



Research Progress on Target Control of Perioperative Blood Pressure in Adults

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Abstract

Intraoperative hypotension frequently occurs and is an essential trigger of postoperative organ dysfunction and surgical patients' mortality. This review was to investigate recent literature regarding the level of perioperative blood pressure control and its relationship with organ injury after surgery. Guiding blood pressure management and ameliorating complications in surgical patients. There is a lack of uniform definition or guidelines regarding blood pressure targets to ensure patient safety. Learning the dynamic nature of blood pressure may give more insight into the mechanism for adverse events and provide optimal intraoperative targets. The goal of blood pressure targets titration is to maintain organ perfusion and optimize the microcirculation - which, therefore, benefits patients' prognosis and outcome. The available evidence suggests that targeting a Mean Arterial Pressure (MAP) of above 65 mmHg (1 mmHg = 0.133 kPa) in a surgical patient without preexisting risk factors is a reasonable threshold. In patients with comorbid conditions, blood pressure management should be individually tailored to an optimal level considering physiology and the clinical situation. Personalized blood pressure management according to individual physiology and particular clinical situation may reduce postoperative organ dysfunction in surgical patients. A magnitude of $\pm 20\% \pm 10\%$ fluctuation based on baseline blood pressure is an optimal blood pressure target for high risk patients. A sensitive biomarker in reflecting optimal blood pressure target and organ ischemic injury threshold helps blood pressure management.

Keywords: Peri-operation; Blood pressure; Personalized; Target

Introduction

Blood pressure refers to the lateral pressure of blood flow in a vessel against the vessel wall per unit area. It is the driving force to promote blood flow in the vessel and is one of the important vital signs. Blood pressure usually refers to arterial blood pressure or systemic blood pressure, which is common, easy to obtain and more intuitive clinical information. In clinical anesthesia, blood pressure is often the most common indicator to guide anesthesia intervention. During anesthesia and surgery, blood pressure is measured at least once every 5 min. The control level of perioperative blood pressure is closely related to postoperative organ function recovery and complications. It is traditionally believed that the fluctuation range of blood pressure during perioperative period should be maintained within 20% of the baseline value, but there are great differences in the control goals of blood pressure among clinical anesthesiologists with different experience and qualifications in clinical practice. Therefore, this paper reviews the objectives of perioperative blood pressure control to provide reference and guidance for clinical work.

Blood Pressure Measurement and Basic Blood Pressure

According to statistics, 80% of the perioperative blood pressure is obtained through the non-invasive cuff using the principle of shock method. The shock method is the most common way to monitor blood pressure during the perioperative period, which can automatically and intermittently measure the blood pressure value [1]. Eripheral artery puncture and catheterization can obtain blood pressure continuously, rapidly and accurately. In most cases, it is considered that the blood pressure measured by invasive artery puncture is closer to the true value than the cuff pressure. But it should be pointed out that, under different conditions noninvasive and invasive arterial pressure cuff pressure difference may exist, idea, etc. to choose 24,225 patients, 63% of cases of simultaneous determination of noninvasive blood pressure cuff and a radial artery blood pressure, 37% of cases and radial artery blood pressure monitoring, it was found that in patients with low blood pressure, especially SBP<111 mmHg (1 mmHg = 0.133 kPa) value of noninvasive blood pressure cuff is often higher than that of invasive arterial pressure measurements [2]. In patients with hypertension,

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Received Date: 23 Feb 2021

Accepted Date: 02 Apr 2021

Published Date: 07 Apr 2021

Citation:

Jianfeng L, Zongming J. Research Progress on Target Control of Perioperative Blood Pressure in Adults. *Clin Surg*. 2021; 6: 3127.

