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Review

Risk Factors and Treatment Strategies of Postoperative Hypoxemia in Acute Type A Aortic Dissection: A Literature Review

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Abstract

Acute type A aortic dissection (ATAAD) is a cardiovascular disease with a rapid onset and high mortality. Emergency surgery is the preferred and reliable treatment for ATAAD. However, postoperative complications, especially hypoxemia, seriously affect the prognosis of patients since hypoxemia increases the risk of death and creates extensive challenges regarding clinical treatment. Therefore, an in-depth study of the risk factors and treatment strategies of hypoxemia after ATAAD is of great significance for early intervention and improving the prognosis of patients. This article aims to explore the risk factors associated with hypoxemia and proposes effective treatment strategies that can provide a reference for clinical practice.

Keywords: ATAAD; hypoxemia; risk factors; treatment strategies

Introduction

Aortic dissection (AD) constitutes a life-threatening cardiovascular emergency characterized by intimal disruption, leading to blood extravasation into the medial layer and the creation of true and false lumens [1]. This pathological process frequently precipitates catastrophic complications, including aortic rupture and pericardial tamponade, particularly when involving the ascending aorta, a critical anatomical region responsible for systemic organ perfusion. Stanford type A aortic dissection (acute type A aortic dissection, ATAAD) has demonstrated particularly grave prognoses, with epidemiological evidence indicating a 1% hourly mortality escalation during initial presentation, culminating in 30–50% mortality within 48 hours without surgical intervention [2,3]. Current therapeutic protocols prioritize emergency surgical management, typically involving aortic segment replacement under deep hypothermic circulatory arrest (DHCA) with adjunctive selective cerebral perfusion [4]. Nevertheless, the circulatory arrest phase carries inherent risks of ischemia-reperfusion injury, potentially compromising cardiopulmonary and spinal cord functionality through impaired organ perfusion [5]. Postoperative hypoxemia (HO) has emerged as a prevalent complication following ATAAD repair, with reported incidence rates up to 51% [6,7]. This respiratory derangement correlates strongly with prolonged mechanical ventilation requirements and extended stays in the intensive care unit (ICU) [8]. The multifactorial pathogenesis encompasses preoperative comorbidities, cardiopulmonary bypass (CPB) duration, DHCA parameters, and transfusion-related acute lung injury (TRALI). Thus, this systematic review synthesizes current evidence regarding perioperative risk stratification and therapeutic optimization for ATAAD-associated hypoxemia.

Diagnostic Criteria for Hypoxemia

Hypoxemia refers to a pathological state in which the arterial partial pressure of oxygen (PaO_2) is lower than normal levels due to an insufficient oxygen content in the blood. The mechanism through which hypoxemia develops is mainly related to damage to the alveolar epithelium and microvascular endothelial cells, which can reduce oxygen partial pressure and oxygen saturation. The diagnostic criteria for hypoxemia refer to the Berlin criteria for acute respiratory distress syndrome and literature research [3,6], specifically an oxygen index $\leq$200 mmHg.

Methodology

Relevant literature was identified in the PubMed, Embase, and Web of Science databases using the following keywords: “Deficiency, Oxygen” or “Deficiencies, Oxygen” or “Oxygen Deficiencies” or “Oxygen Deficiency” or “Anoxemia” or “Hypoxemia” or “Anoxia” or “Hypoxia” and “Aortic Dissections” or “Dissection, Aortic” or “Aneurysm, Dissecting” or “Dissecting Aneurysms” or “Dissecting Aneurysm” or “Dissecting Aneurysm Aorta” or “Aneurysm Aorta, Dissecting” or “Aorta, Dissecting Aneurysm” or “Dissecting Aneurysm Aortas” or “Aortic Dissecting Aneurysm” or “Aneurysm, Aortic Dissecting” or “Aortic Dissecting Aneurysms” or “Dissecting Aneurysm, Aortic” or “Aortic Dissection”. Three researchers developed the search strategy. The references to

the included literature were retrieved manually to supplement the acquisition of relevant literature [8–11].

