Review Article

Postperfusion lung syndrome: Respiratory mechanics, respiratory indices and biomarkers

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Submission: 09-10-2013
Accepted: 02-07-2014

Abstract:

Postperfusion lung syndrome is rare but lethal. Secondary inflammatory response was the popularly accepted theory for the underlying etiology. Respiratory index (RI) and arterial oxygen tension/fractional inspired oxygen can be reliable indices for the diagnosis of this syndrome as X-ray appearance is always insignificant at the early stage of the onset. Evaluations of extravascular lung water content and pulmonary compliance are also helpful in the definite diagnosis. Multiorgan failure and triple acid-base disturbances that might develop secondary to postperfusion lung syndrome are responsible for the poor prognosis and increased mortality rather than postperfusion lung syndrome itself. Mechanical ventilation with low tidal volume (TV) and proper positive end-expiratory pressure can be an effective treatment strategy. Use of ulinastatin and propofol may benefit the patients through different mechanisms.

Key words:

Acid-base imbalance, cardiopulmonary bypass, mechanical ventilators, multiple organ failure, respiratory insufficiency

Access this article online

Quick Response Code:

Website: www.thoracicmedicine.org

DOI: 10.4103/1817-1737.150736

In 1994, the American-European Consensus Conference on acute respiratory distress syndrome (ARDS) set the criteria for the diagnosis of acute lung injury (ALI) and ARDS.[1] Both ALI and ARDS were characterized by an acute onset, bilateral pulmonary infiltrations on chest X-ray, and pulmonary wedge pressure <18 mmHg. The distinctive criterion for both disorders was arterial oxygen tension/fractional inspired oxygen (PaO_2/FiO_2) <300 mmHg in ALI, while PaO_2/FiO_2 <200 mmHg in ARDS.

ALI is a leading cause of death of patients with severe trauma, infection and complex operations.[2] Postperfusion lung syndrome, that is ARDS that develops early after cardiopulmonary bypass (CPB), is a rare but refractory complication. In the early years, it was reported that the incidence of postperfusion lung syndrome was 1-2%[3], but the mortality could be 91.6%, 70% of which were with multiorgan failure.[2] Postoperative hypoxemia after CPB was mostly subclinical symptoms in response to functional alterations. Only 2% of the patients developed ARDS.[2] Although severe hypoxemia after open heart surgery under CPB was rare, it remains the important cause leading to patients' death.[4]

Mechanisms

The underlying mechanisms still remain uncertain. The "secondary lung injury" theory was the popularly accepted explanation of lung injury after CPB of today.[5] Systemic inflammatory response was considered an inherent intriguing factor and target organ dysfunctions may develop and may cause multiorgan failure. Traumatic ARDS was considered the pulmonary manifestation of systemic inflammatory reactions. The operation is a form of severe trauma, an intriguing factor of ARDS in addition to the input and output of massive fluid during the operation. Thus, postoperative patients are high-risk population of ALI/ARDS. Once ALI/ARDS occurs, disorders of homoeostasis may be induced by acute hypoxia, and further leads to sequential multiorgan dysfunctions.[6,7] Complement is another major factor in the inflammatory response CPB. Complement may be activated by either the classical or alternate pathway during CPB and protamine reversal.[8] Activation of complement products may cause aggregation of granulocyte and hemolysis.[8]

In cardiac surgery, systemic inflammatory response syndrome secondary to contact of the blood components with the artificial surface of the bypass circuit, ischemia-reperfusion injury, endotoxemia, and operative trauma, was considered the prominent etiology[2], leading to activation of complements, neutrophils, monocytes, macrophages, platelets, and endothelial cells, and cause stasis with the lungs. The neutrophils were further activated with the occurrence of hypoxia, hemorrhage, ischemia-reperfusion injury, and release of endotoxins,

releasing oxygen free radicals and proteases and resulting in lung injury. After the operation, patients may have gas exchange disorder, respiratory resistance alteration, including increase of alveolar-arterial oxygen pressure difference [$P(A\text{-}a)O_2$], increase of intrapulmonary shunt and increase of pulmonary vascular resistance. Damage of basal membranes of alveolar capillaries, increased permeability and respiratory membrane thickening negatively influenced the gas exchange.

