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Research Article

Oxygen therapy in the intensive care unit

Ping Wang[1,#], Qixin Huang[1,#], Bin Liu[1], Qiangjun Xu[1], Xingsong Li[2], Guidong Feng[2], Yiming Liu[3,*]

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Abstract

Oxygen therapy is a crucial treatment method for maintaining vital signs in patients in the intensive care unit. However, several controversial issues have emerged regarding its clinical application. This article analyzes current research trends in oxygen therapy in the intensive care unit and provides guidance and recommendations. Relevant literature was retrieved from the Web of Science Core Collection, and keyword co-occurrence and highly cited literature hotspot analyses were conducted using VOSviewer 1.6.19 software. The key topics related to oxygen therapy in the intensive care unit primarily focus on four areas: oxygen therapy and mechanical ventilation in the intensive care unit, extracorporeal membrane oxygenation therapy for coronavirus disease 2019 and its role in reducing mortality, research on hypoxia and oxygen saturation monitoring, and oxygen inhalation therapy in the intensive care unit. The analysis of highly cited literature indicates that the main research hotspots regarding oxygen therapy used in the intensive care unit focus primarily on conservative oxygen therapy, high-flow nasal oxygen therapy, comparisons of high- and low-oxygenation strategies, and research on hyperbaric oxygen therapy. First, the potential of conservative oxygen therapy to reduce mortality rates in the intensive care unit has attracted considerable attention; however, further clinical studies are needed to validate its optimal parameters and suitable patient populations. Second, high-flow nasal oxygen therapy has been shown to be effective in alleviating respiratory distress and reducing the need for intubation. This therapy can deliver oxygen flows of up to 60 L/min, effectively improving respiratory distress and decreasing intubation demands. In patients subjected to high-risk extubation, the combination of high-flow nasal oxygen therapy and noninvasive ventilation significantly lowers the rate of reintubation, making the combined approach one of the best strategies to prevent respiratory failure after extubation in the intensive care unit. Third, there are differences between lower and higher oxygenation strategies regarding their effects on patient mortality, long-term outcomes, and clinician preferences; however, there is currently no clear evidence indicating which strategy is superior. Clinicians' preferences regarding various oxygenation targets may impact the design of future studies. Finally, hyperbaric oxygen therapy is recognized as an effective supportive treatment for various critical conditions and has significant application value in acute severe traumatic brain injury, cerebral resuscitation, and cardiopulmonary resuscitation. Currently, researchers are continually exploring the latest oxygen therapies in the intensive care unit. Several randomized controlled clinical trials investigating automated oxygen control, novel high-flow nasal oxygen therapy, and combined oxygen therapy are underway. The results of these trials should be closely observed. Overall, this article provides a systematic review and valuable reference for the scientific and rational application of oxygen therapy in the intensive care unit. Future research should focus on verifying the optimal parameters of conservative oxygen therapy, assessing oxygen needs in different patient populations, evaluating the long-term effects of oxygen treatment, and developing novel oxygen therapy technologies and devices.

Key Words: extracorporeal membrane oxygenation; high-flow nasal oxygen therapy; hyperbaric oxygen; intensive care unit; mortality rate; noninvasive ventilation; oxygen; oxygen concentration; oxygenation; respiratory distress

Introduction

In current medical practice, patients in the intensive care unit (ICU) often require oxygen therapy to maintain vital signs.[1,2] According to the literature published in the Web of Science Core Collection, the main research topics related to oxygen therapy include dyspnea, respiratory distress, respiratory failure, apnea, hypoxemia, lung compliance, and critical illness (**Figure 1**). As a fundamental and critical treatment method, oxygen therapy is crucial for increasing patients' oxygenation levels and lowering mortality rates.[3,4]

As clinical practice advances, a series of research hotspots and controversial issues have emerged in the application of oxygen therapy.[5-7] Although previous studies have made significant progress in terms of the principles, methods, and efficacy of oxygen therapy, many questions remain unresolved. For example, research on the optimal dosage, duration of treatment, and effects of oxygen concentration on the lungs and other organs remains insufficient.[8] Additionally, excessive or inappropriate oxygen therapy can lead to complications such as oxygen toxicity and acute lung injury, adversely affecting patients' recovery and quality of life.[9-12]

[1]Department of Emergency, ZhuJiang Hospital of Southern Medical University, Guangzhou, Guangdong Province, China; [2]Department of Emergency, The Second People's Hospital of Qingyuan City, Qingyuan, Guangdong Province, China; [3]Department of Emergency and Disaster Medicine, Seventh Affiliated Hospital, Sun Yat-sen University, Shenzhen, Guangdong Province, China
*Correspondence to: Yiming Liu, MS, liuyiming@sysush.com.
https://orcid.org/0009-0002-0176-8591 (Yiming Liu)
#Both authors contributed equally to this work.

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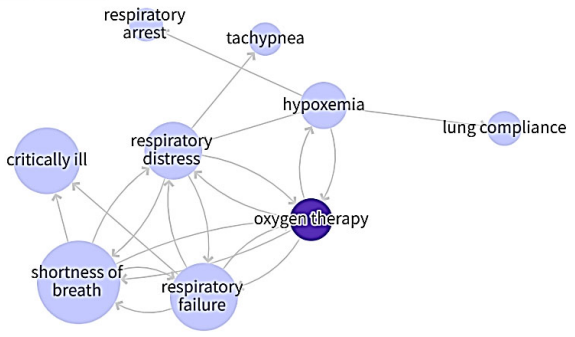


Figure 1 | Research topics related to oxygen therapy in the Web of Science Core Collection (from inception to November 25, 2024).
This figure was generated using the Web of Science Core Collection. The size of each circle reflects the volume of publications associated with that topic, with larger circles indicating more publications. The lines with arrows represent the connections between different topics.

