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Consensus and Guideline

Expert consensus on blood pressure management in critically ill patients ☆

Yuetian Yu [1,#], Ye Gong [2,#], Bo Hu [3], Bin Ouyang [4], Aijun Pan [5], Jinglun Liu [6], Fen Liu [7], Xiu-Ling Shang [8], Xiang-Hong Yang [9], Guowei Tu [10], Changsong Wang [11], Shaolin Ma [12], Wei Fang [13], Ling Liu [14], Jiao Liu [15,*], Dechang Chen [15,*]

[1] *Department of Critical Care Medicine, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai 200001, China*
[2] *Department of Critical Care Medicine, Huashan Hospital, Fudan University, Shanghai 200040, China*
[3] *Department of Critical Care Medicine, Zhongnan Hospital of Wuhan University, Wuhan 430071, Hubei, China*
[4] *Department of Critical Care Medicine, The First Affiliated Hospital of SunYatsen University, Guangzhou 510080, Guangdong, China*
[5] *Department of Critical Care Medicine, The First Affiliated Hospital of USTC, Division of Life Science and Medicine, University of Science and Technology of China, Hefei 230001, Anhui, China*
[6] *Department of Emergency Medicine and Critical Care Medicine, The First Affiliated Hospital of Chongqing Medical University, Chongqing 400016, China*
[7] *Department of Critical Care Medicine, The First Affiliated Hospital of Nanchang University, Nanchang 330000, Jiangxi, China*
[8] *Department of Critical Care Medicine, Fujian Provincial Hospital, Shengli Clinical Medical College of Fujian Medical University, Fujian Provincial Center for Critical Care Medicine, Fujian Provincial Key Laboratory of Critical Care Medicine, Fuzhou 350001 Fujian, China*
[9] *Department of Intensive Care Unit, Emergency & Intensive Care Unit Center, Zhejiang Provincial People's Hospital, Affiliated People's Hospital, Hangzhou Medical College, Hangzhou 310014 Zhejiang, China*
[10] *Cardiac Intensive Care Center, Zhongshan Hospital, Fudan University, Shanghai 200032, China*
[11] *Department of Critical Care Medicine, the First Affiliated Hospital of Harbin Medical University, Harbin 150001, Heilongjiang, China*
[12] *Department of Critical Care Medicine, Shanghai East Hospital, Tongji University School of Medicine, Shanghai 200120, China*
[13] *Department of Critical Care Medicine, Shandong Provincial Hospital Affiliated to Shandong First Medical University, Shandong First Medical University, Jinan, 250014 Shandong, China*
[14] *Department of Critical Care Medicine, Jiangsu Provincial Key Laboratory of Critical Care Medicine, Zhongda Hospital, School of Medicine, Southeast University, Nanjing, 210009 Jiangsu, China*
[15] *Department of Critical Care Medicine, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200025, China*

Introduction

For critically ill patients with unstable hemodynamics, goal-directed therapy for arterial blood pressure is needed with continuous daily bedside monitoring. The prevalence of hypertension in Chinese adults is 25.2%, of which 1–2% of patients may experience a hypertensive emergency, with a mortality rate of 6.9% in the acute phase. The mortality and readmission rates within 90 days of onset are as high as 11%.[1] Furthermore, the mortality rate for patients who experience hypertensive emergencies can reach 50% within 12 months of the incident.[2] The incidence of perioperative hypertension in patients undergoing cardiac surgery is approximately 50%, with this figure dropping to 25% for non-cardiac surgery. Surgery may increase the incidence of perioperative cardio-cerebrovascular adverse events by 3–5%.[3]

Hypotension is a common clinical manifestation of shock and the most frequently monitored measure in the intensive care unit (ICU). In addition, nearly 50 million people worldwide are diagnosed with sepsis every year, of which almost 2 million (3–4%) may develop secondary septic shock, with mortality exceeding 50%.[4] The incidence of cardiogenic shock is 10–20%, and the in-hospital mortality rate for cardiogenic shock related to myocardial infarction is in the range of 27–51%.[5] Hypovolemic shock accounts for 16% of all shock patients admitted to the ICU, mainly because of endogenous or exogenous blood volume loss, which can lead to hypoperfusion of tissues and organs, especially cardiac, cerebral, and renal hypoperfusion.[6]

Thus, it remains challenging to standardize arterial blood pressure monitoring and medication use in critically ill patients, control blood pressure within an ideal range, restore tissue and organ perfusion, correct microcirculation disorders, and reduce

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* Corresponding authors at: Department of Critical Care Medicine, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200025, China.
E-mail addresses: catherine015@163.com (J. Liu), 18918520002@189.cn (D. Chen).
# Yuetian Yu and Ye Gong contributed equally to this work

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related adverse events. With the constant development of critical care medicine, large-cohort studies and randomized controlled trials (RCTs) have provided evidence-based guidelines for goal-directed blood pressure therapy. Targeted blood pressure adjustments lead to various clinical effects in critically ill patients. On the one hand, these effects arise from changes in tissue and organ perfusion pressure caused by blood pressure fluctuations, and on the other hand, they reflect the body's response after drug regulation. These changes are foundational for maintaining pathophysiological homeostasis. However, further clarification is needed about determining individualized regulation for blood pressure goals based on the patient's underlying disease, blood pressure levels, vascular status, organ function, and disease processes. Although it is the era of precision medicine, and individualized therapy is increasingly emphasized, we still need to develop a basic range of blood pressure regulation in different pathophysiological states. Thus, it is anticipated that we could standardize blood pressure regulation as much as possible.

To further optimize blood pressure monitoring and regulation in critically ill patients, the Chinese Society of Critical Care Medicine (CSCCM) commissioned a panel of experts to discuss, summarize, and formulate relevant content using the Grading of Recommendations Assessment Development and Evaluation (GRADE) methodology to develop the *Expert Consensus on Blood Pressure Management in Critically Ill Patients*.

Scope and definition of the consensus

This consensus proposes recommendations mainly focused on the implementation of blood pressure monitoring in critically ill patients, goal-directed blood pressure therapy for patients in shock, hypertension in severely ill patients and emergency treatment of hypertension, and blood pressure management in severely ill patients in different disease states. The consensus is intended to provide a reference for clinicians from the ICU, Emergency and Anesthesiology Departments, and clinical pharmacists for the reasonable regulation of blood pressure in critically ill patients with various pathophysiological conditions.

Consensus development process

In March 2022, a drafting group for the *Expert Consensus on Blood Pressure Management in Critically Ill Patients* was established with 16 critical care experts and two experts in evidence-based medicine. Working meetings were held regularly, leading to an agreement that blood pressure monitoring methods and blood pressure regulating drugs are widely used in critically ill patients despite controversies remaining about the target population, the timing of initiation, dose adjustment, and course of treatment for patients with different pathophysiology. Current clinical care practices and published literature suggest a need to develop expert consensus and associated recommendations to promote standardized management of blood pressure and the reasonable use of vasoactive agents in critically ill patients, ultimately maintaining their blood pressure stability and improving outcomes.

Expert group members searched literature included in PubMed, Cochrane, and Embase databases from 2010 to 2021, and published in English or with English abstracts available. The search terms used to retrieve results included: "critical care," "critically ill patients," "shock," "hypertension," "hypotension," and "perioperative." Systematic reviews, and prospective, and retrospective cohort studies were preferentially selected for inclusion, while case series or case reports were excluded. The titles and abstracts of all articles were screened for relevance by three experts in the drafting group. The full-text content of eligible articles was then compared against inclusion and exclusion criteria. Only studies reporting results in adult patients (≥18 years of age) were included. When papers lacked relevant data on ICU admission, treatment, or death, the studies (or some of the patients) were excluded.

Table 1
GRADE recommendation levels.

Grade	Recommendation	Evidence
Grade 1+	Strongly recommended	High-quality evidence
Grade 2+	Weakly recommended	Low-quality evidence
Expert opinion	Expert advice	Insufficient evidence
Grade 2−	Weakly not recommended	Low-quality evidence
Grade 1−	Strongly not recommended	High-quality evidence

GRADE: Grading of Recommendations Assessment Development and Evaluation.

Clinical questions were proposed by the expert group, and clinical experts responsible for each question were appointed. All the proposed questions were deconstructed according to the PICO principles of research population (Participants), interventions (Interventions), disease controls (Comparisons), and clinical outcomes (Outcomes), which were used to define the eligibility criteria for the literature search and identify the studies for final analysis. Levels of evidence were divided into high or low quality, and in some cases, treatment for specific clinical problems was recommended as "expert advice" because of insufficient literature to support more clearly graded recommendations. The GRADE methodology (Table 1) was adopted to evaluate each recommendation and grade the evidence quality according to evidence-based medicine principles.

After five rounds of discussion by the working group, 25 recommendations were finally developed. Each recommendation was evaluated using the GRADE methodology, and the evaluation process was duplicated to ensure comprehensive recommendations and accurate grading levels for each recommendation. Subsequently, the working group again referred to the latest literature and updated the recommendations based on the summary opinions of the meetings. The first draft of recommendations was completed at the end of February 2023 and was finalized in March 2023. After two rounds of voting, a high level of agreement was reached for all the recommendations.

Monitoring methods and medications for blood pressure in critically ill patients

Monitoring methods for blood pressure control in critically ill patients

Blood pressure monitoring in critically ill patients can be divided into non-invasive and invasive approaches. Non-invasive monitoring uses intermittent and continuous modes, and commonly used intermittent monitoring includes the Korotkoff sound method (mercury sphygmomanometer) and the vibration

method (monitor). Current relatively mature methods of continuous non-invasive blood pressure monitoring include volume-compensation, arterial tonometry, pulse wave velocity, and ultrasonic manometry.[7] These monitoring methods avoid the complications caused by invasive monitoring (such as bleeding, infection, and thrombus) and compensate for the disadvantages of non-real-time intermittent non-invasive monitoring.[8] However, the accuracy and reliability of continuous non-invasive monitoring methods remain controversial compared with invasive approaches.

Question 1: What are the appropriate monitoring methods of arterial pressure for critically ill patients?

Recommendation 1: For patients with hypotension requiring vasopressors or hypertensive emergencies requiring emergency intervention, we suggest invasive arterial pressure monitoring is the first choice (Grade 2+, Weak recommendation).

It is difficult for non-invasive monitoring of arterial pressure to reflect fluctuations in blood pressure over time for critically ill patients with unstable blood pressure. A retrospective study of 27,022 critically ill patients found that intermittent non-invasive arterial pressure monitoring significantly overestimated systolic pressure compared with invasive arterial pressure monitoring during hypotension.[9] In another retrospective study of 263 critically ill patients, the difference between the two measured mean arterial pressures (MAPs) was ≥10 mmHg in 40% of the patients.[8] However, compared with invasive arterial pressure monitoring, the bias and precision of continuous non-invasive monitoring did not reach the level considered acceptable by the Association for the Advancement of Medical Instrumentation.[10] A meta-analysis of 18 studies in 2021 involving 785 critically ill adult patients also showed poor consistency between continuous non-invasive and invasive arterial pressure monitoring.[11] Therefore, for patients with hypotension requiring vasoactive agents, invasive blood pressure monitoring is suggested as the optimal approach.

