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Abstract: *Objective:* To explore the effect of continuous non-invasive blood pressure monitoring on intraoperative hemodynamics and postoperative myocardial injury in craniotomy. *Methods:* 120 cases of elective craniotomy were divided into the self-control group (continuous non-invasive blood pressure monitoring and intermittent cuff non-invasive blood pressure monitoring, CNAP group) and propensity score matching group (only intermittent cuff non-invasive blood pressure measurement in previous craniotomy, PSM group); Goal-directed hemodynamic management in CNAP group included heart rate (HR), blood pressure (BP), stroke volume (SV), stroke variability (SVV), and systemic vascular resistance index (SVRI). The main index is to compare the troponin level within 72 hours after operation between the CNAP group and the PSM group; The secondary indicators are the comparison of the hemodynamic conditions between the CNAP group and the PSM at 10 specific time points. *Results:* The incidence of postoperative myocardial injury in the CNAP group was significantly lower than that in the PSM group (12% vs. 30%, P = 0.01); in the CNAP group hypotensive episodes (6 vs. 3, P = 0.01), positive balance of fluid therapy (700 vs. 500 mL, P < 0.001), more use of vasoactive drugs (29 vs. 18, P = 0.04), more stable hemodynamics medical status (P = 0.03) were recorded. *Conclusion:* The hemodynamic management strategy based on continuous non-invasive blood pressure monitoring can reduce the incidence of myocardial injury after elective craniotomy and maintain a more stable hemodynamic state.

Keywords: Continuous non-invasive blood pressure monitoring; Propensity score matching; Self-control; Elective surgery; Craniotomy; Hemodynamics state; Myocardial injury

Online publication: September 25, 2023

1. Introduction

Craniotomy is a common surgical procedure of neurosurgery. Due to the long operation time and frequent

changes of intracranial pressure during the operation, the application of intracranial pressure-lowering drugs, and the complexity of surgical operations, blood pressure (BP) monitoring is required. Invasive blood pressure monitoring is regarded as the gold standard ^[1], but arterial catheter insertion requires specially trained personnel, is invasive, time-consuming, and has risks such as embolism, tissue damage, local infection, and so on ^[2].

In clinical practice, invasive blood pressure monitoring is mostly limited to be used in high-risk cases. The traditional cuff intermittent non-invasive blood pressure (NIBP) monitoring method is simple, safe, and reliable, even in about 50% of high-risk surgeries, NIBP is also used ^[3]. However, motion artifacts, cuff size, and long intermissions are also significant disadvantages of NIBP. If blood pressure is not monitored timely, it may lead to delays in recognition and treatment, which may have adverse effects. Previous study has shown that hypotension is associated with postoperative stroke, myocardial injury, and acute kidney injury ^[4]. Even if the mean arterial pressure is lower than 55 mmHg for a short period, it is also closely related to the occurrence and development of myocardial injury. Monk *et al.* found that the mortality rate will increase by 1.36 times per minute when the systolic blood pressure is less than 80 mmHg ^[5]; at the same time, the mean arterial pressure variability is closely related to the 30-day mortality rate of non-cardiac surgery patients ^[6].

Another hemodynamic monitoring method is the continuous non-invasive monitoring technology of pressure waveform. This device can calculate cardiac output and blood pressure through digital pulsation and pressure waveform analysis. Like invasive arterial monitoring, it can continuously obtain blood pressure, indexes such as cardiac output, cardiac index, stroke volume (SV), stroke variability (SVV), and systemic vascular resistance index (SVRI) are relatively advanced hemodynamic monitoring technologies and equipment ^[7].

In craniocerebral surgery, especially craniotomy, due to the complexity of the operation and the brain as the central nervous system of the whole body, intracranial pressure changes continuously with the operation steps, and the application of drugs such as reducing intracranial pressure has a great impact on the autonomic nervous system, and systemic catecholamines have a greater impact which can easily lead to extremely unstable hemodynamics in the perioperative period, high incidence of complications and all-cause mortality, and postoperative myocardial injury ^[8]. Therefore, for this type of surgery, not only continuous monitoring of vital signs such as heart rate (HR), BP, body temperature (T), and oxygen saturation (SpO₂) but also real-time and continuous monitoring of cardiac function and fluid is required.