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the measured value of the latter is higher than the non-invasive cuff pressure value in most cases, especially SBP [3]. The main reason is that direct blood pressure measurement by peripheral arteries (often radial arteries) will amplify the blood pressure signal, especially in patients with hypertension; the signal amplification is more obvious, so the higher SBP value is more obvious. In clinical practice, when there is a great difference between the two values, especially when the invasive blood pressure is significantly hypotensive, the non-invasive cuff pressure should be measured. At this time, the non-invasive cuff pressure is closer to the actual value of central blood pressure, so relevant treatment should be carried out on the basis of the non-invasive cuff pressure, and the difference between the calculated average blood pressure should be paid attention to at the same time [4]. In addition, the vasotonic and volumetric clamp techniques can be used to continuously measure arterial blood pressure without arterial puncture. However, due to data interpretation, error and technical factors, its clinical use is limited. The level of blood pressure is closely related to the individual's biological rhythm, emotional state, activity, co-existing diseases and climate change, etc., and blood pressure is variable. For example, a person's blood pressure varies significantly between reading a newspaper quietly and strenuous exercise and these two very different blood pressure levels can meet the needs of the same individual. Basal blood pressure is an important reference for setting the control level of blood pressure during the perioperative period. However, how to define the basic blood pressure during the perioperative period has always been controversial. In some studies, baseline blood pressure was measured immediately before induction of general anesthesia, 30 min in the preparation room before surgery, and 5 min in the quiet ward before surgery, and averaged for 3 times, etc., but it could not reflect the true baseline blood pressure before surgery. Salmasi et al. [5] retrospective analysis found that compared with 20% value of blood pressure fluctuations, perioperative blood pressure control, based on 65 mmHg in the prediction of postoperative myocardial injury and the sensitivity of renal impairment has equal value, and the absolute value is simple, and easy to use, the study recommended perioperative blood pressure control basis irrespective of preoperative blood pressure. A study selected 40 to 65 - year - old marked non cardiac surgery patients with general anesthesia as the research object, preoperative induction of 24 h ambulatory blood pressure monitoring and anesthesia before the blood pressure, blood pressure and the average intraoperative blood pressure after induction comparison, found that after first before anesthesia induction measuring blood pressure and daytime dynamic correlation between average blood pressure difference ($r=0.429$), and about two-thirds of patients after induction minimum intraoperative minimum average blood pressure and blood pressure were significantly lower than that of patients with the lowest dynamic blood pressure values at night, prompt before anesthesia induction blood pressure cannot be regarded as a daytime blood pressure [6]. General anesthesia suppresses the sympathetic nervous system tone and thus reduces oxygen consumption. Similar to physiological sleep, it is reasonable to assume that patients can tolerate their lowest nocturnal blood pressure during the perioperative period, and that ideal blood pressure control should be based on this standard. The problem is that 24 h dynamic blood pressure monitoring before operation for every patient as the reference basis of basal blood pressure is not practical. Therefore, it is still necessary to further study to find a simple and feasible method to determine the basic blood pressure level in line with clinical practice.

Clinical Study on Blood Pressure and Organ Damage during Perioperative Period

Many vital organs of the body, such as the brain and kidney, have a certain range of autoregulation of perfusion pressure. When the perfusion pressure is significantly lower than the minimum threshold of its self-regulation, insufficient perfusion of heart, brain, kidney and other important organs will occur. According to the duration and severity, different degrees of organ function damage may occur. Severe cases may increase the risk of perioperative complications and death. The target level of perioperative blood pressure is an important determinant of organ perfusion pressure, and intraoperative hypotension is the most direct factor to induce organ hypoperfusion.