A retrospective study in 2021 included 147 patients with hypertensive emergencies and found that – compared with invasive arterial pressure monitoring – intermittent non-invasive arterial pressure monitoring resulted in systolic pressure values lower than 10 mmHg in 68% of patients, which may have led to the poorly controlled arterial pressure in these patients.[12] Similar results were noted in a prospective study of hypertensive patients with acute aortic disease. Therefore, invasive arterial pressure monitoring is also suggested as the first choice for patients experiencing hypertensive emergencies that require rapid reduction.[13]

Question 2: Which site should be selected for invasive arterial pressure monitoring?

Recommendation 2: We suggest the radial artery as the preferred site for invasive arterial pressure monitoring (Grade 2+, Weak recommendation).

The radial artery is often preferred for arterial puncture because of its fixed and superficial location, ease of puncture and cannulation, presence of collateral circulation from the ulnar artery, and low complication rates. In a retrospective study of 57,787 patients, radial artery cannulation was performed in 94.5% of patients, with vascular complications or nerve injury occurring in 21 patients (0.034%).[14] The central (femoral) artery can also be used as a site for invasive arterial pressure monitoring.

A prospective study in 2022 that included 32 patients with refractory shock found that the MAP in the radial artery was 7.6 mmHg lower than in the femoral artery.[15] Similarly, in a prospective study of critically ill patients with sepsis, the MAP of the radial artery was lower than that of the femoral artery (66±2.2 mmHg *vs.* 81±2.5 mmHg) when high-dose norepinephrine was used.[16] Therefore, when administering large doses of vasoactive agents, central arteries (such as the femoral artery) can be used for invasive blood pressure monitoring.

Intravenous drug therapy for blood pressure control in critically ill patients

The blood pressure of critically ill patients fluctuates considerably, and medications need to exert a rapid and strong effect in controlling blood pressure. Thus, intravenous administration is often used. This section focuses on the mechanisms of action, dosage, onset, duration of action, contraindications, and adverse reactions of commonly used agents in blood pressure regulation (Supplementary Tables 1 and 2).

Blood pressure management in patients with shock

Blood pressure management in patients with septic shock

According to the Sepsis 3 definition, septic shock requires vasopressors to maintain MAP greater than 65 mmHg and arterial blood lactate greater than 2 mmol/L[17] after adequate fluid resuscitation to the underlying sepsis. Pathophysiologically, it is characterized mainly by distributive shock caused by pathological vasodilation. In septic shock, hypotension leads to inadequate oxygen delivery and tissue perfusion. Thus, blood pressure management is necessary to restore the balance between systemic oxygen delivery and oxygen consumption as rapidly as possible.[18] The target level of blood pressure management and the use of vasoconstrictor drugs may vary because of the diversity of precipitating factors for septic shock and individual differences.

Question 3: What is the target blood pressure for initial resuscitation in patients with septic shock?

Recommendation 3: For patients with septic shock requiring vasopressors, the experts recommend an initial target MAP ≥65 mmHg (Grade 1+, Strong recommendation).

A multicenter RCT (SEPSISPAM) found no significant difference between 28-day (Hazard Ratio[HR]=1.07; 95% confidence interval[CI]: 0.84–1.38; *P*=0.57) and 90-day (HR=1.04; 95% CI: 0.83–1.30; *P*=0.74) mortality in patients with septic shock on vasopressors with target MAPs of 65–70 mmHg or 80–85 mmHg; the group with a higher target had a greater incidence of new-onset atrial fibrillation than the lower target group.[19] Another study included patients over 65 years of age who received vasopressors because of vasodilatory hypotension. Participants were randomized into a conventional treatment group (vasopressor use and MAP target were at the discretion of the clinicians) or the permissive hypotension group (MAP target maintained at 60–65 mmHg). The final results showed that the MAP of the con-

ventional treatment group was 72.6 mmHg, while the intervention group's MAP was 66.7 mmHg. The two groups showed no significant difference in the 90-day mortality rate (HR=−2.85%, 95% CI: −6.75 to 1.05; *P*=0.15). In addition, the study suggests that minimizing the use of vasopressors may be beneficial in elderly patients with vasodilatory hypotension.[20] In their research – with the same outcomes as the two RCTs described above – Lamontagne et al.[21] found that in patients with septic shock, there was no significant difference in-hospital mortality between the low (60–65 mmHg) and high (75–80 mmHg) MAP groups (30% *vs.* 33%, *P*=0.84). Even for patients older than 75 years, lower MAP targets were associated with reduced hospital mortality (*P*=0.015).

Question 4: What is the blood pressure target in initial resuscitation for patients with septic shock with chronic hypertension?

Recommendation 4: For patients with septic shock with chronic hypertension, we suggest that the initial MAP should be maintained at 80–85 mmHg or normal levels (Grade 2+, Weak recommendation).

Arteriole lesions are the most important pathological changes in hypertension. Patients with hypertension are more prone to tissue hypoperfusion because of impaired endothelial cell function and abnormal mitochondrial function. Thus, the demand for organ perfusion pressure levels may be higher for hypertensive patients.

The optimal target for MAP in hypertensive patients with septic shock remains undetermined. A single-center study showed that patients with septic shock complicated by chronic hypertension required norepinephrine to maintain MAP ≥65 mmHg. Increasing MAP from 65 mmHg to normal levels by increasing the dosage of norepinephrine was associated with an increase in cardiac output and central venous oxygen saturation. Meanwhile, the density of perfused small vessels (*P*=0.009), the proportion of perfused small vessels (*P*=0.002), and the microvascular flow index (*P*=0.009) were significantly increased.[22] The study suggests that in early resuscitation of patients with septic shock complicated by chronic hypertension, increasing MAP to normal levels may significantly improve microcirculation. In the subgroup analysis of the SEPSISPAM study, it was found that patients with hypertension had a reduced incidence of acute kidney injury (AKI) and renal replacement therapy in the high MAP target group (80–85 mmHg) compared with the low MAP group (65–70 mmHg), suggesting that higher MAP may be required in patients with septic shock and chronic hypertension.[19]

Lamontagne and colleagues[20] found in septic shock patients with chronic hypertension, the permissive hypotension approach was associated with a lower 90-day mortality rate, however, the permissive hypotension group's MAP was 66.7 mmHg and the usual care group's MAP was 72,6 mmHg. The blood pressure level in the usual care group was lower than 80–85 mmHg, which may be the reason for the opposite result.

Question 5: What target diastolic blood pressure (DBP) **should be maintained in patients with septic shock?**

Recommendation 5: For patients with septic shock, we suggest that diastolic arterial pressure should be maintained at >50 mmHg (Grade 2+, Weak recommendation).

DBP is one of the hallmarks of vascular tension. The reduction of DBP in septic shock is related to the severity of arteriolar vasodilation, and left ventricular myocardial perfusion may be impaired when DBP <50 mmHg. Low DBP is an early predictor of mortality in septic shock. In an analysis of patients with septic shock requiring continuous norepinephrine for at least 72 h, DBP >50 mmHg (odds ratio[OR]=24.8, 95% CI: 2.9–215.9, *P*=0.0036) was found to be an independent predictor of short-term survival.[23] Therefore, diastolic pressure, as an important parameter reflecting vascular reactivity in patients with septic shock, provides an easily measured and reliable indicator for goal-directed treatment of septic shock. Studies suggest that for patients with septic shock and MAP less than 85 mmHg, the dose of vasopressors should be titrated to maintain DBP ≥50 mmHg – shown to be similarly significant as maintaining MAP ≥65 mmHg in patients with septic shock.[19,24]

Question 6: For patients with septic shock, which vasopressor should be selected to maintain the target blood pressure?

Recommendations 6: (a) For patients with septic shock, norepinephrine is recommended as the preferred vasopressor (Grade 1+, Strong recommendation); and (b) For patients with septic shock requiring norepinephrine, if target MAP cannot be achieved, we suggest co-administration of vasopressin rather than escalating the dose of norepinephrine (Grade 2+, Weak recommendation).

Two meta-analyses that included high-quality RCTs with patients with septic shock indicated that norepinephrine is associated with a lower incidence of mortality and arrhythmia compared with dopamine.[25,26] Although dopamine β1 activity improves cardiac function in patients with cardiac dysfunction, the higher incidence of arrhythmias limits its use.

Vasopressin is a V1 receptor agonist on vascular smooth muscle. Studies have shown that vasopressin levels are elevated in the early stages of septic shock but fall to the normal range in most patients within 24–48 h as the shock progresses.[27] Unlike most vasopressors, vasopressin is usually administered at a fixed dose of 0.03–0.04 IU/min to treat septic shock, with higher doses associated with cardiac, peripheral, and visceral ischemia. The timing of initiating vasopressin remains unclear. Based on the VANISH trial results, we recommend considering vasopressin when the dose of norepinephrine is in the range of 0.16–0.55 μg/kg/min, which may reduce the risk of norepinephrine-related adverse reactions.[28]

The VANISH trial directly compared the use of vasopressin and norepinephrine, finding no significant difference in 28-day mortality between the two groups (30.9% *vs.* 27.5%, risk ratio (RR): 1.13 [95% CI: 0.85–1.51]). However, the use of vasopressin may reduce the risk of renal replacement therapy.[28] In terms of combination therapy, there was no significant difference in 28-day mortality between norepinephrine alone and norepinephrine combined with vasopressin (0.01–0.03 U/min) (VASST trial) (39.3% *vs.* 35.4%, *P*=0.26). However, in subgroup analysis, patients with septic shock receiving norepinephrine <15 μg/min tended to have improved survival with a combination of vasopressin (26.5% *vs.* 35.7%, *P*=0.05).[29] Another systematic review found that the combination of vasopressin and norepinephrine was associated with a lower risk of atrial fibrillation compared with norepinephrine alone.[30]

There is insufficient evidence regarding the optimal treatment strategy for shock requiring high doses of vasopressors.

Epinephrine is recommended as the second or third line of vasopressor in patients with septic shock. When high levels of norepinephrine are used, α1 receptors may be saturated and downregulated. Therefore, using another epinephrine targeting the same receptors may have limited utility, whereas vasopressin may be more effective in that case. An analysis comparing epinephrine and vasopressin revealed no significant difference in mortality (RR: 0.94; 95% CI: 0.47–1.88).[31]

Angiotensin II exerts a significant vasoconstriction effect by stimulating the renin-angiotensin system. Recently, its artificial preparation has become available for clinical use. In an RCT with 344 patients with vasodilatory shock (approximately 90% with confirmed or suspected sepsis), 114 of 163 patients in the angiotensin II group and 37 of 158 patients in the placebo group had MAPs increased by at least 10 mmHg or to 75 mmHg (69.9% *vs.* 23.4%, $P<0.001$). The use of angiotensin II did not increase the incidence of adverse events.[32] Angiotensin II antagonists should not be considered as first-line agents but may be used as adjunct vasopressors because of their physiological effects. To date, there is insufficient evidence regarding angiotensin II antagonists and their safety for treating septic shock.