Risk factors

ARDS is frequently a part of a multiorgan failure complexity where pulmonary injury is not necessarily the cause of death.[2] Pulmonary morphology, respiratory mechanics and mechanical ventilation strategies can be different between ARDS caused by pulmonary and extrapulmonary etiologies.[9] The pulmonary ARDS at an early stage is characterized pathologically by increased pulmonary capillary permeability, interstitial edema and decreased alveolar surfactants mediated by inflammatory mediators and toxins usually manifesting pulmonary consolidation; whereas the extrapulmonary ARDS was often a result of an indirect alveolar damage from pathogens and the toxins, and therefore alveolar edema and fibrosis and accumulations of massive necrotic tissues, microorganisms, neutrophils and erythrocytes leading to collapsed alveoli are the main pathological findings. Hypoxemia of the extrapulmonary ARDS may show good response to mechanical ventilation and positive end-expiratory pressure (PEEP) therapy, however, the pulmonary ARDS did not.[10]

CPB may cause pulmonary dysfunction, which can be proven by the detections of alveolar-arterial oxygenation gradient, intrapulmonary shunt, degree of pulmonary edema, pulmonary compliance and pulmonary vascular resistance.[2] Predisposing risk factors for postperfusion lung syndrome were age, cardiac and renal function impairments, pulmonary hypertension, prolonged CPB duration and postoperative dopamine and milrinone requirements. Prolonged crossclamp and CPB times primarily trigger systemic inflammatory reactions and pulmonary ischemia-reperfusuion injury in patients receiving a cardiac operation with the aid of CPB. This is particularly prominent in patients in a poor condition.[11] Hypoxemia is commonly complicated the cardiac operation, which is usually disclosed by low PaO_2 and low PaO_2/FiO_2.[8]

Byrick and Noble[12] examined the role of the oxygenator in the postperfusion lung syndrome on 16 patients undergoing coronary artery bypass with a bubble and 14 similar patients with a membrane. Postoperative pulmonary dysfunction in the bubble oxygenator group was characterized by increased pulmonary vascular resistance and extravascular lung water (EVLW). EVLW increase was noted on three successive measurements after bubble oxygenation, whereas no EVLW increase was found at any measurement time in the patients with the use of the membrane oxygenator. The postoperative pulmonary vascular resistance and EVLW were significantly elevated in the bobble group than in the membrane group, indicating that the a membrane oxygenator was associated with greater blood component damage in the lung.[12] Additionally, bubble oxygenators were associated with more leukocyte sequestrations.[13]

Pulmonary hypertension predisposes pulmonary vascular wall thickening, increased pulmonary resistance, decreased cardiac index and decreased pulmonary capillaries. Poor elasticity of the lung tissues, increased pulmonary capillary permeability with pulmonary interstitial edema and alveolar collapse are easily present as mediated by numerous inflammatory mediators in elderly patients. Therefore, functional residual capacity increased with age, however, pulmonary compliance would not significantly decrease and no obvious pulmonary edema displays on chest X-ray films but only hypoxemia. Heart dysfunction especially of the left heart can be associated with increase of the left atrial pressure and pulmonary microcirculation. Mild pulmonary interstitial edema may be compensated however, decompensation may develop in the presence of alveolar edema, pulmonary parenchymal consolidation and heart dysfunction resulting in ARDS. Preoperative heart failure was therefore a risk factor of postoperative hypoxemia. Use of more than 3 immunosuppressive agents, arterial carbon dioxide tension ($PaCO_2$) $\geq$ 50 mmHg, $PaO_2/FiO_2 \leq$ 150 mmHg, acute physiology and chronic health evaluation (APACHE) II $\geq$19 points were reported to be independent risk factors of poor prognosis of ARDS patients.[14]

