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RECENT ADVANCES IN PHARMACOLOGICAL AND NON-PHARMACOLOGICAL STRATEGIES OF PNEUMOPROTECTION: A NARRATIVE REVIEW

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Abstract

Acute lung injury (ALI), acute respiratory distress syndrome (ARDS), ventilator-induced lung injury (VILI), pulmonary ischemia-reperfusion (I/R) injury, and inflammatory lung diseases remain major causes of morbidity and mortality in critically ill patients worldwide. Despite significant advances in respiratory support, lung injury continues to represent a major therapeutic challenge due to the complex interaction between inflammatory, oxidative, mechanical, and cellular pathways. The concept of pneumoprotection encompasses endogenous and exogenous mechanisms capable of attenuating pulmonary damage and preserving alveolar-capillary integrity. These protective responses may be stimulated by pharmacological interventions, including antioxidants, nitric oxide modulators, corticosteroids, mesenchymal stem cell-derived therapies, and mitochondrial-targeted agents, as well as non-pharmacological approaches such as lung-protective ventilation, prone positioning, ischemic conditioning, and physical rehabilitation strategies. Recent advances in molecular biology have revealed critical signaling pathways involved in pneumoprotection, including PI3K/Akt, Nrf2/HO-1, NF-κB, HIF-1α, mitochondrial permeability transition pore regulation, and inflammatory cytokine modulation. This narrative review summarizes current evidence regarding pharmacological and non-pharmacological strategies for pneumoprotection and discusses future perspectives for translational and clinical research.

Keywords: pharmacology; acute lung injury; acute respiratory distress syndrome; mechanical ventilation; oxidative stress; pneumoprotection.

Authors

1. Introduction

Acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) remain major causes of morbidity and mortality worldwide, frequently associated with sepsis, pneumonia, trauma, aspiration, ischemia-reperfusion injury, and mechanical ventilation, with mortality rates that may exceed 40% in severe cases [1,2,3]. ARDS is characterized by diffuse alveolar damage, disruption of the alveolar-capillary barrier, and severe impairment of gas exchange; the Berlin Definition has long been the standard framework for diagnosis and severity classification[4], and was recently expanded by a new global definition that incorporates patients

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receiving high-flow nasal oxygen, the SpO_2 /FiO_2 ratio, and lung ultrasound[5]; current ESICM guidelines summarize the evidence on definition, phenotyping, and respiratory support strategies[6]. Its pathophysiology is multifactorial, involving inflammatory mediators, oxidative stress, endothelial and epithelial injury, coagulation abnormalities, mitochondrial dysfunction, and dysregulated immune responses [2,3].

Mechanical ventilation, although indispensable in respiratory failure, may itself aggravate pulmonary damage through ventilator-induced lung injury (VILI) when inappropriate settings are used [7]. Recognition that pulmonary tissue possesses endogenous mechanisms capable of limiting injury has led to the concept of pneumoprotection, which, analogous to cardioprotection and neuroprotection, encompasses physiological and pharmacological interventions that preserve pulmonary structure and function by attenuating inflammation, oxidative stress, mitochondrial dysfunction, and cell death [2,7].

This narrative review provides a critical and integrative synthesis of pharmacological and non-pharmacological strategies for pneumoprotection, emphasizing biological mechanisms of pulmonary injury and protection. Rather than following a systematic methodology, it aims to highlight established concepts, emerging therapeutic approaches, and current research trends, integrating evidence from experimental, translational, and clinical studies addressing inflammatory signaling, oxidative stress, mitochondrial dysfunction, immune regulation, and endogenous adaptive responses, to support future mechanistic, translational, and clinical investigation in pulmonary protection.