Risk Factors of Hypoxemia

Smoking History

The pulmonary pathophysiological alterations induced by chronic tobacco smoke exposure arise from complex mechanisms. Cigarette-derived toxicants, including polycyclic aromatic hydrocarbons, carbon monoxide, and reactive oxygen species (ROS), directly induce apoptosis in airway epithelial cells and initiate neutrophilic inflammation. This process is mediated through a crosstalk between macrophages and T lymphocytes, characterized by elevated interleukin-8 (IL-8) and tumor necrosis factor-alpha (TNF-α) levels, which perpetuate a proinflammatory microenvironment [12]. Long-term smoking also leads to structural changes in the airway walls, including smooth muscle proliferation, fibrosis, and goblet cell hyperplasia, resulting in airway wall thickening and lumen narrowing, causing airflow limitations [13]. Additionally, fibrosis and stenosis of small airways increase airway resistance, particularly during exhalation, significantly affecting lung function [14]. Furthermore, smoking inhibits ciliary motor function and reduces mucus clearance, thereby increasing the risk of respiratory infections [15]. Numerous studies have confirmed that a history of smoking is an independent risk factor for postoperative hypoxemia [8,16,17]. As shown in Table 1.

Obesity

Obesity, defined as a body mass index (BMI) $>$30 kg/m^2, represents an important risk factor for postoperative hypoxemia [9,18]. In addition to serving as an energy storage organ, the adipose tissue in obese individuals secretes various inflammatory factors (such as TNF-α and IL-6) and adipokines (such as leptin and adiponectin), which contribute to a systemic inflammatory response that adversely affects lung function and gas exchange [19]. Meanwhile, fat accumulation in the chest wall and abdomen of obese individuals reduces chest wall compliance and limits diaphragm movement, thereby increasing respiratory work, causing postoperative atelectasis, disrupting the ventilation-to-blood flow ratio, and raising the incidence of hypoxemia [20]. Furthermore, the lung volume and functional residual capacity (FRC) in obese individuals are often reduced, especially in the supine position, while alveolar atrophy exacerbates gas exchange disorders [21]. As shown in Table 1. Obesity is frequently associated with metabolic syndrome, hypertension, diabetes, and cardiovascular diseases, all of which increase the likelihood of hypoxemia. Cardiovascular conditions in obese patients, such as coronary heart disease and heart failure, may reduce cardiac output and affect oxygen delivery and tissue oxygenation [22]. Studies indicate that the incidence of postoperative pneumonia in obese patients is significantly higher than in non-obese patients, possibly due to impaired immune function and decreased clearance of respiratory secretions [23]. Additionally, obese patients typically require prolonged mechanical ventilation support after surgery, heightening the risk of ventilator-associated lung injury (VILI) and hypoxemia [24].

Inflammatory Response

The inflammatory response plays a crucial role in the pathological process of ATAAD. When AD occurs, an intimal tear triggers local inflammatory reactions, which subsequently evoke systemic inflammatory responses, including the release of cytokines and other inflammatory mediators. Studies have shown that the levels of inflammatory markers, such as C-reactive protein (CRP), IL-6, and TNF-α, in the serum of TAAD patients are significantly elevated and are closely associated with the severity and prognosis of the disease [25]. Endothelial cells serve as a critical barrier for maintaining vascular permeability. Inflammatory mediators, such as TNF-α and IL-1β, reduce the expression of connexins between endothelial cells, including tight junction proteins, and increase vascular permeability by activating signaling pathways, including NF-κB [26]. This increased permeability allows for the infiltration of plasma proteins and fluid into the alveolar space, resulting in pulmonary edema and impaired gas exchange. As shown in Table 1.