Intraoperative blood pressure and postoperative acute kidney injury

Walsh et al. [7] retrospectively analyzed 33,330 patients and found that the incidence of perioperative acute kidney injury and myocardial injury were 7.4% and 2.3% respectively. Further analysis of the relationship between map <55 mmHg during operation and postoperative acute kidney injury and myocardial injury in patients undergoing non-cardiac operation showed that map <55 mmHg increased the risk of postoperative acute kidney injury and myocardial injury regardless of the length of time. Sun et al. [8] conducted a retrospective cohort analysis of 5,127 patients undergoing non-cardiac surgery. The results showed that map <60 mmHg for more than 20 min and map <55 mmHg for more than 10 min were directly related to postoperative acute kidney injury. This study clearly suggests that a certain target level of map is necessarily associated with postoperative organ dysfunction. Therefore, individualized blood pressure control goal can reduce the occurrence of adverse events, and low map level should be avoided during and after operation. Recently, Ahuja et al. [9] prospectively enrolled 23,140 patients undergoing non-cardiac surgery. Radial artery puncture was used to record SBP, DBP, and map and pulse pressure difference per minute. The relationship between blood pressure and postoperative acute kidney injury was analyzed. The results showed that SBP <90 mmHg, map <65 mmHg and pulse pressure difference >35 mmHg were related to postoperative acute kidney injury, while map <65 mmHg during operation. It is the most sensitive predictor of postoperative acute kidney injury. This suggests that the absolute level of hypotension is an important independent risk factor for postoperative acute kidney injury.

Intraoperative blood pressure and postoperative myocardial injury

Perioperative myocardial injury or infarction will increase postoperative complications and mortality. Intraoperative hypotension may be directly related to postoperative myocardial injury. Hallqvist et al. [10] evaluated 300 patients with postoperative myocardial injury after major non-cardiac surgery, and found that patients with SBP decreased more than 50% of the basic value and lasted more than 5 min were prone to postoperative myocardial injury. Sessler and Khanna [11] retrospectively analyzed the patients with coronary stent implantation and normal preoperative troponin level who underwent high-risk surgery. Although there was no direct relationship between intraoperative blood pressure level and myocardial injury, the study showed that a large dose of positive inotropic drugs was needed to improve blood pressure level in order to avoid myocardial injury. Another retrospective cohort study on the postoperative prognosis of elderly patients with vascular surgery pointed out that the decrease of map during operation was more than

40% before anesthesia induction and lasted for 30 min, which was a high-risk factor for postoperative myocardial injury [12].

Intraoperative blood pressure level and brain function damage

Peri-operative brain damage includes postoperative delirium, postoperative cognitive dysfunction and stroke. Maintaining map at 50 mmHg to 150 mmHg can maintain the stability of cerebral blood flow through self-regulation. When low or high pressure exceeds the lower or upper limit of brain autoregulation threshold, the imbalance between cerebral perfusion and cerebral blood flow occurs, which is not conducive to the normal function of brain. At present, researches on the relationship between intraoperative blood pressure and brain function mainly focus on cardiac surgery, but there are many controversies about the appropriate map level during CPB. In 2011, a randomized single center prospective study showed that maintaining 80 mmHg to 90 mmHg high-pressure perfusion during CPB with relative low-pressure perfusion can reduce the incidence of postoperative delirium [13]. However, another observational study held a different view: during CPB, it is not hypotension, but high map exceeding the upper limit of cerebral blood flow autoregulation range is a risk factor for postoperative delirium, suggesting that appropriate map within cerebral blood flow autoregulation range may reduce the risk of delirium [14]. Vedel et al. [15] a randomized controlled study maintained two different levels of perfusion in patients with CPB Map (40 mmHg to 50 mmHg and 70 mmHg to 80 mmHg) showed that there was no significant difference in the incidence of new cerebral infarction and infarct size between the two perfusion pressure levels. Hori et al. [16] used transcranial Doppler technology to measure the self-regulating range of cerebral blood flow during CPB in real time. The results showed that the lower limit, upper limit and optimal map of cerebral self-regulating pressure during CPB were (65 ± 12), (84 ± 11) mmHg and (78 ± 11) mmHg respectively. The perfusion pressure is lower than the lower limit of pressure significantly increased the incidence of perioperative stroke. This suggests that individualized blood pressure level control is the most favorable for the outcome of patients. Recently, there was a literature review on the risk factors affecting the recovery of neurological function in patients with acute ischemic stroke after vascular interventional therapy. The results showed that the decrease of map more than 40% during operation was an independent risk factor for poor prognosis of neurological function [17]. However, the following studies suggested that there was no significant relationship between perioperative blood pressure level and postoperative neurological dysfunction (ischemic stroke). It can be seen that the blood pressure control levels obtained by different research objects and measurement methods are different, but individualized blood pressure control to achieve appropriate intraoperative blood pressure maintenance plays an important role in the recovery of neurological function in high-risk groups.

