Literature Review

Aeromedical Concern for Patients with Acute Respiratory Distress Syndrome (ARDS) during Air Medical Evacuation

Monica Djaja Saputera,*[1] Mia Elhidsi,[2] Retno Wibawanti[1]

[1]Aerospace Medicine Division, Department of Community Medicine, Faculty of Medicine, Universitas Indonesia, Jakarta
[2]Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Indonesia, Persahabatan General Hospital, Jakarta

Corresponding Author:
Monica Djaja Saputera | Aerospace Medicine Division, Department of Community Medicine, Faculty of Medicine, Universitas Indonesia, Jakarta | monicdjaja@gmail.com

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Abstract

Acute respiratory distress syndrome (ARDS) is a clinical syndrome of acute respiratory failure characterized by arterial hypoxemia and bilateral pulmonary opacities. In recent years, the incidence of ARDS has rapidly increased due to Coronavirus Disease 2019 (COVID-19). This has resulted in an increased need for patient referral to more adequate health care facilities using air ambulance through air medical evacuations. The purpose of this study is to synthesize the aeromedical concerns in ARDS patients undergoing air medical evacuation, focusing on physiological challenges and mechanical ventilation issues in flight. Acute hypobaric hypoxia that occurs during air medical evacuation inside the cabin (altitude 6,000–8,000 ft) will trigger a hyperventilation response that can lead to respiratory alkalosis. This condition will not only worsen the hypoxemia state but also deteriorate the patient's clinical symptoms. Additionally, changes in altitude and atmospheric pressure inside the aircraft cabin also pose risks to patients using invasive mechanical ventilation. Not only can it disrupt the settings of medical equipment, but it can also cause pulmonary barotrauma, which can lead to pneumothorax. To prevent these various impacts, air medical evacuation must be carried out by a multidisciplinary team with considerations for the use of medications and manoeuvres for invasive mechanical ventilation. The key parameters to assess fitness-to-fly among ARDS patients include the vital signs, heart rhythm, tidal volume, end-tidal carbon dioxide, neuromuscular blockade, inspiratory pressure peak, along with some parameters related to the use of invasive mechanical ventilation, such as oxygen pressure, FiO_2, atmospheric pressure, power status, turbine function, and malfunction indicator.

Keywords: acute respiratory distress syndrome, air ambulance, air medical evacuation, hypobaric hypoxia, mechanical ventilation

INTRODUCTION

The vastness of Indonesia can potentially cause health problems for citizens of 284.44 million people.[1] Although existing regulations already state that access to health care facilities is a right for every citizen, not all health care facilities are well-distributed across all areas.[2]

Limited health care facilities and inadequate access in remote areas are the most common challenges for health care workers to provide the best health care.[3]

One of the most challenging health problems for every country is acute respiratory distress syndrome (ARDS), which causes morbidity and mortality in critically ill patients.[4] A study of 29,144 patients undergoing treatment in the Intensive Care Unit (ICU) in Europe reported that the prevalence of ARDS during the study period was 10.4%, with a mortality rate up to 40%.[5]

In China, a study of 18,793 patients undergoing treatment in the ICU also reported that 672 patients met the Berlin ARDS criteria. The mortality rate in this study reached 46.3%, with the most common predisposing factor being pneumonia (77%).[6] Meanwhile, in Indonesia, several studies reported that the mortality rates of ARDS patients were higher compared with those in previous studies. The mortality rates of ARDS patients in Indonesia were 71%–75.3%.[7,8]

The morbidity rate of ARDS was also reported to have increased significantly during the Coronavirus Disease 2019 (COVID-19) pandemic.[9] Several studies in European countries illustrate the incidence of ARDS in COVID-19 patients, prompting local governments to carry out medical evacuations. During the pandemic, air medical evacuation has become an option to relocate ARDS patients to more adequate healthcare facilities.[10–12]

During the one year of the pandemic (March 2020 – March 2021), there were several studies that conducted air medical evacuations of 96 patients. Most patients did not experience any problems during the flight and were able to reach the destination hospital in stable condition.[10–12] Although it is relatively safe, the risk of health disturbance during flight remains. This is because of the unique environment inside the aircraft cabin.

