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Identification and Management Strategies for Low Cardiac Output Syndrome After Cardiac Surgery

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ABSTRACT

Low cardiac output syndrome is one of the common complications after cardiac surgery, and is also the main cause of postoperative death. In this paper, the risk factors, prediction models, diagnosis and treatment of low cardiac output syndrome were reviewed in recent years, so as to provide reference for early identification and appropriate management of low cardiac output syndrome.

1. Background

Low cardiac output syndrome (LCOS) is a clinical syndrome characterized by decreased cardiac output and inadequate peripheral organ perfusion. It is one of the most serious complications after cardiac surgery, with an incidence rate of up to 10% and a mortality rate that may exceed 20% [1-3]. Severe LCOS leads to prolonged use of ventilators, increased risk of acute kidney injury and pulmonary infection, prolonged stay in intensive care units (ICU), prolonged hospitalization, increased costs, and even patient death, posing great challenges to clinical doctors and imposing a heavy burden on society. Therefore, studying the potential risks of LCOS, understanding its occurrence and development patterns, and being able to identify and handle it in a timely manner are of great significance for improving the prognosis of patients after cardiac surgery.

2. Identification of LCOS

2.1. Potential Risk Factors for LCOS Occurrence

By analyzing literature, it was found that depending on the type of heart disease and surgical approach, the risk factors for LCOS vary and can be divided into three categories: (1) Heart valve surgery: Researchers have studied that the risk factors for LCOS are low body weight, cardiothoracic ratio > 0.7, preoperative renal insufficiency, pulmonary hypertension, preoperative left ventricular ejection fraction (LVEF) < 40%, cardiopulmonary bypass (CPB) time > 140 minutes, and postoperative bleeding volume [4-6]. (2) Coronary artery bypass grafting (CABG): studies had shown a history of myocardial infarction, preoperative arrhythmia, and heart function grade II to IV and LVEF < 45%, intraoperative CPB time > 100 minutes and blood loss > 800 ml are risk factors for postoperative LCOS; a study in Brazil identified risk factors for LCOS after CABG surgery: age > 60 years, emergency surgery, incomplete revascularization, and LVEF < 50% [6-9]. (3) Complex congenital

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heart disease surgery: studies suggested that low age, small body weight, long aortic occlusion time and CPB time, increased postoperative CPB resistance and preoperative pulmonary hypertension are risk factors for postoperative LCOS; a Meta-analysis study pointed out that the independent significant risk factors of LCOS including age > 65 years, LVEF < 50%, CABG, emergency surgery or CPB and incomplete revascularization [6]. Diabetes mellitus and preoperative renal dysfunction are not independent predictors, but the combination of the two increases the risk of LCOS by 50% [10-12].

To sum up, older patients with preoperative LVEF < 50%, long operation time, more blood transfusion and unsatisfactory anatomic correction have a high incidence of postoperative LCOS, while children with complex congenital heart disease who are small months old and low weight have a much higher incidence of postoperative LCOS than adult cardiac surgery [6].

2.2. Related Research on Predicting the Occurrence of LCOS

There are many risk factors for LCOS, but its prediction model has not been uniformly recognized. At present, EuroSCORE II is widely used in the risk assessment model of cardiac surgery, which can predict the perioperative cardiovascular changes sensitively [13, 14]. By analyzing the data of 41729 CABG patients in Chinese Cardiac Surgery Registry (CCSR) database from 2013 to 2015, researchers established a new risk prediction model using 21 risk factors to predict, and verified it with the data of 15047 CABG patients in CCSR database in 2016. It was found that the new risk prediction model could more accurately predict the in-hospital mortality after CABG in patients in mainland China, which was helpful to identify high-risk patients before surgery [15, 16]. However, this model has not been widely used in clinic yet and needs further research.