2. Cellular and Molecular Mechanisms Involved in Pulmonary Injury

Acute pulmonary injury results from coordinated activation of innate immunity, inflammatory signaling, oxidative stress, mitochondrial dysfunction, metabolic impairment, and programmed cell death, converging to disrupt alveolar-capillary barrier integrity regardless of the initiating insult—sepsis, pneumonia, trauma, ischemia-reperfusion injury, or mechanical ventilation [2,8]. Among the earliest events is activation of pattern-recognition receptors by pathogen- and damage-associated molecular patterns (PAMPs/DAMPs); Toll-like receptor 4 (TLR4), which recognizes lipopolysaccharide and endogenous danger signals, triggers MyD88- and TRIF-dependent signaling and transcriptional activation of inflammatory genes [9,10]. A central downstream event is stimulation of nuclear factor-kappa B (NF-κB), a principal transcriptional regulator of inflammation whose persistent activation is consistently associated with worse outcomes in experimental and clinical ARDS [10].

NF-κB activation drives transcription of tumor necrosis factor-alpha (TNF-α), produced primarily by activated macrophages and neutrophils and correlated with edema severity and impaired gas exchange, interleukin-1 beta (IL-1β, generated via NLRP3 inflammasome/caspase-1 activation), and interleukin-6 (IL-6), whose elevated plasma and bronchoalveolar concentrations are associated with disease

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severity, ventilation duration, and mortality through the IL-6/JAK/STAT3 axis [11,12,13]. High-mobility group box-1 protein (HMGB1), released from necrotic or activated cells, interacts with TLR4 and RAGE receptors to further amplify NF-κB- and MAPK-mediated responses, while chemokines such as CXCL10 sustain recruitment of activated lymphocytes, monocytes, and natural killer cells, particularly in viral and sepsis-associated lung injury [8,14]. The mitogen-activated protein kinase (MAPK) family (ERK, JNK, p38) regulates inflammatory gene expression, cytokine production, and apoptosis in parallel; experimental MAPK inhibition attenuates pulmonary inflammation and edema [15].

Oxidative stress, driven by activated inflammatory cells and dysfunctional mitochondria, generates excessive reactive oxygen species (ROS) that cause lipid peroxidation, protein oxidation, endothelial dysfunction, and DNA damage, further amplifying inflammatory signaling [16,17]. Mitochondrial dysfunction has emerged as a central mechanism linking inflammation to cellular injury: impaired oxidative phosphorylation progressively depletes intracellular ATP, compromising ion transport, membrane integrity, and alveolar fluid clearance, and disrupting ATP-dependent calcium transport [18,19]. Consequent cytosolic and mitochondrial calcium overload favors mitochondrial permeability transition pore (mPTP) opening, dissipation of the mitochondrial membrane potential, cytochrome c release, and apoptotic activation, directly driving epithelial and endothelial cell death and increasing alveolar–capillary permeability[20,21]. Collectively, activation of TLR4, NF-κB, TNF-α, IL-1β, IL-6, HMGB1, CXCL10, and MAPK signaling, together with oxidative stress, ATP depletion, calcium dysregulation, and mitochondrial permeability transition, forms the molecular basis of pulmonary injury and represents the principal target of contemporary pneumoprotective therapies [2,19] (Figure 1).