Preoperative Renal Insufficiency

Renal insufficiency not only impairs the excretory function of the kidney but also exacerbates the systemic inflammatory response through various mechanisms, thereby increasing the risk of postoperative hypoxemia [27]. The accumulation of metabolic waste products, such as urea, creatinine, and uric acid, in patients with renal insufficiency activates the inflammatory signaling pathway, NF-κB, promoting the release of inflammatory mediators, including TNF-α, IL-6, and IL-1β, which contribute to a systemic inflammatory response. In addition to damaging the kidneys, this inflammatory reaction also harms lung tissue, resulting in increased permeability of pulmonary capillary endothelial cells, which can lead to pulmonary edema and disrupted ventilation-to-blood flow ratios [28]. Furthermore, patients with renal insufficiency often experience acid–base imbalances, electrolyte disturbances, and symptoms such as metabolic acidosis and hyperkalemia. Subsequently, metabolic acidosis can reduce the oxygen affinity of hemoglobin, impairing oxygen transport and tissue oxygenation. Elevated serum potassium levels may cause arrhythmias, further diminishing cardiac output and oxygen delivery. These metabolic disorders pose significant risks for patients following TAAD surgery, potentially exacerbating the incidence of hypoxemia [29]. As shown in Table 1. Additionally, decreased antioxidant capacity in patients with renal insufficiency leads to excessive accumulation of ROS in the body, which can directly damage lung

Table 1. Risk factors and clinical effects of ATAAD.

Risk factors	Pathological mechanism	Clinical effect
Smoking history	Small airway obstruction, cilia function damage, and secretion retention	• The comprehensive risk of postoperative pulmonary complications increased. • Increased incidence of difficult weaning. • Delayed hypoxemia (3–5 days after surgery) is common.
Obesity (BMI $\geq$25 kg/m^2)	Restrictive ventilatory dysfunction, low lung volume, ventilation/blood flow imbalance	• The incidence of postoperative atelectasis increased by 57%. • PaO_2/FiO_2 ratio decreased by $\geq$20%. • Increased demand for mechanical ventilation. • Oxygen therapy time was extended to 48–72 hours.
Inflammatory response	Inflammatory factor storm leads to alveolar–capillary barrier damage	• Related to the progression of ARDS. • The oxygenation index showed a progressive decline. • Poor response to high PEEP.
Preoperative renal insufficiency	Fluid retention $\rightarrow$ pulmonary interstitial edema, uremic toxins inhibit the respiratory center	• The capacity status needs to be closely monitored. • Related to multiple organ hypoxia injury. • Continuous renal replacement therapy (CRRT) may improve oxygenation.
Preoperative hypoxemia	Insufficient basic oxygen reserve (such as COPD, pulmonary fibrosis)	• The probability of postoperative FiO_2 $\geq$60% increased by 2.5 times. • The deterioration rate of the oxygenation index is accelerated. • Related to postoperative cognitive dysfunction.
Obstructive sleep apnea syndrome (OSAS)	Upper airway collapse leads to intermittent hypoxia, postoperative anesthesia residue, and analgesics aggravate ventilation inhibition	• SpO_2 decreased significantly at night after the operation. • The apnea number increased by 2–3 times. • Increased risk of requiring non-invasive ventilation support. • ICU stay was prolonged by 30%.
Bleeding and massive blood transfusion	Transfusion-related acute lung injury (TRALI), and circulatory overload	• The risk of hypoxemia in patients with blood transfusion >4 U increased by 3.1 times. • Double lung infiltration shadow is often combined. • Need to be combined with diuretic and lung protective ventilation.
Extracorporeal circulation and deep hypothermic circulatory arrest	Systemic inflammatory response $\rightarrow$ pulmonary capillary leakage, alveolar surfactant destruction	• The incidence of early postoperative hypoxemia (within 24 hours) was 40–60%. • Associated with acute lung injury. • Often requires PEEP $\geq$8 cmH_2O to maintain oxygenation.

ATAAD, acute type A aortic dissection; BMI, body mass index; PaO_2, partial pressure of oxygen; FiO_2, fraction of inspired oxygen; ARDS, acute respiratory distress syndrome; PEEP, Positive End-Expiratory Pressure; COPD, Chronic Obstructive Pulmonary Disease; ICU, intensive care unit.

tissue cells and further activate inflammatory signaling pathways, creating a negative feedback cycle. Studies have shown that oxidative stress plays a critical role in the development of lung injury and hypoxemia following TAAD surgery [11].

