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Research on the Mechanisms of Lung Injury in Cardiopulmonary Circulation (CPB)

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Abstract: Very common complications in cardiopulmonary bypass (CPB) surgery include lung injury, and there are many risk factors for such complications, such as systemic inflammatory response syndrome, ischemia-reperfusion injury, long turnaround, emergency surgery, preoperative inetsufficiency, etc .At the present stage, the intervention programs for CPB lung injury mainly include mechanical intervention, surgical technical intervention, anesthesia management, drug protection, etc., which can effectively reduce blood dilution, leukocyte agglomeration, systemic inflammatory response syndrome, and contact activation response caused by CPB. The relevant mechanisms, risk factors, and lung protection strategies of CPB lung injury are reviewed below.

1. Introduction

One of the important auxiliary technologies in cardiac surgery is CPB, which can supply the blood of the main organs of the body when the heart is stopped, and then prevent the production of hypoxia and functional organs in the body organs. However, when CPB is applied in surgery, its artificial pipeline will contact with the blood, which will activate the body's immune system and blood coagulation system, causing an inflammatory reaction to the body, and then damage the body[1]. The organs in the body that can accept all cardiac ejection are the lungs, which has gas exchange capacity and blood supply capacity, which will further increase the sensitivity of the lungs to inflammatory reactions, and then increase the risk of lung injury caused by CPB. One common complication of cardiac surgery is CPB lung injury, mild in mild and respiratory distress syndrome or acute lung injury in severe cases. Due to the higher mortality caused by CPB lung injury, about 1/2, it can be seen that this complication is also an important factor causing the death of patients after CPB. However, the mechanism of CPB lung injury is more complicated, and most scholars agree that ischemia-reprovision injury and systemic inflammatory response syndrome is the main factors, Interventions during CPB can significantly improve the lung injury situation[2], Furthermore, this paper reviews the relevant mechanisms and lung protection strategies of CPB lung injury.

2. Relevant mechanisms of CPB lung injury

The mechanism of CPB lung injury is complicated. At present, various clinical studies and scholars agree and believe that lung ischemia-reprovision injury and systemic inflammatory response syndrome is the main role.

2.1 Pulmonary ischemia-reprovision injury

The lungs have a special structure and have a high risk of ischemia-reprovision injury. Pulmonary artery and bronchial artery are an important pulmonary blood vessels, and pulmonary blood flow only 1% -3% by bronchial artery, if in CPB, one is enough to cava resistance, artificial right heart blood is mainly introduced by vena cava, the process without cava artery, pulmonary blood supply mainly by bronchial artery, easily affect the lung blood supply, cause ischemia or blood supply[3]; Second, the CPB operation needs to be completed at a sub-low temperature state, A higher temperature in the blood of the lung tissue during this process, Lung tissue has a higher metabolism, And because of the lack of hypoxia metabolic substrate, Leading in a reduced content of adenosine triphosphate synthesized by the cells, At this time, the lungs will be in a high metabolism, high temperature, high oxygen consumption state, This leads to the lung tissue occurrence of ischemia, hypoxia situation; Jump the heart after developing the ascending aorta, Then restore the normal pulmonary artery blood transport, Lung tissue with peroxidative peroxidase and hyperoxide dismutase skin balance, Leading to the accumulation and release of large oxygen free radicals, It then produces pulmonary cell oedema to produce lung injury[4]. Clinical studies have shown that the oxygen free radical produced by mitochondria after lung tissue ischemia and reperfusion plays a key role in lung cell damage. In addition, lung ischemia and reperfusion can also induce lung cell death, while cell death is one of the important factors of CPB lung injury[5]. Lung ischemia and reperfusion can disturb the antioxidant and oxidation balance, cause inactivation of sodium pump, calcium overload in cells, cell necrosis and apoptosis; lung ischemia and reperfusion injury can induce poly ADP ribose activation, MP , MP, Caspase pathway, and eventually produce lung dysfunction.

2.2 Systemic inflammatory response syndrome

CPB is a kind of cardiac surgery auxiliary technology, belongs to the nonphysiological circulation, in the process of CPB, the equipment and pipeline will contact with the body blood, coupled with surgery, anesthesia, destroy blood components, protamine and heparpled in drug use factors, will activate the body complement system, and under the action of inflammatory factors and endotoxemia produce a variety of reactions.

2.2.1 Cytokines

CBP tumor necrosis factor plays an important role in lung inflammation, directly induces apoptosis, affects pulmonary vascular endothelial cells and alveolar epithelial cells, and indirectly regulates immune cell function, causing lung injury; in addition, endothelial cells, macrophages and other immune cells activate pro-inflammatory cytokines (interleukin and tumor necrosis factor), nitric oxide synthase, NADPH oxidase, reactive oxygen species, cell surface molecules, produce super inflammatory response, damage cells and tissues, reduce lung compliance and reduce gas exchange[6].

2.2.2 Complement activation

CBP process will activate the body complement system, and glycoprotein is the main component of

complement, enzymatic activity, activation will enhance C3 in the blood, and generate complement active fragment allergic toxin, such as C5a, C4a and C3a, affect mast cells and alkalophils, promote the release of inflammatory mediators, and improve lung epithelial and endothelial cell permeability, and promote lung small vasoconstriction, and eventually cause pulmonary edema[7].