Individualized Blood Pressure Management Strategy

Perioperative goal-directed hemodynamic management is to set a certain level of map based on the results of population data, in order to control the level of map, optimize the organ perfusion pressure and provide the most suitable oxygen supply for the tissue. The target values of hemodynamics were set in advance by means of liquid infusion, vasoactive drugs and positive inotropic drugs. However, the concept of goal-directed hemodynamic management is vague, needs a complete set of equipment, and the operation is complicated, so its

clinical application is limited. Tissue hypoperfusion is an important factor in inducing organ injury. Organ perfusion pressure depends on the difference between inlet pressure and outlet pressure, and inlet pressure is the difference between map and critical arterial closure pressure. As we all know, the inlet pressure and outlet pressure of each organ are very different. Therefore, setting a "fixed" map cannot meet the more suitable perfusion pressure and the most suitable pressure range of all organs. In addition, most organs have self-regulating function on blood flow; when perfusion pressure is lower than organ specific self-regulating threshold level, there is a linear relationship between organ blood flow decrease and perfusion pressure, and it depends on map level. To sum up, when determining the target of blood pressure regulation during perioperative period, we should comprehensively consider the patient's basic blood pressure, pathophysiological status and coexisting diseases, and implement individualized blood pressure management strategy [18]. Large sample retrospective and observational studies indicated that map should be controlled at 60 mmHg to 70 mmHg in general patients during perioperative period to reduce the incidence of postoperative acute kidney injury, while patients with a history of hypertension need higher map level (>70 mmHg) [19,20]. However, there are many confounding factors in these studies, and it is difficult to determine the inevitable relationship between blood pressure management and patient outcomes. In a multicenter randomized clinical press study, adult patients with high risk of postoperative complications were divided into individualized blood pressure management group (patients with SBP fluctuation less than 10% of the baseline value maintained by infusion of norepinephrine) and standard treatment group (patients with SBP <80 mmHg or $<60\%$ of the baseline value maintained by intermittent intravenous injection of ephedrine). The results showed that the systemic inflammatory response syndrome in the individualized blood pressure management group was significantly lower than that in the standard treatment group at 7 days after operation (38.1% vs. 51.7%, $P<0.001$), and the risk of renal insufficiency in the individualized blood pressure management group at 30 days after operation (Relative Risk, $RR=0.70$, 95% CI 0.53 to 0.92) and the risk of organ dysfunction ($RR=0.66$, 95% CI 0.52 to 0.84) were significantly reduced, which suggested that individualized blood pressure management was very important for the outcome of patients [21]. 678 elderly patients with hypertension were randomly divided into three map levels groups (65 mmHg to 79 mmHg group, 80 mmHg to 95 mmHg group, 96 mmHg to 110 mmHg group). The patients were treated with goal-directed fluid control (stroke volume variation 8% to 13%) and four vasoactive drugs to control blood pressure in the target range. The results showed that the incidence of postoperative acute kidney injury in 80 mmHg to 95 mmHg group was significantly reduced [22]. In patients with cardiac CPB, Ono et al. [23] continuously monitored the pressure range of cerebral blood flow autoregulation by near infrared mass spectrometry as the map value of each patient during CPB perfusion. The results showed that it was not the absolute value of map, but the blood pressure lower than the threshold of cerebral autoregulation, which was closely related to postoperative acute kidney injury. The results of the above studies confirmed that individualized blood pressure control with reference to individual pathophysiological characteristics and specific clinical conditions can reduce the occurrence of adverse events and improve the prognosis of patients. The important problem is how to achieve individualized blood pressure target control and ultimately improve patient outcomes through a simple and fast process in clinical work? The process of "5T" can provide reference for rapid individualized