Therefore, this article aims to synthesize the aeromedical concerns in patients with ARDS undergoing air medical evacuation, with a focus on physiological challenges as well as prevention and management of mechanical ventilation issues in flight.

METHOD

This narrative review was conducted by searching the relevant literature. Relevant studies were identified using electronic databases such as PubMed and Embase. The search terms included air medical evacuation, air transportation, air ambulance, ARDS, COVID-19, mechanical ventilation and hypobaric hypoxia. The publication timeframe was limited to approximately the past 10 years.

ACUTE RESPIRATORY DISTRESS SYNDROME

Since it was introduced in 1967, the definition of ARDS has undergone a series of updates.[13,14] The latest update of the definition of ARDS was made by the American Thoracic Society (ATS) in 2024. ARDS is a clinical syndrome of hypoxemic acute respiratory failure that occurs due to

acute and diffuse pulmonary inflammation in the lungs.[14] Various predisposing factors usually trigger this condition. Some direct predisposing factors of ARDS are pneumonia, aspiration, inhalation injury, etc., and indirect predisposing factors of ARDS include non-pulmonary infections, trauma, blood transfusions, burns, shock, etc.[13–15]

Acute respiratory distress syndrome occurs when exposure to pathogens or various predisposing factors causes injury to the alveolar epithelium or endothelium. This activates alveolar macrophages to release inflammatory mediators, with neutrophils dominating the response.[15] This inflammatory reaction will increase the permeability of the alveolar wall, which can lead to the accumulation of oedematous fluid in the alveolar space. This excessive accumulation will cause alveolar collapse and lead to an acute lung injury.[14,15]

The symptoms of ARDS usually occur within one week after the exposure. Typical clinical manifestations of ARDS are arterial hypoxemia and bilateral pulmonary opacities, which are associated with increased shunting and alveolar dead space.[14] In contrast to the Berlin criteria for ARDS, which use blood gas analysis to measure the hypoxemic condition, the new guideline from ATS adds pulse oximetry to measure the hypoxemic condition.[13,14]

Some indicators measured in blood gas analysis under the Berlin criteria are the partial pressure of oxygen in arterial blood (PaO_2)/fraction of inspired oxygen (FiO_2), and the peripheral oxygen saturation (SpO_2) measured by pulse oximetry. However, the use of pulse oximetry is not recommended for patients with a history of haemoglobin abnormalities, as it can falsely measure SpO_2. As is known, the hypoxemic criteria according to the new guidelines from ATS are PaO_2/FiO_2 <300 mmHg or SpO_2/F_iO_2 <315 (note: SpO_2 <97%).[14]

In addition to hypoxemic conditions, the diagnosis of ARDS also needs to be strengthened by bilateral pulmonary opacities on chest X-ray or CT scan.[14] An additional imaging examination that is also recommended is ultrasound.[14,16] Lung ultrasonography (LUS) is chosen to help establish the diagnosis of ARDS in health care facilities that have limited advanced imaging.[16] The most common finding in ultrasound is a loss of lung aeration that cannot be explained by other causes.[14,16] This examination can be considered a feasible and recommended assessment method in selected situations, especially during critical care transport.

As a non-invasive and portable imaging modality, LUS has several advantages when used in air medical evacuation, including real-time monitoring of patient conditions and assisting in the early detection of pneumothorax during flight. However, the use of LUS still faces limitations related to the availability of equipment, along with adequately trained and competent personnel. Shekhar et al emphasized that LUS implementation requires adequate personnel competence because LUS assessment accuracy is highly dependent on operator skill and experience.[17] Therefore, the use of LUS

requires consideration of the availability of equipment, training and resource readiness.

Based on the latest guidelines, management of ARDS has involved the use of medications and medical devices. Recommended medications include corticosteroids and neuromuscular blocking agents, while the recommended medical devices are Veno-venous extracorporeal membrane oxygenation (VV-ECMO), mechanical ventilation with a restriction of tidal volume of 4-8 mL/kg with a plateau pressure of $\leq$30 cmH_2O and prone position.[18]

Among ARDS patients, the use of oxygen can be with or without intubation. If the patients are non-intubated, they will receive non-invasive respiratory support such as continuous positive airway pressure (CPAP), high-flow nasal oxygen (HFNO), or conventional oxygen therapy.[18–21] The use of CPAP and HFNO is usually preferred compared to the use of conventional oxygen therapy. This is because of the lower risk of the need for intubation in the future. Furthermore, close monitoring is needed to detect signs of respiratory failure.[22]

On the other hand, if the patients are intubated, some of the complications may arise due to use of invasive mechanical ventilation.[22] However, the benefit of invasive mechanical ventilation is that it allows gas exchange while providing an opportunity for the lung to recover.