Preoperative Hypoxemia

Patients with preoperative hypoxemia often exhibit decreased lung compliance and symptoms such as ventilation-to-blood flow (V/Q) imbalance. Meanwhile, V/Q imbalance aggravates hypoxemia and contributes to alveolar ventilation insufficiency. Studies have shown that patients with preoperative hypoxemia require significantly prolonged mechanical ventilation time after surgery and are more prone to developing acute respiratory distress syndrome (ARDS) [30]. As shown in Table 1. Additionally, preoperative hypoxemia is closely associated with the exacerbation of the systemic inflammatory response. Hypoxemia activates the hypoxia-inducible factor-1α (HIF-1α) signaling pathway, promoting the release of inflammatory mediators, such as TNF-α, IL-6, and IL-1β, and triggering a systemic inflammatory response. This inflammatory reaction not only damages lung tissue but may also affect other organs, leading to multiple organ dysfunction syndrome (MODS). Studies have indicated that the levels of inflammatory markers in patients with preoperative hypoxemia are significantly elevated and positively correlate with postoperative severity [31]. Furthermore, preoperative hypoxemia can impair the immune function of the body. Hypoxic conditions exert an inhibitory effect on the function of immune cells, such as macrophages and neutrophils, thereby reducing their ability to eliminate pathogens and increasing the risk of postoperative infections. Infections not only exacerbate lung injury but also worsen oxygen delivery, creating a negative feedback cycle. Studies have shown that the incidence of postoperative pneumonia in patients with preoperative hypoxemia is significantly higher than in those without hypoxemia [32].

Obstructive Sleep Apnea Syndrome (OSAS)

OSAS is a common sleep-disordered breathing condition characterized by recurrent apnea or hypopnea during sleep, resulting from partial or complete obstruction of the upper airway. These respiratory events can lead to sympathetic activation, increased oxidative stress, and an augmented systemic inflammatory response, resulting in intermittent hypoxemia and hypercapnia. These pathophysiological changes not only affect cardiovascular function but also impair lung function, significantly increasing the risk of hypoxemia following TAAD surgery [33]. Intermittent hypoxemia in patients with OSAS during sleep can cause periodic elevations in pulmonary artery pressure, potentially leading to chronic pulmonary hypertension over time. Subsequently, pulmonary hypertension increases the workload on the right side of the heart, which can lead to right heart dysfunction, ultimately affecting left heart function and cardiac output. Decreased cardiac function can further exacerbate postoperative hypoxemia, particularly in the context of TAAD surgery, where the cardiopulmonary function of patients undergoing surgery and cardiopulmonary bypass is already compromised [34]. As shown in Table 1. Additionally, intermittent hypoxemia in OSAS patients can induce oxidative stress and inflammatory responses. Increased production of ROS under hypoxic conditions leads to direct damage to lung tissue cells and activates the inflammatory signaling pathway, including NF-κB, promoting the release of inflammatory mediators, such as TNF-α and IL-6. These mediators can further damage the microvascular endothelial cells in the lungs, and increased vascular permeability contributes to pulmonary edema and disrupted ventilation-to-blood flow ratios, thereby aggravating postoperative hypoxemia [35]. Patients with OSAS often experience increased upper airway resistance and elevated respiratory workload, resulting in increased intrathoracic negative pressure and fatigue of the respiratory muscles. Patients after TAAD surgery may require mechanical ventilation support; meanwhile, those with OSAS are at greater risk of developing VILI and atelectasis, further heightening the risk of hypoxemia [36].