This article reviews the literature on oxygen therapy in the ICU published in the Web of Science Core Collection. It offers a comprehensive analysis of current research hotspots in this field and critically examines the key issues highlighted in recent clinical studies. The objective is to provide clinicians with a detailed and systematic overview of trends in oxygen therapy research within the ICU, serving as a valuable resource for both clinical practice and future investigations. By conducting a thorough analysis of existing research, this article aims to promote a more scientific and rational application of oxygen therapy in the ICU, ultimately enhancing patient treatment outcomes and survival rates.

Methods

Data sources

Database

Web of Science Core Collection.

Retrieval time

November 25, 2024.

Publication date

No restrictions.

Search query

TI=(Oxygen*) AND TI=("Intensive Care Unit*" OR ICU).

Search results

436 publications.

Data analysis

Reference data, including full records and citation information, were exported from the Web of Science Core Collection in plain text (TXT) format. The file was subsequently imported into VOSviewer 1.6.19 software to create a scientific knowledge map that visually depicts the evolution and structural connections of scientific knowledge. The focus is on the co-occurrence analysis of author keywords, which allows for the generation of both keyword visualization maps and density visualization maps. All metrics were calculated using full counting, which means that each co-occurrence or cocitation indicator was assigned equal weight. The detailed steps and standard guidelines for using VOSviewer 1.6.19 software are based on previous literature to generate keyword visualization maps.[13] The content of highly cited seminal papers among the 436 publications was analyzed to identify key advancements and emerging trends in oxygen therapy in the ICU.

Analysis of the clinical trial registration protocol

Clinical trial registrations related to oxygen therapy in the ICU were searched on ClinicalTrials.gov (https://classic.clinicaltrials.gov/), and the latest trends in clinical trials registered in 2024 were analyzed.

Primary outcome measures

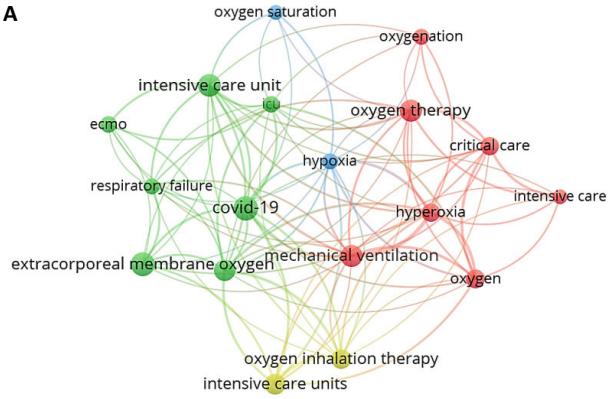
This article focuses on key aspects of oxygen therapy in the ICU, including the characteristics of trending topics, hotspots in highly cited research, development trends, application strategies, and clinical trial registration protocols.

Results

Characteristics of trending topics in oxygen therapy in the intensive care unit

A co-occurrence analysis of keywords from 436 publications was conducted via VOSviewer 1.6.19 software, resulting in a co-occurrence map of keywords that appeared more than 10 times (**Figure 2**). In this map, the top five most frequent keywords related to oxygen therapy in the ICU were COVID-19, extracorporeal membrane oxygenation (ECMO), intensive care unit, oxygen therapy, and mechanical ventilation. The keywords can be grouped into four main clusters: cluster 1: oxygen therapy and mechanical ventilation in the ICU; cluster 2: ECMO for COVID-19 to reduce mortality; cluster 3: hypoxia and oxygen saturation monitoring studies; and cluster 4: oxygen inhalation therapy in the ICU. These four clusters represent the primary research directions in this field.

A



B

Cluster 1 (7 items)	Cluster 2 (7 items)
critical care	covid-19
hyperoxia	ecmo
intensive care	extracorporeal membrane
mechanical ventilation	oxygenation
oxygen	icu
oxygen therapy	intensive care unit
oxygenation	mortality
	respiratory failure
Cluster 3 (2 items)	**Cluster 4 (2 items)**
hypoxia	intensive care units
oxygen saturation	oxygen inhalation therapy

Figure 2 | Keyword visualization and cluster analysis of keywords related to oxygen therapy research in the intensive care unit (Web of Science Core Collection).
(A) Keyword network visualization map; (B) keyword cluster statistics map. In the map, larger keyword nodes represent higher frequencies of keywords, whereas thicker lines indicate more frequent cooccurrences between keywords. The different colors in the map correspond to different keyword clusters. The images were created using VOSviewer 1.6.19 software.

Hotspots of highly cited literature regarding research on oxygen therapy in the intensive care unit

The key topics in highly cited literature on oxygen therapy in the ICU, as published in the Web of Science Core Collection, were analyzed (**Table 1** and **Box 1**).[14-23]

Table 1 | Summary of the top 10 highly cited publications on oxygen therapy in the ICU from the Web of Science Core Collection