Bacteremia and hypotensive episodes regardless of CPB duration can be risk factors for postperfusion lung syndrome in patients receiving cardiac surgical procedures.[2] The duration of heart operation is an important factor for mechanical ventilation but not necessarily for the development of postperfusion lung syndrome. With operation duration increases, colloidal osmotic pressure decreases and EVLW increases. Sustained aspiration of dry cold pure oxygen predisposes alveolar collapse, diffuse atectasis, oxygen exchange abnormalities, and ventilation/perfusion imbalance requiring mechanical ventilation. Reduced plasma albumin level may result in decreased colloidal osmotic pressure, increased EVLW and decreased PaO_2/FiO_2. Therefore, plasma albumin can be an independent predictive factor for mechanical ventilation, and a predisposing risk factor for prolonged ventilation and even extubation failure.

Respiratory indices

PaO_2/FiO_2, PaO_2 and alveolar-arterial oxygen pressure ratio [$P(A/a)O_2$] are indicators of pulmonary gas exchange. Due to the oxygen therapy in most the postoperative patients, PaO_2 is easily influenced by aspiration, territory difference and age. $P(A\text{-}a)O_2$ reflects the gas exchange (oxygen intake) function, more sensitive than PaO_2. The PaO_2 changes are closely associated with FiO_2, therefore PaO_2/FiO_2 is more reliable than PaO_2.[15] PaO_2/FiO_2, also termed oxygen index, is a common indicator of pulmonary gas exchange, and a main diagnostic index of diagnosing ARDS. Its normal range is 430-560 mmHg. PaO_2/FiO_2 is a stable index especially when $FiO_2 > 0.50$ and shunting rate >30%.[2] It is the most preferable non-traumatic pulmonary oxygen index, reflecting pulmonary vascular bed and alveolar injuries. The increase of PaO_2/FiO_2 may indicate oxygenation exchange abnormalities secondary to lung injury, with an etiology of ventilation/perfusion mismatch, pulmonary interstitial disorder and pulmonary edema and diffuse disorder as a result of ARDS. The PaO_2/FiO_2 ratio in patients with moderate shunts (<30%) varied considerably with alteration in FiO_2. Patients with larger shunts (> 30%)

had greater PaO_2/FiO_2 ratios at low FiO_2; while the PaO_2/FiO_2 ratios decreased to relatively stable values at FiO_2 values of > 0.5.[16] It is of high sensitivity and specificity. However, doubts arose after the establishment of the criteria. Therefore, how PaO_2/FiO_2 relates to patients' survival is still uncertain. It has been noted that a high $PaO_2/FiO2$ at the onset of ARDS was an independent risk factor of the patients.[17] Bone *et al*.[18] found the PaO_2/FiO_2 values showed significant differences between the survived and deceased only at 24 hours after traditional mechanical ventilation. Miller *et al*.,[19] found, by observing 343 ARDS patients that elder patients (>65 years) had a mortality of 51.9% and that of those younger than 65 years was 41.7% without significant differences. Villar *et al*.[20] proposed that the criteria could not reflect the severity and progression of the disease, and all four diagnostic criteria $PaO_2/FiO_2 \leq 200$ mmHg irrelevant of the PEEP level, bilateral pulmonary infiltrates and no evidence of left heart failure were of poor specificity. The differences in the respiratory severity index during the first 24 hours of inclusion, PaO_2/FiO_2 ratio at baseline and at 24 hours, maximum plateau airway pressure, maximum level of PEEP and number of organ system failures during the Intensive Care Unit stay were statistically significant. Pulmonary functional disorder post-CPB was predominantly oxygen exchange disorder, showing a reduced PaO_2, increased $P(A\text{-}a)O_2$ and respiratory index (RI).