AIR MEDICAL EVACUATION

History

Air medical evacuation is the act of relocating sick and injured patients using an air ambulance, and it began in the early 20th century. The first air ambulance was designed by two American soldiers at Fort Barrancas in 1910, and could only fly as far as 500 meters at an altitude of 100 ft. Then, the air ambulance concept continued to develop, and the first air ambulance that successfully supported the relocation process was built in France and called the Dorand AR II.[22,23]

One year later, the United States also co-designed the Curtiss JN-4 Jenny into an air ambulance equipped with stretchers.[22] At that time, air ambulances were widely used by military soldiers to transport and relocate sick and injured soldiers during the war. Furthermore, rotary-wing aircraft (helicopters) began to be widely used around 1950, when the Korean War broke out.[23] Helicopters were chosen because of their ability to evacuate patients in remote areas.

The use of air ambulances was very common in the military and finally started to shift to civilian society right after the Vietnam War, in 1973.[22,23] There are many commercial providers who provide various types of air medical evacuation, such as scene response, transfers, speciality care and evacuation.[24]

Scene response usually happens in emergencies where the responder needs to evacuate the patient in remote areas, while transfers and speciality care are the evacuation of patients between hospitals that generally require treatment with more advanced facilities. Generally, speciality care is the one that requires medical devices, such as mechanical ventilation,

extracorporeal membrane oxygenation, etc., so it should be directly supervised by the health care workers.[24]

Meanwhile, evacuation is the transfer of patients who require further treatment to a referral hospital, both nationally and internationally.[24] In addition, this kind of evacuation can also be carried out for repatriation or travellers who get sick while travelling to another country.

Based on the previous case reports during the COVID-19 pandemic, it was reported that there were several collective air medical evacuations held by the military air forces in Europe. French Air Force reported that 36 ARDS patients on mechanical ventilation underwent air medical evacuation for interhospital transfer.[12] Other studies with the same purpose of air medical evacuation also reported this among 55 ARDS patients in France.[10,11] From these studies, we can summarize that the purpose of all cases evacuated by air ambulance during the pandemic was interhospital transfer.

Types of Air Ambulance

There are two commonly used types of air ambulance: fixed-wing aircraft and rotary-wing aircraft.[22,23] Many fixed-wing aircraft, such as commercial airplanes and business jets, are usually designed with pressurized cabins. Every fixed-wing aircraft can cruise at an altitude of 30,000-50,000 ft. Rotary-wing aircraft, such as helicopters, are not usually designed with pressurized cabins because they operate at lower altitudes, in the range of 10,000 ft.

Some aspects that need to be considered when choosing the type of aircraft are the purpose of evacuation, the location and the necessary medical equipment.[23] Airplanes are generally chosen for air medical evacuation with longer distances (more than 321 km) and longer flight durations (more than 3 hours). In addition, airplanes are also preferable if the evacuation requires advanced medical devices.[22,23]

Meanwhile, helicopters are generally chosen for the evacuation of patients in emergencies where the location is difficult to reach and requires a vertical take-off and/or landing (such as sea, mountainous areas, construction areas, etc.). Helicopters are also more suitable if the distance is less than 321 km. However, the biggest disadvantage of using helicopters in air medical evacuation is their dependence on weather conditions.[22,23]

Physiology of The Aviation Environment

The aviation environment has unique characteristics compared with the ground environment. The main difference is the difference in altitude. To provide the comfort and safety of passengers, every fixed-wing aircraft is usually designed with a pressurized cabin.[25,26]

The pressurized cabin will be set within the physiological zone (6,000–8,000 ft), which allows humans to breathe without the need for oxygen supplementation.[25–27] It will remain constant even though the fixed-wing aircraft will be cruising at altitudes around 30,000-50,000 ft, with an average cruising altitude of around 35,000 ft.[26]