Author/Publication year	Study design	Oxygen therapy methods/Outcome measures	Patient type	Study findings	Journal	Number of citations
Girardis et al.[14]/ 2016	A single-center, open-label, randomized clinical trial	Conservative oxygen therapy *versus* conventional oxygen therapy	All adult patients in the ICU with an expected length of stay of 72 h or more	In critically ill patients with an ICU stay of 72 h or longer, the conservative oxygen therapy approach more greatly reduced ICU mortality compared to conventional therapy.	*JAMA-Journal of the American Medical Association*	487
INSPIRATION Investigators[15]/ 2021	A 2 x 2 factorial design multicenter randomized trial	ECMO	Patients with COVID-19	Regular use of medium-dose prophylactic anticoagulation therapy is effective in unselected COVID-19 patients admitted to intensive care units.	*JAMA-Journal of the American Medical Association*	465
ICU-ROX Investigators and the Australian and New Zealand Intensive Care Society Clinical Trials Group[16]/ 2020	Randomized controlled trial	Conservative oxygen therapy during mechanical ventilation	Adult patients requiring mechanical ventilation in the ICU	For adults on mechanical ventilation in the ICU, conservative oxygen therapy shows no significant difference in the number of ventilator-free days compared with conventional oxygen therapy.	*New England Journal of Medicine*	299
de Jonge et al.[17]/ 2008	A retrospective observational study	Oxygen therapy during mechanical ventilation	Patients in the ICU receiving mechanical ventilation treatment	The actual arterial oxygen saturation values achieved in Dutch ICU patients were higher than those generally recommended in the literature. High fractions of inspired oxygen, low PaO_2, and high PaO_2 within 24 hours after admission were closely associated with in-hospital mortality rates among ICU patients.	*Critical Care*	292
Sztrymf et al.[18]/ 2012	A prospective observational study	High-flow nasal cannula oxygen therapy	Patients with acute respiratory failure in the ICU	The use of high-flow nasal cannula oxygen therapy in patients with persistent acute respiratory failure significantly and sustainably improved clinical and biological parameters.	*Journal of Critical Care*	210
Papazian et al.[19]/ 2016	A narrative review	High-flow nasal oxygen therapy	Adult patients in the ICU	High-flow nasal oxygen therapy may help improve preoxygenation and can be used after extubation. Similarly, high-frequency NIV can be used for obese patients or to prevent respiratory deterioration in patients with hypoxemia who require bronchoscopy, or for aerosol treatments.	*Intensive Care Medicine*	208
Jaber et al.[20]/ 2016	A randomized, controlled, single-center trial	Nasal high-flow oxygen therapy combined with NIV for preoxygenation during intubation treatment	Hypoxemic patients in the ICU	Nasal high-flow oxygen therapy combined with NIV for preoxygenation during intubation may be more effective in reducing the severity of oxygen saturation decline.	*Intensive Care Medicine*	154
Morris et al.[21]/ 2004	A retrospective case analysis	ECMO	Pediatric cardiac ICU patients	In a study of 137 patients receiving ECMO therapy in the pediatric cardiac ICU, the survival rate at discharge was 39%.	*Critical Care Medicine*	146
Young et al.[22]/ 2020	A prospective nonrandomized controlled trial	Conservative oxygen therapy	Adult patients with sepsis undergoing mechanical ventilation	The point estimate results of conservative oxygen therapy on the 90-d mortality rate indicate that this intervention may pose clinically significant harm to patients with sepsis.	*Intensive Care Medicine*	68
Gottlieb et al.[23]/ 2022	A retrospective cohort study	Noninvasive positive pressure ventilation and high-flow nasal cannula oxygen therapy	Patients with hypoxemia in the ICU	Asian, Black, and Hispanic patients received less supplemental oxygen than White patients, which is associated with differences in the performance of pulse oximeters.	*JAMA Internal Medicine*	67

COVID-19: Coronavirus disease 2019; ECMO: extracorporeal membrane oxygenation; ICU: intensive care unit; NIV: noninvasive ventilation.

The most significant finding from these studies is the implementation of conservative oxygen therapy strategies for ICU patients. The Oxygen-ICU study demonstrated that conservative oxygen therapy can reduce mortality rates and complications among ICU patients. This finding is important for the practice of intensive care, as it offers a potential approach to improve patient outcomes. However, further multicenter, randomized clinical trials are necessary to validate these preliminary results andrefine the optimal parameters and target populations for conservative oxygen therapy. Based on the research findings, we identify six main areas of focus in this field, which represent the six most highly cited aspects among researchers.

Box 1 Summary of the main research hotspots in the top 10 most cited papers

Best practices for oxygen therapy:
Conservative oxygen therapy strategies (maintaining PaO_2 between 70–100 mm Hg (1 mmHg = 0.133 kPa) or SpO_2 between 94–98%) have shown potential life-saving benefits in ICU patients, but larger-scale clinical trials are needed to validate these findings.

Relationship between oxygen therapy and patient prognosis:
The relationship between oxygen therapy and patient prognosis is complex. In ICU patients, the fraction of inspired oxygen and PaO_2 levels are associated with inpatient mortality, suggesting that hyperoxia may increase mortality rates. However, moderate-dose prophylactic anticoagulation therapy for COVID-19 in ICU patients has not demonstrated greater efficacy compared to standard-dose prophylactic anticoagulation.

Individualized oxygen therapy:
Racial and ethnic differences can influence both the effectiveness and safety of oxygen therapy. Asian, Black, and Hispanic patients may need higher levels of oxygen to achieve adequate blood oxygen saturation because pulse oximeters may perform differently in these populations.

Monitoring and evaluation of oxygen therapy:
Pulse oximeters may overestimate blood oxygen saturation, particularly in minority patients, which could result in inadequate oxygen therapy. Therefore, clinicians should use pulse oximeter data with caution and consider additional monitoring indicators to assess a patient's oxygenation status.

Safety of oxygen therapy:
In patients in the ICU with COVID-19, medium-dose prophylactic anticoagulation did not significantly enhance the primary efficacy outcomes compared to standard-dose prophylactic anticoagulation; however, it did increase the risk of bleeding and thrombocytopenia.

New technologies and equipment for oxygen therapy:
High-flow nasal oxygen therapy has demonstrated significant benefits in improving clinical and biological indicators in patients with acute respiratory failure, such as a decrease in respiratory rate and an increase in oxygen saturation. Furthermore, high-flow nasal oxygen may assist in minimizing decreases in oxygen saturation before intubation; however, additional studies are necessary to verify its applicability and safety.

Research development trends of highly cited literature on oxygen therapy in the intensive care unit

Oxygen toxicity risk in the intensive care unit: a focus since 1999

In 1999, Mao et al.[24] conducted a study to examine attitudes and practices related to oxygen therapy in Canadian University-Affiliated Adult ICUs. They introduced a new descriptive index and highlighted significant differences in how oxygen was managed. The findings showed that although all respondents were aware of the risks associated with oxygen toxicity, there were inconsistencies in their approaches to assessing tissue oxygenation and adjusting the fraction of inspired oxygen. The study addressed the importance of documenting current practices and developing decision support systems.