blood pressure regulation, that is, identifying high-risk patients; early intervention measures can be started to control blood pressure before anesthesia induction; the types of intervention include liquid therapy to enhance intravascular volume, vasoactive drugs to optimize cardiac after load and positive inotropic drugs to enhance myocardial contractility; target variables should be set as far as possible dynamic hemodynamic parameters were selected to guide the treatment and target blood pressure.

Suggestions on Blood Pressure Management Objectives in Clinical Practice

Blood pressure is an important hemodynamic index in perioperative period. Reasonable blood pressure is very important for the prognosis of patients. When setting a blood pressure range in clinical work, the following factors need to be considered [24]: 1. The blood pressure value cannot be regarded as the perfusion pressure of an organ, and the blood volume is the basis and key to determine the perfusion; 2. The blood pressure is the result of the joint action of blood flow and vascular resistance; 3. The special conditions of patients (such as the type and stage of shock, bleeding, sepsis, etc.); 4. The results showed that the elderly patients with complications underwent major surgery or the healthy young people underwent simple surgery; 5. Strict blood pressure management is better than laissez faire or loose management for the maintenance of patients' organ function; 6. One size fits all management may cause some patients to suffer from obvious hypoperfusion and organ function damage. Special attention should be paid to the duration of this blood pressure target.

There are three situations in clinical practice: Low basal blood pressure (SBP<90 mmHg, DBP<50 mmHg), normal basal blood pressure (SBP 90 mmHg to 139 mmHg, DBP 50 mmHg to 89 mmHg) and high basal blood pressure (SBP \geq 140 mmHg, DBP \geq 90 mmHg). It is recommended in the literature that the goal of blood pressure management for patients with hypotension undergoing non cardiac surgery should be to keep map \geq 60 mmHg and blood pressure fluctuating within 100% to 120% of the baseline as far as possible, and the maximum allowable map is 76 mmHg [25]. It should be emphasized that maintaining map \geq 60 mmHg during perioperative period is a minimum requirement for such patients. When patients with normal basal blood pressure undergo non-cardiac surgery, the goal is to keep blood pressure at 90% to 110% of the basal value and map at 65 mmHg to 95 mmHg. For patients with high basal blood pressure, strict blood pressure control measures should be taken. Because this group is prone to severe fluctuations of blood pressure during perioperative period. It is suggested that the blood pressure drop should be controlled within 20% of the basic value, while the blood pressure rise should be set within 10% of the basic value, because if the latter is 20%, it may lead to unnecessary hypertension. The research results suggest that the perioperative SBP of such patients should be maintained <160 mmHg [26].

Conclusion and Prospect

The goal of blood pressure control is a dynamic management process. The ultimate goal of blood pressure target setting is to maintain effective organ perfusion and improve microcirculation, which is conducive to the prognosis and outcome of patients. According to the basic blood pressure, strict blood pressure control, that is, the fluctuation range maintained at 10% to 20% of the basic blood pressure, may be the most suitable blood pressure target control

mode for patients' physiological needs. Large sample studies suggest that map should be maintained >65 mmHg in patients without comorbid diseases during perioperative period, but the results of group studies should be carefully applied to the blood pressure control of individual patients; patients with multiple risk factors should be individualized according to specific pathophysiological characteristics. At present, there is a lack of prospective research on the target of individualized blood pressure control in patients with different pathophysiological states. It is of great significance to select biological indicators sensitive to organ ischemia/hypoxia to guide blood pressure control in order to further clarify the individualized blood pressure control in different disease states.

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