Table 1. Effect of Altitude on Atmospheric Pressure, PO_2, PaO_2 and FiO_2

Altitude (ft)	Atmospheric Pressure (mmHg)	PO_2 (mmHg)	PaO_2 (mmHg)	FiO_2 (%)
0	760	159.6	99.7	21
6,000	609	127.9	68	16.6
8,000	564	118.4	58.6	15.1
10,000	523	109.8	50	14
20,000	349	73.3	13.4	8.9

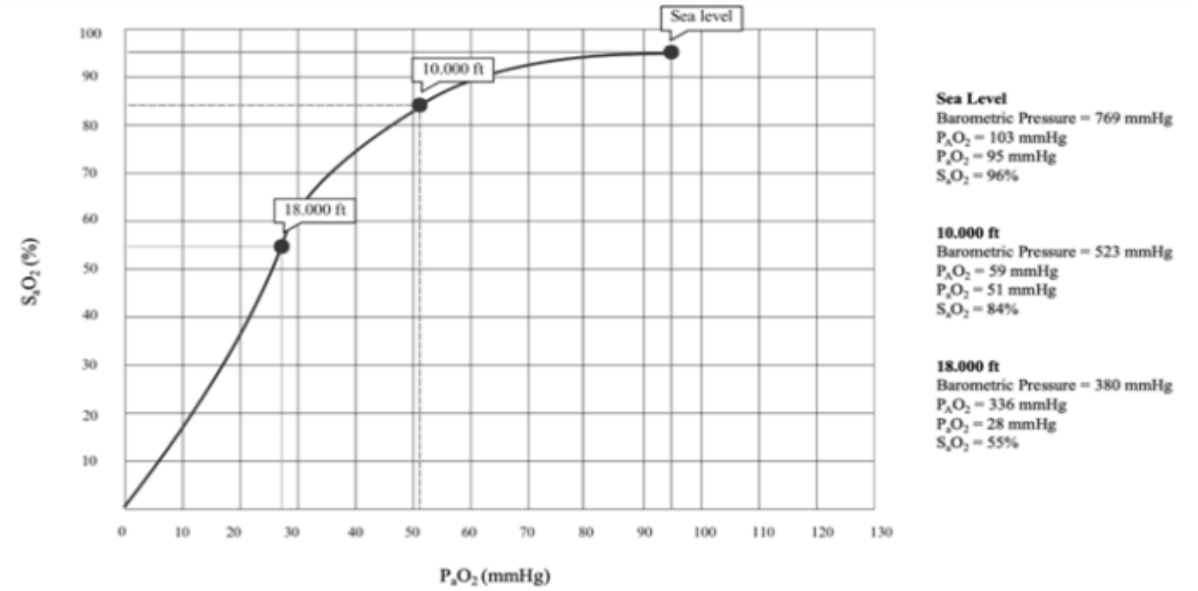


Figure 1. Oxyhaemoglobin Saturation Levels Relative to Different Altitudes

In addition, the change in altitude is also directly related to the change in atmospheric pressure and partial oxygen pressure (PO_2). As the altitude increases, the atmospheric pressure, PO_2 and PaO_2 decrease, as shown in Table 1.[25,26]

At sea level, the atmospheric pressure is 760 mmHg with FiO_2 of 21%, PO_2 of 159.6 mmHg and PaO_2 of 99.7 mmHg. While at a cabin altitude of 8,000 ft, the atmospheric pressure will decrease to 564 mmHg, FiO_2 to 15% and PaO_2 to 53-64 mmHg.[25,26] This condition will induce mild hypoxia, but is well tolerated by most healthy passengers.[28] This condition still lies on the flat part of the oxyhaemoglobin dissociation curve with PaO2 of 58.6 mmHg, and the SaO2 remains in the range of 90%, as shown in Figure 1.[25,26]

However, it will decrease slightly in passengers with underlying health conditions, especially in passengers with anaemia or any other cardiovascular-pulmonary disease. Passengers with underlying pulmonary disease may already have a low SaO_2 at sea level. This will lead to a steep decline in SaO_2 in the cabin environment and can induce symptoms.[26]