Conservative oxygen therapy strategy to lower mortality rates: a 2016 proposal

In 2016, Girardis et al.[14] conducted a randomized controlled trial to assess a conservative oxygen therapy strategy that included all adult patients in the medical-surgical ICU at Modena University Hospital in Italy who were expected to stay for 72 hours or longer. They evaluated whether a conservative oxygen supplementation strategy can improve the prognosis of patients in the ICU. All these adult patients were randomly assigned to one of two treatment groups: one group received oxygen therapy aimed at maintaining their arterial partial pressure of oxygen (PaO_2) between 70 and 100 mmHg (1 mmHg = 0.133 kPa) or maintaining arterial oxygen saturation (SpO_2) between 94% and 98% (conservative treatment group). The other group followed standard ICU practices, which involved increasing the PaO_2 to 150 mmHg (1 mmHg = 0.133 kPa) or maintaining the SpO_2 between 97% and 100% (conventional control group). The findings revealed that for critically ill patients with an ICU stay of 72 hours or longer, the conservative oxygen therapy approach was associated with lower mortality rates compared to conventional therapy. However, in 2016, Ferguson[25] raised concerns regarding the validity of the trial by Girardis et al.[14] He suggested that prior to further validation of the trial results on this matter, it would be more prudent to carefully measure and monitor supplemental oxygen in the ICU. This approach aims to achieve normal physiological levels of PaO_2 while avoiding the potential dangers of hyperoxia.

Combination of high-flow nasal oxygen therapy and noninvasive ventilation to reduce oxygen saturation requirements: a concept first proposed in 2016

In 2016, Jaber et al.[26] highlighted the serious risks associated with tracheal intubation in the ICU, such as severe hypoxemia. To mitigate these risks, researchers have recommended preoxygenation before intubation. They posited that noninvasive ventilation (NIV) could be a beneficial preoxygenation method, as it can increase blood oxygen saturation levels through positive end-expiratory pressure to prevent alveolar collapse during intubation. However, they acknowledged a critical issue: the NIV mask must be removed for mouth intubation, leaving hypoxemic patients without oxygen and at risk for severe hypoxemia. To address this, they suggested that high-flow nasal oxygen therapy might enable apneic oxygenation during the apnea period following NIV preoxygenation. The question remains whether combining high-flow nasal oxygen therapy and NIV could more effectively mitigate the reduction in oxygen saturation levels during intubation for patients with acute respiratory failure and hypoxemia in the ICU compared to NIV alone. In the same year, Jaber et al.[20] conducted a single-center, randomized controlled trial known as OPTINIV. This two-arm study aimed to investigate the effectiveness of combining high-flow nasal cannula oxygen therapy with NIV to reduce desaturation during intubation in critically ill patients with hypoxemia. The results suggested that a new preoxygenation strategy using high-flow nasal oxygen therapy for noninvasive oxygenation in hypoxemic patients prior to intubation may be more effective in minimizing the severity of desaturation compared to the use of NIV alone.

Advantages of conservative oxygen therapy: evidence from 2017 to 2020

A randomized controlled trial conducted by Young et al.[27] in 2017 revealed that patients receiving conservative oxygen therapy spent significantly more time at an FiO_2 of 0.21 in the ICU than did those receiving standard oxygen therapy. Conversely, patients with SpO_2 levels ≥ 97% spent less time in the ICU than patients receiving standard oxygen therapy did, confirming the advantages of conservative oxygen therapy. In 2020, Young et al.[22] reported a study that examined oxygen therapy in mechanically ventilated adult patients in the ICU. This study compared the effects of conservative oxygen therapy with those of conventional oxygen therapy. In the conservative oxygen therapy group, the upper limit for SpO_2 was set at 97%, whereas the conventional oxygen therapy group had no specific SpO_2 limit. The primary outcome measured was the number of ventilator-free days, defined as the time patients remained alive and free from mechanical ventilation from randomization to day

28. The results revealed no significant difference in the effect of the two therapies on ventilator-free days. However, patients in the conservative oxygen therapy group spent more time receiving an FiO_2 of 0.21 in the ICU, while they had shorter durations with SpO_2 exceeding 96%. Additionally, there was no significant difference in 180-day mortality rates between the two groups. Therefore, conservative oxygen therapy did not have a significant effect on the number of ventilator-free days compared with conventional oxygen therapy.

Efficacy of high versus low oxygenation strategies: findings from studies conducted in 2022–2023

In 2022, Rasmussen et al.[28] conducted the HOT-ICU trial, which analyzed 110 critically ill COVID-19 patients assigned to two oxygen therapy groups: a low oxygenation group (PaO_2 = 8 kPa) and a high oxygenation group (PaO_2 = 12 kPa). The results indicated that both groups had similar 90-day mortality rates; however, the low oxygenation group had more days without the need for life support.

This study suggests that maintaining a lower PaO_2 may be beneficial for ICU patients with COVID-19, although the conclusions remain uncertain. In 2022, Crescioli et al.[29] assessed the outcomes of ICU patients with severe hypoxemia 1 year after being assigned to lower *versus* higher oxygenation targets. They reported that, in critically ill adults with severe hypoxemia, a lower oxygenation target (8 kPa) did not improve 1-year survival rates or health-related quality of life compared with a higher target (12 kPa). In 2022, a systematic review by Crescioli et al.[30] included 17 randomized controlled trials that evaluated the long-term outcomes of adult ICU patients receiving low *versus* high oxygenation strategies. The results indicated that the evidence regarding cognitive function and health-related quality of life was very uncertain, with no significant effect found on the 6-minute walk test or lung diffusion capacity test. In 2023, Li et al.[31] conducted a systematic review assessing the benefits and potential harms of conservative (low oxygenation target) *versus* liberal (high oxygenation target) oxygen therapy in ICU patients. The review included 10 studies with a total of 5429 patients. The findings revealed no significant differences in all-cause mortality rates at 28 days, 90 days, or the longest follow-up period between conservative oxygen therapy and liberal oxygen therapy. This study concluded that conservative oxygen therapy does not demonstrate a clear advantage or disadvantage in reducing all-cause mortality among critically ill adult patients in the ICU.

