonary fibrosis, and severe hypoxemia. Computational fluid dynamics further compliments this by simulating airflow distribution and oxygen transfer through the lung structures[33].

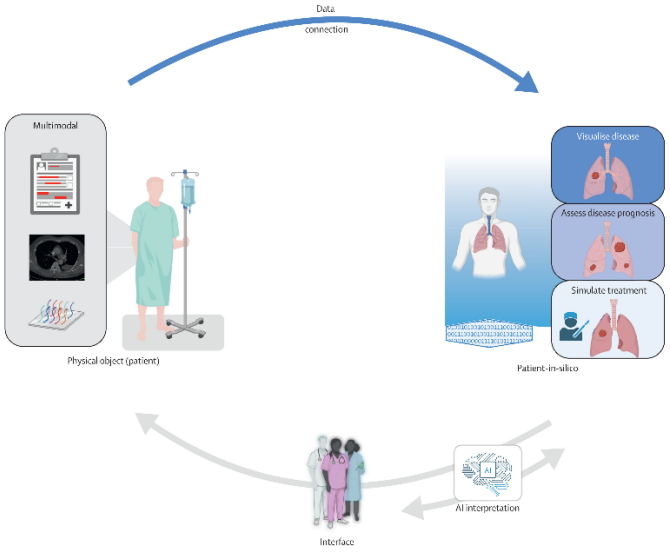

Figure 3. AI-Enabled Digital Twin Framework for Precision Respiratory Medicine.

With the help of AI, digital twins, and computational physiology, the effectiveness of clinical decision support systems has been enhanced due to continuous analysis of physiologic information, ventilator settings, lab tests, and imaging modalities[34]. Intelligent systems will help the clinicians in predicting the respiratory deterioration, optimizing the oxygen delivery, and individualizing the ventilation settings. But still, for a successful implementation, external validation and dataset standardization are needed.

4.3 Three-Dimensional Fingerprinting, Explainable AI, and Future Clinical Implementation

3D fingerprinting has become a viable computational tool for identifying variations in structure and physiology associated with disorders related to oxygen. Using three-dimensional medical imaging, computational reconstruction, radiomics, and quantitative morphometry, 3D fingerprinting allows a better evaluation of the structure of lungs, alveoli, pulmonary vasculature, and regional ventilation. Such quantitative models allow better characterization of the disease and serve as biomarkers for its diagnosis, severity, and treatment monitoring.

With AI being more widely implemented in healthcare, interpretability of models has become equally essential as prediction performance. Explainable Artificial Intelligence (XAI) increases interpretability through providing a clearer insight into how clinical parameters affect predictions of models. SHAP, LIME, feature importance and attention methods are commonly used to ensure explainability of AI-based predictions especially for respiratory critical care.

It is anticipated that future precision medicine approaches in respiratory health care based on AI will comprise explainable AI, digital twins, three-dimensional physiological fingerprinting, wearable biosensors, Internet of Medical Things (IoMT) devices, cloud computing, and real-time clinical analytics[35]. They will enable timely detection of oxygen dysregulation, personalized oxygen treatment, and disease progression monitoring. However, the clinical implementation of these systems will depend on data standardization, multi-center validation, regulation compliance, cybersecurity, and collaboration between clinicians, biomedical engineers, computational scientists, and health policy makers.

Table 2. Comparative Analysis of Representative Studies on Oxygen Homeostasis, Hypoxia,

Author(s) & Year	**Study Focus**	**Methodology / Approach**	**Major Findings**
Warren & Partridge (2016)[36]	Role of necrosis, acute hypoxia, and chronic hypoxia in PET imaging	Computational modeling of 18F-FMISO PET image contrast	Demonstrated that different hypoxic conditions significantly influence PET image contrast, improving quantitative assessment of tissue oxygenation and hypoxic regions.
Xu et al. (2017)[37]	NIV in acute hypoxemic respiratory failure	Systematic review and meta-analysis	Reported that NIV improves oxygenation and reduces respiratory distress in selected patients, although careful patient selection remains essential.
Yeo (2019)[38]	Molecular relationship between hypoxia and aging	Comprehensive molecular review	Highlighted the involvement of hypoxia-inducible factors, oxidative stress, and mitochondrial dysfunction in aging and age-associated pathological conditions.
Yu et al. (2020)[39]	Prediction of dissolved oxygen and hypoxia	Machine learning-based prediction model	Developed an accurate ML model for predicting dissolved oxygen concentration and hypoxic conditions, demonstrating the predictive capability of AI-based approaches.