Blood pressure management in patients with hemorrhagic shock

Hypovolemic shock is caused by decreased intravascular volume. Its common causes include blood loss, fluid accumulation in the third space, and burns. Hemorrhagic shock is the main cause of hypovolemic shock in critically ill patients and is characterized pathophysiologically by decreased cardiac output because of decreased preload resulting from blood loss. Hemorrhagic shock should be treated by stopping bleeding as rapidly as possible, eliminating etiology, and restoring blood volume. An appropriate pressure level is essential for maintaining tissue perfusion, but excessively high target blood pressure may lead to aggravated bleeding during the treatment of hemorrhagic shock. Furthermore, the use of higher doses of vasoactive drugs to achieve target blood pressure levels may lead to therapeutic injury. Thus, good blood pressure management is vital for the effective management of patients with hemorrhagic shock.

Question 7: What is the target blood pressure in patients with hemorrhagic shock with uncontrolled bleeding?

Recommendation 7: (a) For patients with traumatic hemorrhagic shock without traumatic brain injury (TBI), we suggest a permissive hypotension strategy (systolic blood pressure [**SBP] ≥70 mmHg, MAP 50–60 mmHg) should be adopted until bleeding is controlled (Grade 2+, Weak recommendation). (b) For hemorrhagic shock patients with severe TBI (Glasgow Coma Scale [GCS] ≤8), we suggest maintaining SBP >90 mmHg (Grade 2+, Weak recommendation).**

Damage control strategies – such as reducing target blood pressure – play an important role in the management of patients with trauma. For critically ill patients with severe trauma and uncontrolled bleeding, resuscitation with lower target blood pressure or permissive hypotension may be beneficial. The purpose of permissive hypotension resuscitation is to maintain sufficient vital organ perfusion and avoid iatrogenic injury, such as increasing blood loss caused by maintaining excessively high target blood pressure.

Dutton et al.[33] randomized 110 patients with traumatic hemorrhagic shock into two fluid resuscitation groups: target SBP >100 mmHg (conventional) or target SBP of 70 mmHg (low). Fluid therapy was titrated to this endpoint until definitive hemostasis was achieved. Results showed no difference in injury severity score (19.65±11.8 *vs.* 23.64±13.8, $P=0.11$) and active bleeding duration (2.97±1.75 h *vs.* 2.57±1.46 h, $P=0.20$) between the two groups, with four deaths in each group. The authors concluded that titration of initial fluid therapy to lower than normal SBP during active hemorrhaging did not affect mortality. Schreiber et al.[34] evaluated the feasibility and safety of controlled resuscitation (CR group, maintaining radial pulse or SBP ≥70 mmHg) *vs.* standard resuscitation (SR group, maintaining SBP ≥110 mmHg) in 192 patients with traumatic shock. ICU-free days, ventilator-free days, renal injury, and renal failure did not differ between the groups. Among patients with blunt trauma, 24-h mortality was lower in the CR group (3% *vs.* 18%, OR=0.17) whereas there was no difference among patients with penetrating trauma. The authors concluded that CR may offer an early survival advantage in blunt trauma. Tran et al.[35] compared the efficacy and safety of permissive hypotension in five randomized trials with a total of 1158 trauma patients. The target blood pressure in the hypotensive group was SBP in the range 50–70 mmHg, or MAP ≥50 mmHg. Compared with conventional resuscitation, the pooled OR of survival in the hypotensive resuscitation group was 0.70 (95% CI: 0.53–0.92), suggesting a survival benefit for permissive hypotension – those patients received fewer blood products and had less estimated blood loss. Scholars who undertook a meta-analysis of 30 RCTs on the efficacy of hypotensive resuscitation in patients with traumatic hemorrhagic shock, found that the hypotensive resuscitation group experienced a statistically significant decrease in mortality (RR: 0.50, 95% CI: 0.40–0.61), and reduced use of packed red cell transfusions and fluid resuscitations. A protective effect was observed relative to multiple organ dysfunction and ARDS.[36] Cerebral perfusion pressure (CPP) and cerebral blood flow (CBF) may be decreased in patients with hemorrhagic shock with TBI, CPP, and CBF may be critically decreased in TBI patients complicated with increasing intracranial pressure (ICP), which will result in increased mortality. Therefore, for patients with hemorrhagic shock with TBI, it is necessary to balance the appropriate cerebral perfusion and the need for hypotensive fluid resuscitation. Analysis of 13,114 patients with TBI recruited over 10 years in a single center by Huang et al.[37] showed that SBP <90 mmHg was significantly associated with increased mortality. A European multicenter cohort study of 5057 patients with TBI showed that the mortality rate of patients with SBP <90 mmHg doubled, while the mortality rate of SBP <70 mmHg increased five-fold ($P<0.01$). It is recommended that SBP <90 mmHg is the threshold of TBI hypotension.[38] However, another analysis based on data from the IMPACT study showed that patients with SBP of 120 mmHg had better prognoses.[39] The target blood pressure for patients with hemorrhagic shock and TBI requires further confirmation given the lack of large-scale RCTs. However, available evidence suggests that for patients with severe TBI (GCS ≤8), a target SBP ≥90 mmHg should be maintained. In addition, the pressure reactivity index (PRx) developed from parameters such as MAP, ICP, and CPP, may provide a better reference and more guidance for determining target blood pressure in this population.[40]

Question 8: What is the target blood pressure in initial resuscitation for patients with hemorrhagic shock?

Recommendation 8: For patients with hemorrhagic shock, we suggest a relatively lower target MAP of 60–70 mmHg for initial resuscitation (Grade 2+, Weak recommendation).

The treatment of hemorrhagic shock mainly involves timely hemostasis, but eliminating etiology, restoring blood volume, and ensuring blood pressure meets the appropriate targets can also help ensure organ tissue perfusion. Thus, we need to determine the target blood pressure to guide treatment when resuscitating patients with hemorrhagic shock. Safiejko et al.[41] conducted a meta-analysis of 28 RCTs with 4503 patients with hemorrhagic shock. The analysis showed that hypotensive fluid resuscitation significantly reduced the mortality rate: patients receiving hypotension fluid resuscitation compared with conventional fluid resuscitation were less likely to die (12.5% *vs.* 21.4%; RR=0.58; $P<0.001$), had fewer incidents of acute respiratory distress syndrome (ARDS) (7.8% *vs.* 16.8%) and multiple organ dysfunction syndrome (8.6% *vs.* 21.6%). Lamontagne et al.[21] enrolled 118 shock patients from 11 centers requiring vasoactive drugs to increase blood pressure. They found that among patients aged ≥75 years, a lower target MAP (60–65 mmHg) was associated with reduced mortality (13% *vs.* 60%, $P=0.03$). Shao et al.[42] estimated the most appropriate target blood pressure by monitoring inflammatory markers and hemodynamics in 60 patients with traumatic hemorrhagic shock. The moderate MAP group (65 mmHg≤MAP<70 mmHg) evidenced a strong linear correlation between MAP and the expression of inflammatory markers, such as TNF-α ($P<0.01$). The authors believe that the effect of reducing the systemic inflammatory response and improving hemodynamics is optimal when MAP is 65–70 mmHg. Thus, do patients benefit from lower targeted blood pressure? Lee et al.[43] analyzed 336 patients with non-variceal upper gastrointestinal bleeding and found that hypotension during hospitalization (systolic blood pressure [SBP] <90 mmHg) was an important predictor of 30-day mortality. Meanwhile, Singh et al.[44] also found systolic pressure <90 mmHg or MAP <65 mmHg was a risk factor for severe lower gastrointestinal bleeding. These results suggest that MAP <65 mmHg or SBP <90 mmHg should be avoided in patients with gastrointestinal bleeding.

In summary, we recommend targeting lower levels of blood pressure (MAP 60–70 mmHg) for resuscitation in patients with hemorrhagic shock.

Blood pressure management in patients with cardiogenic shock

Cardiogenic shock is a low cardiac output state that results in life-threatening end-organ hypoperfusion and hypoxia. Acute myocardial infarction with left ventricular dysfunction is the most common cause of the condition, and other causes include severe valvular disease, pericardial disease, arrhythmias, and myocarditis. Cardiogenic shock carries high morbidity and mortality despite significant advances in diagnosis and treatment.[45,46] Hypotension in cardiogenic shock can lead to poor tissue perfusion. Thus, blood pressure management is important for the treatment of patients with cardiogenic shock.

Question 9: What is the initial blood pressure target in patients with cardiogenic shock?

Recommendation 9: For patients with cardiogenic shock requiring vasopressors, we suggest a target MAP 65–70 mmHg (Grade 2+, Weak recommendation).

A *post hoc* analysis of a single-center RCT comparing dobutamine to milrinone in patients with cardiogenic shock (CAPITAL DOREMI Trial) revealed several conclusions. The composite primary outcome(all-cause mortality, resuscitated cardiac arrest, need for cardiac transplantation or mechanical circulatory support, non-fatal acute myocardial infarction, transient ischemic attack or stroke, or the initiation of renal replacement therapy) occurring in the low MAP group (average MAP <70 mmHg over the 36 h following randomization) was higher than that of the high MAP group and increased all-cause mortality (57.8% *vs.* 28.9%, adjusted RR=0.56; 95% CI: 0.40–0.79; $P<0.01$). Findings indicated that low MAP targets in patients with cardiogenic shock secondary to decompensated heart failure are associated with poor clinical outcomes.[47]

The MAP target of 65 mmHg in patients with cardiogenic shock is weakly supported by a single central study.[48] A retrospective study was conducted to determine the relationship between MAP during the first 24 h and mortality in patients with cardiogenic shock. The authors analyzed 1002 patients with an admission diagnosis of cardiogenic shock in the cardiac ICU. Hospital mortality was inversely associated with the mean of all MAP values during the first 24 h ($mMAP_{24}$). Hospital mortality was inversely associated with the mean of all MAP during the first 24 h (mMAP24). Patients with mMAP24 <65 mmHg were at higher risk of hospital mortality (57% *vs.* 28%, adjusted OR=2.0, 95% CI: 1.4–3.0, $P<0.001$); no differences were observed between patients with mMAP24 65-<75 mmHg *vs.* ≥75 mmHg ($P>0.100$). These findings provide indirect support for a MAP target ≥65 mmHg for patients with cardiogenic shock.

In summary, we suggest an initial blood pressure target 65–70 mmHg for patients with cardiogenic shock. We should pay attention to the importance of the phenotype of cardiogenic shock and how to titrate different subsets of cardiogenic shock. However, limited RCT data exist regarding the optimal MAP target for patients with cardiogenic shock. Optimal MAP targets will vary for individuals, and the balance between hypoperfusion/ischemic risks with lower MAP, and arrhythmias with higher MAP, should be considered. Blood pressure targets should be set individually based on patients' organ and tissue perfusion.

Question 10: For patients with cardiogenic shock, at what level should DBP be maintained?