Oxygen application strategies in the intensive care unit

Upon further analysis of the literature on oxygen application strategies in the ICU, the primary applications of oxygen therapy can be categorized into three key aspects: oxygen management strategies, assessment of the effects of oxygen therapy, and the clinical decision-making process. These aspects highlight the various strategies for using oxygen in critical care, their effects on patient outcomes, and the decision-making processes of clinicians involved in oxygen management.

Oxygen management strategies

In the ICU, the optimal target range for oxygen therapy is still uncertain, resulting in ongoing discussions about the merits of low- *versus* high-oxygenation strategies. For example, research has shown that conservative oxygen therapy might limit oxygen exposure, but it does not significantly affect the 90-day mortality rate of patients.[16,22]

Assessment of the effects of oxygen therapy

Studies have shown that there is no significant difference in the 28- and 90-day mortality rates between low- and high-oxygenation strategies.[31,32] Compared with conventional oxygen therapy, conservative oxygen therapy does not significantly affect the number of days without ventilation.[16] Additionally, excessive oxygen exposure is associated with an increased mortality rate, highlighting the need for careful management of oxygen therapy.[33]

Clinical decision-making process for oxygen therapy

In the ICU, clinicians recognize the issue of excessive oxygen exposure in oxygen management; however, the primary focus of care is not necessarily on achieving the lowest possible oxygen levels. Research suggests that clinical decision-making often depends on collaboration within interdisciplinary teams rather than relying solely on individual clinical evidence. Therefore, there is a need to develop and evaluate evidence-based oxygen management protocols to promote more conservative use of oxygen.[34,35] Despite the variety of available oxygen therapy strategies, there are no significant differences in key outcomes, such as mortality rates and days without ventilation, among various oxygen therapies. Therefore, more cautious and evidence-based management of oxygen therapy is required in clinical practice.

Strategies commonly used for oxygen therapy in the intensive care unit

Conservative oxygen therapy in the intensive care unit

Efficacy of conservative oxygen therapy in the intensive care unit: Compared with conventional oxygen therapy, conservative oxygen therapy does not significantly affect the 90-day mortality rate; however, it may result in clinically important harm.[22] Compared with that in patients receiving conventional oxygen therapy, the duration of mechanical ventilation in patients receiving conservative oxygen therapy is shorter, and the incidence of new organ dysfunction is lower.[36] Research indicates that conservative oxygen therapy may be associated with fewer cases of radiographic atelectasis and may facilitate earlier weaning from mechanical ventilation.[37]

Treatment goals and strategies for conservative oxygen therapy: Scholars have compared various oxygen saturation targets (such as 88–92% *versus* above 96%) in critically ill patients.[31,38] The results indicate no significant differences in the incidence of new organ dysfunction or the 90-day mortality rate between the 88–92% oxygen saturation target and the targets above 96%. The implementation of conservative oxygen strategies may help reduce oxygen exposure, thereby decreasing oxidative damage to the lungs and other organs.[16] Evidence supports the use of conservative oxygen therapy in patients requiring mechanical ventilation, which suggests that conservative oxygen therapy is a viable alternative.[38]

Clinician evaluation of conservative oxygen therapy: Most critical care clinicians consider oxygen-related lung injury to be a significant concern and have a positive attitude toward the implementation of conservative oxygen therapy. Specifically, 91.1% of clinicians believe that conservative oxygen therapy is easy to implement, and the majority express a desire to continue using this strategy.[39] Despite the high acceptance of conservative oxygen therapy, further education and research are needed to clarify its potential benefits and risks.

In conclusion, conservative oxygen therapy may offer potential benefits in reducing the duration of mechanical ventilation and the incidence of new organ dysfunction; however, its effect on the mortality rate requires further investigation.

High-flow nasal oxygen therapy in the intensive care unit

High-flow nasal oxygen therapy can deliver oxygen flow rates of up to 60 L/min, helping to alleviate respiratory distress and reduce the need for intubation.[19,40] It has proven effective in patients with acute hypoxemic respiratory failure, particularly in the ICU.[40,41] The mechanisms of high-flow nasal oxygen therapy include flushing

out the oropharyngeal dead space, reducing airway resistance, and enhancing oxygen delivery.[40] In patients subjected to high-risk extubation, the combination of high-flow nasal oxygen therapy and NIV can significantly reduce the reintubation rate. The use of both NIV and high-flow nasal oxygen therapy together leads to a notable decrease in the incidence of respiratory failure and reintubation.[19,42] This combination therapy is regarded as one of the most effective strategies for preventing postextubation respiratory failure in the ICU. High-flow nasal oxygen therapy has shown good tolerance and effectiveness in patients with acute respiratory failure, which helps alleviate respiratory distress.[43] Research indicates that high-flow nasal oxygen therapy can improve oxygenation in patients with hypoxemic acute respiratory failure of various tiologies.[40] Despite the increasing use of high-flow nasal oxygen therapy, further studies are needed to clarify its indications and contraindications.[40,41]

In conclusion, both high-flow nasal oxygen therapy and NIV have demonstrated significant clinical benefits in managing patients with acute hypoxemic respiratory failure by improving oxygenation and reducing reintubation rates. Future studies will help further define the optimal applications and effectiveness of these two strategies.