Zhao et al. (2019)[40]	Computer-aided diagnosis of fetal hypoxia	CNN integrated with recurrence plot analysis	Proposed a deep learning framework that accurately identified fetal hypoxia from physiological signals, improving automated diagnostic performance.

5. DISCUSSION

Regulation of oxygen homeostasis is a very well-coordinated physiological process in which respiratory, cardiovascular, hematology, and cellular systems interact to maintain oxygen supply and consumption. This review proves that the malfunctioning of any system involved in this integration can trigger a series of pathophysiological consequences culminating in hypoxemia, tissue hypoxia, alveolar dysfunction, respiratory dysfunction, and oxygen toxicity. In addition to the conventional physiology of oxygen homeostasis, the progress made in molecular biology, computational medicine, and AI research in recent years allowed the significant deepening of our understanding of oxygen homeostasis mechanisms.

5.1 Interpretation and Analysis of Findings

The results derived from this review indicate that dysregulated oxygen metabolism is a multi-factor process due to derangements in ventilation of alveoli, pulmonary diffusion of gases, ventilation-perfusion coupling, oxygen transport by cardiovascular system and cellular oxygen utilization that result in reduced tissue oxygenation and aggravate the development of diseases. The molecular pathogenesis underlying such derangements includes hypoxia-induced factor pathway activation, increased oxidative stress, inflammation, endothelial dysfunction and impaired mitochondrial metabolism. Additionally, the increasing contribution of artificial intelligence, machine learning, computational physiology, digital twins and three-dimensional physiological fingerprinting in prediction of hypoxemia and personalization of oxygen therapy is discussed in the review.

5.2 Implications and Significance

The increasing prevalence of respiratory and oxygen-based disease calls attention to the significance of optimal oxygen balance for better therapeutic outcomes. Detection of dysregulated oxygen balance at an early stage helps in prompt treatment, avoids organ damage, and provides individualized treatment with oxygen therapy, avoiding the hazards related to its overuse. Application of AI, computational simulation, digital twin, and digital health technologies open many avenues for continuous monitoring of the patients, risk prediction, optimization of

ventilation strategies, and individualized clinical decision making. In general, all these developments may revolutionize respiratory medicine.

5.3 Research Gaps and Limitations

However, despite considerable progress in understanding the mechanisms underlying oxygen homeostasis and AI-based computational methods, several limitations persist. In particular, modern studies face limitations associated with an uncoordinated approach to interdisciplinary integration, small and heterogeneous sample sizes, insufficient validation, and different clinical protocols. At the same time, the incorporation of digital twins, computational physiology, and three-dimensional fingerprints into clinical practice is limited by the absence of standardization of computational frameworks, explainability of AI, and data security issues. Solving these problems is critical to implementing intelligent systems of respiratory health care.

5.4 Future Research Directions

Future research needs to focus on the creation of integrative computational approaches that incorporate physiological information, imaging, molecular biomarkers, wearable technologies, and EHRs in the same AI platform. Multicenter and diverse population-based studies will be necessary to ensure better robustness, validation, and clinical relevance of models, and more attention needs to be paid to the development of explainable AI to increase transparency and clinical acceptance. Progress in the field of digital twins, three-dimensional physiology fingerprints, multimodal omics integration, and real-time monitoring is expected to contribute to personalized respiratory medicine even further. Clinical, biomedical, computational scientists and policymakers will continue their collaboration to implement these advances into clinical practice.

6. CONCLUSION

Oxygen homeostasis refers to a well-coordinated physiological phenomenon of pulmonary, cardiac, and cellular regulation of sufficient tissue oxygen delivery. Imbalance of the regulatory mechanisms leads to the development of hypoxemia, hypoxia, alveolar dysfunction, respiratory failure, and oxygen intoxication, thus significantly contributing to morbidity of respiratory and general diseases. The aim of this review is to describe the physiologic, molecular, clinical, and computational aspects of oxygen dysregulation with special attention to the recently recognized role of artificial intelligence, machine learning, digital twins, computational physiology, and 3D physiologic fingerprinting in precision respiratory medicine. Despite some difficulties with standardization of the data and validation of the models, the development of the intelligent computational approach is expected to positively influence the management of oxygen-related diseases.

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