Is the serum glucose/potassium ratio a reliable prognostic factor for aneurysmal SAH?

TO THE EDITOR: We studied with keen interest the article by Fujiki et al.1 regarding the role of the serum glucose/potassium ratio in predicting the outcome of aneurysmal subarachnoid hemorrhage (SAH) (Fujiki Y, Matano F, Mizunari T, et al: Serum glucose/potassium ratio as a clinical risk factor for aneurysmal subarachnoid hemorrhage. J Neurosurg [epub ahead of print November 17, 2017. DOI: 10.3171/2017.5.JNS162799]). We commend the authors for their attempt to revisit this question because biomarkers for predicting poor prognosis following aneurysmal SAH have not yet been established. However, we would like to bring forth a few issues in this article that need further consideration. In their retrospective study design involving 565 subjects, they did not mention any inclusion or exclusion criteria. In their patient selection, there was no account of any pre-existing cause of hyperglycemia, which can be attributed to diabetes, metabolic syndrome, or insulin resistance. The drug status on admission—that is, taking oral hypoglycemic agents, insulin, or beta blockers—was not mentioned. The authors did not mention hypertensive status on admission or BMI in their summary of patient characteristics, which could have been potential confounders of a poor outcome.

There was no time cutoff from SAH to admission. The range of time from SAH to admission was 1 hour to 16 days (mean time 20.1 ± 19.07 hours). Hence, the time from SAH to admission could be an independent factor affecting prognosis, with late admissions faring worse. Moreover, the authors did not mention whether it was a single value or a mean value of serum glucose or potassium estimation at the time of admission. Also, there was no account of those patients who were normoglycemic at admission but later developed hyperglycemia. The authors report that they used sliding scale insulin for post-admission hyperglycemia control, but it would have been insightful to know the insulin dosage, which could highlight the degree of hyperglycemia and metabolic stress. The study fails to answer a pertinent question, that is, whether the glucose/potassium ratio is associated with the risk of vasospasm/delayed cerebral injury. Moreover, no correlation of the serum glucose/potassium ratio with the Glasgow Outcome Scale (GOS) score at 3 months was assessed, which misses out on patients who could have delayed recovery.

Finally, we would like to congratulate the authors on bringing to light an interesting scientific issue. Their article lays the groundwork for a larger prospective study design to evaluate these biomarkers in aneurysmal SAH to aid in treatment policy decisions.

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References

Disclosures
The authors report no conflict of interest.

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Response
Thank you for your helpful comments regarding our article.

All patients with acute endogenous SAH (confirmed by CT or lumbar puncture) were eligible for study participation and were included if they or their health care decision surrogate provided consent. Patients with traumatic SAH and cardiopulmonary issues on arrival were excluded. Additionally, pre-existing hyperglycemia was defined by a history of diabetes, the use of oral hypoglycemic agents, the use of insulin, and an HbA1c value > 7.0. Among the 565 treated patients, 46 had these conditions of pre-existing hyperglycemia. We found that 34 patients were using oral hypoglycemic agents, 3 were using insulin, and 5 were using beta blockers. With regard to the hypertensive status and BMI of the patients, we did not find a significant correlation between a poor outcome (GOS scores 1–3) and these factors.
A nonsignificant trial result does not mean that two procedures are equal

TO THE EDITOR: Vieira et al.1 contribute to the accumulating evidence on the commonly performed procedure of decompressive craniectomy by reporting the results of their randomized controlled study comparing 2 surgical techniques for decompressive craniectomy (DC): with watertight duraplasty and without watertight duraplasty (Vieira E, Guimarães TC, Faquini IV, et al: Randomized controlled study comparing 2 surgical techniques for decompressive craniectomy: with watertight duraplasty and without watertight duraplasty. J Neurosurg [epub ahead of print November 17, 2017. DOI: 10.3171/2017.4.JNS152954]).

Although one must greatly appreciate such randomized controlled trials with blinded evaluation of outcomes, there are a few methodological flaws in the trial. The authors give the impression that the experimental procedure is safe and hence equivalent to the traditional watertight cranioplasty. They come to the conclusion that rapid-closure DC without watertight duraplasty is a safe procedure and that it is not associated with a higher incidence of surgical complications. Assuming that a procedure is equivalent or non-inferior to another procedure just because there was no statistically significant difference is fundamentally wrong. Failure to reject the null hypothesis that the experimental procedure is not superior to the control procedure should not automatically prompt one to accept the null hypothesis and conclude that both procedures are equivalent in terms of safety.

In situations where one anticipates that one procedure is likely to be nearly equivalent to the other, as in the present case, a non-inferiority trial design should be used.

The authors describe a composite outcome of several complications, including CSF leak, subgaleal collection, and infective complications, as the primary outcome. The sample size should have been calculated to power the trial to find the primary outcome. However, the authors calculated sample size to find a significant difference in the duration of the surgery, which resulted in extremely low power to detect superiority in terms of complications. A retrospective calculation shows that the trial had only 5% power to detect a statistically significant difference for the primary outcome.

Consider a hypothetical example in which the control arm has only 1 complicating event compared to the same 5 complications that occurred in the experimental arm. The trial would still have shown no statistically significance!

<table>
<thead>
<tr>
<th>Trial Arm</th>
<th>Complications</th>
<th>No Complications</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (watertight)</td>
<td>1</td>
<td>27</td>
<td>28</td>
</tr>
<tr>
<td>Experimental (non-watertight)</td>
<td>5</td>
<td>22</td>
<td>27</td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
<td>49</td>
<td>55</td>
</tr>
</tbody>
</table>

The Fisher exact test statistic value is 0.101181 (not significant, p > 0.05).