Recommendation 10: We suggest maintaining the target DBP >60 mmHg for patients with cardiogenic shock (Expert opinion).

The coronary artery is perfused mostly during diastole, and perfusion is closely related to the DBP level. Coronary blood flow is higher in diastole than in systole because the diastolic phase is longer than the systolic phase in a cardiac cycle. Thus, DBP and the diastolic period length are important for coronary blood flow. A DBP of 60 mmHg or less has been shown to be associated with low myocardial perfusion and high myocardial infarction risk or even cerebral circulation damage.[49,50] Appro-

priate DBP is extremely important for coronary artery perfusion in patients with cardiogenic shock.

A large cohort study of patients with hypertension and coronary artery disease found that DBP of less than 60 mmHg was associated with cardiovascular death, myocardial infarction, or stroke (adjusted HR[95%CI]=2.01 [1.50–2.70] for DBP of less than 60 mmHg).[51] This provides indirect support for DBP of no less than 60 mmHg.

A retrospective analysis found that only the minimum DBP was an outcome predictor in patients with cardiogenic shock: 41±7 mmHg for survivors and 37±8 mmHg for non-survivors. There was no difference in the highest diastolic pressure between the two groups.[52] The TRIUMPH study found that 30-day mortality was associated with SBP and creatinine clearance in patients with persistent vasopressor-dependent cardiogenic shock complicating acute myocardial infarction at least 1 h after established infarct-related artery patency. Though not included in further analysis, the DBP was different for survivors and non-survivors (54.5 [46.0, 61.0] mmHg *vs.* 50.0 [40.0, 58.0] mmHg, $P<0.01$).[53] This indicated that low diastolic pressure is associated with poor prognosis in patients with cardiogenic shock. Thus, we need to pay attention to DBP in addition to MAP. We suggest maintaining a DBP of 60 mmHg or more for patients with cardiogenic shock. Further RCTs are needed to establish optimal DBP targets in patients with cardiogenic shock.

Question 11: What is the initial blood pressure target for patients with cardiogenic shock requiring veno-arterial extracorporeal membrane oxygenation (VA-ECMO)?
Recommendation 11: We suggest a MAP ≥65 mmHg as the initial target blood pressure for patients with cardiogenic shock requiring VA-ECMO (Expert opinion).

In a recent systematic review with meta-analysis investigating the impact of targeted perfusion parameters during extracorporeal cardiopulmonary resuscitation (ECPR) in out-of-hospital and in-hospital cardiac arrest, the author conducted random and mixed-effects meta-analyses, which included a total of 51,282 ECPR patients from 20 ECPR studies. Flow values were categorized as high (>2.2 L/min/m^2, 4.22 L/min, 60 mL/kg/min), medium (1.5–2.2 L/min/m^2, 2.88–4.22 L/min), or low (<1.5 L/min/m^2, 2.88 L/min), and MAP targets were categorized as high (70 mmHg), medium (65–70 mmHg), and low (<65 mmHg). The analysis did not prove the heterogeneity of flow and MAP independently affected the outcome variable. In a second mixed-effect model, a combination of medium flow and high MAP showed advantages for survival and neurological outcomes.[54] Several other studies found that higher MAP (65 mmHg or higher) was associated with better neurological outcomes among survivors who received VA-ECMO ECPR.[55,56]

We suggest MAP ≥65 mmHg as the optimal initial blood pressure target for patients with cardiogenic shock receiving VA-ECMO, which will ensure sufficient tissue perfusion without an increased afterload.

Management of hypertension in critically ill patients and hypertensive emergencies

Hypertension is commonly seen in ICU patients. A survey in India showed that among 4076 critically ill patients, hypertensive emergencies occurred in 50 patients, with a prevalence of 1.22%.[57] Severely ill patients typically have elevated blood pressure because of pain, discontinuation of analgesic or antihypertensive drugs, sound and light stimulation, bladder retention, acidosis, hypoglycemia, or nursing interventions.

Hypertension is also associated with poor prognosis in critically ill patients. A re-analysis of MIMIC data showed that elevated nocturnal MAP in critically ill patients was associated with mortality in ICU (OR=1.34; 95% CI: 1.10–1.65), in-hospital mortality (OR=1.34; 95% CI: 1.10–1.65), 28-day mortality (HR=1.27; 95% CI: 1.10–1.48), and 1-year mortality (HR=1.24; 95% CI: 1.10–1.40).[58] Furthermore, a similar trend was observed in patients with coronavirus disease 2019 (COVID-19). Pranata et al.[59] pooled data from 30 studies involving 6560 COVID-19 patients, and found that hypertension increased the composite adverse outcome (HR=2.11; 95% CI: 1.85–2.40), including mortality, severity, incidence of ARDS, ICU admission, and disease progression. Therefore, careful attention should be given to the management of hypertension in critically ill patients.

Question 12: Which patients with acute and severely elevated blood pressure should be admitted to the ICU?
Recommendation 12: We suggest patients with acute onset SBP >180 mmHg and/or DBP >110 mmHg accompanied by organ dysfunction should be admitted to the ICU (Grade 2+, Weak recommendation).

Acute onset SBP >180 mmHg and/or DBP >110 mmHg can cause acute damage to the heart, brain, and microvasculature. According to the meta-analysis of 123 studies by Ettehad et al.[60] involving 613,815 hypertensive patients, for every 10 mmHg decrease in SBP, the risk of major cardiovascular events (RR=0.80), coronary heart disease (RR=0.83), stroke (RR=0.73), or heart failure (RR=0.72) significantly increased. The all-cause mortality in the study population decreased by 13% (0.87). Even without acute target organ damage, acute severe blood pressure elevation can affect patients' long-term outcomes. In a study of 2435 patients with a history of previous transient ischemic attacks, an isolated systolic pressure greater than 180 mmHg was associated with a five-fold increase in stroke risk during the subsequent 3 years of follow-up compared with normotensive patients.[61] The autoregulation of organ blood flow can ensure relatively stable organ perfusion within a wide range of fluctuations. Limited data suggest that this autonomic regulatory response may take months to improve in patients with acute severe hypertension >180/110 mmHg, but only weeks in patients with <180/110 mmHg. Therefore, patients with acute severe hypertension accompanied by organ dysfunction should be admitted to the ICU for urgent blood pressure reduction with close monitoring.

Question 13: Whether antihypertensive therapy should be the routine treatment for patients admitted to the ICU with severe hypertension?
Recommendation 13: We suggest antihypertensive therapy should be administered intravenously for patients with SBP >180 mmHg and/or DBP >110 mmHg with organ dysfunction (Grade 2+, Weak recommendation).

Although there are few RCTs enabling comparison of treatment strategies for most cases of acute severe hypertension, it is generally believed that oral medication can be considered

if there is no target organ damage mediated by hypertension. However, urgent blood pressure reduction treatment is required for concurrent events such as acute ischemic or hemorrhagic stroke. Zhao et al.[62] reviewed and analyzed two groups of patients with acute hemorrhagic stroke – one group of 351 patients with an SBP control target of <180 mmHg within 1 h, and another group of 308 patients with an intensified treatment target of <140 mmHg within 1 h. The intensified treatment used a combination of intravenous medication as the main treatment plan and blood pressure monitoring every 10 min. The results showed that the incidence of hematoma expansion significantly reduced in the intensified blood pressure reduction treatment group (43 of 308, 13.9% *vs.* 74 of 351, 21.1%, P=0.018), while the length of ICU stay, and the incidence of severe adverse events were similar in both groups. The goal of blood pressure reduction treatment for acute severe hypertension is to prevent or limit further target organ damage, while avoiding secondary damage caused by excessive blood pressure reduction. In this scenario, short-acting, titratable intravenous antihypertensive drugs can achieve better organ protection. Oral medication to ensure stable absorption is difficult to administer to critically ill ICU patients because of intubation and gastrointestinal dysfunction.

Question 14: For patients with acute severe hypertension admitted to ICU, how should the rate of blood pressure reduction be set?

Recommendation 14: For patients with acute severe hypertension, we suggest a stepwise strategy for antihypertensive therapy. Except for acute aortic dissection, the SBP should be reduced by no more than 25% in the first hour, then reduced to 160/100–110 mmHg in the next 2–6 h, and cautiously reduced to the normal level in the following 24–48 h (Grade 2+, Weak recommendation).

The 2018 American Heart Association guidelines for the management of hypertension and the 2019 position paper and recommendations of the European Society of Cardiology on the management of hypertensive emergencies suggest the initial decrease in blood pressure for hypertensive emergencies should not exceed 20–25% in the first hour. This should then be followed by a decrease to 160/100–110 mmHg over 2–6 h.[63,64] Mayer et al.[65] analyzed 1566 patients enrolled in the Studying the Treatment of Acute Hypertension (STAT) registry study. The initial blood pressure level was 183/95 mmHg, and the group of patients who died experienced lower blood pressure level than the survival groups (median 103/45 mmHg *vs.* 118/55 mmHg, P<0.0001). Excessive blood pressure lowering requires immediate discontinuation of intravenous medications and, in some cases, administration of vasopressors or fluid therapy for a short time. Long-acting antihypertensive drugs should be resumed concurrently with intravenous antihypertensive drugs to ensure a smooth transition of treatment. As hypotension is most likely to occur during the first 6 h of antihypertensive therapy, oral medication should be added after 6–12 h of intravenous therapy. The speed and intensity of antihypertensive therapy need to be adjusted appropriately in clinical scenarios, particularly in cases of aortic dissection, preeclampsia, and pheochromocytoma crisis. Antihypertensive therapy for ischemic stroke should be more conservative to avoid peri-infarctional hypoperfusion.

Management of hypertension in special types of critically ill patients

Blood pressure management in patients with abdominal compartment syndrome

Increased intra-abdominal pressure (IAP) of critically ill patients can be directly transmitted to other chambers of the body, affecting systemic hemodynamics and leading to a decrease in intraperitoneal perfusion pressure, which results in hypoperfusion of abdominal viscera. Intra-abdominal hypertension (IAH) is defined as a continuous or repeated elevation in IAP ≥12 mmHg. Abdominal compartment syndrome is defined as a sustained IAP >20 mmHg. Abdominal perfusion pressure (APP) is defined as the difference value between MAP and IAP. In IAH and abdominal compartment syndrome, the intra-abdominal and intrathoracic pressure are evaluated, and compress the superior and inferior vena cava and cardiac contraction, which can lead to a decreased venous return to the heart, decreased cardiac preload, increased right ventricular afterload, cardiac dysfunction, and decreased cardiac output.[66] These changes result in lower MAP, higher IAP, and a distinct reduction in APP. However, a lack of evidence persists regarding APP-guided target blood pressure management in patients with abdominal compartment syndrome.

Question 15: Can intraperitoneal perfusion pressure be used instead of MAP as the endpoint of shock resuscitation in patients with IAH during shock resuscitation?

Recommendation 15: For patients with IAH, we suggest maintaining the intraperitoneal perfusion pressure at 60 mmHg on the basis of controlling the IAP (Expert opinion).