AEROMEDICAL CONCERN

The Effect of Cabin Environment On ARDS

Exposure to acute hypoxia during flight will lead to activation of peripheral chemoreceptors, causing hyperventilation.[25,26,29,30] Hyperventilation is the normal response to hypoxic pressure

(PaO_2=55-60 mmHg), increasing the respiratory frequency to meet oxygen needs and expel excess carbon dioxide. However, prolonged hyperventilation will result in respiratory alkalosis that can shift the oxyhaemoglobin dissociation curve to the left.[25,26]

Under normal conditions, the alveoli have an important role in exchanging oxygen and carbon dioxide. However, in patients with ARDS, changes in the anatomical structure of the alveolus will have an impact on perfusion and diffusion disorders, so that the patient is in a hypoxemic condition.[14,15]

Exposure to the hypoxic condition during flight can aggravate the patient's clinical condition due to inadequate hyperventilation, which directly also leads to the worsening of the patient's clinical condition.[26] Worsening clinical condition among ARDS patients may manifest as a progressive respiratory failure due to impaired gas exchange and deterioration of lung function. This condition could initially cause hypocapnia and lead to respiratory alkalosis.

Persistent hypoxemia among ARDS patients, along with exposure to hypobaric hypoxia during flight, can also trigger hypoxic pulmonary vasoconstriction. This will increase pulmonary vascular resistance and lead to pulmonary hypertension. The increase in right ventricular load caused by these conditions can lead to right ventricular dysfunction and cardiovascular complications.[29]

Apart from those circumstances, there is a risk of pathogen transmission from HFNO and CPAP use during flight. This warrants special attention and investigation because the unique characteristic of the cabin environment is a confined space with dedicated air circulation systems. Clinical warnings are warranted regarding the potential for aerosolization of pathogens during the use of high-flow oxygen therapy or non-invasive ventilation in the cabin, as well as the importance of using adequate viral filtration systems.

These concerns actually arose during COVID-19 and remain relevant and can be applied in the air medical evacuation situation for patients with infectious respiratory diseases. The experience with air medical evacuation of COVID-19 patients suggests that the use of portable medical isolation units can be a mitigation strategy to reduce the risk of pathogen exposure during transport. Ravi et al demonstrated that these protocols allow the air medical evacuation of infectious patients safely while maintaining the protection of the medical crew and air crew as part of the team.[31]

The Effect of Cabin Environment On The Use of Invasive Mechanical Ventilation

The use of invasive mechanical ventilation in ARDS patients who will undergo an air medical evacuation requires some special consideration in terms of aviation physiology.[22] This generally relates to the effect of the cabin environment on the use and arrangement of medical equipment that may threaten

patient safety.[18] There are several physical laws involved in aviation physiology, such as Boyle's law, Dalton's law, Gay-Lussac's law, and Henry's law.[18,25,26]

Boyle's law states that at a constant air temperature, the volume of a gas is inversely proportional to the atmospheric pressure ($P_1 \times V_1 = P_2 \times V_2$).[18,25,26] It has an important role in the regulation of the cuff pressure of the endotracheal tube or the laryngeal tube, as well as the regulation of the tidal volume in mechanical ventilation. If invasive mechanical ventilation is used, the ventilation mode settings (such as tidal volume and positive end-expiratory pressure/PEEP) need to be closely monitored.[18,22,25,26] This is closely related to the risk of pulmonary barotrauma during flight, which can lead to pneumothorax, pneumomediastinum, and subcutaneous emphysema.[22]

Due to these possible complications, pre-flight preparation and in-flight emergency management strategies are crucial. In patients with a complication of pneumothorax during flight, chest tube placement should be performed with attention to several related issues. In flight, the chest tube should be connected to a reliable drainage system that allows continuous evacuation of air while preventing backflow into the pleural cavity. One-way valve-based drainage systems or waterless drainage systems are preferred over conventional water-seal systems. The main reason is that they are safer and less prone to disruption during air medical evacuation.[32]

Meanwhile, in the human body, another effect of atmospheric pressure is the increase in gas volume during flight, which can cause trapped gas. Trapped gas is a common phenomenon that occurs in various hollow organs, such as ears, paranasal sinuses, teeth, and gastrointestinal organs.[18,25,26]