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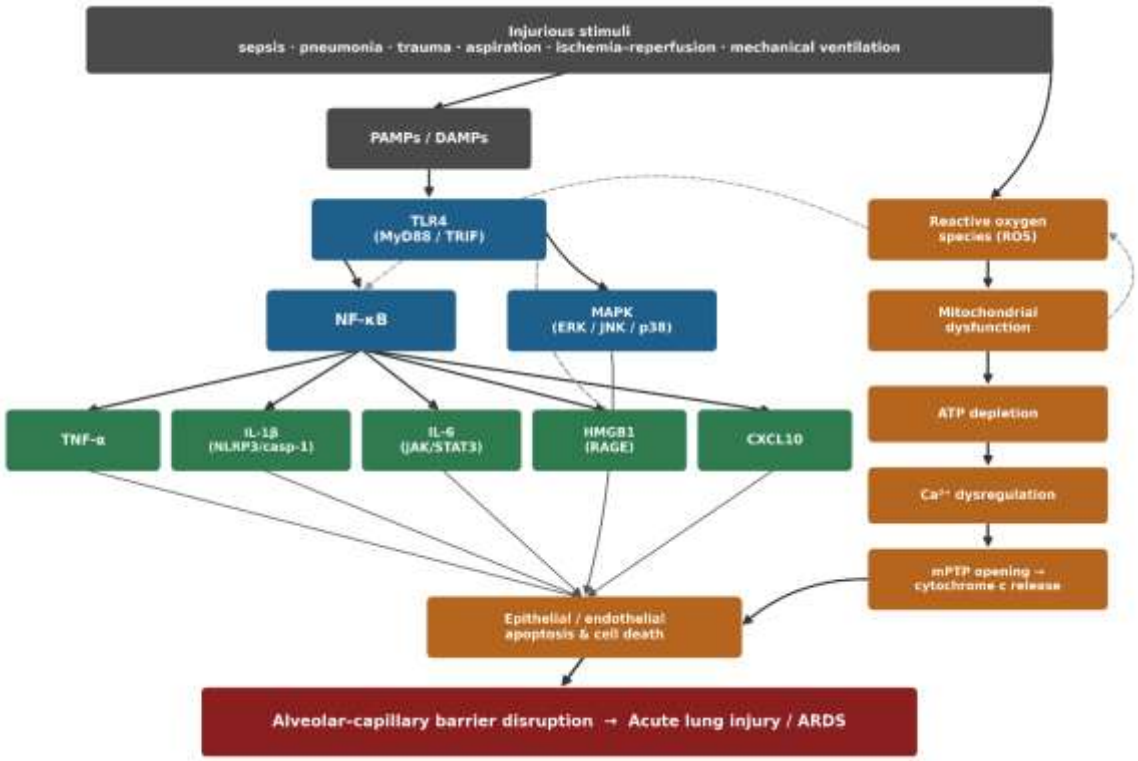


Figure 1. Overview of the cellular and molecular mechanisms of acute pulmonary injury. Injurious stimuli (sepsis, pneumonia, trauma, aspiration, ischemia–reperfusion, mechanical ventilation) release pathogen- and damage-associated molecular patterns (PAMPs/DAMPs) that activate TLR4/NF-κB and MAPK signaling, driving production of TNF-α, IL-1β, IL-6, HMGB1, and CXCL10 (left/centre pathway). In parallel, reactive oxygen species and mitochondrial dysfunction deplete ATP, dysregulate calcium homeostasis, and trigger opening of the mitochondrial permeability transition pore (mPTP) (right pathway). Both pathways converge on epithelial and endothelial apoptosis, culminating in alveolar–capillary barrier disruption and acute lung injury/ARDS. Dashed arrows indicate amplifying feedback loops between pathways. Figure generated with an artificial intelligence image-generation tool (Claude, Anthropic) and reviewed by the authors.

3. Ventilator-Induced Lung Injury (VILI)

When inappropriate ventilatory parameters are applied, mechanical ventilation may itself induce or aggravate pulmonary damage—a process termed ventilator-induced lung injury (VILI)—independent of the underlying disease [7,22]. Its pathophysiology involves alveolar overdistension (volutrauma), elevated airway pressures (barotrauma), repetitive alveolar collapse and reopening (atelectrauma), and mechanical stress-induced inflammatory activation (biotrauma), together disrupting epithelial and endothelial integrity [7].

Mechanical stretch activates mechanotransduction pathways that convert physical forces into biochemical signals, engaging TLR4, NF-κB, and MAPK signaling and increasing production of TNF-α, IL-1β, and IL-6, alongside release

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of HMGB1 and other DAMPs that sustain a positive feedback loop of inflammatory injury [7,23]. Excessive mechanical stretch also increases reactive oxygen species (ROS) generation and impairs mitochondrial oxidative phosphorylation, culminating in epithelial and endothelial apoptosis [17,18].

The clinical relevance of VILI was definitively demonstrated by the landmark ARDS Network trial, which showed that lower tidal volume ventilation significantly reduced mortality in ARDS, establishing lung-protective ventilation as the cornerstone of modern respiratory support [24]. Beyond tidal volume, driving pressure and mechanical power have since been proposed as additional determinants of ventilator-associated risk, with driving pressure showing the strongest association with survival among ventilatory variables in ARDS[25,26]. Understanding VILI as a syndrome of mechanotransduction, inflammation, oxidative stress, and mitochondrial dysfunction has been fundamental to the development of contemporary pneumoprotective strategies aimed at minimizing ventilator-associated pulmonary damage [7].