At present, no clinical evidence exists from RCTs relating to APP value as an endpoint of resuscitation. In 12 observational studies of patients with IAH or abdominal compartment syndrome, reduced APP was considered as an independent risk factor for poor prognosis in critically ill patients.[67] However, the high heterogeneity and strong bias of the enrolled patients in these studies resulted in low-quality conclusions. Increased APP associated with higher MAP may result in an additional intake of excess fluid or an increased risk of vasoactive drugs. For example, when IAP is 20 mmHg and a target APP is set to 60 mmHg, MAP needs to be increased to 80 mmHg. Although no clinical studies have confirmed whether APP evaluation can improve clinical outcomes, an APP of 60 mmHg can meet the perfusion demand of abdominal organs from a physiological perspective.

Clinical evidence is still lacking about whether restricted fluid resuscitation and aggressive use of vasoactive agents or inotropic drugs may improve APP during shock resuscitation.[68] Excessive fluid resuscitation may lead to aggravated abdominal visceral edema and increased IAP, and vasoactive agents may lead to vasoconstriction and hypoperfusion in abdominal viscera. Therefore, balancing fluid resuscitation and vasoactive agents during shock in IAH patients warrants further clinical research.

Blood pressure management in patients with severe brain injury

Blood pressure management in patients with TBI

Either hypotension or hypertension could be harmful in patients with TBI. Blood pressure management is crucial, directly affecting the prognosis and mortality of patients with TBI.[69–71]

First, maintaining the CPP at 60–70 mmHg in patients with increased ICP requires an adequate MAP, as CPP=MAP − ICP. Meanwhile, hypotension reduces CBF directly while cerebral autoregulation is impaired in patients with TBI. Besides, hypotension may also trigger the dilation of blood vessels in the brain, leading to a further increase in ICP.[69,70]

In contrast, relatively high blood pressure or hypertension could also cause cerebral hemorrhage and aggravates cerebral edema in TBI.[71]

Recent studies found that individual blood pressure management with brain multimodal monitoring could be helpful for patients with TBI. Brain multimodal monitoring has been applied in clinical practice with synchronously monitoring blood pressure, ICP, cerebral oxygen, and CBF. Computer software is used to analyze and integrate multiple parameters, and an optimal CPP (CPPopt) is calculated for each individual patient. Studies have shown that CPPopt and optimal blood pressure improve patients' TBI prognosis.[72,73]

Question 16: What is the target blood pressure in patients with moderate to severe TBI?

Recommendation 16: For patients with hypotension, we suggest maintaining SBP >100 mmHg and MAP >80 mmHg (GRADE 2+, Weak recommendation). For patients with hypertension, we suggest maintaining SBP <160 mmHg, and focusing on the etiology and treatment of inductive factors (Expert opinion).

Early studies showed that hypotension (SBP <90 mmHg, MAP <65 mmHg) was significantly associated with poor neurological prognosis in patients with TBI.[74,75] Recent studies have indicated that the threshold of hypotension in patients with TBI needs to be redefined. A retrospective cohort observation in 2007 included 8 RCTs and 3 observational studies, and a total of 13,447 patients with TBI were recruited. This study showed that SBP at 120–150 mmHg or MAP at 85–110 mmHg improved the prognosis of patients.[76] To observe the effect of blood pressure on mortality, another large-scale retrospective cohort study was performed in 2012, which included 15,733 patients with moderate to severe TBI. This study found that maintaining blood pressure >100 mmHg can minimize mortality in patients aged 50–69 years. While in younger (15–49 years) or older (≥70 years) patients, maintaining blood pressure >110 mmHg minimized mortality.[77] Another prospective cohort study was performed in 2012, which included 60 patients with TBI. The effects of blood pressure on mortality and 12-month prognosis were observed. It showed that avoiding SBP <110 mmHg within 48 h post-injury can reduce the risk of death and avoiding SBP <120 mmHg within 48 h post-injury improves the long-term prognosis of patients.[76] In 2017, an observational study of 3844 patients was performed to observe the effects of pre-hospital blood pressure and on mortality in patients with severe TBI. This study found a significant linear relationship between pre-hospital SBP (40–119 mmHg) and mortality.[78] Based on these studies, we conclude that maintaining SBP >100 mmHg and MAP >80 mmHg reduces mortality and improves the prognosis in patients with TBI.

Two observational studies were undertaken for the threshold of hypertension in patients with TBI. In 2012, a large study recruited 42,500 patients with TBI from a large database. It showed that SBP >160 mmHg was associated with poor prognosis, regardless of whether hypertension occurred on admission or during hospitalization.[79] However, these patients' hypertension was associated with ICP and disease severity. Treatment of hypertension in these patients requires attention paid to the patient's original disease and status, including reducing intracranial hypertension, sedation, and analgesia. Another study included 194 patients with TBI. This study showed that either SBP <90 mmHg or ≥140 mmHg was an independent risk factor for mortality in patients with TBI (OR=18, P=0.012).[71]

Question 17: How does one individualize the target blood pressure in patients with TBI?

Recommendation 17: We suggest targeting individualized blood pressure according to ICP and CPP for patients with TBI. Multimodal monitoring can be performed in experienced medical units (Expert opinion).

Studies have shown that maintaining CPP at 60–70 mmHg can improve patient prognosis. In recent years, multimodal brain monitoring has been gradually incorporated into clinical practice. CPPopt can be found in each individual patient by monitoring ICP, CBF, or cerebral oxygen synchronously with blood pressure based on optimal cerebral autoregulation. The optimal blood pressure can be calculated through multimodal brain monitoring. Depreitere's[72] retrospective case series included 180 patients with TBI. It found that a closer difference between actual CPP and CPPopt was associated with a better prognosis. In Steiner's [80] retrospective study of 114 patients with TBI, an actual perfusion pressure closer to optimal perfusion pressure indicated a better prognosis. A single-center prospective study by Dias et al.[73] investigated the effects of continuous multimodal brain monitoring on TBI patients' outcomes. They explored the effect of individualized blood pressure management guided by brain multimodal monitoring on TBI patients' 6-month outcomes. The results showed that blood pressure management guided by dynamic bedside assessment of brain multimodality was associated with better GCS scores (P=0.01) and better clinical outcomes (P=0.01).

Blood pressure management in stroke patients

Stroke is the second leading cause of death and the third leading cause of disability worldwide. Accounting for 77.8% of strokes, ischemic stroke is the most common type, followed by cerebral hemorrhage and subarachnoid hemorrhage (SAH).[81] Hypertension is a main risk factor for stroke, and there is a continuous, graded, and predictable relationship between hypertension and stroke. Blood pressure management should be carried out throughout the diagnosis and treatment of stroke. Disease severity and the needs associated with specialized treatment methods should also be considered to comprehensively improve the overall prognosis and neurological outcome, together with judging the goals and timing of blood pressure control and the choice of drugs. Controversies remain regarding the regulation strategy and target level of blood pressure in the early post-stroke phase. The following recommendations were made

based on a summary of related research to standardize the blood pressure management of patients with acute stroke.

Question 18: What is the target blood pressure in acute ischemic stroke patients without intravenous thrombolysis or mechanical thrombectomy?

Recommendation 18: For acute ischemic stroke patients without intravenous thrombolysis and mechanical thrombectomy, we suggest initiating antihypertensive therapy if SBP ≥220 mmHg and/or DBP ≥120 mmHg and reducing SBP by 10–25% within 24 h (Grade 2+, Weak recommendation).

Studies report that BP ≥220/120 mmHg exceeds the upper limit of CBF regulation, and some guidelines point out that antihypertensive therapy should then be initiated by default in clinical practice. In 2014, the China Antihypertensive Trial in Acute Ischemic Stroke (CATIS) recruited 4071 patients with acute ischemic stroke who had not received intravenous thrombolysis or thrombectomy (baseline BP <220/120 mmHg). In this multicenter controlled clinical trial, patients were divided into two groups: the antihypertensive treatment group (SBP reduced by 10–25% within 24 h, with blood pressure maintained at 140/90 mmHg, *n*=2038) and the non-antihypertensive treatment group (*n*=2033). No significant difference was reported between the two groups in death and severe disability at 14 days post-onset or on hospital discharge, with the recurrence rate of stroke in the antihypertensive treatment group presenting a decreasing trend.[82] In 2019, Zhang et al.[83] published in the JAMA network open to sharing a re-analysis of CATIS subgroups, and found that early antihypertensive treatment in patients with ischemic strokes and hypertension could reduce the risk of recurrent stroke within three months. Thus, the evidence leads to our recommendation that patients with acute ischemic stroke who have not received intravenous thrombolysis and mechanical thrombectomy start antihypertensive therapy if SBP ≥220 mmHg and/or DBP ≥120 mmHg, and, further, it may be safer to reduce SBP by 10–25% within 24 h.

Question 19: What is the target blood pressure in acute ischemic stroke patients receiving intravenous thrombolysis?

Recommendation 19: Before intravenous thrombolysis, we suggest initiating antihypertensive therapy if BP ≥180/105 mmHg. After thrombolytic recanalization, we suggest maintaining SBP within 130–140 mmHg (Grade 2+, Weak recommendation).

Blood pressure levels before and after intravenous thrombolytic therapy, variability in blood pressure, and intervention timing significantly affect the prognosis of patients with stroke. Relevant guidelines in China and other countries suggest that keeping blood pressure below 185/105 mmHg may be safe during thrombolytic therapy. However, more research is required to justify the exact blood pressure target. In 2019, the Enhanced Control of Hypertension and Thrombolysis Stroke Study (ENCHANTED) enrolled 2196 patients with acute ischemic stroke who received alteplase treatment. Compared with the standard antihypertensive group (SBP target <180 mmHg), the hemorrhagic transformation rate was significantly reduced in the intensive antihypertensive group (SBP target: 130–140 mmHg).[84] A *post hoc* analysis of the ENCHANTED data found that compared with the standard blood pressure reduction group, intracranial hemorrhage was significantly reduced in the intensive blood pressure reduction group (especially massive intracerebral hemorrhage [ICH]), with a better clinical prognosis.[85] Therefore, before intravenous thrombolysis, we suggest initiating antihypertensive therapy if blood pressure ≥180/105 mmHg. After thrombolytic recanalization, SBP should be maintained in the 130–140 mmHg range.

Question 20: What is the target blood pressure post mechanical thrombectomy in acute ischemic stroke patients?

Recommendation 20: We suggest maintaining SBP at 130–140 mmHg within 24 h post mechanical thrombectomy (Grade 2+, Weak recommendation).

In 2019, a multicenter retrospective study investigated 703 patients with acute ischemic stroke who underwent mechanical thrombectomy for subgroup analysis. Compared with patients whose median SBP ≥140 mmHg, patients with SBP <140 mmHg after recanalization had better clinical prognoses and lower three-month mortality.[86] A multicenter RCT in 2021 included 324 patients with large vessel occlusions in the anterior circulation caused by acute ischemic stroke who received successful reperfusion after mechanical embolectomy. Compared with the standard treatment group (SBP: 130–185 mmHg), mechanical embolectomy under intensive SBP control at 100–129 mmHg could not reduce radiographic intraparenchymal hemorrhage rates at 24 h.[87] Therefore, controlling the SBP of patients with acute ischemic stroke at 130–140 mmHg within 24 h of mechanical embolectomy may be beneficial.