We hypothesized that in elective craniotomy surgery, the use of continuous non-invasive blood pressure monitoring-guided perioperative hemodynamic management strategies can maintain a more stable intraoperative hemodynamic state and reduce the incidence of postoperative myocardial injury, thereby improving the initial perioperative outcomes and prognosis in cranial surgery.

2. Materials and methods

2.1. General information

This study is a single-center, self-control, and propensity score-matched inter-group control clinical study aimed at improving intraoperative hemodynamics and short-term postoperative outcomes in patients undergoing craniotomy. This study is approved by the Ethics Committee of Dazhu Hospital. The subjects of this study were elective surgery patients who were hospitalized in Dazhu County People's Hospital from October 2018 to February 2023 and underwent craniotomy.

Inclusion criteria included patients between 50 to 65 years old, patients with American Society of Anaesthesiologists (ASA) grade I–II, patients with a body mass index (BMI) of $18-25 \text{ kg/m}^2$, and patients who signed the informed consent form.

Exclusion criteria included: (1) Patients allergic to general anesthesia and other commonly used

perioperative drugs or have drug contraindications; (2) Patients with bilateral radial arteries who are not suitable for installing non-invasive blood pressure monitoring devices; (3) Combined preoperative patients with myocardial injury, heart failure and arrhythmia; (4) Patients with electrolyte abnormalities, liver and kidney insufficiency, coagulation dysfunction, etc. before surgery; (5) Patients with uncontrolled hypertension before surgery; (6) Patients with diabetes before surgery; (7) Patients with severe macrovascular disease and peripheral vascular disease before surgery; (8) Patients with disturbance of consciousness before surgery; (9) Long-term use of sedatives or antidepressants before surgery, alcoholism or drug dependence patients; (10) Patients who participated in other clinical studies in the past three months; and (11) Patients who were evaluated by researchers for other conditions that were not suitable for inclusion.

Elimination criteria included: (1) Patients with interrupted or incomplete intraoperative non-invasive blood pressure (continuous or traditional) monitoring data; (2) Intraoperative or postoperative massive bleeding (bleeding volume > 500 mL) or hemorrhagic shock; (3) Intraoperative or postoperative bleeding Patients with post-consciousness disorder or more than 24 hours without awakening; (4) Patients who had complications with sepsis during hospitalization; and (5) Patients who underwent craniocerebral surgery or lumbar drainage during hospitalization.

The definition of postoperative myocardial injury is high-sensitivity troponin > 15 ng/L within 72 hours after surgery ^[9].

2.2. Sample size and grouping

The sample size is 120 cases in total, 60 cases of self-control group (continuous non-invasive blood pressure monitoring (TL-300) and traditional cuff intermittent non-invasive blood pressure monitoring at the same time, the interval time is set to 3 min, hereby known as CNAP group), 60 craniotomy patients who underwent only conventional intermittent non-invasive blood pressure monitoring were matched 1:1 based on propensity scores, hereby known as PSM group.

2.3. Implementation method

2.3.1. Anesthesia method

Preoperative fasting of 6–8 hours, water deprivation of 2 hours, monitoring of vital signs such as HR, T, SpO_2 , BP (including continuous non-invasive blood pressure monitoring and intermittent cuff blood pressure monitoring), end-tidal CO₂ (PetCO₂), and muscle relaxation were performed. Anesthetic gas was monitored after entering the operation room, an open peripheral/center intravenous channel was built, and no special medication was given before anesthesia. General anesthesia was induced with midazolam, propofol, sufentanil, and rocuronium bromide. Remifentanil and propofol were continuously infused, and inhalation of sevoflurane was maintained at an appropriate depth of anesthesia, with intermittent bolus injections of rocuronium bromide to maintain muscle relaxation. All drugs were given according to conventional dosages.

2.3.2. Fluid infusion

The fluid infusion of the CNAP group adopts the standard infusion method. A total of 300 mL compound sodium chloride injection was given before the start of anesthesia, supplement fluid was given at 5–7 mL/kg.h, and infusion of compound sodium chloride:hydroxyethyl starch at a ratio of 2:1 was given when the blood loss is less than 500 mL; When the patient has hemoglobin < 10 g/dL, red blood cell transfusion can be considered. During this period, the plasma colloid osmotic pressure (COP) and coagulation function of the patient can be dynamically monitored, and if necessary, colloid (COP < 25 mmHg) or albumin (colloid infusion cannot supplement COP) or fresh frozen plasma (during coagulation dysfunction) can be infused.