High- and low-oxygenation strategies in the intensive care unit

Low- *versus* high-oxygenation strategies: In critically ill patients undergoing mechanical ventilation, a low oxygenation strategy did not significantly reduce the 28-day mortality rate compared with a high-oxygenation strategy.[31] For patients with acute hypoxemia, there was no significant difference in the 90-day mortality rate between the low oxygenation strategy and the high-oxygenation strategy.[32] Additionally, there was no significant difference in ventilator-free days between patients receiving conservative oxygen therapy and those receiving conventional oxygen therapy.[16]

Long-term effects of oxygen therapy: Two systematic reviews indicate that there is no conclusive evidence regarding the effects of low- *versus* high-oxygenation strategies on cognitive function and quality of life.[30,32] Evidence suggests that oxygen therapy may have both beneficial and detrimental effects on the long-term health outcomes of critically ill patients in the ICU; however, the quality of this evidence is low.[32,45] Furthermore, there is currently no thorough evaluation of the impact of oxygen therapy on long-term outcomes for ICU patients, other than its effects on mortality and quality of life.[44]

Clinician preferences for oxygenation: A survey performed by Schjørring et al. found that 52% of ICU physicians consider PaO_2 to be the most important parameter for assessing oxygenation.[46] The survey revealed that physicians have varying preferences for target PaO_2 levels depending on specific pathological conditions. For example, the target PaO_2 for patients with chronic obstructive pulmonary disease is approximately 8 kPa, whereas for patients with healthy lungs, it is approximately 10 kPa. Consequently, many physicians are willing to accept lower PaO_2 targets in clinical trials, indicating that these preferences for oxygenation levels may affect the design of future clinical research. Despite the lack of conclusive evidence from existing studies on the merits of various oxygenation targets, understanding preferences for oxygen therapy and their potential effects remains critical for designing future clinical trials.

Hyperbaric oxygen therapy in the intensive care unit

Hyperbaric oxygen therapy is recognized as an effective supportive treatment for various critical conditions. However, its implementation requires careful assessment of both the patient's specific situation and the treatment environment. Hyperbaric oxygen therapy is widely used to treat many critical illnesses, including carbon monoxide poisoning, gas embolism, and necrotizing fasciitis.[47,48] For critically ill patients, the use of hyperbaric oxygen therapy requires a risk–benefit assessment to ensure that it does not delay or interrupt overall management.[49-51] Hyperbaric oxygen therapy can improve tissue oxygenation by increasing the amount of dissolved oxygen in plasma and reduce tissue inflammation in COVID-19 patients.[52]

During hyperbaric oxygen therapy, it is essential to ensure that patient monitoring and treatment are not compromised. All equipment and procedures must undergo rigorous evaluation and testing.[49] Specialized equipment and trained personnel are required to manage critically ill patients to ensure the safety and effectiveness of the treatment.[47] During hyperbaric oxygen therapy, the oxygenation status of critically ill patients can sometimes decline, necessitating adjustments to mechanical ventilation parameters.[53] A previous study has shown that blood pressure in critically ill patients may increase following hyperbaric oxygen therapy, but this effect is usually minor and related to the number of treatments.[54] In critically ill patients undergoing hyperbaric oxygen therapy, oxygenation may significantly decrease after treatment, which could necessitate temporary adjustments to ventilator settings.[53] Although hyperbaric oxygen therapy is considered effective in certain situations, a previous study suggested that its role in acute carbon monoxide poisoning remains controversial.[55]

In summary, hyperbaric oxygen therapy is considered a vital supportive treatment in the ICU. However, its implementation demands careful management of patients and thorough risk assessment. When combined with proper monitoring and equipment, hyperbaric oxygen therapy can be safely administered to critically ill patients, improving their treatment outcomes.

Oxygen therapy for brain resuscitation

Hyperbaric oxygen therapy has shown promising results in treating acute traumatic brain injury, making the optimization of oxygen delivery crucial for improving patient outcomes. This therapy has demonstrated significant physiological benefits without causing cerebral or pulmonary toxicity, potentially enhancing clinical results.[56] A preclinical study consistently reported positive therapeutic effects of hyperbaric oxygen therapy across various outcome measures, with minimal safety concerns.[56] After hyperbaric oxygen therapy, the levels of PaO_2 in brain tissue significantly increase, leading to improved cerebral blood flow and enhanced oxygen metabolism.[57]

Research suggests that implementing a protocol-driven approach to enhance oxygen delivery can shorten the duration of brain hypoxia and potentially reduce mortality rates in patients with severe traumatic brain injury.[58] Clinical guidelines advise increasing the oxygen supply by adjusting the mean arterial pressure, intracranial pressure, and blood oxygen-carrying capacity while simultaneously lowering the oxygen demand through sedation and pharmacologic coma.[58] Despite the increasing interest in brain tissue oxygenation, many treatment methods still lack strong clinical evidence to support their effectiveness.[58] Furthermore, evidence exists that administering 100% oxygen may result in cerebral hyperperfusion and elevated oxygen delivery, which could be linked to oxidative stress-related damage in brain tissue.[59]

In summary, hyperbaric oxygen therapy is promising for treating acute severe traumatic brain injury. Optimizing oxygen delivery is essential for improving patient outcomes, and the effects of brain hypoxia and hyperoxia highlight the importance of carefully managing the oxygen concentration during treatment. These findings offer a valuable theoretical foundation for future clinical trials and treatment protocols.

Oxygen therapy in cardiopulmonary resuscitation

In cases of cardiac arrest, failure to provide immediate resuscitation

can result in irreversible damage to the brain and other vital organs within 4–6 minutes. Therefore, cardiopulmonary resuscitation must be initiated without delay after cardiac arrest. Currently, oxygen therapy in cardiopulmonary resuscitation primarily involves the following two aspects:

Extracorporeal membrane oxygenation therapy

The use of ECMO therapy in patients experiencing cardiac arrest has been associated with higher survival rates, particularly in cases of refractory cardiac arrest.[60] Research indicates that ECMO therapy can significantly increase in-hospital survival rates compared with traditional cardiopulmonary resuscitation.[61] However, the implementation of ECMO therapy also carries risks of complications, such as infection.[62]

Oxygen management strategies

In cases of out-of-hospital cardiac arrest, addressing low oxygen saturation may not significantly increase in-hospital survival rates.[63] Research indicates that excessively high concentrations of oxygen can increase the risk of reperfusion brain injury, highlighting the need for careful management of oxygen concentrations.[63] Early oxygen management strategies should consider the individual circumstances of each patient to optimize outcomes after resuscitation. In summary, ECMO and oxygen management strategies are currently key areas of research in the intensive care management of cardiac arrest, reflecting a commitment to improving both survival rates and neurological recovery for these patients.