Question 21: What is the target blood pressure in patients with acute ICH?

Recommendation 21: We suggest maintaining SBP within 130–140 mmHg if SBP is 150–220 mmHg and maintaining the SBP within 140–180 mmHg if SBP >220 mmHg (Grade 2+, Weak recommendation).

The 2013 INTERACT-2 cohort study included 2839 patients with an SBP of 150–220 mmHg within 6 h of ICH onset. Controlling SBP below 140 mmHg significantly improved the modified Rankin Scale (mRS) score at 90 days compared with 140–180 mmHg.[88] The 2016 ATACH-2 cohort study included 1000 patients whose SBP >180 mmHg within 4.5 h after ICH onset. SBP was controlled to <140 mmHg or 140–180 mmHg within 2 h and maintained for 24 h. Compared with SBP at 140–180 mmHg, SBP <140 mmHg did not affect the hematoma growth rate within 24 h or the mRS score and mortality at 90 days, but a significant increase in the incidence of adverse renal events was noted within 7 days.[89]

When SBP is controlled to <130 mmHg, antihypertensive treatment may worsen the prognosis of patients. The *post hoc* meta-analysis of INTERACT-2 and ATACH-2 in 2019 revealed that for hypertensive patients receiving antihypertensive therapy after cerebral hemorrhage, every 10 mmHg reduction in SBP increased the probability of functional recovery in patients with cerebral hemorrhage by 10%. However, when the SBP dropped to 120–130 mmHg, the incidence of early deterioration of neurological function increased.[90] Based on this evidence, we suggest maintaining SBP within 130–140 mmHg if SBP is in the 150–220 mmHg range.

For patients whose SBP ≥220 mmHg with ICH, early control of SBP <140 mmHg is harmful. The 2020 ATACH-2 *post hoc*

analysis included 228 ICH patients whose SBP ≥220 mmHg, and found that controlling SBP between 110 and 139 mmHg and 140–180 mmHg significantly increased the risk of 24-hour neurological deterioration and the incidence of adverse renal events.[91] For patients with renal failure, early control of SBP <140 mmHg is also harmful. In 2021, another *post hoc* analysis of ATACH-2 data included 974 ICH patients with recorded glomerular filtration rates. Controlling SBP at 110–139 mmHg increased the risk of death at 90 days or disability among patients with renal failure.[92] Therefore, it is recommended that the target SBP be controlled to 140–180 mmHg for patients with renal failure or whose SBP ≥220 mmHg in the acute phase after ICH.

Question 22: Does variability of SBP affect prognosis in acute ICH patients with hypertension?

Recommendation 22: High variability of SBP is associated with poor prognosis. Thus, we suggest continuous, consistent antihypertensive therapy (Grade 2+, Weak recommendation).

SBP variability refers to the fluctuation of SBP within a specific period, including instantaneous variability, acute phase, and medium- and long-term variability. Commonly used monitoring indicators for SBP variability include standard deviation, coefficient of variation, and mean absolute change. Several studies confirm an increase in SBP variability after ICH, which is associated with the deterioration of clinical function scores. However, there is no definitive conclusion about the exact scale of SBP variability increase that would cause harmful effects. An RCT in 2018 indicated that the increase in the index of SBP variability in the hyperacute and acute stages after ICH would lead to a worsening of the mRS score at 90 days.[93] In 2019, a retrospective study (n=762) showed that increased SBP variability during the acute and subacute phases was associated with adverse clinical outcomes at 90 days.[94] However, there are few studies on the reduction of SBP variability after ICH. Continuous and steady antihypertensive therapy may reduce the variability of SBP after ICH, thereby improving prognosis.[95] It can be concluded that high variability of SBP is associated with poor prognosis. Therefore, we suggest continuous and steady antihypertensive therapy.

Blood pressure management in patients with SAH

SAH is bleeding into the subarachnoid space between the brain and the surrounding membrane causing related clinical symptoms and accounting for 5–10% of all types of stroke. Intracranial aneurysms are the most common cause of SAH (85%). In recent years, severe SAH has been defined as severe headache – grade II or above using the Yasargil grading method – and CT showing extensive hemorrhage in the basal and sylvian cisterns.

Question 23: What is the target of blood pressure in SAH patients?

Recommendation 23: There is no definitive evidence to support the magnitude of blood pressure reduction and optimal blood pressure levels in acute SAH, and the recommended control goals prior to aneurysm management are to maintain SBP <160 mmHg and MAP around 80 mmHg; Blood pressure management after aneurysm management should be individualized with reference to basal blood pressure and cerebral multimodal monitoring to determine the individualized optimal blood pressure. In the case of delayed cerebral ischemia (DCI), blood pressure may be increased by 20% depending on the situation. (Grade 2+, strong recommendation, Level of Evidence B); We do not recommend the routine use of 'triple-H therapy' to prevent and treat DCI. (Grade 2-, strong recommendation, Level of Evidence B)

Observations that high blood pressure after aneurysmal SAH is related to poor outcomes and that treating high blood pressure can reduce rebleeding have existed for almost half a century. Blood pressure management is subdivided into two phases: pre and post-aneurysm management. Before aneurysm management, the main aim of blood pressure management was to reduce the risk of exacerbation of hypertension-related bleeding. Studies have shown that blood pressure should be controlled with titratable agents from the onset of SAH symptoms to the resolution of the aneurysm to balance the risk of stroke and hypertension-related rebleeding and maintain the CPP.[96] In an observational study of 273 patients admitted within 24 h of an initial SAH, systolic arterial pressure >160 mmHg was a possible risk factor for rebleeding (OR=3.1).[97] A meta-analysis of four retrospective studies found that the SAH rebleeding ratio was as high as 2.52 when systolic pressure was >160 mmHg.[98] Therefore, it is beneficial to control systolic pressure <160 mmHg and maintain it steady before aneurysm management. Also, attention needs to be paid to the increased risk of cerebral ischemia due to excessive hypotension. A study of 30 patients with low-grade SAH showed that CPP <70 mmHg was associated with metabolic crisis (OR=2.1), and cerebral hypoxia (OR=2.0) may increase the risk of secondary cerebral palsy in SAH patients.[99] A multicenter study of 1167 cases showed an increased risk of rebleeding with MAP >100 mmHg, and MAP <60 mmHg was associated with an increased risk of DCI, suggesting maintaining MAP at around 80 mmHg.[100] After aneurysm management, rebleeding is no longer the main clinical intervention target, but cerebral edema, increased intracranial pressure and cerebral vasospasm are the main clinical problems, and blood pressure management is aimed at maintaining cerebral tissue perfusion and preventing ischemic injury.[101] Usually, the blood pressure can be increased by 20% as appropriate for the specific condition and cerebral perfusion needs, and the target value can be modified by referring to the patient's pre-onset basal blood pressure to avoid hypotension and excessive blood pressure variability.[102] The use of multimodal testing such as transcranial Doppler ultrasound, electroencephalography, and cerebral oxygen to individualize the guidance of blood pressure management, reduce cerebral vasospasm, and improve cerebral perfusion has good clinical application.

A meta-analysis of RCTs of prophylactic nimodipine in patients with SAH showed that nimodipine treatment increased the ratio of a favorable outcome after SAH (OR=1.86), reduced the rate of dysfunction or death due to vascular spasticity (OR=0.46), and CT infarction rate (OR=0.58), compared with placebo. The clinical efficacy of other calcium antagonists, either orally or intravenously, remains uncertain. Triple-H (hemodilution, hypervolemia, and hypertension) therapy lacks relevant RCT evidence for preventing and treating DCI.[103] In an RCT including 41 patients with a SAH, DCI was compared with the treatment of induced hypertension, which showed that induced hypertension did not improve clinical outcomes but in-

creased the ratio of serious adverse effects, such as arrhythmia, myocardial infarction, and even death, to 2.1.[104] We suggest preventing DCI by maintaining fluid balance and normal circulating blood volume. However, in cases where the aneurysm has been treated and cerebral vasospasm is present, a higher blood pressure should be maintained to prevent cerebral vasospasm and cerebral ischemia.

Blood pressure management in patients with AKI

The kidneys receive 25% of cardiac output and have strong autonomous regulation of renal blood flow. Within the range of arterial blood pressure of 80–180 mmHg and renal perfusion pressure (RPP) of 60–100 mmHg, the body regulates the tension of afferent and efferent arterioles of the renal glomerulus through tubuloglomerular feedback, the sympathetic nervous system, and the renin–angiotensin–aldosterone system to maintain renal perfusion stability.[105] In critically ill patients with sepsis, shock, major surgery, or chronic hypertension, the autonomous regulation of renal blood flow may be impaired. Then, low or high blood pressure levels can lead to further alterations in renal perfusion, resulting in more severe kidney injury. Therefore, maintaining appropriate blood pressure, especially RPP, is an important aspect of renal protection.

Question 24: What is the target blood pressure in patients with AKI without a history of hypertension?

Recommendations 24: We suggest maintaining MAP ≥65 mmHg for AKI patients without a history of hypertension (Grade 2+, Weak recommendation).

Meta-analysis showed a significantly increased risk of AKI in non-cardiac surgery patients with intraoperative MAP <60 mmHg for 1 min and more, and a significant increase in 30-day mortality with MAP <60 mmHg for 5 min and more.[106] A study of 8782 patients in septic shock in 110 US hospitals showed that the risk of AKI increased by 7% for each 1 mmHg increase in time-weighted average MAP (TWA-MAP) <65 mmHg, and by 37% when MAP <65 mmHg lasted for 6–8 h.[107] In post-operative cardiac shock with AKI, increasing MAP from 60 mmHg to 75 mmHg by norepinephrine increased renal oxygen delivery and glomerular filtration rate by 13% and 27%, respectively; renal oxygen extraction decreased by 7.4%. However, when MAP was raised to 90 mmHg, it only increased renal vascular resistance without improving renal oxygen delivery and glomerular filtration rate.[108] Increasing the dose of vasopressors to elevate MAP >70 mmHg for septic shock means patients might face an increase in AKI risk instead.[109] This indicates that increasing the dose of vasopressors based solely on MAP as a resuscitation target may increase the incidence of AKI. Therefore, for AKI patients without a history of hypertension, we suggest maintaining MAP ≥65 mmHg.

Question 25: What is the target MAP for AKI patients with a history of hypertension?

Recommendation 25: We suggest maintaining MAP at 80–85 mmHg or at basal blood pressure levels for AKI patients with a history of hypertension (Grade 2+, Weak recommendation).

