Does the Reperfusing Brain Recover Better Under Pressure?

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Patients who have return of spontaneous circulation (ROSC) after cardiac arrest have a postarrest syndrome involving hemodynamic instability and neurologic dysfunction including coma. The post–cardiac arrest inflammatory cascade leads to disruption of autoregulation in the cerebral vasculature, and cerebral blood flow becomes pressure dependent. The blood pressure (BP) range for optimal neurologic improvement is currently unknown.

Most of the investigations on BP and neurologic outcome have been in the setting of acute ischemic stroke (AIS) or intracerebral hemorrhage (ICH). Although more regional than in cardiac arrest, in AIS, there is hypoperfusion of the brain in the affected vascular territory. In a retrospective review of the international stroke trial, the clinical outcome in relation to systolic BP (SBP) followed a U-shaped association, with SBP lower than 120 mm Hg or higher than 200 mm Hg associated with worse neurologic outcomes (1). A higher SBP was associated with increased strokes, and lower SBP was associated with adverse cardiac events. BP fluctuations during the acute phase of ischemic stroke have shown mixed results. One observational study reported poorer neurologic outcomes for a 10 mm Hg drop in SBP below 180 mm Hg as well as above 180 mm Hg (2). Another prospective observational study reported that a decrease in SBP of 10% within the first 24 hours of AIS resulted in worse neurologic outcomes at 3 months (3). Data analyzed from the Trial of ORG 10172 in Acute Stroke Treatment study (4) reported that a 30% change in BP within the first 24 hours of AIS was not predictive of poor neurologic outcome. During AIS, active lowering of BP in the first few hours or days has shown no difference in functional well-being (5), and in some cases, it has been detrimental to neurologic outcome (6). In the Continue or Stop Post-Stroke Antihypertensives Collaborative Study, patients with AIS either stopped their preexisting antihypertensive medications or continued them for 2 weeks. No significant difference was found in the rate of disability between the two groups at 6 months per modified Rankin score (7).

Lower BPs (< 140 mm Hg SBP) are also associated with worse neurologic outcomes after ICH (8).

In this issue of Critical Care Medicine, the study by Kilgannon et al (9) investigates the association between BP and neurologic outcomes in post–cardiac arrest patients with ROSC and is an interesting “look” into a very basic but key variable. This is a prospective but observational study where the investigators assessed the BP at 15-minute intervals for 6 hours after cardiac arrest, without any manipulation of BP, which was left at the discretion of the primary treating physicians. They calculated a time-weighted average-mean arterial pressure (TWA-MAP) and found that a threshold TWA-MAP of more than 70 mm Hg had the strongest association with good neurologic outcome as defined as a Cerebral Performance Category (CPC) of 1–2.

Scarc data exist regarding the association between BP and neurologic outcomes in patients with cardiac arrest. A recent retrospective study (10) of patients who had undergone cardiac arrest reported an association with improved neurologic outcomes (CPC 1–2) at even higher MAPs than that reported by Kilgannon et al (9). Vasopressor use was associated with poorer outcomes, which is likely due to a higher severity of illness in these patients (10). In another retrospective observational study, the initial MAPs within 5 minutes after cardiac arrest were not associated with outcome, but time-weighted MAPs (75–100) averaged over 2 hours demonstrated better neurologic outcome (11). The mean MAPs were 76 and 87 in patients with poor versus better neurologic outcomes, respectively (11). A recent study of patients with out-of-hospital cardiac arrests found the highest survival rate when the SBP was between 120 and 129 mm Hg in patients presenting with an initial shockable rhythm (i.e., ventricular tachycardia/ventricular fibrillation [VT/VF]) but no such association in patients with nonshockable rhythm (i.e., pulseless electrical activity [PEA/asystole]) (12).

The findings of Kilgannon et al (9) lend further support to the existing body of data, although not conclusively proven, indicating that low BP during low flow states to the brain is not beneficial in the acute phase of injury. The authors point out many of the limitations of their study. It is observational in nature; therefore, only associations not causations can be determined.

Most of the patients had in-hospital cardiac arrest with an initial PEA/asystole rhythm. An important finding is that although a TWA-MAP of more than 70 mm Hg had the strongest association with good neurologic outcome, this was in the patient group that naturally maintained TWA-MAP of more than 70 mm Hg without the use of vasopressors. The group of patients on vasopressors with a TWA-MAP of more than 70 mm Hg actually had a significantly poorer neurologic outcome. This may indicate that the “general well-being” of the individual plays a more significant role in determining neurologic outcomes than...
artificially maintaining higher MAP. Regardless of vasopressor use, patients with TWA-MAP of less than 70 mm Hg had the poorest outcomes and were obviously sicker with higher Charlson comorbidity scores, a greater number of arrests occurring in the ICU, and a greater rate of PEA/asystolic arrest.

It should be noted that in the current study, even when the patients were on vasopressors, some presumably in the ICU, no arterial catheters were inserted. As there is discordance between invasive and noninvasive BP measurements (even MAPs), monitoring invasive BP would likely change the “cut-off” BP variable for a good outcome (13).

The use of therapeutic hypothermia in PEA/asystole arrest is not recommended but was left to the discretion of the treating physician, yet 78% of the patients receiving therapeutic hypothermia had PEA/asystole as the initial rhythm. Another peculiar observation is that the rate of good neurologic outcomes was the same (29%) for both initial rhythm VT/VF and initial rhythm PEA/asystole. Outcomes would be expected to be much worse in the PEA/asystole group (14). This suggests the presence of confounding unmeasured variables in this relatively small, single-center study.

In conclusion, although observational in nature, this study raises important questions about the role of BP in post–cardiac arrest neurologic outcomes. There is a need for a randomized trial to prospectively target BP ranges to evaluate what BPs are conducive to better neurologic outcomes after cardiac arrest. It is also likely that “one size does not fit all,” and ideally the control of BP should be based on real-time monitoring of cerebral perfusion and function at the bedside. Until such tools become available, it is prudent to avoid hypotension. No human studies to date have established an optimal BP or MAP, but recommendations are to keep the MAP more than or equal to 65 after cardiac arrest ROSC (15).

REFERENCES