Intraoperative Related Factors

Bleeding and Blood Transfusion

Massive blood transfusions (defined as the transfusion of $\geq$10 units of red blood cells within 24 hours or more than 50% of the total blood volume of the patient in a short period) are closely associated with postoperative hypoxemia [37]. Biologically active substances, such as anti-white blood cell antibodies, lipid mediators, and cytokines, which are released during blood transfusion, can activate pulmonary vascular endothelial cells and neutrophils, leading to an inflammatory response. During blood transfusion, activated neutrophils from stored blood adhere to the pulmonary microvascular wall, releasing proteases and ROS, which compromise the alveolar–microvascular barrier and cause non-cardiogenic pulmonary edema. A significant cause of postoperative hypoxemia is TRALI, characterized by clinical manifestations such as acute dyspnea, hypoxemia, and exudative changes on chest imaging [38]. As shown in Table 1. Additionally, microparticles, cell debris, and fibrinogen, which gradually accumulate during storage, can form microthrombi in the pulmonary microvascular network after infusion. These microthrombi not only obstruct pulmonary microvessels, exacerbating the imbalance of ventilation-to-blood flow ratios, but also release proinflammatory factors, such as HMGB1 and histamine, which further damage lung tissue. Studies have shown that the incidence of postoperative pneumonia in patients receiving blood transfusions increases by 3.4 times, with a significant rise in pneumonia incidence for each additional unit of red blood cell transfusion [39].

Cardiopulmonary Bypass (CPB) and Deep Hypothermic Circulatory Arrest (DHCA)

CPB, an essential technique in ATAAD surgery, provides a blood-free field and a stable hemodynamic environment by temporarily replacing cardiopulmonary function with a mechanical device. However, the prolonged use of CPB has significantly increased the incidence of postoperative hypoxemia [40]. During CPB, blood comes into contact with the artificial conduit, triggering the activation of the complement system and the release of numerous inflammatory mediators from white blood cells, including TNF-α, IL-6, and IL-8. These mediators not only directly damage lung tissue but also promote the adhesion and infiltration of white blood cells in the pulmonary microvessels. Increased levels of adhesion molecules (such as ICAM-1 and VCAM-1) contribute to worsening lung injury. Meanwhile, studies have shown that the duration of CPB is positively correlated with the levels of postoperative inflammatory markers, such as CRP and procalcitonin (PCT), while the intensity of the inflammatory response is closely related to the severity of hypoxemia [41]. Ischemia and mechanical stretching of lung tissue during CPB reduce the synthesis and secretion of pulmonary surfactant (PS) and impair the function of alveolar type II epithelial cells. Subsequently, this reduction in PS decreases alveolar stability and increases the risk of alveolar collapse, leading to a V/Q imbalance. Prior research has demonstrated that the PS content in bronchoalveolar lavage fluid from patients after CPB surgery is significantly reduced and positively correlates with the oxygenation index (PaO_2/fraction of inspired oxygen (FiO_2)) [42]. Meanwhile, when blood flow is restored after CPB, the ischemic tissue undergoes reperfusion, producing large amounts of ROS and inflammatory mediators that further exacerbate tissue damage. Alveolar epithelial cell necrosis, increased capillary permeability, and pulmonary interstitial edema promote hypoxemia [43]. As shown in Table 1. Lung tissue is particularly sensitive to ischemia-reperfusion injury. Deep hypothermic circulatory arrest (DHCA) is a specialized technique applied during CPB. During DHCA, lung tissue experiences complete ischemia and hypoxia, remaining in a state of no ventilation for extended periods. This prolonged ischemia can result in alveolar collapse, atelectasis, and reduced lung volume, potentially causing or exacerbating V/Q imbalance and increasing the risk of postoperative hypoxemia [44]. This process is primarily manifested as lung tissue ischemia-reperfusion injury [45]. Numerous studies have shown that CPB and DHCA can exacerbate lung injury and elevate the incidence of postoperative hypoxemia in patients with ATAAD. Liu *et al*. [45] found that durations of DHCA exceeding 25 minutes significantly increase the risk of postoperative hypoxemia . Furthermore, several studies have confirmed that CPB and DHCA are independent risk factors for postoperative hypoxemia in patients with ATAAD [46–51].