4. Pneumoprotection Induced by Ischemic Postconditioning

Ischemic postconditioning (IPostC) consists of brief, intermittent cycles of ischemia and reperfusion applied immediately after a prolonged ischemic insult. Originally described in the myocardium, it has since shown protective effects in other organs, including the lungs, by attenuating inflammation, oxidative stress, endothelial dysfunction, and mitochondrial damage [27,28]. The lung is particularly susceptible to ischemia-reperfusion (I/R) injury given its extensive vascular network; restoration of blood flow, although essential, paradoxically triggers inflammatory and oxidative cascades that may exacerbate tissue damage in settings such as transplantation, cardiopulmonary bypass, and hemorrhagic shock [29].

Postconditioning attenuates innate immune activation by reducing TLR4/NF-κB signaling and downstream production of TNF-α, IL-1β, and IL-6, and by limiting HMGB1 release and chemokine-mediated leukocyte recruitment, thereby preserving alveolar-capillary barrier integrity [28]. It also enhances endogenous antioxidant defenses, reducing ROS-mediated lipid peroxidation and DNA damage, and shifts MAPK signaling away from pro-apoptotic p38/JNK activity toward pro-survival ERK1/2 signaling [15,17].

Mitochondrial preservation represents one of the most important mechanisms of postconditioning-mediated protection: brief I/R cycles inhibit mPTP opening during early reperfusion, preserving membrane potential and preventing cytochrome c release, while also maintaining ATP-dependent calcium transport [20,30]. Remote ischemic postconditioning (RIPostC), in which transient ischemia is applied to a distant organ or limb, induces systemic protection via neural, humoral, and immunological pathways and has attracted considerable interest for perioperative and critical care applications given its non-invasive, low-risk profile [31,32]. Although evidence remains largely experimental, ischemic postconditioning is among the most promising non-pharmacological

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pneumoprotective strategies, warranting translational and clinical trials to define optimal protocols [31,32].

5. Physiological and Pathological Conditions Potentially Stimulating Pneumoprotective Responses

The lung can activate endogenous adaptive mechanisms—analogous to ischemic tolerance in the heart and brain—that increase resistance to subsequent injurious stimuli, involving coordinated regulation of inflammatory signaling, oxidative stress, mitochondrial function, cellular metabolism, and tissue repair [33,34].

5.1. Hypoxic Adaptation and Permissive Hypercapnia

Moderate or intermittent hypoxia induces stabilization of hypoxia-inducible factors (HIF-1α/HIF-2α), transcription factors regulating angiogenesis, glucose metabolism, antioxidant defense, and mitochondrial adaptation; experimental activation of HIF signaling attenuates pulmonary inflammation, preserves endothelial barrier function, and reduces injury during subsequent inflammatory or ischemic insults, in part through reduced ROS generation and more efficient oxygen utilization [33,35]. Controlled, permissive hypercapnia—common during lung-protective ventilation—similarly attenuates NF-κB activation and reduces TNF-α, IL-1β, and IL-6 production, and may reduce oxidative stress and preserve barrier integrity, although excessive hypercapnia may be detrimental and moderate degrees are therefore preferred [36,37].

5.2. Exercise, Hormesis, and Ischemic Conditioning

Regular physical activity induces systemic adaptive responses that extend beyond the cardiovascular system, enhancing endogenous antioxidant defenses (superoxide dismutase, catalase, glutathione peroxidase), increasing mitochondrial biogenesis, improving endothelial function, and suppressing basal NF-κB/MAPK/inflammasome activity, collectively increasing pulmonary resilience to inflammatory and oxidative insults [38,39,40]. This parallels the concept of hormesis, whereby exposure to low-intensity stress—such as mild oxidative stress—activates nuclear factor erythroid 2-related factor 2 (Nrf2) signaling, upregulating heme oxygenase-1 (HO-1), glutathione synthesis enzymes, and other cytoprotective and detoxification systems, attenuating pulmonary inflammation, oxidative stress, and mitochondrial dysfunction [41,42]. Both ischemic preconditioning and postconditioning, as well as remote organ crosstalk, in which brief sublethal ischemia in skeletal muscle or intestine activates neural, humoral, and immunological pathways, reduce injury in distant organs including the lungs, providing rationale for clinically applicable remote conditioning strategies [31,32].

