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Mean arterial pressure and outcomes in critically ill patients: is there a difference between high and low target?

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Adult critical illness is one of the conditions that generates the substantial burden of disease and is expensive globally. Sepsis, acute lung injury, and mechanical ventilation are the most representative conditions in this specialty[1]. The barriers and deficiencies of health systems in low- and middle-income countries make the approach to this type of disease even more complex, forcing the reproduction of the best evidence-based decision-making with the least use of resources[1]. This contemplates the ongoing discussion of emerging evidence and the evolution of traditionally used clinical concepts that are essential in the pathophysiology and health care of critically ill patients. Systemic mean arterial pressure (MAP) is a hemodynamic parameter that reflects the perfusion pressure of vital organs. In critically ill patients with resolution therapy, supportive care is essential to ensure survival, reduce morbidity, and reduce the risk of sequelae[2,3]. There has been much discussion on the MAP value that is most appropriate to maintain in critically ill patients[2,3]. However, the scientific evidence shows that this may vary depending on the baseline characteristics of the patients, the disease being treated, and the goal the intensivist wants to achieve. Some guidelines differ between these values, recommending values ranging from 65–70 mmHg to 80–85 mmHg but relying mainly on 30- or 90-day mortality outcome[2-4]. Then, is there a difference between high and low target? What does the evidence say about it?

Recently, Carayannopoulos et al.[4] conducted a meta-analysis of randomized controlled trials, including six trials with a total of 3,690 patients, in order to assess whether the target of higher vs. lower MAP in adults with shock produces significant differences in outcomes in critically ill patients. The authors found that high vs. low target MAP does not produce significant differences in mortality outcome (RR: 1.06; 95%CI: 0.98–1.15, I2=0%, p=0.12), nor in renal replacement therapy (RR: 0.96; 95%CI: 0.83–1.11, I2=24%, p=0.57). However, it was evident that a high target MAP in patients with a history of arterial hypertension may reduce the risk of renal replacement therapy (RR: 0.83; 95%CI: 0.71–0.98, I2=0%, p=0.02) compared to those without arterial hypertension (RR: 0.83; 95%CI: 0.71–0.98, I2=0%, p=0.02). Thus, the authors concluded that there is no difference between the MAP targets in terms of mortality, but a higher MAP can be considered in patients with arterial hypertension[4]. Another similar meta-analysis[5], which evaluated additional outcomes in 3,753 patients with the same conditions, showed that there was no significant difference between MAP targets and duration of mechanical ventilation (SMD: 0.51; 95%CI: -0.29 to 1.31, p=0.21), or length of stay in intensive care (SMD: 0.22; 95%CI: -0.07 to 0.5, p=0.14). However, there was a statistically significant difference in the reduction of ICU length of stay in post-cardiac arrest patients with high MAP targets (SMD: 0.55; 95%CI: 0.31–0.80, p<0.000001)[5].

Other recent studies useful in understanding the impact of MAP variation on outcomes in critically ill patients include those by How et al.[6] and Yoshimoto et al.[7] In the first one, the authors explored the relationship between MAP variability and short- and medium-term mortality in a cohort study. They included a total of 12,867 patients (1,320 died in-hospital, 1,399 died within the first 28 days, and 2,734 died within 1 year), finding that the average real variability of MAP ≥7. 2 mmHg was associated with higher in-hospital (OR: 1.44; 95%CI: 1.21–1.72), 28-day (HR: 1.28; 95%CI: 1.1–1.5), and 1-year mortality (HR: 1.27; 95%CI: 1.14–1.42)[6]. This association was maintained independently of the sequential organ failure assessment (SOFA) score. In the Yoshimoto et al.'s[7] study, in which three randomized controlled trials on 3,357 patients with vasodilator shock were meta-analyzed and the optimal

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blood pressure target was evaluated, there was no difference in mortality (RR: 1.06; 95%CI: 0.98–1.16) between the two groups evaluated (60–70 mmHg vs. >70 mmHg), nor in patients with arterial hypertension or older than 65 years. There were also no differences in adverse events observed between the two groups (RR: 1.04; 95%CI: 0.87–1.24). However, it was observed that the frequency of supraventricular arrhythmias was significantly higher in the higher MAP group (RR: 1.73; 95%CI: 1.15–2.60) and that the need for renal replacement therapy in hypertensive patients was lower in this same group (RR: 0.83; 95%CI: 0.71–0.98)[7]. Although these results allow us to observe a heterogeneous trend in terms of MAP targets and mortality, the positive association between higher MAP and a lower need for renal replacement therapy in hypertensives is more evident. However, the risk of supraventricular tachycardia was also reported, which may be an important factor in patients with a history of heart disease. Also, there were no differences in terms of duration of mechanical ventilation or length of stay in intensive care. However, differences were found in post-cardiac arrest patients.

Other variables to consider, which have been studied but not evaluated in the meta-analyses described above, are the time of day of the measurement or MAP variability. A cohort study involving 5,185 individuals found that nocturnal MAP rising was significantly associated with intensive care (OR: 1.34; 95%CI: 1.10–1.65), in-hospital (OR: 1.35; 95%CI: 1.12–1.63), 28-day (HR: 1.27; 95%CI: 1.10–1.48), and 1-year mortality (HR: 1.24; 95%CI: 1.10–1.40). Similar to the evidence discussed previously, this estimate was independent of the SOFA score[8]. Likewise, differences have also been found in the outcomes of surgical patients with hypotensive events during the postoperative stay in intensive care. Those with events with MAP values ≤65 mmHg had up to 1.52 times higher risk of suffering an adverse cerebrovascular or cardiac event at 30 days[9]. Thus, care must be taken in the interpretation and critical reading of the evidence, since numerous additional factors may be associated with the control of MAP in intensive care, as well as mortality outcomes, duration of mechanical ventilation, and length of hospital stay.

In Latin American countries, such as Brazil, the quality of labor contracting, barriers, and economic and infrastructure limitations of the health system impedes the systematic reproduction of decision-making[10-12], which would explain the lack of data available to perform similar studies on this topic and to corroborate if the hemodynamic behavior and its association with short- and long-term outcomes are similar to those reported in the literature. A significant prevalence of burnout has been described in nurses and intensive care technicians in Brazil, which can make it difficult to strictly monitor MAP in a personalized way by disease or patient, in a unit with a large volume of patients[12]. The Brazilian Research in Intensive Care Network[11] highlighted the progressive and relevant advances that the country has made in recent years. However, among the future perspectives proposed is to strengthen the country's research, education, and infrastructure in order to further reduce mortality from critical illnesses[11]. The monitoring and regulation of MAP is an indicator associated with outcomes in intensive care; therefore, its constant evaluation and control should also be included in the technical challenges in order to reduce the burden of critical illnesses in adults.

AUTHORS' CONTRIBUTIONS

DCBP: Conceptualization, Formal Analysis, Investigation, Writing – original draft, Writing – review & editing. **JAFS:** Conceptualization, Formal Analysis, Investigation, Writing – original draft, Writing – review & editing. **AFTS:** Conceptualization, Writing – original draft, Writing – review & editing. **MGOS:** Conceptualization, Formal Analysis, Investigation, Writing – original draft, Writing – review & editing.

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