2.3. Diagnosis and Controversy of LCOS

The expert consensus of LCOS in 2018 defined cardiac index < 2.0 L/min/m2 as low cardiac output [17]. The results of questionnaire survey catch by Shanghai Children's Medical Center showed that only 77% of the centers could monitor cardiac output and 41% could monitor microcirculation in China[18]. Therefore, for some centers with incomplete monitoring equipment, the diagnosis of LCOS is difficult to clarify and prone to missed diagnosis. At present, some cardiac centers have quantified the diagnosis of LCOS and found slight differences in its criteria through literature analysis. The diagnostic criteria of Beijing Anzhen Hospital include: (1) LVEF < 40%; (2) Cardiac index < 2.3 L/min/m2; (3) Persistent hypotension; (4) Oliguria (urine output < 1 ml/kg/h without diuretics); (5) Lactic acid > 3.0 mol/L; (6) Central venous oxygen saturation < 50%; (7) Vasoactive inotropic score > 15.5. When any one of (1) or (2), or any three of (3) - (7) appears after surgery, it is diagnosed as postoperative LCOS [19]. Another study refined the diagnostic criteria into 9 items, and patients who met two or more of items 1-8, or who developed item 9, were directly diagnosed with LCOS: (1) Cardiac index < 2.5 L/min/m2; (2) Postoperative echocardiography measured LVEF < 50%; (3) Systolic blood pressure < 90 mmHg, or mean arterial pressure < 60mmHg, or continuous decrease in systolic blood pressure exceeding 20% of preoperative baseline blood pressure for more than 2 hours; (4) Central venous pressure > 13 mmHg, or pulmonary capillary pressure > 15 mmHg, or central venous oxygen saturation < 50%; (5) Postoperative dopamine dosage > 10 ug/kg/min is required to maintain systolic blood pressure and cardiac output, and the duration of medication should exceed 30 minutes; (6) Lactic acid > 3.5 mmol/L or metabolic acidosis (pH < 7.4, lactic acid > 3.0 mmol/L, base excess < -2 mmol/L); (7) Urine output < 0.5ml/kg/h when diuretics are not used; (8) Insufficient peripheral perfusion, coldness and cyanosis at the extremities; (9) The patient needs intra-aortic ballon pumps (IABP) due to hemodynamic disorders [6]. The essence of LCOS is a decrease in cardiac output leading to inadequate tissue perfusion and an imbalance between cellular oxygen supply and consumption. The different stages of pathological and physiological changes in LCOS patients, as well as the differences in intervention methods, intervention intensity, and intervention effects received by patients, can lead to heterogeneity in clinical manifestations and related monitoring indicators. Therefore, people can fully understand that different studies will propose different diagnostic criteria for LCOS, and they can also understand why the incidence of LCOS varies greatly among different studies.

2.4. Monitoring Methods for the Development and Changes of LCOS

At present, mature monitoring methods of LCOS include: (1) Ultrasound technology: In recent years, echocardiography developed rapidly in the field of cardiac surgery, including ultrasound-guided interventional closure surgery in congenital heart disease surgery and evaluation of valve function in valve surgery. echocardiography has become the second eye of surgeons. After cardiac surgery, echocardiography can reveal the type of LCOS and evaluate ejection fraction, cardiac volume, systolic and diastolic function, valve pathology, pulmonary circulation, ventricular filling pressure, pericardial effusion, and fluid reactivity [20]. As a portable and non-invasive examination method, echocardiography can provide targeted real-time assessment of the patient's condition in a short period of time, guide the rapid treatment of LCOS causes, provide intuitive and rapid evaluation of treatment outcomes [21]. However, echocardiography has a high degree of technical dependence on the operator, subjective examination results, and cannot provide continuous hemodynamic measurements. (2) The pulmonary artery floating catheter (PAC), also known as the Swan-Ganz balloon floating catheter, can provide reliable hemodynamic parameters that reflect changes in the patient's cardiac output per unit of time. In addition, it can also provide pulmonary artery pressure, right heart and pulmonary artery capillary filling pressure, peripheral blood vessel and pulmonary artery resistance [22, 23]. However, placing PAC in the right heart is an invasive surgery that may lead to cardiovascular complications such as pneumothorax, pulmonary artery rupture, arrhythmia, pericardial tamponade, infection, catheter entanglement, thromboembolism, etc. Currently, it is not widely used in clinic. (3) Pulse index continuous cardiac output (PICCO) is a novel minimally invasive hemodynamic monitoring technique that measures a series of clinical monitoring indicators, such as CO, stroke volume (SV), stroke volume variation (SVV), global end diastolic volume (GEDV), intrathoracic blood volume (ITBV), and indicators related to cardiac preload or afterload, through a central vein and arterial catheter using thermal dilution method. Therefore, some clinical doctors use it as a substitute for PAC [24]. The safety of PICCO operation is higher than PAC. However, the measurement of data requires calibration with low-temperature saline, which can easily cause arrhythmia after cardiac surgery and is limited in use. (4) The FloTrac/Vigileo system: With only one arterial catheter, cardiac output can be continuously and timely calculated by collecting arterial waveforms and combining them with the patient's basic information (age, gender, height, body mass, etc.) to analyze and calculate cardiac output, SV, SVV easily, but the accuracy is low in patients with severe arrhythmia or severe aortic valve insufficiency. Currently, large-scale clinical applications have not been carried out.