5.3. Endogenous Resolution of Inflammation and Mitochondrial Adaptive Responses

Beyond mechanisms that limit injury, the lung possesses pathways that actively promote resolution of inflammation: specialized pro-resolving mediators

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(SPMs)—lipoxins, resolvins, protectins, and maresins—regulate termination of inflammatory responses, clearance of apoptotic cells, and tissue repair, and their failure has been implicated in persistent injury, fibrosis, and prolonged dysfunction, while their enhancement is beneficial experimentally [43,44]. Mitochondria also function as central regulators of cellular adaptation to stress, and mild metabolic stress can stimulate mitochondrial biogenesis, mitophagy, and cytoprotective signaling that preserve ATP production, maintain calcium homeostasis, reduce ROS generation, and prevent mPTP opening; enhancement of mitochondrial quality control is increasingly recognized as a fundamental component of endogenous pneumoprotection, associated with reduced inflammation and improved epithelial barrier function [18,45]. Collectively, these adaptive stimuli converge on common molecular targets—HIF signaling, Nrf2 activation, NF-κB inhibition, and mitochondrial preservation—that may be harnessed to develop innovative pneumoprotective strategies [35,41].

6. Pharmacological Strategies for Pneumoprotection

Growing mechanistic understanding has stimulated pharmacological interventions that directly target the inflammatory, oxidative, and mitochondrial processes responsible for pulmonary injury, rather than merely addressing its physiological consequences [3].

6.1. Anti-Inflammatory and Cytokine-Targeted Therapies

Corticosteroids, the most extensively investigated anti-inflammatory agents, suppress NF-κB activation and pro-inflammatory cytokine transcription, with recent trials suggesting benefit in selected ARDS populations, particularly during early inflammatory phases [46,47]. Biological therapies directed against TNF-α, IL-1β, and IL-6 signaling reduce leukocyte recruitment and barrier disruption experimentally, though clinical translation remains limited by disease heterogeneity [48,49].

6.2. Antioxidant and Mitochondria-Targeted Therapies

N-acetylcysteine (NAC), a glutathione precursor, remains extensively studied and reduces pulmonary edema and oxidative injury experimentally [50]. Melatonin has emerged as a particularly attractive agent owing to combined antioxidant, anti-inflammatory, anti-apoptotic, and mitochondrial-protective properties [51,52]. In a small experimental study using a rat model of intestinal ischemia-reperfusion-induced lung injury, both melatonin and NAC attenuated pulmonary injury and increased superoxide dismutase activity, with greater reductions in TNF-α in the melatonin group [53]; as these findings derive from a single model, they require independent confirmation. Mitochondria-targeted antioxidants (e.g., MitoQ, SS-31) and pharmacological inhibition of mPTP opening have also shown experimental benefit in preserving membrane potential and preventing apoptotic cascades [30,54].

6.3. Nitric Oxide, TLR4/NF-κB/MAPK Modulation, and Cell-Based Therapies

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Nitric oxide (NO) regulates vascular tone, endothelial function, and pulmonary perfusion; inhaled NO acts as a selective pulmonary vasodilator that improves ventilation-perfusion matching and oxygenation and continues to be used as rescue therapy in selected patients with refractory hypoxemia, although mortality benefit remains unproven in meta-analyses [55,56]. Because TLR4, NF-κB, and MAPK occupy central positions in the inflammatory cascade, experimental inhibition of these pathways attenuates cytokine production (TNF-α, IL-1β, IL-6, HMGB1), leukocyte recruitment, oxidative stress, and endothelial injury, while also preserving mitochondrial function [57,58,59]. Mesenchymal stromal cells (MSCs) have emerged as one of the most promising translational approaches, exerting immunomodulatory and tissue-reparative effects via secretion of growth factors, extracellular vesicles, and mitochondrial transfer; experimental administration reduces cytokine production, attenuates alveolar-capillary permeability, and improves alveolar fluid clearance and survival [60,61].