RI is the ratio of $P(A\text{-}a)O_2$ to PaO_2. It is a simple and reliable indicator for the evaluation of post-CPB pulmonary function. Its normal range of RI is 0.1-0.3. An increased RI may represent oxygen exchange dysfunction. RI may reach a peak value 15 min in patients after open heart operation followed by a gradual reduction showing a minimal value at 90 min. A second peak appeared at 12 hours after the operation, and then returned to normal range gradually. Moreover, pulmonary water content increased significantly after CPB with decreased pulmonary compliance, surface active substances and functional residual capacity and diffuse alveolar atectasis. As a result, postoperative RI increased.

RI is superior to PaO_2 and PaO_2/FiO_2 in the early diagnosis of ARDS. Acute respiratory failure can be divided into three types: ventilation dysfunction, ventilation/perfusion imbalance and intrapulmonary shunting types. During the course of disease, three types may coexist or present independently reciprocal transformation. The respiration failure of ARDS belongs to the third type — intrapulmonary shunting type. RI ≥ 2.5 is a high risk indicator for ARDS, and RI ≥ 3.0 can be a diagnostic criterion for early diagnosis of ARDS. RI < 2.5 by repeated blood-gas analysis with 24 hours is one of safe indicators for tracheal extubation.[21] RI decrease indicates amelioration of the patient condition, while if RI keeps high or even increase, it means the patient was in a critical condition.[22] Postoperative sustained hypoxia with significant increased RI may lead to the diagnosis of ARDS. In extreme cases, hypoxia persists for over 48 hours with a sustained high RI, the patients are prone to develop low output syndrome and acute renal failure. It was reported that two patients were extubated successfully when RI was <1.45, but died of heart failure and renal failure on postoperative days 7 and 9, respectively. It illustrated that prolonged RI increase is not only a critical indicator but may have negative impact on other organs leading to eventual multiorgan failure.[23]

Respiratory mechanics

At the early stage of ALI, mechanical ventilation may prevent from the further development of respiratory failure, and may decrease the complications such as lung injury, circulatory inhibition, ventilator associated pneumonia and oxygen poisoning under small PEEP and short period of high FiO_2 (>0.60) requirements. Mechanical ventilation may rectify hypoxemia when the lung injury progresses into ARDS, but higher PEEP and inspiration pressure support were prone to respiratory tract damage and intra-alveolar pressure increases leading to lung injury and circulatory inhibition with decreased cardiac output and hypotension. Prolonged mechanical ventilation is usually associated with ventilator associated pneumonia and may induce or exaggerate systemic inflammatory response syndrome, multiorgan dysfunction syndromes and even multiorgan failure. Prolonged (>12 hours) and high concentration (>0.60) of FiO_2 easily result in oxygen poisoning and increase mortality.[24]

PEEP can increase functional residual capacity, re-expand the atectastic alveoli, ameliorate gas exchange, lessen intrapulmonary shunting and thus lowering the RI. For the patients with RI > 1.45 at 15 min postoperation, PEEP is routinely given and a good outcome is anticipated. It has been suggested that extubation at RI < 1.45 can be safe.[23] Liu *et al*.[25] found in 14 ALI patients whose PaO_2/FiO_2 continued to increase with an increase of PEEP. When oxygen supply reached a maximal value with a PEEP of 15 cmH_2O, PaO_2/FiO_2 did not reach a maximum, but decreased with the increase of PEEP; when PEEP was 20 cmH_2O, oxygen supply began to decrease, obviously due to the decrease of cardiac output. When PEEP was 10-15 cmH_2O, static lung compliance was kept at a stable level (33.6 ± 8.3 cmH_2O), and oxygen supply was at a maximal value but when PEEP increased to 20 cmH_2O, static lung compliance and oxygen supply decreased while peak airway pressure increased remarkably. Han *et al*.[26] were in line with Liu *et al*.[25] in terms of relations between respiratory mechanics and PaO_2/FiO_2 in ARDS patients. According to their results, linear correlations could be noted between PEEP, cardiac output or peak pressure of airway and PaO_2/FiO_2, but correlations between oxygen supply or static lung compliance were weak.[25] Pulmonary dynamic compliance and oxygenation index in patients (treated from day 1-15) with ARDS showed a direct correlation in both cured and dead patients.[26]