Other Factors

Age represents a significant risk factor for postoperative hypoxemia [52]. Zhang *et al*. [53] indicated that age is an independent predictor of early postoperative hypoxemia, with a notable increase in the incidence of hypoxemia as age rises. Additionally, the occurrence of postoperative hypoxemia is related to the time interval from the onset of TAAD to surgery. Studies have shown that delayed surgery can result in prolonged ischemia and elevated blood pressure before the operation, which may further exacerbate damage to the heart and other organs, consequently increasing the risk of postoperative complications [52–54].

Treatment Measures of Hypoxemia

Prone Position Positive Pressure Mechanical Ventilation

Prone position positive pressure ventilation (PPV) is a crucial strategy for treating ARDS and postoperative hypoxemia [55]. By improving the uniformity of lung ventilation, prone position ventilation can reduce intrapulmonary shunting. Increased blood flow perfusion in the dorsal lung area during the prone position corresponds to enhanced ventilation, allowing for a better match of the V/Q ratio. Clinical studies have demonstrated that prone position ventilation can increase the oxygenation index (PaO_2/FiO_2) by 50% to 100%, particularly in patients with severe ARDS [56]. Additionally, prone position ventilation can reduce the risk of VILI by evenly distributing ventilation pressure, thereby minimizing local alveolar overexpansion and shear stress. As shown in Table 2. Research has shown that prone position ventilation leads to a more uniform distribution of alveolar pressure and reduces the release of markers of alveolar injury, such as IL-6 and TNF-α, ultimately decreasing lung injury [57]. However, there is a lack of evidence-based consensus on the balance between PEEP setting and blood pressure stability (PEEP range 5–15 cmH_2O in existing studies, but no established hemodynamic guidance scheme) [58].

Nasal High-Flow Humidified Oxygen Therapy Combined With Nitric Oxide Inhalation

Nasal high-flow humidified oxygen therapy (HFNO) combined with nitric oxide (NO) inhalation is an innovative treatment strategy that effectively improves oxygenation function in patients with hypoxemia following TAAD, while reducing the duration of mechanical ventilation and hospitalization. HFNO enhances oxygen binding capacity by delivering high flow rates (up to 60 L/min) of heated and humidified oxygen. The high-flow gas helps to eliminate dead space in the nasopharynx, reducing the re-inhalation of carbon dioxide (CO_2) and increasing ventilation efficiency. Studies have shown that HFNO can reduce anatomical dead space by 30% to 40%, significantly improving oxygenation function [59]. Additionally, HFNO promotes alveolar recruitment by generating a certain level of positive airway pressure (typically 2 to 5 cmH_2O), which helps to reduce

Table 2. The mechanism of action, clinical outcomes, and major limitations of ATAAD treatment strategies.

Treatment strategy	Action mechanism	Clinical results	Main limitations
Prone position positive pressure mechanical ventilation	• Improves the ventilation/blood flow ratio; reduces dorsal alveolar collapse through lung recruitment in the gravity-dependent area	• PaO_2/FiO_2 increased $\geq$50 mmHg. • Reduced 28-day mortality by 22%.	Hemodynamic instability taboo; need a professional team operation
Nasal high flow oxygen therapy (HFNC) and NO inhalation	• Synergistic improvement of oxygenation: HFNC provides • Constant FiO_2 and reduces the work of breathing. iNO selectively expands the pulmonary vessels in the ventilation area and reduces pulmonary artery pressure	• Intubation rate decreased by 34% vs. HFNC alone. • PaO_2/FiO_2 increased by 38 $\pm$ 12 mmHg (vs. 22 $\pm$ 9 mmHg).	The cost of iNO is high; long-term use may cause methemoglobinemia
Venovenous extracorporeal membrane oxygenation (VV-ECMO)	• Complete or partial replacement of lung function; provides *in vitro* oxygenation/CO_2 clearance to achieve lung protective ventilation	• The 90-day survival rate of patients with refractory hypoxemia increased to 63%, but the bleeding complications increased by 2.1 times.	Need anticoagulant therapy; high equipment/technical threshold
Ulinastatin	• Inhibition of TNF-α, IL-6, IL-1β, and other signaling pathways reduces the release of inflammatory mediators	• The incidence of moderate to severe ARDS was reduced by 41%, but the dose-effect relationship was not clear.	Patients with renal insufficiency need to adjust the dose; however, there is a lack of long-term follow-up data
Methylprednisolone	• Inhibits the inflammatory cascade; blocks the nuclear translocation of NF-κB and reduces the production proinflammatory factors; stabilizing lysosomal membrane: reducing cell damage	• Early application (preoperative) increased the improvement rate of PaO_2/FiO_2 by 29%, but increased the risk of infection by 1.8 times.	Timing sensitive (postoperative use may increase blood glucose control difficulties)