In addition to Boyle's law, another law that needs to be applied in conducting an air medical evacuation is Dalton's law. This law states that the total pressure of a mixture of gases is equal to the sum of the partial pressures of its constituent gases ($P = P_1 + P_2 + P_3 + P_4 + \ldots + P_n$). Meanwhile, the Gay-Lussac law is a law that plays a role in regulating the pressure in the oxygen cylinder, i.e. the pressure will increase as the temperature increases.[18,25,26]

These two laws have a big role in calculating oxygen needs during flight. The calculation of oxygen demand during flight will be based on the calculation of PO_2, atmospheric pressure at the expected altitude (P_B) and FiO_2. The formula of the calculation of PO_2 is:[18]

$$PO_2 = P_B \times FiO_2$$

After calculating PO_2 requirements, the conversion rate of airflow velocity in the provision of oxygen in flight is generally 1.3 times higher than on the ground. This is important because it relates to the supplies that must be prepared for the flight.

Strategies to reduce the effect of the cabin environment on mechanical ventilation include restricting cruising

altitude, adjusting tidal volume, performing PEEP manoeuvres, placing the patient in a prone position, using ECMO, and administering medications (such as corticosteroids, neuromuscular blocking agents and pulmonary vasodilation with inhalation of nitric oxide).[22,33–36] The correction factor in ARDS patients, according to their categorization during flight, needs to be adjusted to their cruising altitude. The formula that can be used to calculate the correction factor at an altitude >3280 ft:[14]

$$\frac{(PaO^2 \text{ or } SpO_2)}{FiO_2} \; x \; \frac{atmospheric\ pressure\ at\ a\ certain\ altitude}{760}$$

The expected ventilation target in ARDS patients is 4-8 mL/kg predicted body weight with a plateau pressure of <30 cmH_2O.[18]

AEROMEDICAL CONSIDERATIONS: PASSENGERS' FITNESS TO FLY

According to medical guidelines from the International Air Transport Association (IATA) in 2020, there are no specific requirements for passengers experiencing ARDS, but there are specific requirements for passengers who use mechanical ventilation. Critically ill passengers who use mechanical ventilation need to be assessed by a doctor who has experience in the field of aviation. In addition, the use of invasive and non-invasive respiratory support also needs to be considered to determine the need for medical equipment during evacuation.[37]

Furthermore, the decision on fitness to fly will be discussed with the airline's medical personnel. If the cause of ARDS is related to a respiratory tract infection, it is necessary to ascertain whether the disease has a risk of transmission through airborne transmission or not.[37]

The two main aspects that need to be considered by the medical team during the flight are the patient and medical equipment aspects. Some medical examinations that need to be considered in ARDS patients are vital signs (including blood pressure, respiratory rate, heart rate, SaO_2, and body temperature), electrocardiogram, tidal volume, and end-tidal carbon dioxide, neuromuscular blockade and inspiratory pressure peak.[38]

Meanwhile, other things that need to be considered in the aspect of invasive mechanical ventilation equipment are oxygen pressure, FiO_2, power status, turbine function and malfunction indicator.[38] For the non-invasive respiratory support equipment, some things that need to be considered are respiratory frequency, SaO_2, PaO_2/FiO_2 ratio, PCO_2, expired tidal volume and respiratory effort assessment.[21]

Fitness-to-fly assessment for ARDS patients should be performed on an individualized basis and not based on a single absolute parameter. Several clinical parameters need to be considered, including disease severity, haemodynamic stability, the need for ventilatory support, and the risk of in-flight emergency.

Evaluation of oxygenation status is also a crucial component that needs special attention and includes the PaO_2, the PaO_2/FiO_2 ratio, and the calculation of the need for oxygen supplementation, as well

as the respiratory support device that will be used. Therefore, the decision to perform an air medical evacuation for ARDS patients must involve a multidisciplinary approach that takes into account the patient's clinical condition, the capacity of the transport facility, and the clinical judgment of the treating and evacuation team.

