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Acute stroke: low baseline blood pressure equals low seven-day life expectancy?

Acidente vascular cerebral agudo: pressão arterial baixa à admissão implica em redução na expectativa de vida em 7 dias?

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Normal cerebral autoregulation maintains uniform cerebral blood flow despite fluctuations in cerebral perfusion pressure between 50-150 mm Hg. This autoregulation is impaired during acute stroke resulting in a linear relationship between cerebral blood flow and cerebral perfusion pressure[1]. Elevated systolic blood pressure (SBP) and mean arterial pressure at presentation have been associated with poor outcomes, including early death[1,2,3,4]. There have been few studies that have also shown increased mortality with low SBP at baseline showing a U-shaped curve of mortality with blood pressure[1,5]. These studies have been largely inclusive of minor and severe strokes and there is a paucity of research done to establish an association of mortality and acute blood pressure (BP) in high-risk patients.

In this issue of the journal, Furlan et al.[6] report the findings of their single center study among 146 acute stroke patients admitted to the intensive care unit, which examined relationships between BP obtained at presentation and at 48-hours, and the occurrence of early mortality (within seven days). Among the 101 ischemic patients, they observed that baseline systolic BP, baseline diastolic BP, 48-hour mean systolic BP, and 48-hour mean diastolic BP were all significantly lower in patients who died within seven days compared with survivors; and in multiple regression analysis, the 48-hour mean systolic BP remained significantly associated with odds of early mortality. Moreover, a 48-hour mean systolic BP of ≤ 131 mmHg was determined to be the most optimal cut-off for discriminating odds of early mortality. Among the 45 hemorrhagic stroke patients there were no significant associations between BP and occurrence of early mortality.

The authors are to be commended for investigating this important yet controversial issue, especially given the plethora of studies over the years that have sought to improve our understanding about how best to manage blood pressure for these patients, taking into consideration the different pathophysiology of the main stroke types (ischemic vs. hemorrhagic), and even subtypes (large vessel occlusion vs. small vessel ischemic disease). Nonetheless, the interpretation of findings observed among their ischemic stroke patients should be looked at carefully.

First, information about the various mechanisms of ischemic stroke was not available, although one may presume that since these were all critically ill patients requiring admission into the neurointensive care unit, chances are that the majority had large vessel occlusive disease (although patients with small vessel disease strokes and multiple comorbidities or new-onset complications can also find themselves in a critical unit). Ischemic strokes secondary to large artery atherosclerosis may be more prone to hypoperfusion-related extension or recurrence of ischemic stroke than other etiologies of ischemic stroke. This phenomenon was noted in patients with ipsilateral (sub-group analysis of SCAST[7]) and bilateral severe carotid disease (meta-analysis of ECST, NASCET, and UK-TIA trial by Rothwell et al.[8]*)*.

Second, was the difference between the baseline SBP and 48-hour mean SBP. The survivor group had a decline of 26 mm Hg from baseline to 48-hour SBP whereas the difference was only 3 mm Hg in the non-survivor group. Elevated blood pressure is common in the acute phase and can be seen in two-thirds to three-quarters of cases[9,10]. The fact that the non-surviving group of ischemic strokes had uniformly low SBP in the first 48 hours may point towards an underlying hemodynamic confounder. While the authors did due diligence by performing the ***post hoc*** regression analysis to include possible confounders such as infection and myocardial

infarction, they were unable to assess the potential impact of chronic or acute-on-chronic congestive heart failure due to limited information on cardiac function. Several community-based studies have shown that congestive heart failure is independently associated with greater mortality[11-16] and undiagnosed congestive heart failure could have been the unaccounted-for confounder. Should oral antihypertensive medications that patients were using before stroke onset be temporarily held back or lowered in dose during acute ischemic stroke treatment to prevent inadvertent dramatic drops in BP? This is still not clear, but expert consensus guidelines recommend that the approach be individualized based on select patient and stroke features. However, beyond the initial 24–48 hours, it is not unreasonable to begin antihypertensive drug treatment given that the ischemic penumbra usually goes away within the initial 24 hours.

Third, the sample size is relatively small and the population is restricted to only patients admitted to the intensive care unit. In the case of the former (especially with intracerebral hemorrhage patients), the possibility of a type I error is high and in the case of the latter, the ability to generalize these findings to all stroke patients is questionable. Moreover, with hemorrhagic stroke, the low number of patients limits interpretation of the results. From the INTERACT-2[17] and ATACH-2[18] trials, we learned that achieving a target SBP of 140 mm Hg acutely in intracerebral hemorrhage is safe and is possibly associated with improved outcomes, but targeting an SBP of ≤ 130 mm Hg does not add any benefit while it increases the risk of renal complications. The mean 48-hour SBP in the surviving (143 mm Hg) and fatal (133 mm Hg) groups of hemorrhagic stroke patients were not overtly different from the target SBP achieved acutely in the active arm of the INTERACT-2 trial (139 mm Hg within six hours) and, hence, it is not surprising that no significant difference was found between the two arms of hemorrhagic stroke by Furlan et al.[6].

Despite its limitations, the authors have identified an important sub-group of patients admitted to the intensive care unit with acute ischemic stroke. The presence of baseline and 48-hour mean SBP of ≤ 130 mm Hg should be identified as a marker of poor outcomes, and carefully selecting such patients for further cardiac workup, such as echocardiography, should be done in centers with limited resources to identify and optimize the compromised hemodynamic state. In ischemic stroke, the current consensus-based guidelines recommend that there is no clear benefit in starting antihypertensive treatment in the acute setting after an ischemic stroke unless there is a strong indication to control elevated BP for a comorbid condition such as post-thrombolysis bleed or aortic dissection[19]. This study reinforces these guidelines and suggests it may not be appropriate to start antihypertensive agents within 48 hours in patients presenting with SBP of 130-140 mm Hg unless indicated for another reason.

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