NO, nitric oxide; TNF-α, Tumor Necrosis Factor-α; IL, interleukin; NF-κB, Nuclear Factor kappa-light-chain-enhancer of activated B cells.

atelectasis. As shown in Table 2. Clinical studies demonstrate that HFNO can increase the oxygenation (PaO_2/FiO_2) index by 20% to 30% [60]. Meanwhile, the warming and humidification functions of HFNO also decrease airway dryness and mucus viscosity, enhancing patient tolerance, comfort, and reducing the risk of re-intubation. NO is a selective pulmonary vasodilator that increases cyclic guanosine monophosphate (cGMP) levels by activating soluble guanylate cyclase (sGC), improving the V/Q ratio. Studies have indicated that NO inhalation can increase the oxygenation index by 30% to 50% [61]. Furthermore, NO also reduces intrapulmonary shunting by raising the arterial partial pressure of oxygen (PaO_2). Clinical research has shown that NO inhalation can decrease the intrapulmonary shunt rate by 20% to 30% [62]. The combination of HFNO and NO inhalation significantly reduces postoperative mechanical ventilation time in patients with hypoxemia [58]. The two synergistically improve oxygenation: HFNC provides constant FiO_2 and reduces respiratory work, while NO selectively dilates the pulmonary vessels in the ventilation area and reduces pulmonary artery pressure [63].

Extracorporeal Membrane Oxygenation

Extracorporeal membrane oxygenation (ECMO) is an advanced life support technique that provides *in vitro* gas exchange to enhance oxygenation and improve carbon dioxide clearance in patients with severe ARDS. For patients with severe hypoxemia following TAAD, ECMO is a critical alternative when conventional mechanical ventilation fails to enhance oxygen absorption effectively. ECMO facilitates oxygenation and CO_2 removal through an extracorporeal circulation system, either replacing or partially supporting lung function. The membrane oxygenator in ECMO effectively eliminates CO_2 from the blood while delivering O_2, significantly improving the arterial PaO_2. Studies have shown that ECMO can increase the oxygenation index (PaO_2/FiO_2) by 50% to 100% [64]. As shown in Table 2. Additionally, ECMO reduces the risk of VILI by lowering the pressure and tidal volume of mechanical ventilation, thereby preventing alveolar overexpansion and shear stress. Clinical studies indicate that ECMO can decrease mechanical ventilation pressure by 30% to 40%, significantly reducing the release of lung injury markers, such as IL-6 and TNF-α [65]. Furthermore, ECMO can provide cardiopulmonary support for patients with cardiac insufficiency by enhancing cardiac output and tissue perfusion in the veno-arterial (VA) mode [66].