Clinical registration protocol

The most recent relevant randomized controlled trial protocols registered on ClinicalTrials.gov in 2024 are displayed in **Table 2**.

The essential information and content of the latest randomized controlled trial protocols on oxygen therapy in the ICU, which were registered in 2024 and are presented in **Table 2**, are as follows:

Improving the precision of oxygen therapy: The NCT06622161 study used an automated oxygen control system in the neonatal intensive care unit to accurately regulate FiO_2 and keep SpO_2 within the desired range, thereby minimizing the occurrence of hypoxemia and hyperoxemia.

Reducing patient complications and mortality rates: The NCT06593509 study compared the effectiveness of NIV, high-flow nasal cannula oxygen therapy, and conventional nasal oxygen therapy as postextubation respiratory support. This study aimed to reduce reintubation rates, shorten the ICU length of stay, and decrease mortality within 48 hours. Additionally, the NCT06213168 study examined the effect of combining continuous positive airway pressure with a high-flow nasal cannula on the mortality rate in patients suffering from acute respiratory failure.

Comparison of different oxygen therapy strategies: The NCT06398951 study compared the effectiveness of two different sizes of high-flow nasal cannulas in extubated ICU patients, focusing on arterial blood gas values, physiological data, and patient comfort. The NCT06350864 study assessed the effectiveness of high-flow nasal cannula oxygen therapy compared with conventional nasal oxygen therapy during prolonged gastrointestinal endoscopy. The NCT06306651 study compared standard oxygen therapy with high-flow nasal cannula oxygen therapy in the postoperative ICU, focusing on SpO_2 levels, extubation times, ICU length of stay, and continuous positive airway pressure requirements. Additionally, the NCT06247397 study evaluated the effectiveness of high-flow oxygen therapy for patients requiring long-term oxygen treatment.

Table 2 | **Top 10 randomized controlled trial protocols on ICU oxygen therapy registered on ClinicalTrials.gov in 2024 (arranged by initial registration date)**

NCT number	Study title	Study design	Interventions	Enrollment (*n*)	First posted	Study status
NCT06622161	Automated *versus* manual oxygen control in preterm babies on respiratory support	A randomized crossover trial	Automated oxygen *versus* manual oxygen	26	October 1, 2024	Recruiting
NCT06593509	The effectiveness of high flow nasal cannula *versus* noninvasive ventilation and conventional oxygen therapy	A randomized parallel trial	Maquet, Servo I. *versus* Vapotherm *versus* venturi mask	60	September 19, 2024	Completed
NCT06494410	Effect of high *versus* low fraction of inspired oxygen during alveolar recruitment	A randomized parallel trial	High *versus* low fraction of inspired oxygen	80	July 10, 2024	Completed
NCT06492382	The effects of home monitors used with home oxygen therapy	A randomized parallel trial	Diagnostic test: Home oxygen monitors	20	July 9, 2024	Not yet recruiting
NCT06398951	HFNC *versus* two nare HFNC in extubated patients	A randomized crossover trial	Two nare HFNC oxygen therapy	50	May 3, 2024	Active, not recruiting
NCT06350864	HFNC *versus* conventional oxygen therapy in prolonged upper gastrointestinal endoscopy in the ICU	A randomized parallel, single-blind trial	Conventional nasal oxygen therapy *versus* HFNC oxygen therapy	70	April 5, 2024	Completed
NCT06306651	High flow nasal cannula and conventional oxygen therapy in the postoperative management of patients with mild to moderate obstructive sleep apnea	A randomized parallel, single-blind trial	High-flow nasal cannula therapy *versus* conventional oxygen therapy	60	March 12, 2024	Recruiting
NCT06247397	Effect of high-flow therapy in long-term oxygen therapy	A randomized parallel trial	Added high-flow oxygen therapy *versus* standard care	310	February 7, 2024	Recruiting
NCT06213168	Impact on mortality of a strategy including continuous positive airway pressure plus high flow nasal cannula oxygen therapy *versus* high flow nasal cannula oxygen therapy alone in patients with *de novo* acute hypoxemic respiratory failure: a prospective, randomized controlled trial	A randomized parallel trial	HFNC *versus* CPAP and HFNC	1084	January 19, 2024	Not yet recruiting
NCT06202586	Effect of different oxygen concentration on postoperative pulmonary complications after pulmonary reexpansion	A randomized parallel, triple-blind trial	Low FiO_2 *versus* high FiO_2	300	January 11, 2024	Recruiting

CPAP: Continuous positive airway pressure; FiO_2: inspired fraction of oxygen; HFNC: high-flow nasal cannula; ICU: intensive care unit.

New technologies for high-flow nasal cannulas: The NCT06398951 study presented a new high-flow nasal cannula designed with nozzles of varying diameters to deliver different levels of positive pressure, thereby increasing oxygenation.

Long-term effects of oxygen therapy in patients with chronic obstructive pulmonary disease and interstitial lung disease: The NCT06247397 study assessed the long-term effects of high-flow oxygen therapy in patients with chronic obstructive pulmonary disease and interstitial lung disease.

Discussion

Result analysis

The article analyzes literature on oxygen therapy in the ICU from the Web of Science Core Collection, summarizing and examining key research areas in this field. Keyword clustering reveals that research on oxygen therapy in the ICU has focused on four main areas: the relationship between oxygen therapy and mechanical ventilation, the impact of ECMO for COVID-19 on mortality reduction, studies on hypoxia and oxygen saturation monitoring, and oxygen inhalation therapy in the ICU.

The analysis of highly cited literature underscores the significant interest in the potential of conservative oxygen therapy to lower mortality rates in the ICU. However, additional research is needed to determine the optimal parameters and identify suitable patient populations. Furthermore, the relationships between oxygen therapy and patient prognosis, individualized treatment approaches, monitoring and assessment practices, safety considerations, and the development of new technologies and equipment also need further investigation.