Ventilation/perfusion imbalance is mainly due to the hypostasis pulmonum (lower dorsal and basal). Due to the effect of gravity, there is abundant blood flow in these regions. There would be no effective oxygenation when blood flows through the collapsed or consolidated alveolar capillaries, resulting in poor blood-gas exchange with a ventilation/perfusion ratio of much smaller than 0.8 and eventual ventilation/perfusion mismatch.[27]

Lung water

The increase of EVLW is an important pathophysiological change of ARDS. One of the major etiologies for hypoxemia of ARDS was increase of EVLW. PaO_2/FiO_2 increased by 33% in patients with low EVLW index (EVLWI), whereas it only changed by -1% in the patients with high EVLWI. A significant difference was noted between two groups.[28] ELVW is the fluid

distributed outside of the pulmonary vessels. It is composed of intracellular fluid, bronchoaleolar fluid and pulmonary interstitial fluid, which was produced from the respiratory bronchioles, alveolar epithelium and adjacent pulmonary alveoli, filtered from the alveoli, entering into the lymphatic system, reabsorbed through pulmonary vessels or exudated from the pleura or secreted from the respiratory tract.[29] Normally, ELVW should be less than 7 ml/kg. Mean EVLWI indexed to actual body weight (ActBW) in females was 7.4 ml/kg, and mean EVLWI indexed to predicated body weigh in females was 9.1 ml/kg.[30] A comparative study has revealed that EVLWI is more sensitive than the current American European Consensus Committee criteria.[31] Clinical observations revealed that the ELVW was significantly increased and PaO_2/FiO_2 significantly decreased in ARDS patients comparing with non-ARDS patients. On the other hand, PaO_2/FiO_2 only reflects the result instead of the cause of oxygenation, although there is a close relation between PaO_2/FiO_2 and ELVW. Due to the fact that the clinical application of pulse-indicated continuous cardiac output (PiCCO) technique, bedside monitoring of ELVW has come to true. Significant negative correlation was found of EVLWI and PaO_2/FiO_2 ($r = –0.45$, $P < 0.01$) in patients with severe sepsis/septic shock-related ALI/ARDS.[32] Linear correlations between PaO_2/FiO_2 and EVLWI was noted as, $PaO_2/FiO_2 = 190.31\text{-}2.674 \times EVLWI$ ($p = 0.000$, $r = –0.772$). There showed a significant negative correlation.[33]

Intrapulmonary shunting

A pulmonary shunt is a physiological condition when the alveoli are perfused with blood as usual, but ventilation fails to supply the perfused region. Normal value of pulmonary shunt is 0-5%.[34] The intrapulmonary shunt is the best indicator of outlining hypoxic hypoxemia. It reflects the degree to which the lung separates from ideal as an oxygenator of pulmonary blood. PaO_2/FiO_2, with a close relation to intrapulmonary shunting, is more sensitive than PaO_2 in the evaluation of the pulmonary function. Exact calculation of the intrapulmonary shunt requires measurements of oxygen concentration in both arterial and mixed-venous blood samples. A shunt of 10-19% seldom would require significant support. A calculated shunt of 20-29% may be life-threatening with limited cardiovascular function. A calculated shunt >30% usually requires significant cardiopulmonary support. The necessity of sampling mixed-venous blood seems to be the most limiting factor for a widespread clinical use of shunt calculations.[35]