Postoperative Drug Intervention

Drugs such as ulinastatin (UTI) and methylprednisolone have significant effects on alleviating inflammatory responses and improving lung function, particularly in the treatment of hypoxemia following TAAD. UTI is a broad-spectrum protease inhibitor with anti-inflammatory, antioxidant, and cytoprotective properties. UTI reduces the release of inflammatory mediators by inhibiting signaling pathways such as NF-κB, IL-6, and IL-1β, thereby alleviating systemic inflammatory responses and lung tissue damage [67]. Methylprednisolone is a potent anti-inflammatory and immunosuppressive glucocorticoid that reduces the synthesis and release of inflammatory mediators by inhibiting the NF-κB and AP-1 signaling pathways, subsequently diminishing the inflammatory response in lung tissue. Numerous clinical studies have demonstrated that UTI and methylprednisolone are effective in treating hypoxemia after TAAD. A study involving 120 patients following TAAD surgery showed that the oxygenation index in the UTI treatment group was significantly higher than that in the control group (PaO_2/FiO_2: 280 vs. 220 mmHg). Additionally, the duration of mechanical ventilation was reduced by an average of 2.5 days [68]. As shown in Table 2. However, the existing randomized clinical trial (RCT) dose range is too wide (300,000-1 million IU/day). Moreover, there is a lack of phase III dose exploration trials, and no dynamic adjustments are combined with biomarkers (such as the decline in IL-8 levels). The effects of different doses of ulinastatin, the timing of hormone use (preoperative vs. CPB), and the combination of ventilation strategies on hypoxemia should be further investigated.

Prognostic Implications of Postoperative Hypoxemia

Previous studies have shown that patients with hypoxemia have longer hospital and ICU stays than patients without hypoxemia. Some studies have also reported that patients with hypoxemia have longer hospital stays in the ICU and hospitals [69–71]. The prolonged length of ICU stay may be due to patients often requiring mechanical ventilation, non-invasive positive pressure ventilation, and nasal high-flow systems. Meanwhile, the prolonged hospital stay may be because hypoxemia prevented rehabilitation from progressing and made it difficult to investigate the effects of exertion on blood pressure elevation. Compared with the non-hypoxemia group, the hypoxemia group had longer ICU and hospital stays (median 20 days and 16 days, respectively; $p = 0.039$). The median durations were 7 days and 5 days, respectively $p < 0.001$ [72].

Prospect

Hypoxemia is a common serious complication after ATAAD, and its occurrence is related to various risk factors, including smoking history, obesity, inflammatory response, preoperative renal insufficiency, preoperative hypoxemia, obstructive sleep apnea syndrome, age, CPB, DHCA time, and intraoperative blood transfusion. There is a lack of standardized regimen for UTI dose and mechanical ventilation parameters in treatment, no clinical transformation of key biomarkers, and a lack of dynamic data on long-term lung function and neurological prognosis. Future re-

search should focus on conducting biomarker-driven precision intervention trials (such as stratified RCT to verify the optimal dose of ulinastatin); developing a dynamic prediction model for integrating intraoperative real-time monitoring data; meanwhile, we should be simultaneously incorporating interdisciplinary technologies and multi-center collaborative networks to build a closed-loop system of "monitoring-warning-intervention" to promote the transformation of clinical practice to a dynamic and precise model. Hypoxemia not only prolongs the mechanical ventilation and ICU treatment times of patients, but also significantly reduces their survival rate. Therefore, for ATAAD patients with risk factors of postoperative hypoxemia, comprehensive preoperative evaluation and perioperative management should be performed, and appropriate intervention measures should be taken to reduce the incidence of postoperative hypoxemia.

Conclusion

Hypoxemia is a common and severe complication following surgery for ATAAD. Its occurrence is associated with multiple risk factors, including smoking history, obesity, inflammatory response, preoperative renal insufficiency, preoperative hypoxemia, OSAS, age, CPB and DHCA, and intraoperative blood transfusion. Hypoxemia not only prolongs the duration of mechanical ventilation and ICU stay but also significantly reduces survival rates. Therefore, for ATAAD patients with risk factors for postoperative hypoxemia, comprehensive preoperative evaluation and perioperative management should be implemented, along with appropriate interventions to reduce the incidence of postoperative hypoxemia.

Author Contributions

JM, XM, SY and HL designed the research study. JM performed the research. JM analyzed the data. JM drafted the manuscript. All authors contributed to critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

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Conflict of Interest

The authors declare no conflict of interest.

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