FUTURE AIR MEDICAL EVACUATION PROTOCOL IN INDONESIA

As we know, there is no specific regulation governing the air medical evacuation protocol in Indonesia. Unlike other countries, Indonesia only has a guideline on the specifications of air ambulances.[37] Meanwhile, guidelines regarding the personnel involved in air ambulance services have not yet been established.[37,39]

According to the study conducted by Ayuningtyas et al in 2024, it was stated that the biggest obstacle to air medical evacuation services in Indonesia is the lack of regulations. Meanwhile, other obstacles that disrupt air medical evacuations are inadequate infrastructure and the limited number of medical personnel who have the appropriate qualifications and experience.[30]

The current situation shows that the medical personnel who join air medical evacuations are mostly general practitioners. Sometimes it involves aviation specialists, related specialists, and nurses. The aviation specialist, along with the doctor in charge, is responsible for determining fitness to fly. Besides medical personnel, the researchers also stated that the administration team plays a major role in taking care of field technicians and coordinating with related stakeholders.[30]

For the air medical evacuation of ARDS patients, the authors propose the following protocol, which involves the pulmonologist and other related specialists (Figure 2).

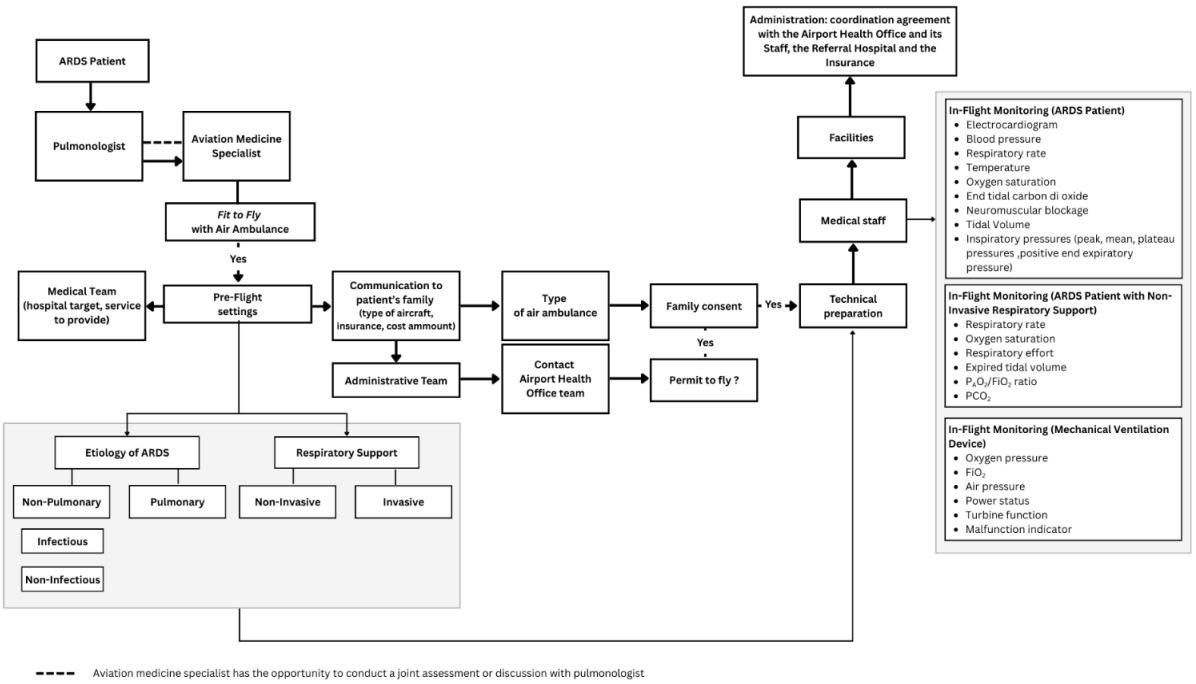


Figure 2. Air Medical Evacuation Protocol for ARDS Patients in Indonesia[30,31]

CONCLUSION

Air medical evacuation of ARDS patients requires a comprehensive risk evaluation carried out by the multidisciplinary team (including an aviation specialist, pulmonologist and any other related specialists) and an individualized, case-by-case decision. Several factors, such as the patient's clinical condition, respiratory support device and emergency in-flight preparation, are the primary considerations in determining fitness-to-fly in these patients. In the future, the development of a formal protocol based on Indonesian conditions is needed to support clinical decision-making, optimize transport preparation, and enhance patient safety during air medical evacuation.

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