2.3.3. Hemodynamic targeting and treatment flow chart

The goal of hemodynamics is to maintain the mean arterial pressure (MAP) within the range of \pm 15%. Specific measures include fluid load (administration of compound sodium chloride injection 2 mL/kg within 5 minutes), norepinephrine, ephedrine or atropine, uradil/nitroglycerin, esmolol, cedilan, etc. The processing flow is shown in **Figure 1**.



Figure 1. Management of hemodynamic abnormalities

2.4. Observation indicators

The main observation indicator of this study is the incidence of postoperative myocardial injury between the 2 groups.

The secondary indicator of this study is the observation of both groups after entering the operation room (T1), immediately after induction (T2), immediately after intubation (T3), immediately after head nail installation (T4), immediately after scalp incision (T5), cuff and continuous non-invasive measurement of BP and HR before flap removal (T6), after bone flap removal (T7), before dura mater incision (T8), after dura mater incision (T9), at the end of surgery (T10).

2.5. Statistical methods

Data analysis was performed using SPSS 22.0 and R language. If it satisfied a normal distribution, it was expressed as mean \pm standard deviation (SD). The traditional cuff blood pressure measurement group and the continuous non-invasive blood pressure measurement group were matched 1:1 according to the propensity score. If the main indicators met the normal distribution, the analysis of variance was used; for the data of two groups with multiple repeated measurements, the paired sample *t*-test was used; if not, the non-parametric test will be used. *P* < 0.05 means a statistically significant difference.

3. Results

3.1. The basic characteristics of included patients

A total of 203 patients who underwent craniotomy were screened in this study, and 120 patients (60 in each group) were included in the study (**Figure 2**). There were no significant statistical differences between the two groups in demographic characteristics and anesthesia-related data (**Table 1**).



Figure 2. Patients allocation

| | CNAP group | PSM group | <i>P</i> value |
|------------------------|--------------|--------------|----------------|
| Age, years | 59.7 ± 8.9 | 58.9 ± 8.1 | 0.63 |
| Gender (female) | 27 | 28 | 0.91 |
| BMI | 23.6 ± 3.5 | 24.2 ± 3.9 | 0.83 |
| ASA grade | | | 0.75 |
| Ι | 6 | 5 | |
| II | 54 | 55 | |
| Type of surgery | | | 0.85 |
| Tumor | 39 | 40 | |
| Aneurysm | 21 | 20 | |
| Duration of anesthesia | 239 ± 61 | 243 ± 59 | 0.83 |

Table 1. Characteristics, anesthesia, and procedure data

During the operation, the hemodynamics of the CNAP group were more stable, and there was no significant difference in BP at each time point (P > 0.05), while the traditional cuff intermittent blood pressure measurement group had no significant difference before and after the installation of head nails, opening of the skull, and key nodes such as before and after dura mater opening are more prone to hemodynamic

fluctuations (P = 0.03). In the CNAP group at the T1–10 timepoint, continuous non-invasive blood pressure can detect hemodynamic abnormalities in real-time, which is more sensitive and specific than intermittent cuff measurement, and the treatment measures are more directional. The results of the CNAP group and the PSM group combined showed that hemodynamic management under the guidance of continuous non-invasive blood pressure monitoring had a higher recognition rate and was related to more timely and effective interventions. Compared with traditional non-invasive blood pressure monitoring, CNAP group intervention measures were precise (**Table 2**).