6.4. Specialized Pro-Resolving Mediators and Emerging Targets

Unlike conventional anti-inflammatory agents, SPMs actively promote resolution of inflammation while preserving host defense, reducing pulmonary edema and fibrosis in experimental models [62,63]. Additional emerging targets under investigation include Nrf2 activation, autophagy modulation, inflammasome inhibition, ferroptosis regulation, and enhancement of mitochondrial quality control, aiming to restore cellular homeostasis rather than merely suppress inflammation [41,64]. Collectively, experimental evidence suggests that simultaneous modulation of oxidative and inflammatory pathways may be a promising strategy for clinical translation [41,52].

7. Non-Pharmacological Strategies for Pneumoprotection

Non-pharmacological interventions remain the foundation of contemporary pneumoprotection, acting by reducing mechanical stress, optimizing gas exchange, and limiting inflammatory activation, with many strategies directly influencing the molecular pathways described above [7,65].

7.1. Lung-Protective Ventilation and PEEP Optimization

Lung-protective ventilation, established by the landmark ARDS Network trial, remains the cornerstone of modern pneumoprotection, minimizing volutrauma, barotrauma, atelectrauma, and biotrauma and thereby limiting NF-κB/MAPK-driven cytokine production [24]. Appropriate positive end-expiratory pressure (PEEP) prevents repetitive alveolar collapse and reopening, improving oxygenation and ventilation-perfusion matching, though excessive PEEP may cause overdistension and hemodynamic compromise, underscoring the need for individualized titration [65,66].

7.2. Prone Positioning, ECMO, and Fluid Management

Prone positioning redistributes transpulmonary pressures and improves oxygenation while reducing regional overdistension; the PROSEVA trial demonstrated significant mortality reduction with early, prolonged prone

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positioning in severe ARDS [67,68]. Extracorporeal membrane oxygenation (ECMO) permits ultra-protective ventilation in patients with severe, refractory respiratory failure, with expanded use in severe ARDS and during recent viral pandemics [69,70]. Conservative fluid management minimizes hydrostatic pulmonary edema and has been shown to improve oxygenation and shorten mechanical ventilation duration, as demonstrated in the FACTT trial and subsequent studies [71,72].

7.3. Remote Conditioning, Rehabilitation, Nutrition, and Oxygen Titration

Remote ischemic conditioning reduces pulmonary inflammation, oxidative stress, and mitochondrial injury through neural, humoral, and immunological mechanisms, though clinical evidence remains limited [32]. Early mobilization and rehabilitation counteract immobilization-related respiratory muscle dysfunction and systemic inflammation, and may improve recovery of pulmonary performance [73]; however, the multicenter TEAM trial in 750 ventilated adults found that intensified early active mobilization did not increase days alive and out of hospital and was associated with more adverse events, so mobilization intensity should be individualized[74]. Adequate nutritional support is recommended by international guidelines as a component of comprehensive critical care, whereas routine high-dose supplementation with omega-3 fatty acids—precursors of SPMs—is not supported by current guidance [75]. Individualized oxygenation targets that avoid both hypoxemia and hyperoxia limit ROS-mediated oxidative damage, as supported by recent trials of conservative oxygen therapy [76,77].

7.4. Integrated Approaches

Current evidence indicates that no single intervention is sufficient to fully prevent pulmonary injury. Optimal pneumoprotection likely requires integration of multiple complementary strategies—lung-protective ventilation, individualized PEEP, prone positioning, conservative fluid management, early rehabilitation, optimized oxygen therapy, and selective extracorporeal support—which converge on shared biological pathways of inflammation, oxidative stress, mitochondrial dysfunction, and endothelial injury. Future personalized approaches combining pharmacological and non-pharmacological interventions may further improve outcomes in patients at risk for acute lung injury and ARDS [7,65].