The blood pressure control target for AKI patients with a history of hypertension has not yet been determined. An appropriate MAP might minimize the risk of AKI occurrence in critically ill patients with prior hypertension. For elderly patients with hypertension undergoing gastrointestinal surgery, the lowest incidence of AKI was observed in the group with MAP between 80 mmHg and 95 mmHg compared with 65–79 mmHg and 96–110 mmHg.[110] A multicenter RCT also demonstrated that maintaining MAP at 80–85 mmHg, compared with 65–70 mmHg, reduced the incidence of AKI stage 2 and the need for renal replacement therapy in septic shock patients with chronic hypertension.[19] For patients with prior hypertension who developed AKI within 24 h of septic shock, a higher MAP target of 80–85 mmHg – compared to a standard MAP target of 65–70 mmHg – was associated with significantly greater glomerular function.[111] A total of 45–70% of critically ill patients admitted to the ICU have a history of chronic hypertension, and 48–72% of ICU patients in shock and on vasoactive drugs experience relative hypotension compared to basal hypertension, usually expressed as blood pressure deficit [(actual blood pressure − baseline blood pressure)/baseline blood pressure], closely related to the occurrence of AKI.[112] Therefore, we suggest maintaining MAP at 80–85 mmHg or at the patient's baseline blood pressure during shock resuscitation for AKI patients with prior hypertension.

Question 26: To avoid the occurrence or progression of AKI, what RPP should be targeted in critically ill patients?

Recommendation 26: RPP should be maintained at ≥60 mmHg in critically ill patients to avoid the occurrence or progression of AKI. We suggest titrating the blood pressure level according to the RPP, if possible (Grade 2+, Weak recommendation).

Optimizing renal perfusion is the main therapeutic method for critically ill patients to avoid or ameliorate AKI progression. RPP is defined as the difference between systemic MAP and central venous pressure (CVP): RPP=MAP − CVP. Studies show that the renal mean perfusion pressure (MPP) deficit [(actual MPP − baseline MPP)/baseline MPP] was significantly higher in patients with septic shock who developed severe AKI compared to those who did not (29% *vs.* 24%), with the difference mostly depending on a CVP effect.[113] A retrospective study of 746 ICU patients undergoing elective cardiac surgery in 14 ICUs also showed that high CVP, low MPP, and prolonged duration of MPP <60 mmHg, were independent risk factors for the development of AKI.[114] Together, these studies indicate that RPP is a relatively more reliable target for blood pressure management in critically ill patients and that an RPP >60 mmHg should reduce the incidence of AKI and ameliorate its progression. We suggest titrating the blood pressure level according to the RPP, if possible.

Question 27: What is the target blood pressure for critically ill patients on continuous renal replacement therapy (CRRT)?

Recommendation 27: Hypotension is associated with a high risk of mortality during CRRT. Thus, we suggest maintaining the RPP ≥60 mmHg as a reasonable target (Expert opinion).

Reports indicate that 97% of patients experience at least one new episode of hypotension during CRRT, with 43% of these

episodes occurring within the first hour of CRRT initiation.[115] The frequency and duration of hypotension during CRRT, particularly hypotension episodes within the first hour of CRRT initiation, are independent risk factors for poor prognosis.[115] A machine-learning model for predicting the occurrence of hypotension during CRRT has been constructed with an AUROC of 0.828.[116] However, the target blood pressure for critically ill patients during CRRT has not yet been determined. A retrospective analysis of 2292 AKI patients on CRRT found that low MAP, particularly when MAP <82.7 mmHg, was associated with high ICU mortality.[117] Therefore, it is necessary to closely monitor MAP during CRRT and take measures as early as possible to avoid hypotensio, with the help of predictive models. We suggest the target MAP could be individualized based on premorbid basal blood pressure and hemodynamic status, ensuring at least an RPP >60 mmHg.

Perioperative blood pressure management in cardiac surgery

Question 28: What is the target blood pressure post coronary artery bypass grafting (CABG)?
Recommendation 28: We suggest maintaining MAP ≥70 mmHg in patients post-CABG to ensure adequate myocardial perfusion (Expert opinion).

CABG is an effective treatment for severe coronary artery disease. Patients with coronary artery disease often have hypertension, diabetes, congestive heart failure (CHF), and other diseases and are prone to experience blood pressure fluctuations during the perioperative period. Sufficient MAP should be maintained for patients after CABG to ensure adequate myocardial perfusion. Patients with coronary heart disease depend greatly on sufficient diastolic filling to maintain coronary blood flow. Therefore, diastolic pressure should be a focus for patients after CABG, along with ensuring that MAP meets the needs of myocardial oxygen uptake.

An RCT evaluated the effectiveness of amrinone and dobutamine on patients with preoperative left ventricular dysfunction presenting with postoperative low cardiac output syndrome. The treatment objectives were to achieve a CI ≥2.4 L/min/m^2 and a MAP ≥70 mmHg.[118] In another study of blood pressure management after CABG, patients were randomly allocated to receive either clevidipine or sodium nitroprusside after their MAP had reached >90 mmHg for at least 10 min; the target MAP was set at 70–80 mmHg. There was no significant difference in blood pressure attainment between the two groups.[119] In a study of clevidipine on blood pressure control after CABG, the target MAP was set at 70–80 mmHg, and found that myocardial lactate metabolism was unaffected.[120] El-Rahmany et al. also set the target MAP after CABG between 70 mmHg and 80 mmHg. They found that forced-air warming after CABG could reduce the need for vasodilator drugs.[121] For early goal-directed hemodynamic management after CABG, one RCT set target MAP at 70 mmHg and SV index ≥35 mL/m^2 as the goals of hemodynamic management and found that this protocol shortened the duration of CABG patients' hospital stay from 13.9 days to 11.4 days (P=0.02). Furthermore, ICU bed utilization was reduced by 23%, providing indirect evidence for the scientific rationale of the cited blood pressure goals.[122]

Question 29: What is the target blood pressure during the perioperative period in patients with aortic dissection?
Recommendation 29: We suggest perioperative SBP of patients with aortic dissection should be controlled within 100–120 mmHg. The heart rate should be controlled at approximately 60 beats/min. Perfusion of vital organs should be maintained with the premise of preventing rupture and bleeding (Grade 2+, Weak recommendation).

Heart rate and blood pressure should be strictly controlled in patients with aortic dissection to reduce the shear stress of blood flow on the aorta, thereby limiting the progression of dissection. Perioperative blood pressure management should fully consider the individual's age, basal blood pressure, history of stroke, liver and kidney function, and the degree of dissection to organs and blood vessels to control blood pressure at the lowest level while maintaining the perfusion of vital organs. Extremities that are not affected by the dissection should be selected for blood pressure measurement to ensure accurate monitoring.

Although there are no RCTs of blood pressure control in patients with acute aortic dissection, observational studies have shown that antihypertensive therapies can slow the progression of dissection. A retrospective study analyzed 224 patients with type B aortic dissection, in which the SBP was controlled at 120 mmHg with medication. Based on the average heart rate on the 3rd, 5th, and 7th day post-onset, patients were divided into strict heart rate control (<60 beats/min) and conventional heart rate control (≥60 beats/min) groups. The incidence of aortic events (such as organ ischemia and aortic rupture) was compared between the two groups, showing that the incidence of aortic events in patients in the strict heart rate control group was significantly reduced.[123]

β-blockers are typically used as first-line drugs for controlling heart rate and reducing the contractility of the left ventricle, thereby reducing the aortic shear force and slowing down disease progression to a great extent. If patients have potential conditions that cannot tolerate β-blockers, such as asthma, bradycardia, or heart failure, esmolol with a shorter half-life may be an alternative. If β-blockers fail to lower systolic pressure sufficiently, urapidil, nicardipine, or sodium nitroprusside can be combined to reach the target blood pressure. Urapidil has a rapid onset of action, little effect on perioperative organ perfusion, and no adverse reactions such as coronary steal syndrome. Nitroprusside can cause reflex activation of the sympathetic nervous system, and thus, it is suggested to give β-blockers to control heart rate before using sodium nitroprusside. When managing postoperative blood pressure, β-blockers should still be used as the first-line drug. Chen et al.[124] conducted a retrospective study of 4275 patients with acute type A aortic dissection who underwent surgery, and found that postoperative use of β-blockers could significantly reduce all-cause mortality (16.2% *vs.* 23.7%) and the incidence of cardiovascular and cerebrovascular events (19.2% *vs.* 29.0%). This further confirms the protective effects of β-blockers on patients following aortic dissection.

Question 30: What is the target blood pressure post left ventricular assist device (LVAD) implantation?
Recommendation 30: We suggest maintaining MAP at 70–80 mmHg post-LVAD implantation because high blood pressure may be related to poor neurological prognosis (Grade 2+, Weak recommendation).

The low pulse pressure in patients after LVAD makes it difficult to measure blood pressure non-invasively. Therefore, we recommend using invasive arterial blood pressure monitoring. Pulmonary artery catheter (PAC) and echocardiography are recommended for hemodynamic monitoring in the early postoperative period to evaluate patients' volume status and cardiac function. Excessively high blood pressure may lead to neurological complications, bleeding, and decreased LVAD flow, while excessively low blood pressure may lead to increased LVAD flow and right heart failure.

A study based on INTERMACS data found that the three-year survival rate of patients with low MAP (≤75 mmHg) was 58±1.8%, while those with normal (76–90 mmHg), high (91–100 mmHg), and very high (>100 mmHg) MAPs were 70±0.9%, 71±1.5%, and 63±3.0%, respectively. These findings suggest that extreme blood pressure values during LVAD support increase the risk of adverse events. Therefore, it is recommended that MAP be maintained at 70–90 mmHg.[125] In a prospective observational study of 96 patients with LVAD, patients who did not receive standardized antihypertensive treatment had significantly more neurological complications based on the MAP target of ≤80 mmHg. Through strict blood pressure management, only 3% of patients developed moderate or severe aortic regurgitation during a follow-up period of up to 201 days.[126] In a retrospective study of 123 patients with LVAD, patients were divided into a hypertension group (greater than 90 mmHg), a moderate blood pressure group (80–90 mmHg), and a blood pressure control group (less than 80 mmHg) according to MAP. The adverse events (such as intracranial hemorrhage, thrombotic events, and aortic regurgitation) of the three groups were 30%, 13%, and 3%, respectively. The increased MAP in patients with LVAD significantly increases the risk of adverse events, and controlling MAP below 80 mmHg can help reduce complications after LVAD.[127] These studies suggest that for patients receiving LVAD, a target MAP of 70–80 mmHg should be maintained.

Postoperative blood pressure management in patients with non-cardiac surgery

Most cardiovascular events occur after surgery in patients undergoing non-cardiac surgery, especially during transfer to the ICU. Hypotension and hypertension have a high incidence and a long duration and are associated with myocardial and renal injury and other adverse prognoses.[128–131]

Question 31: Do non-cardiac surgery patients need postoperative blood pressure monitoring?

Recommendation 31: For hemodynamically stable patients, routine non-invasive arterial blood pressure (NIBP) monitoring is recommended. For hemodynamically unstable patients, invasive arterial blood pressure (IBP) monitoring should be performed (Expert opinion).