A study demonstrated that the RI to intrapulmonary shunting (Qsp/Qt) ratio was significantly increased in patients who developed fatal ARDS compared with those who did not develop ARDS, or with those whose ARDS resolved. Owing to the increased oxygen consumption in ARDS patients in association with their severe limitations in gas exchange and increased Qsp/Qt, surviving ARDS patients may have a significant increase of cardiac index.[36] PaO_2/FiO_2 had good correlations with intrapulmonary shunting and alveoli-artery oxygen difference. The latter two, in spite of high sensitivities, cannot be used as diagnostic indicators of ARDS instead of PaO_2/FiO_2, but can be primary screening indicators for ARDS patients. When $P(A\text{-}a)O_2$ is >75 mmHg, ARDS should be suspected of; while intrapulmonary shunt <15% and $P(A\text{-}a)O_2$ difference <75 mmHg are helpful to exclude ARDS. Intrapulmonary shuntings expressed in equations, are: $Y = 998.708\text{-}2846.05X$, $P = 0.000$ (Y was PaO_2/FiO_2, and X was intrapulmonary shunting); $Y = 233.54\text{-}0.3X$, $P = 0.000$ (Y was PaO_2/FiO_2, and X was alveolar-arterial oxygen pressure difference); $Y = –682.14 + 3536.312X$, $P = 0.024$ (Y was alveolar-arterial oxygen pressure difference, and X was intrapulmonary shunting).[37]

Biomarkers

Lungs have special capillary beds, playing a role in leukocyte sequestration. Alveolar macrophages are easily activated, releasing a series of inflammatory mediators such as tumor necrosis factor (TNF)-α, interleukin (IL)-6 and IL-8 and superoxide dismutase, etc., thereby damaging vascular endothelium and alveolar epithelium, with lungs being the primary target organ. Recent research has demonstrated that leukocyte accumulation and the adhesion to the endothelial cells, damages to the endothelial cells and the "respiratory burst" requires the participation of adhesion molecules. Hyperviscosity of the neutrophils is associated with the expression and adjustment of CD11/CD18 of the neutrophils. Intercellular adhesion molecule (ICAM)-1 is the ligand of the CD11/CD18 system of the leukocytes. The elevated expression may mediate the activation of the leukocytes and the tight adhesiveness with vascular walls. Experimental study revealed antisense oligonucleotides inhibited upregulation of ICAM-1 mRNA at 4 and 24 hours after instillation of endotoxin in a dose-dependent manner, indicating that antisense oligonucleotides targeted to ICAM-1 might inhibit the endotoxin-induced upregulation of ICAM-1 in the lung and could be effective as anti-ICAM-1 antibodies in preventing neutrophil emigration.[38]

TNF-α and IL-6 may lead to direct lung injury by inducing early inflammatory reactions, releasing toxic products and increasing pulmonary permeability. TNF-α combines the TNF-α receptors in the lungs and damages the hemolase rendering enzyme leakage and further lung injury. It can also stimulate the adhesions of the endothelial cells and neutrophils, and impact a toxic effect by release of proteases, oxygen free radicals and superoxide dismutase. Productions of ILs including ILs –1, –2, –6 and –8 would be increased by stimulations of mono-macrocytes exaggerating the lung injury. An early appearance of TNF-α heralds the imitator of ARDS and the synthesis and secretion of IL-6.

Yu *et al*.,[39] prospectively studied the effects of penehyclidine hydrochloride on lung function in cardiac surgical patients. They noted elevated plasma TNF-α and IL-6 at all sampling points during and after the operation. Administration of penehyclidine hydrochloride was associated significantly reduced $P(A\text{-}a)O_2$ and RI as well as reduced TNF-α and IL-6. Respiratory parameters, both RI and $P(A\text{-}a)O_2$, were closely related to the concentrations of TNF-α and IL-6. The correlation was better in the penehyclidine hydrochloride than in the control.