3. Management Strategy of LCOS

3.1. Basic Principles of LCOS Management

The treatment for the etiology of LCOS includes several aspects: (1) Actively correcting reversible factors that lead to low cardiac output, especially for LCOS caused by surgical factors, it must be resolved as soon as possible. (2) Optimize capacity status to maintain optimal preload levels. (3) The application of vasoactive drugs stabilizes heart rate and rhythm, and ensures atrioventricular synchronization in pacemaker dependent patients. (4) Mechanical circulation assisted therapy is used when the drug treatment effect is invalid [17].

3.2. Vasoactive Drugs

Goal-directed fluid therapy (GDFT) refers to the therapeutic concept of using monitoring technology for hemodynamic management, individualized fluid replacement based on the patient's cardiac function, load status, and fluid needs. Therefore, hemodynamic management not only includes individualized volume management, but also means individualized treatment with vasoactive drugs.

Vasoactive drugs mainly regulate the cardiovascular system by acting on adrenergic and non-adrenergic receptors, including positive inotropic drugs, vasopressors, and vasodilators. According to the different stages of hemodynamic changes in LCOS, the direct effects of drugs on myocardium and vascular tension can be divided into four categories: (1) Cardiac vasodilators: dobutamine, milrinone; (2) Simple vasodilator: Sodium nitroprusside; (3) Cardioconstrictors: Norepinephrine, epinephrine, dopamine; (4) Simple vasoconstrictors: epinephrine, vasopressin. In addition, levosimendan is a novel calcium sensitizing positive inotropic drug and an ATP sensitive potassium channel opener that enhances myocardial contractility, dilates peripheral and coronary vessels, improves the hemodynamic effects of heart failure and clinical symptoms of patients without increasing myocardial oxygen consumption. It can effectively prevent or treat LCOS after cardiac surgery. Researches had shown that levosimendan can improve postoperative cardiac output and tissue perfusion, reduce the occurrence of LCOS, then improve survival rate [25, 26]. European experts suggested that levosimendan can effectively stabilize the hemodynamics of patients undergoing cardiac surgery, thereby reducing the need for positive inotropic drugs and mechanical circulatory support [27]. The optimal time for preoperative treatment of levosimendan is the day before surgery, with a recommended dose of 0.1 μg/kg/min and continuous infusion for 24 hours. The latest meta-analysis showed that levosimendan can reduce the mortality rate of preoperative LVEF patients, but does not affect the overall mortality rate. The adverse reactions of levosimendan include hypotension and ventricular arrhythmia, which should be selected according to the patient's condition [28].

The application of vasoactive drugs should be based on clinical pathological and physiological status as well as hemodynamic conditions, and appropriate drugs and doses should be selected to reduce potential adverse reactions. According to a survey questionnaire from Shanghai Children's Medical Center, dopamine is the main medication used for preventive medication in each center [18]. The selection of therapeutic drugs is basically the same for each center: (1) Milrinone is used for LCOS with increased systemic circulation resistance; (2) Dopamine and adrenaline are used to reduce systemic circulation resistance in LCOS; (3) LCOS with increased pulmonary circulation resistance is treated with milrinone, catecholamines, and pulmonary vasodilators [18]. A systematic literature review studied positive inotropic drugs after CPB and showed that dobutamine and phosphodiesterase inhibitors are effective drugs for treating LCOS [29]. Another meta-analysis collected data from 2385 individuals and three ongoing studies, showing uncertainty in the impact of vasoactive drugs on LCOS all-cause mortality. Therefore, the effectiveness of drug therapy is limited, and mechanical circulation assisted therapy is an indispensable means of treating LCOS.

3.3. Instrument Circulation Assistance

Optional extracorporeal life support includes IABP, extracorporeal membrane oxygenation (ECMO), ventricular assist devices (VADs), Impella pumps, and etc. The most widely used currently are ECMO and IABP [31].