The incidence of hypotension was reported in a multicenter retrospective study.[132] A total of 3169 patients were transferred to the ICU for non-cardiac surgery, of whom 2674 (84.0%) had a MAP below 75 mmHg and 1688 (53.0%) had a MAP below 65 mmHg in the ICU. Meanwhile, more than 80% of patients had a MAP <75 mmHg for approximately 8 h in the first two postoperative days. Another retrospective study of 2766 patients undergoing non-cardiac surgery showed that approximately 20% of patients had MAPs below 70 mmHg during their postoperative ICU stay, while the increased duration of postoperative hypotension was significantly associated with myocardial and acute kidney injuries.[133]

NIBP monitoring is recommended for patients with stable hemodynamics, but IBP monitoring can more realistically and accurately reflect blood pressure changes in critically ill patients (especially those in shock) compared with NIBP monitoring.

Question 32: What is the threshold for initiating blood pressure management?

Recommendation 32: For hypotensive patients, the threshold for initiating blood pressure management is MAP <65 mmHg (Grade 2+, weak recommendation). For hypertensive patients, the threshold for initiating blood pressure management is SBP >180 mmHg or DBP >110 mmHg, whichever is higher (Expert opinion).

There is insufficient evidence regarding individualized blood pressure management for non-cardiac postoperative procedures. A retrospective study suggested that MAP <65 mmHg significantly increased the risk of 30-day adverse cardiovascular and cerebrovascular events and AKI.[134] In addition, a multicenter retrospective study found that postoperative MAP <65 mmHg was significantly associated with increased 30-day and 90-day mortality, provided that intraoperative MAP was at least 65 mmHg.[5] The threshold of postoperative hypertension is still controversial, and some studies have demonstrated that systolic pressure >180 mmHg or diastolic pressure >110 mmHg is associated with cardiovascular complications.[135,136] There remains a lack of clear evidence on the specific blood pressure intervention threshold for treatment in the ICU after non-cardiac surgery, and RCTs are needed to determine the optimal intervention threshold for postoperative blood pressure levels and treatment strategies.

Question 33: How should postoperative blood pressure be managed in patients undergoing non-cardiac surgery?

Recommendation 33: For hypotensive patients, volume responsiveness should be assessed after excluding residual effects of anesthesia-related medications. For hypertensive patients, predisposing factors (e.g., pain, dyspnea, and anxiety) should be removed before blood pressure management (Expert opinion).

A meta-analysis that included 2260 patients found that fluid responsiveness was present in 50% of postoperative hypotensive patients and that typical signs and symptoms of suspected hypovolemia were not predictive of fluid responsiveness. However, the increased cardiac output after passive leg raising (PLR) is a good predictor of fluid responsiveness. Patients classified by PLR who did not respond to fluids had no increase in cardiac output after fluid resuscitation.[137] If there is no need to increase preload, the use of vasopressors or cardiac stimulants should be considered (for the emergency management of hypertension, please refer to Section 6 of the consensus). In the absence of a hypertensive emergency, an attempt should be made to determine the presence of factors leading to reversible hypertension.[138] Common non-pharmacological interventions depend on predisposing factors, such as adequate analgesia, oxygen therapy, and appropriate sedation.

Management of blood pressure after pheochromocytoma surgery

Pheochromocytoma originates from the chromaffin tissue of neuroectoderm and mainly secretes catecholamines. The clinical symptoms are mainly paroxysmal or persistent hypertension. After tumor resection, the concentration of catecholamines in the body plummets, and the relative increase of vascular volume and decrease of return blood volume and cardiac output may lead to uncontrollable hypotension – a main cause of postoperative death in patients with pheochromocytoma.[139]

Question 34: What are the indications for transfer to ICU in patients with pheochromocytoma post-surgery?
Recommendation 34: For patients experiencing intraoperative hemorrhage or severe hemodynamic fluctuations (MAP <65 mmHg), and/or still requiring vasoactive drugs to maintain blood pressure post pheochromocytoma surgery, transfer to ICU for further monitoring and treatment is recommended (BPS).

The concentration of catecholamines rapidly decreases in the blood of patients after pheochromocytoma resection. The presence of preoperative residual alpha-blocking effects, the decline in peripheral vasoconstriction, and even postoperative hypovolemia can lead to severe hypotension or shock.[139] A multicenter retrospective study showed that hemodynamically stable postoperative patients with MAP >65 mmHg, tumor diameter <6 cm, and estimated blood loss <250 mL did not need to be transferred to the ICU.[140]

Question 35: How should patients with postoperative hypotension be managed?
Recommendation 35: (a) For patients with a significant drop in blood pressure or hypotension, rapid fluid resuscitation and prompt administration of vasoactive drugs should be performed immediately (Expert opinion); (b) Prompt glucocorticoid supplementation is needed when patients develop intractable hypotension (Grade 2+, weak recommendation); and (c) Consideration of intra-aortic balloon counterpulsation (IABP) or ECMO should occur when treatments (a) and (b) above are not effective (Expert opinion).

Intractable hypotension after pheochromocytoma resection may be secondary to choline depletion. Several studies have found that low-dose glucocorticoids can improve intractable hypotension after pheochromocytoma resection and reduce catecholamine doses.[141–144] In the study and case reports by Hekimian et al. and Zhou et al. six out of nine patients administered ECMO survived, and one patient survived by treatment with IABP and ECMO. When intractable hypotension is not reversed by the above-mentioned pharmacological treatments, IABP or ECMO can significantly reduce cardiogenic shock, contribute to subsequent cardiac recovery, and improve patient prognosis.[145–147]

Blood pressure management in critically ill patients with severe heart disease

Severe heart disease is a group of related diseases associated with varying degrees of damage to the cardiovascular system, mainly including acute coronary syndrome (ACS), acute heart failure (AHF), and acute aortic syndrome, and requiring complex cardiac surgery. During the course of treatment, blood pressure fluctuates greatly and hypertensive emergencies are prone to occur, which further leads to functional damage of target organs such as the heart, kidney, and brain, and increases mortality. The goal of blood pressure management in patients with severe heart disease is to maintain effective hemodynamics to match cardiac function with cardiac pre- and postload, avoiding hypertension complications and ensuring perfusion of organs.

Question 36: What is the target blood pressure for ACS?
Recommendation 36: For patients with ACS combined with hypertension, we suggest SBP should be controlled within 120–130 mmHg and DBP ≥60 mmHg to maintain blood flow of the coronary artery (Grade 2+, weak recommendation).

Hypertension is a risk factor for ACS, and pressure and flow are the major determinants of cardiac structure and function. When SBP rises, the resistance of the left ventricular ejection and wall tension increase, leading to increased myocardial oxygen consumption, left ventricular hypertrophy, and even heart failure, making reasonable control of blood pressure essential. Studies have shown a linear relationship between the control of SBP levels and the risk of cardiovascular disease and death. Compared with patients with SBP at 130–134 mmHg, those with SBP of 120–124 mmHg had an HR of 0.71 (95% CI: 0.60–0.83) for the risk of cardiovascular disease and 0.73 (95% CI: 0.58–0.93) for all-cause mortality risk.[148] For hypertensive patients without diabetes, controlling SBP <120 mmHg was associated with a 25% reduction in the incidence of major cardiovascular events compared with those with a blood pressure target of 140 mmHg, but a significant increase in the incidence of serious adverse events, such as syncope, AKI or renal failure.[149] Therefore, it is recommended that SBP should be controlled at 120–130 mmHg for patients with ACS combined with hypertension.

Almost all myocardial perfusion occurs in diastole, and diastolic pressure is the myocardial perfusion pressure. At present, there are no RCTs to support an ideal DBP target value in patients with ACS. The previous GUSTO IIb and PURSUIT studies with ACS patients found that SBP ≤90 mmHg was closely related to 48 h and 30-day mortality.[150] Furthermore, DBP <60 mmHg is associated with increased incidence of cardiovascular events and all-cause mortality in patients without obvious heart disease in the past.[151] Therefore, combined with the pathophysiology of myocardial perfusion and clinical experience, it is recommended that DBP ≥60 mmHg is maintained in ACS patients to ensure myocardial perfusion.

Question 37: What is the target blood pressure for patients with AHF?
Recommendation 37: For patients with AHF combined with hypertension, we suggest SBP be controlled within 120–130 mmHg (Grade 2+, weak recommendation).

Heart failure with reduced ejection fraction (HFrEF) is common and may occur in association with coronary artery disease. Heart failure with preserved ejection fraction (HFpEF) is often caused by increased left ventricular pressure load caused by hypertension, wall thickening, myocardial fibrosis, and subsequent diastolic dysfunction, and, ultimately, increased left ventricular filling pressure. As a result, its prognosis is similar to that of HFrEF. Therefore, the two conditions share the same blood pressure thresholds and pharmacological targets.[152]

A meta-analysis of the effects of blood pressure goals on the prognoses of hypertensive patients showed that stricter control of blood pressure significantly reduced the risk of stroke, coronary-related cardiovascular events, and death but had little effect on the occurrence of heart failure.[153] In the same year, a meta-analysis of the effects of intensive blood pressure controlling (SBP <133 mmHg) on cardiovascular events and renal function in hypertensive patients also reached similar conclusions.[154] Studies have shown that controlling SBP levels below 120 mmHg can significantly reduce the risk of sudden heart failure.[155] However, when patients are readmitted for AHF, lower SBP (<120 mmHg) levels are significantly associated with all-cause mortality.[156] A recent study of elderly (>75 years) hypertensive patients with HFpEF found that, compared with SBP >130 mmHg, there was no difference in 30-day, 12-month, and 6-year all-cause mortality in patients with SBP <130 mmHg, while the risk of death increased at 120 mmHg.[157] Thus, the optimal diastolic pressure target for patients with heart failure is unclear. The results from the reanalysis of TOPCAT data by Sandesara et al.[158] showed that both DBP >90 mmHg and <60 mmHg were significantly associated with the risk of adverse outcomes.

Patients with AHF have multiple comorbidities, which complicate their treatment and affect prognosis. Therefore, it is recommended that AHF patients have well-controlled SBP <130 mmHg, as soon as possible, to reduce cardiac load and relieve symptoms. However, SBP <120 mmHg is not appropriate for these patients.

Summary

Blood pressure management of critically ill patients is essential. The working group summarized results from recent trials, conducted GRADE classification based on evidence-based medical data, and formulated a national expert consensus on blood pressure management in critically ill patients, including shock, hypertension, ACS, severe craniocerebral injury, severe kidney disease, the perioperative period, and severe heart disease. The aims of this consensus were to clarify optimal approaches of blood pressure monitoring, blood pressure targets, clinical management, and related pharmacotherapy options for critically ill patients. The consensus provides references for blood pressure management in critically ill patients and guides the clinical practice of blood pressure management for clinicians.

However, there are still limitations to this consensus. A systematic review was not conducted, but the recommendations based on GRADE still provide strong guiding evidence for clinicians. Several recent and important trials were not included because of time constraints. The consensus group welcomes further suggestions to advance the development of the next version of the consensus and looks forward to adding more evidence-based medical data in the future to upgrade the expert consensus into guidelines for the blood pressure management of critically illness.

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Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary Materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jointm.2023.06.001.

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