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CORRESPONDENCE

Risk of overestimating loss of cerebral autoregulation

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Abbreviations: CA, Cerebral Autoregulation; CBF, Cerebral Blood Flow; Mxa, Mean Flow Index; CPP, Cerebral Perfusion Pressure; MAP, Mean Arterial Pressure; Vm, Mean velocity

Editor—We wish to comment on the study by Manquat and colleagues, which explored an interesting and innovative noninvasive method for monitoring cerebral autoregulation (CA). Alterations in dynamic CA leave the brain vulnerable to periods of hypo- or hyper-perfusion that may increase the chance of secondary cerebral injury. A reliable approach to quantifying CA is essential to comprehend cerebral haemodynamic alterations and to guide individualised treatment.

We analysed the data presented by Manquat and colleagues[1] and found that patients in the impaired CA group (CA−; n=18) were older, had a higher frequency of comorbidities such as arterial hypertension (38.9% *vs* 16.7%) and diabetes (22.2% *vs* 0%), and included more ASA 3 cases (27.8% *vs* 0%) when compared with the group with preserved CA (CA+). Advanced age by itself is associated with the presence of white matter lesions also known as white matter hyper-intensities. Arterial hypertension and diabetes contribute to the development of endothelial dysfunction. These changes may alter the capacity to autoregulate cerebral blood flow (CBF), the plateau of the CA curve, and the limits of CA itself. This, in turn, leaves the patient more susceptible to haemodynamic changes caused by anaesthetics.

The mean flow index (Mxa), described by Czosnyka and colleagues[2] in 1996, is considered a dynamic measurement of CA that can be measured at the bedside and correlates with spontaneous fluctuations of cerebral perfusion pressure (CPP) and CBF velocity in the middle cerebral artery. This has been evaluated as an indicator for loss of CA.[3,4] When the MAP is within the limits of autoregulation of CBF, Mxa is close to 0, but when the MAP is not within these limits, Mxa is closer to 1. (In other words, CBF depends on the MAP and is correlated to it.) Through the Mxa, it is possible to define the inferior limit of this autoregulation. Nonetheless, Mxa varies according to how the measurement signal is processed and the method used for its measurement.[3] As an alternate approach, when a measurement of intracranial pressure is not readily available, invasive or noninvasive MAP quantification has been used to calculate CPP. This measurement has been typically referred to as Mxa as well.

Mxa has been evaluated by different authors as an indicator for loss of CA.[3] The methodology and interpretation of Mxa and related indices have been noted to be incoherent, generating inaccurate and variable results, making it an unreliable method.[4] Mxa was recently evaluated in healthy subjects, with a basal Mxa greater than 0.3 (the most commonly used threshold to describe loss of CA) found in more than 50% of them. This indicates that measurements of CA based on this method can overestimate the diagnosis of impaired CA or at least indicate that it is not reliable. In the study by Manquat and colleagues,[1] the reliability of Mxa could be even lower, especially because the time used to measure it was short, at approximately 5 min. The percentage of patients with loss of CA in this study might therefore be overestimated.

The risk of developing cerebral hypoperfusion is even greater when MAP is constantly low, especially for older

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patients with clinical or sub-clinical cerebrovascular disease. Given the importance of maintaining MAP higher than the value needed to preserve autoregulation, we find it interesting that high doses of propofol and remifentanil were used by Manquat and colleagues,[1] especially taking into account that the procedures performed involve relatively low levels of noxious stimuli and the doses used might risk hypotension and therefore altered CA. Furthermore, the anaesthetic doses were adjusted to maintain a patient state index of 25–35. These are relatively low values within the usual target range of this index, which is between 25 and 50. The anaesthetic protocol, in addition to the patient characteristics of group CA–, could have generated an increased tendency towards systemic hypotension. The study describes an average MAP of 70.6 (*vs* 71.1 in CA+) in patients with altered CA and a higher need for intraoperative vasopressor support with norepinephrine in this group.

In addition to the arguments presented previously, reported loss of CA might be related to the low values of the mean velocity (Vm) of the middle cerebral artery (28 m s^{-1} in average). This might have generated a higher risk of reporting cerebral hypoperfusion, considering that Vm of the middle cerebral artery in healthy subjects is around 60 cm s^{-1}.[5–8] In fact, several studies have evaluated the effect of anaesthesia maintenance with propofol on Vm[5,6] and also the effect of anaesthesia induction with sevoflurane.[7] They have all reported a decrease in Vm in relation to its basal value but never lower than 40 cm s^{-1}.

We consider that there is a need to find a multimodal monitoring method to evaluate CA. Although alterations noted in the electroencephalogram might be a valuable indicator to predict changes in CA, the aforementioned arguments might indicate that the number or patients with suspected loss of CA is overestimated in this study. It is essential to design studies with a larger sample size and in controlled and favourable conditions from a systematic point of view to obtain a diagnosis with less variability and more specificity and sensitivity.

Declarations of interest

The authors declare that they have no conflicts of interest.

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