3.3.1. ECMO

In the 1970s, ECMO was applied clinically as a respiratory and cardiac function support technology, but its application was limited in the early stages due to the high incidence of complications. With the continuous development of technology, complications are gradually decreasing, and the application of ECMO is becoming more and more common. Its applications in the field of cardiac surgery include the treatment of postoperative cardiogenic shock, severe donor organ failure after heart transplantation, the installation of VAD or transitional treatment for heart transplantation in the end-stage of heart failure, and the prevention and treatment of right heart failure after LVAD [32]. According to literature reports, the incidence of ECMO use in patients after cardiac surgery ranges from 0.4 to 3.7% [33]. Maxwell and colleagues evaluated over 9000 ECMO patients from the National Inpatient Sample Database in the United States from 1998 to 2009, and found 4493 patients, approximately 50% of patients had postoperative cardiogenic shock [34]. The basic working principle of ECMO is to drain the patient's venous blood outside the body, oxygenate it, and then return it to the patient's artery or vein, replacing or partially replacing the patient's heart and lung function. It can maintain the patient's basic vital signs for a period of time to strive for the opportunity for recovery and functional recovery of heart and lung lesions, or provide transitional time for the next step of transplantation. At present, most cardiac surgeries in China use the venous-arterial (V-A) mode for ECMO assisted circulation [35]. Existing studies had shown that ECMO increases systemic perfusion through countercurrent blood, reduces LV preload, increases LV afterload, reduces stroke volume, increases myocardial oxygen demand, and reduces PAWP. A meta-analysis [36] showed that the hemodynamic support provided by V-A ECMO has a reasonable survival benefit with medium and long-term results in the treatment of intractable cardiogenic shock after cardiac surgery in adults. A research showed that ECMO is an important support method for the treatment of reversible cardiopulmonary failure after cardiac surgery, the timing of ECMO, the application of protective pulmonary ventilation, and the effective control and prevention of bleeding are the key factors for the success of ECMO treatment [37]. In addition, patients who established ECMO within 24 hours after operation had a higher survival rate than patients who established ECMO after 24 hours after operation, and the incidence of complications such as acute renal failure and ischemic hepatitis was lower [38, 39]. In conclusion, the success rate of ECMO treatment is high. Ariyaratnam et al. classified the causes of cardiac dysfunction after cardiac surgery into three categories: (1) Reversible, caused by myocardial stunning, which can be restored by short-term support of ECMO. (2) Potentially reversible, mainly caused by localized small focal acute myocardial infarction and acute pulmonary edema, which may require long-term ECMO support. (3) Irreversible, caused by severe heart failure, extensive myocardial infarction, and chronic pulmonary hypertension, ECMO cannot play a fundamental role in the treatment, and heart transplantation should be considered [40]. This explains the reason why ECMO, as the most powerful device support at present, still has high mortality [41]. ECMO is expensive and can lead to serious complications, so its benefits and risks need to be weighed.

3.3.2. IABP

Since the application of IABP in clinic in the 1960s, more than one million patients have received therapy. Since 1973, when IABP was first used in cardiac surgery to assist CPB during operation, IABP has been more and more widely used in cardiac surgery [42]. IABP inflates the balloon in diastole and deflates the balloon in systole, which plays an auxiliary role in the heart. Compared with ECMO, it only has circulation support function, but has no respiratory or circulatory replacement effect. However, because of its simplicity, effectiveness and relatively low price, IABP is widely used and plays an irreplaceable role in the management of LCOS after cardiac surgery. In addition, the timing of intervention is still an important factor affecting the outcome of circulatory assistance. A randomized controlled study pointed out that 1 hour before operation, prophylactic implantation of IABP can reduce the mortality and incidence of LCOS in patients with high-risk CABG [43]. ECMO and IABP cannot be replaced by each other. At present, it is considered that the effect of their combined application is good, but the timing is still controversial. Studies have shown that ECMO combined with IABP in the treatment of high-risk coronary heart disease can significantly improve the hemodynamic indexes of patients, reduce the in-hospital mortality [44]. For patients with LCOS, there is no clear consensus on whether IABP or ECMO should be implanted first, which needs further research.

4. Summary and Prospects

In conclusion, the occurrence of LCOS after cardiac surgery is inevitable, and effective treatment can reduce the mortality. Preoperative comprehensive consideration should be given to various factors of patients, screening high-risk patients with LCOS and carrying out goal-directed therapy based on adequate monitoring, which is conducive to the early identification and appropriate treatment of LCOS.

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