2.3 Plectasis

During CPB, especially during the full flow process, due to the influence of alveolar collapse and stopped breathing, the condition of alveolar surfactant was inactivated and lost, which then caused atelectasis. Even after continuous positive pressure ventilation and PEEP ventilation, the patient still develops atelectasis. Studies have suggested that patients increase the ineffective cavity by 24% and 3% after surgery, while the normal areas will decrease significantly[8]. It can be seen that the incidence of postoperative atelectasis is high, and postoperative atelectasis will not only cause hypoxemia, but also easily cause lung infection and improve the risk of lung injury.

3. Risk factors for CPB lung injury

CPB lung injury is a complication caused by the influence of multiple factors, and the analysis and deep understanding of the risk factors of CPB lung injury is critical to prevent and mitigate such complications.

3.1 Blood transfusion factors

Large blood transfusion can produce related circulatory overload and cause related lung injury. Blood transfusion can activate the body's immune system and aggravate CPB lung injury. Studies have found that the increase of red blood cells from patients will improve the lung permeability after surgery, and vice versa, compared with patients without blood transfusion, the respiratory support time will prolong the CPB and improve the lung capillary permeability[9]. Furthermore, the incidence of pulmonary complications was significantly increased in patients used with old red blood cell suspension. Another study showed prolonged postoperative mechanical ventilation in patients infused with fresh frozen plasma or stock plasma, and a significantly increased postoperative reintubation rate[10].

3.2 Surgical factors

Postoperative lung injury rate was higher in patients with acute surgery, patients with secondary surgery, patients with CPB time over 77 minutes, and patients with intraoperative renphic phrenic nerve renphic nerve injury.

3.3 Combined with disease factors

At present, most patients with a variety of diseases, some diseases will increase CPB lung injury to a large extent. Studies have shown that patients with renal dysfunction, lung dysfunction, cardiac dysfunction and other diseases, the risk of lung injury after CPB is significantly increased. In one study, the incidence of CPB lung injury and mortality was also significantly increased after CPB procedures in patients with less than 60% LV ejection fraction, patients with a history of chronic obstructive pulmonary disease, and patients over 70 years of age[11].

3.4 Patient factors

Patients' own pathological changes are a major influence factor of CPB lung injury, and the risk of CPB disease lung injury is higher if the patient belongs to a specific gene type. Studies have found that patients with 607 C / C and A1-75 G / A genes have a higher risk of postoperative lung injury than patients with other genes[12]. In addition, lung injury is also related to the patient's weight and age.

4. Lung protection strategy

4.1 Surgical and technical interventions

In general, patients will suffer from lung function damage to varying degrees. However, the CPB technology performed in cardiac surgery will cause further damage to the patient's lungs. In recent years, the continuous development of non-stop jumping coronary artery bypass grafting related technology has helped to lay the foundation for the further acting skills of CPB technology for its own postoperative lung function injury. Related studies of intraoperative cardiac skipping and intraoperative cardiac arrest showed that CPB will affect the clinical outcome of patients. The postoperative extubation time of patients with intraoperative cardiac skipping is earlier, but there is no significant difference in the incidence of pulmonary complications[13]. However, the continuous jumping technology is less suitable for surgery, which is now only used in coronary artery bypass grafting, but is not suitable for heart valve-related surgery. Then it can effectively reduce the turning time of CPB, which can prevent acute lung injury to a certain extent. During aortic blockade, enhanced myocardial protection can reduce the damage caused by the inflammatory factors produced during lung reperfusion. The main factors mediating the release of inflammatory factors include perfusion pathway and arrest solution. In the application of CPB technology, the control of internal cardiac suction pipe and the reduced internal cardiac attraction is applied as much as possible, and reducing the gas entering in the CPB pipeline system can promote the recovery of patients' lungs after surgery.

4.2 Mechanical intervention

4.2.1 Outer cycle line

The factors that induce the systemic inflammatory response syndrome after CPB includes the contact between the blood and the artificial cardiopulmonary machine circulating line, which can reduce the contact surface of the blood and the artificial cardiopulmonary machine circulating line, which can reduce the inflammatory response to a certain extent. In recent years, with the innovation and development of medical technology, the new mini pipeline system has come out, with the characteristics of smaller volume, can reduce the precharge capacity, and reduce the degree of blood dilution, alleviate the damage of perfusion organs in the operation, but also can reduce the amount of blood transfusion. At present, there are many studies and experiments related to biological histobility, and the current focus includes heparin. Heparan sulfate is stored on the surface of vascular endothelial cells, and the first coating material studied was heparin. Heparin layer can later inhibit C5、C3The activation, and by inhibiting the activation of endothelial cells, neutrophils and platelets and reduce the release of inflammatory factors, effectively improve the lung injury after CPB[14]. In particular, some complicated cardiac procedures with aortic blockade time of more than 1 hour have obvious advantages for clinical outcomes.