The main strategies for applying oxygen therapy in the ICU include oxygen management approaches, assessments of the effectiveness of oxygen therapy, and the clinical decision-making process. Research indicates that, despite various oxygen therapy strategies being employed, there are no significant differences in key outcomes among them. This indicates the need for more cautious, evidence-based oxygen management in clinical practice.

Currently, conservative oxygen therapy and high-flow nasal oxygen therapy are commonly used treatment strategies in the ICU. Studies suggest that conservative oxygen therapy may reduce the duration of mechanical ventilation and the incidence of new organ dysfunction, whereas high-flow nasal oxygen therapy effectively improves oxygenation and decreases the rate of reintubation.[31,36,38]

Comparative studies of high- and low-oxygenation strategies reveal differences in mortality rates, long-term outcomes, and clinician preferences. At present, there is no definitive evidence indicating which strategy is superior; however, clinicians' preferences for different oxygenation targets may influence the design of future research. Hyperbaric oxygen therapy is regarded as an effective supportive treatment for various critical conditions, particularly demonstrating positive outcomes in the management of acute severe traumatic brain injury. Additionally, high-oxygenation strategies hold significant value in brain resuscitation and cardiopulmonary resuscitation.

The latest results from randomized controlled trial protocols registered with ClinicalTrials.gov in 2024 indicate that automated oxygen control, novel high-flow nasal oxygen therapy, and continuous positive airway pressure combined with high-flow nasal oxygen therapy aim to increase the accuracy and safety of oxygen therapy. These strategies seek to reduce the incidence of hypoxemia and hyperoxemia, offer more effective oxygen therapy solutions for diverse patient populations (including combination therapies and long-term efficacy assessments), and lower complications and mortality rates. This initiative is designed to foster innovation and development in oxygen therapy devices and technologies.

Current research focus and controversial issues

Optimal oxygen therapy strategies

Preliminary findings suggest that conservative oxygen therapy has advantages in managing the risk of hyperoxia; however, further research is required to identify the optimal parameters and identify suitable patient populations. Additionally, emerging technologies such as high-flow nasal oxygen therapy have demonstrated promise in increasing oxygenation rates and lowering reintubation rates, but their specific indications and contraindications still need to be clearly defined.

Selection of high- and low-oxygenation strategies

Current research has not yet clearly defined the benefits and drawbacks of high- *versus* low-oxygenation strategies in relation to mortality, long-term effects, and clinician preferences. Additional studies are needed to evaluate the effects of various oxygenation targets on patient outcomes and to develop evidence-based guidelines for effective oxygen management.

Individualization of oxygen therapy strategies

Differences in race and ethnicity may influence the efficacy and safety of oxygen therapy. More research is required to gain insights into the oxygen requirements of various populations and to develop personalized oxygen therapy plans.

Long-term effects of oxygen therapy strategies

Current research on the long-term effects of oxygen therapy is limited. Further studies are needed to assess its influence on cognitive function, quality of life, and other related factors, as well as to develop effective prevention and intervention strategies.

Limitations

This review primarily depends on a literature analysis, which may introduce biases and limitations in the information provided. There is considerable variation in the quality of the studies included, with some having small sample sizes, raising concerns about how broadly the results can be applied.

Summary and outlook

This article reviews findings from highly cited research literature, revealing that while some studies suggest that high concentrations of oxygen can lead to oxidative stress, lung injury, and increased mortality, other studies do not show significant differences. Furthermore, the effectiveness of moderate-dose prophylactic anticoagulation in COVID-19 ICU patients is not greater than that of standard dosing, which raises questions about the effects of oxygen therapy on patient prognosis. Recent findings indicate that targeting a PaO_2 of 60 mmHg in oxygen therapy for ICU patients with COVID-19 increases the number of days alive without life support at 90 days, compared to targeting a PaO_2 of 90 mmHg. However, there is no significant difference in mortality rate between the two targets.[64-66] This conservative approach highlights potential benefits in the treatment of COVID-19.

The literature analysis revealed that one of the most well-established and extensively studied aspects of oxygen therapy in the ICU is the application of conservative oxygen therapy. This method focuses on maintaining patients' blood oxygen saturation (SpO_2) within a lower range, generally between 94% and 98%, to reduce the risks linked to high oxygen levels, such as oxidative stress and lung injury. Many studies have shown that conservative oxygen therapy can lower

mortality rates and reduce the incidence of complications in ICU patients compared with traditional higher saturation targets.

Future research should focus on several key areas. First, further validation of the optimal parameters and appropriate patient populations for conservative oxygen therapy, along with the development of evidence-based guidelines for oxygen management is essential. Second, comprehensive studies are needed to explore the indications and contraindications of new technologies, such as high-flow nasal oxygen therapy, and to evaluate their long-term effects. Third, large-scale, multicenter, randomized controlled trials should be conducted to assess the effects of different oxygenation targets on patient outcomes. Additionally, it is crucial to investigate the oxygen requirements of different patient populations and develop personalized oxygen therapy regimens.[67] It is also important to assess the long-term effects of oxygen therapy and to implement appropriate preventive and intervention strategies. Moreover, the development and use of new technologies and equipment for oxygen therapy should be prioritized to improve treatment effectiveness and safety. Improving the education and training of clinicians in oxygen therapy will enhance the overall management of this treatment. Ongoing research and practical implementation hold great promise for enhancing the evidence-based and effective use of oxygen therapy in the ICU. This can lead to improved patient outcomes, increased survival rates, and a better quality of life for those receiving treatment.

Conclusions

Research on oxygen therapy in the ICU has made significant progress, particularly with the emergence of conservative oxygen therapy strategies that may reduce mortality and complications. However, further studies are needed to refine optimal parameters and identify suitable patient populations for these approaches. Additionally, the effectiveness of novel technologies, such as high-flow nasal oxygen therapy, requires further evaluation. Future research should also emphasize the development of individualized oxygen therapy plans for various patient populations and assess the long-term effects of oxygen therapy. Furthermore, it is essential to develop appropriate preventive and intervention strategies. Prioritizing the development and use of new technologies and equipment for oxygen therapy will improve both treatment effectiveness and safety.

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