Another experimental study on rabbit ALI models also revealed the pertinent relations between respiratory indices and inflammatory mediators. When ICAM-1 antibody 2 mg/kg was given to the rabbit 30 min before operation, plasma soluble ICAM-1 was significantly reduced comparing with the control. Linear correlation analysis revealed significant direct correlation between RI and plasma soluble ICAM-1s,

and significant negative correlation between PaO_2/FiO_2 and soluble ICAM-1s. The correlations seemed to be weaker in the experimental than in the control.[40]

Acid-base disturbances

The insidious onset of ARDS often leads to a delayed diagnosis as there are usually no abnormal findings on chest X-ray films at an early stage. Respiratory alkalosis is the common type of acid-base disturbances in ARDS patients. Combined respiratory and metabolic alkalosis is more commonly seen at the early stage of ARDS, the pulmonary ventilation is still normal in spite of decreased PaO_2. However, metabolic alkalosis might occur with the use of overdose alkaline drugs, refrigerant diuretics and glucocorticoids. Improper supplements of alkaline drugs for the compensated HCO_3^- decrease would cause respiratory alkalosis with metabolic alkalosis, which can be life-threatening in critical patients. With a decreased HCO_3^- associated with hypokalemia, a possible respiratory alkalosis should be taken into consideration. There were mainly two types of triple acid-base disturbances (TABD): respiratory alkalosis type and respiratory acidosis type. The respiratory alkalosis type TABD, that is, respiratory alkalosis + metabolic acidosis + metabolic alkalosis, may occur when the ARDS patients were with severe hypoxia, shock, hepato-renal functional impairment, use of refrigerant diuretics and glucocorticoids, improper supplements of alkaline drugs and upper gastrointestinal bleeding. This type of TABD often represents the presence of obstructive ventilatory dysfunction, indicating a perilous condition and a poor prognosis. The respiratory acidosis type TABD, that is, respiratory acidosis + metabolic acidosis + metabolic alkalosis, may develop at the late stage of ARDS, but less common.[41] Clinical observations on 110 ARDS patients revealed different degrees of acid-base imbalances. Types of acid-base imbalances were different between the survived and deceased patients. Respiratory alkalosis or mixed respiratory and metabolic alkalosis were the main types in the survived patients; whereas mixed metabolic acidosis and respiratory acidosis, triple acid-base disturbances and respiratory acidosis were predominant in the deceased patients.[41] It displayed an incidence of TABD of 12.7% in ARDS patients. TABD is often associated with $Cl^-\downarrow$ and $AG\uparrow$. The respiratory acidosis type TABD may show $pH\downarrow$, $PaCO_2\uparrow$, $HCO_3^-\uparrow$, $AG\uparrow$ and $Cl^-\downarrow$; and the respiratory alkalosis type, $pH\uparrow$, $PaCO_2\downarrow$, $HCO_3^-\downarrow$, $AG\uparrow$ and $Cl^-\downarrow$. However, both types of TABD may present $HCO_3^-\uparrow$ or $HCO_3^-\downarrow$, and the respiratory alkalosis type, may have $pH\downarrow$. For the correct judgments in the diagnosis of TABD, acid-base indicators and AG values have to be taken into consideration in addition to the use of the expected compensation formula. TABD can be diagnosed when blood-gas analysis shows respiratory acidosis type or combined respiratory alkalosis and metabolic alkalosis associated with $AG\uparrow$, or when blood-gas analysis shows respiratory acidosis type or respiratory alkalosis associated with $AG\uparrow$ and potential HCO_3^- over compensatory limit.[42]