8. Emerging Perspectives and Future Directions in Pneumoprotection

Despite substantial mechanistic and therapeutic advances, ALI and ARDS remain associated with major morbidity and mortality, suggesting that future pneumoprotective strategies will require personalized, multimodal approaches. Precision medicine is among the most promising developments: ARDS is increasingly recognized as a biologically heterogeneous syndrome with distinct inflammatory and metabolic phenotypes, and advances in genomics, transcriptomics, and single-cell sequencing may enable identification of patients most likely to benefit from targeted interventions [78,79,80].

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Volatile anesthetics, particularly isoflurane and sevoflurane, have emerged as promising translational pneumoprotective agents beyond their sedative role, reducing TNF-α, IL-1β, IL-6, and HMGB1 production, suppressing TLR4/NF-κB/MAPK signaling, and preserving mitochondrial function via activation of pro-survival pathways (PI3K/Akt, ERK1/2); a randomized trial in thoracic surgical patients demonstrated reduced pulmonary inflammation with sevoflurane[81], but a subsequent multicenter trial in 460 patients found no difference in major postoperative complications between volatile (desflurane) and intravenous (propofol) anesthesia, so clinical benefit remains to be demonstrated [82,83,84]. Artificial intelligence and machine learning are increasingly used to integrate clinical, physiological, and molecular data, supporting early diagnosis, predictive modeling, and individualized optimization of ventilatory and fluid management strategies [85,86].

Extracellular vesicles and cell-free therapies derived from mesenchymal stromal cells offer a promising alternative to whole-cell therapy, attenuating inflammation and promoting epithelial and endothelial repair with lower immunogenicity [87,88]. Mitochondrial medicine—enhancing biogenesis, mitophagy, and oxidative phosphorylation while preventing mPTP opening—and immunometabolism, which links metabolic reprogramming of immune cells to inflammatory and reparative processes, represent further emerging pillars of pneumoprotection [19,89].

The multifactorial nature of pulmonary injury suggests that future success will depend on multimodal, combination strategies integrating pharmacological and non-pharmacological interventions rather than isolated approaches [3]. However, translation from laboratory to clinical practice remains challenging, reflecting species-specific differences, disease heterogeneity, and variability in timing of intervention; future research should prioritize clinically relevant models, biomarker-guided stratification, and multicenter translational studies integrating precision medicine and systems biology to accelerate development of individualized pneumoprotective therapies [90].

9. Conclusions

Pulmonary injury remains one of the most important causes of morbidity and mortality in critically ill patients, representing a common final pathway of sepsis, ischemia-reperfusion syndromes, trauma, major surgery, mechanical ventilation, and ARDS. Growing understanding of its cellular and molecular basis has expanded pneumoprotection from a predominantly mechanical concept into a comprehensive biological strategy targeting inflammation, oxidative stress, mitochondrial dysfunction, and endothelial injury simultaneously [2,19].

This review highlights that endogenous protective mechanisms can be activated by diverse stimuli—hypoxia, hypercapnia, exercise, hormetic stress, ischemic conditioning, and specialized pro-resolving pathways—converging on common mechanisms that enhance cellular resilience and mitochondrial integrity [35,45]. Pharmacological pneumoprotection has evolved substantially through anti-inflammatory agents, antioxidants, mitochondria-targeted therapies, MSC-

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derived therapies, and specialized pro-resolving mediators, although most of this evidence remains experimental and awaits clinical confirmation.

Equally important, non-pharmacological interventions—lung-protective ventilation, individualized PEEP, prone positioning, conservative fluid management, extracorporeal support, early mobilization, and careful oxygen titration—continue to form the foundation of contemporary pneumoprotection, directly influencing the molecular pathways of injury [65,72]. Looking forward, precision medicine, artificial intelligence, extracellular vesicle biology, mitochondrial medicine, and immunometabolism are likely to redefine this field, enabling biomarker-guided, personalized therapeutic approaches [19,78].

In conclusion, pneumoprotection should no longer be viewed solely as a ventilatory concept but as an integrated biological and clinical paradigm encompassing prevention, attenuation, and resolution of pulmonary injury. Continued integration of experimental, translational, and clinical research will be essential for developing strategies capable of preserving pulmonary structure and function and reducing the global burden of acute lung injury and ARDS [7,90].

Conflicts of Interest

None

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