4.2.2 Leukapheresis

There will be stranded activated leukocytes in lung capillaries, which can affect leukocytes and

endothelial cells in each other and participate in the physiological process of CPB lung injury.During CPB, if leukocytes were removed, the patient had less impaired postoperative lung function.Some clinical studies have shown that after leukocyte removal from surgery, the postoperative level of interleukin (10,8 and 6) increased significantly, oxygenation index improved significantly after 48 hours of surgery, and the postoperative mechanical ventilation time was slightly shorter[15]. However, some scholars have found that although patients underwent leukofiltration, it did not reduce mortality and hospital stay[16]. Some studies showed that performing leukapheresis only alleviated the lung ischemia and reperfusion injury at the cell level, and did not effectively improve the long-term clinical outcomes of patients[17].

4.2.3 Hyperiltration

In the CPB operation, the crystal prebilled fluid will be used, because the amount will dilute the blood.Blood dilution has a positive effect in tissue perfusion. When the specific volume level of red blood cells is below 23%, it will cause organ insufficiency and tissue space edema. Animal studies have shown that ultrafiltration in CPB, removing excess liquid components can improve the specific capacity of red blood cells, in addition to helping increase the colloidal osmotic pressure, and then improve lung interstitial edema, to enhance lung function[18]. In addition, most of the inflammatory factors have a small molecular weight, and generally can penetrate the membrane pores of conventional filters, and then hyperpermeable can remove most inflammatory factors, but also can purify endotoxin, and promote the improvement of surfactant levels. The development and improvement of ultrafiltration technology, this technology can also be used in children, which has a positive role in reducing blood transfusion volume, improving coagulation dysfunction, inhibiting inflammatory response, improving postoperative pulmonary function, preventing edema and other aspects[19].

4.2.4 Pre-charging technology of cppipeline

In the research of relevant scholars, comparing the traditional pre-charging technology and autologous blood reverse pre-charging technology, the latter one can reduce the amount of crystal fluid required for pre-charging, which may be the use of self-circulating blood pre-charging pipeline after intubation. Some scholars pointed out that the use of autologous blood reverse precharging technology during surgery can significantly improve the hematocrit of patients, and also significantly improve the cerebral oxygen saturation in patients' CPB[20].

4.3 Anesthesia management

4.3.1 Mechanical ventilation

One of the important factors causing lung injury in CPB is atelectasis. The pulmonary circulation will be interrupted during the transfer of CPB full flow, and the bronchial artery is the only artery supplied by the lung, but only 1% -3% of the pulmonary blood flow is supplied by the bronchial artery, which cannot meet the normal metabolism of lung tissue, and the lung oxygen should be replaced by passive diffusion. During CPB, apnea causes total atelectasis, while also activating multiple enzymes in the pulmonary circulation that can damage lung function. The function of mechanical ventilation during surgery is to avoid atelectasis and prevent and relieve CPB lung injury. During and after CPB, a variety of ventilation strategies can be selected, such as PEEP ventilation, low tidal volume ventilation, continuous respiratory positive pressure ventilation, continuous ventilation, intermittent ventilation, but different ventilation methods have different effects on inflammatory factors and prognosis.

4.3.2 Anesthesia protocol

Some scholars have compared compound anesthesia with total intravenous anesthesia, and found that the serum level of inflammatory factors in patients with the two types of anesthesia methods did not decrease significantly[21]. Clinical studies have also confirmed that inhaled anesthetics, such as sevoflurane, which is used in CPB use, can also reduce the production of cytokines in lung tissue[22]. At the present stage, when CPB is performed in clinical practice, intravenous inhalation compound anesthesia is mainly selected to maintain anesthesia.

4.4 Drug protection

Drugs used for CPB lung protection include steroids that have been used for 30 years, but there is no consistent evidence at this stage. There are large clinical studies that have not determined that glucocorticoids can prevent CPB complications and reduce mortality. Furthermore, the pulmonary protective effect of steroids like CPB still needs further investigation. One of the main factors mediating CPB lung injury is activated neutrophils, which can effectively inhibit the activity of this cell to improve lung injury to some extent, and has a positive effect on lung function protection. Uinastatin and siverlaus sodium are neutrophil elastase inhibitors, which have obvious inhibitory effect on neutrophil elastase activity, which can significantly increase oxygenation index and reduce postoperative extubation time.In cardiac surgery, in order to prevent fibrinysis, the use of serine protease inhibitors, such as aprotinin, can protect and improve the function of various organs after CPB, prevent the generation of pulmonary effusion, increase oxygenation index to reduce mechanical ventilation time, and prevent monsary complications.

5. Conclusion

CPB lung injury is the result of a variety of factors, the main mechanism of CPB lung injury for lung ischemia-reperfusion injury, systemic inflammatory syndrome, atelectasis, current clinical response for CPB lung injury has many, such as surgical intervention, mechanical intervention, anesthesia management, drug protection, etc., its effect is to prevent and alleviate ischemia / reperfusion injury, improve systemic inflammation syndrome, all have certain results, but can not achieve the expected effect, this needs to constantly explore and study the CPB lung injury mechanism, Lay the foundation for improving the CPB lung protection strategy.

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