In postoperative myocardial injury, there were 7 cases (12%) in the CNAP group and 18 cases (30%) in the traditional cuff monitoring group, and there was a significant difference in the incidence of postoperative myocardial injury between the two groups (P = 0.01) (**Table 2**).

| | CNAP Group | PSM group | P value |
|--|---------------------|---------------------|---------|
| Number of detected episodes of hypotension per patient | 6 | 3 | 0.001 |
| Blood loss (mL) | 300 (100-400) | 310 (120-410) | 0.79 |
| Total intake of fluid (mL) | 2,600 (1,700–3,500) | 1,800 (1,500–2,200) | 0.001 |
| Fluid balance (mL) | +700 (500-1,000) | +500 (300-600) | < 0.001 |
| Patients receiving NE | 29 | 18 | 0.04 |
| Patients receiving cediranib | 4 | 0 | 0.12 |
| Patients receiving nitroglycerin | 3 | 0 | 0.24 |
| Patients with myocardial injury | 7 | 18 | 0.01 |

Table 2. Intraoperative hemodynamic management

4. Discussion

This study shows that the goal-directed hemodynamic management strategy based on continuous non-invasive blood pressure (BP, HR, SV, SVV, SVRI) can effectively reduce the incidence of myocardial injury after elective craniotomy. In intraoperative management with non-invasive blood pressure monitoring, the intraoperative hemodynamics of the CNAP group were more stable. Intraoperative hemodynamic management is more precise and effective. Therefore, for those who do not need or have difficulty establishing invasive arteries, or those who need continuous cardiac function monitoring, from the perspective of stable hemodynamics, non-invasive continuous blood pressure monitoring may well be a desirable choice.

Hypotension leads to target organ damage by affecting organ perfusion. However, the effects of hypotension on organ perfusion and outcome are heterogeneous, and hypotension is not equal to hypoperfusion ^[10,11]. Arterial blood pressure is the driving force of organ perfusion. Blood pressure can be obtained, but there are differences in the automatic regulation of blood flow in different organs, resulting in the inaccurate determination of organ perfusion pressure. In our study, since the included cases were considered to be patients with craniotomy, which is categorized as high-risk surgery, and the relationship between mean arterial pressure and perfusion pressure was more closely related, a 20% decrease in MAP was selected as the criterion for hypotension. The same conclusion as previous studies is that they can guarantee the stability of intraoperative hemodynamics, but the difference is that these studies did not report further postoperative outcomes ^[12,13]. We analyzed the possible reasons: (1) The surgical category is craniocerebral surgery, and the hemodynamic management method of continuous non-invasive blood pressure monitoring maintains continuous hemodynamic stability, not just from the perspective of hypotension. The variation of mean arterial pressure was significantly

correlated with the decrease of mortality within 30 days after operation ^[6]; (2) In our study, not only blood pressure control was improved but also heart function, peripheral vascular resistance, and fluid load were focused on, and so the treatment was more precise and individualized; (3) The VISION study is an international, multicenter, prospective cohort study ^[14]. In patients older than 45 years, the incidence of myocardial injury after noncardiac surgery was 8%, and in our control group, the incidence of myocardial injury was as high as 30%. Therefore, the conclusion needs to be confirmed by further multicenter prospective studies.

In the CNAP group, we observed higher total fluid intake and positive fluid balance, consistent with previous studies on goal-directed fluid therapy ^[15,16]. Due to the particularity of craniocerebral surgery, it is difficult to optimize the group solution of fluid. Theoretically, combining objective indicators such as SV, SVV, and SVRI can guide fluid infusion to a certain extent. However, due to different surgical sites, craniotomy adopts different surgical positions. Under general anesthesia and mechanical ventilation, it may interfere with the accuracy of the results of SV, SVV, and SVRI ^[17,18], which needs to be personalized according to the actual situation of the patient's clinical decision-making.

There are still some shortcomings in this study: the main outcome index of this study was generated from a case-control study, there may be many confounding factors, and as the level of medical technology continues to increase, it may have an impact on the patient's outcome. However, craniotomy itself is a high-risk operation, and continuous hemodynamic monitoring should be performed as much as possible under certain conditions. From the perspective of protecting patients, a randomized controlled study was not selected in our study, but a propensity score was adopted to match the two groups which can reduce the risk of bias and confounding; at the same time, the self-control method was used to compare the two hemodynamic monitoring methods; the single-center and included population of this study may limit the generalizability of the results.

5. Conclusion

The hemodynamic management strategy based on continuous non-invasive blood pressure monitoring can reduce the incidence of myocardial injury after elective craniotomy, and at the same time maintain a more stable hemodynamic state. At present, it is based on the principle of real-time data guidance. Whether machine learning can be used to optimize prediction capabilities and achieve early intervention will be the future research direction.

Disclosure statement

The authors declare no conflicts of interest.

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60

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