Management

Use of ulinastatin was associated with lower malondialdehyde, higher superoxide dismutase and lower physiological dead space to tidal volume ratio, PaO_2/FiO_2 and $P(A\text{-}a)O_2$ after CPB.[43] Relations between RI and multiorgan failure or mortality have been demonstrated. Higher RI was usually associated with more involved organs and higher mortalities.[44] For pulmonary protection, the mechanical ventilation modes that were currently applied are mainly small tidal volume (6-8 ml/kg), limit of transpulmonary pressure and permissive hypercapnia in order to protect the lungs from damage of mechanical ventilation. Permissive hypercapnia is not applicable to all patients with ARDS, for example to those with increased intracranial pressure and heart disease.[45] With proper PEEP, it is feasible to expand and reopen collapsed lung tissue.[46] Due to the fact that the pulmonary lesions are not evenly distributed in ARDS patients, small tidal volume may result in over ventilation in part of the alveoli but cannot reopen other part of collapsed alveoli and therefore leading to hypoventilation, increased carbon dioxide retention and hypercapnia. Lung-protective mechanical ventilation strategies are designed to prevent injury from over distention by using lower TV and lower inspiratory pressures (volume- and pressure-limited ventilation) or injury from ventilation with atelectasis and alveolar flooding at end-expiration (open-lung ventilation).[47] Pulmonary controlled inflation is a novel method to increase the pulmonary effective volume. It is developed from the Sigh principle. At the start of inspiration, sufficient pressure is impacted on the air way at 30-50 cmH_2O and for 30-60 s, to fully reopen the collapsed alveoli and keep them reopening for long time for example for 4 hours. In this way, the pulmonary volume can be significantly increased and the pulmonary compliance can be improved. Meanwhile, ventilator associated lung injuries could be avoided and hypoxia could be improved for a long time.

Airway resistance, work of breathing and peak and mean airway pressures may increase significantly 2 hours after the operation in the patients undergoing valve replacement, and the parameters may reach peak values at 6 hours after the operation. It was thus recommended that mechanical ventilation should be kept for at least 6 hours in the surgical patients.

CPB-related ALI is related to CPB-induced systemic inflammatory reactions. Propofol is not only an intravenous general anesthetic, but also an agent inhibiting inflammatory reactions and protecting organs from ischemia-reperfusion injury. A study revealed that patients with propofol administration had significantly decreased RI, plasma malondialdehyde and IL-8 comparing with the control.[48] IL-8 originates from the pulmonary vascular beds, produced by alveolar macrophage, neutriphils and endothelial cells, and it may produce inflammation mediators induced by endotoxins, IL-1 and TNF-α. With IL-8 increase, the damage from oxygen free radicals seems to be more severe and the RI increases with compromised oxygenation function. Clinical anesthetic dose of propofol may attenuate the lipid peroxidation reactions caused by release of oxygen free radicals, inhibit the release of inflammatory mediator IL-8 and decrease RI. Propofol may also inhibit respiratory burst and decrease pulmonary leukocyte aggregation and endothelial damage.[49] Propafol may acts as a calcium-antagnimthe effects similar to those produced by verapamil,[50] and as a free radical scavenger as well.[51] By inactivating and scavenging free radicals, it may inhibit the production of malondialdehyde, thereby inhibiting the synthesis and release of the inflammatory mediators including IL-8.

Conclusions

Postperfusion lung syndrome is rare but lethal. Secondary inflammatory response was the popularly accepted theory

for the underlying etiology. RI and PaO_2/FiO_2 can be reliable indices for the diagnosis of this syndrome as chest X-ray appearance is always insignificant at the early stage. Evaluations of EVLW and pulmonary compliance are also helpful in the definite diagnosis. Multiorgan failure and TABD secondary to postperfusion lung syndrome may be responsible for the poor prognosis and increased mortality rather than postperfusion lung syndrome itself. Mechanical ventilation with low tidal volume and proper PEEP can be an effective treatment strategy. Use of ulinastatin and propofol may benefit the ARDS patients through different mechanisms.

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How to cite this article: Yuan SM. Postperfusion lung syndrome: Respiratory mechanics, respiratory indices and biomarkers. Ann Thorac Med 2015;10:151-7.

Source of Support: Nil, **Conflicts of Interest:** None declared.