Puzzling posology: was the bevacizumab regimen in recurrent glioblastoma misreported?


In those early days, the optimal bevacizumab dosage in this indication was still uncertain, and physicians proceeded cautiously, especially in real-world practice. Consequently, some initially dosed bevacizumab at 5 mg/kg fortnightly, as Virginia Stark-Vance had in her seminal study;2 they subsequently raised the dose to 10 mg as data from larger Phase II clinical trials accrued.1,2,4–8 However, while researching the topic, I was puzzled that the aforementioned *JNS* paper by Ali et al. reported bevacizumab being dosed at 5 mg or 10 mg per square meter (m²) every 2 weeks,1 rather than per kilogram (kg) body weight, as is standard and labelled (https://www.gene.com/download/pdf/avastin_prescribing.pdf). It is surely an elusive typographic error; nevertheless, it would be worthwhile publishing a formal erratum, not only to correct the scientific record, but also to avoid potential confusion or inadvertent propagation by other non-experts besides myself who refer to that paper.

David Neil, PhD
Content Ed Net (Taiwan), Taipei, Taiwan

References

Disclosures
The author report no conflict of interest.

Is preoperative hypoalbuminemia really a risk factor associated with acute kidney injury and mortality after brain tumor surgery?

TO THE EDITOR: With interest, we read the article of Kim et al.1 assessing the association of preoperative hypoalbuminemia with acute kidney injury (AKI) and mortality after brain tumor surgery in a retrospective study (Kim K, Bang JY, Kim SO, et al: Association of preoperative hypoalbuminemia with postoperative acute kidney injury in patients undergoing brain tumor surgery: a retrospective study. *J Neurosurg* [epub ahead of print May 5, 2017].

References
only comparing mean preoperative hemoglobin levels be-
independent risk factor for postoperative AKI. However,
showed that preoperative hemoglobin level was not an
AKI in patients undergoing brain tumor surgery.

be better if title of the article was changed to “Association
hypoalbuminemia with postoperative AKI. Thus, it would
does not evaluate the association of true preoperative
albumin levels, but was not identified as a risk factor for
postoperative AKI. However, patients were arbitrarily stratified
sociation of preoperative hypoalbuminemia with postopera-
tive AKI in patients undergoing brain tumor surgery.”

Second, the multivariate logistic regression analysis
showed that preoperative hemoglobin level was not an
independent risk factor for postoperative AKI. However,
only comparing mean preoperative hemoglobin levels be-
tween patients with preoperative serum albumin levels <
3.8 g/dl and ≥ 3.8 g/dl may have limited clinical value for
prediction of postoperative AKI. In fact, preoperative ane-
mia is highly prevalent in patients undergoing noncardiac
surgery and has been shown to be an important risk factor
for postoperative AKI. Furthermore, postoperative ane-
mia is also strongly associated with AKI after noncardiac
surgery. In a comparison with patients who did not have a
decrease in postoperative hemoglobin, a decrement of 1.1–
2.0 g/dl was associated with an adjusted hazard ratio (HR)
for AKI of 1.51 (95% confidence interval [CI] 1.15–1.98),
and a decrement of > 4.0 g/dl with an adjusted HR of 4.7
(95% CI 3.6–6.2) for AKI.3

Third, in this study, intraoperative lowest mean arte-
rial pressure (MAP) was recorded and was significantly
different between patients with two preoperative serum
albumin levels, but was not identified as a risk factor for
postoperative AKI. Most importantly, the researchers were not
provided with the occurrences of intraoperative hypoten-
sion, which is a known causative factor of postoperative
AKI.3 The available evidence indicates that even a short
duration of an intraoperative MAP < 55 mm Hg can result
in postoperative AKI, with an independently graded re-
lationship between duration of intraoperative hypotension
and postoperative AKI.3 In particular, the combination of
intraoperative anemia, transfusion, and hypotension can
synergistically act to increase the risk of postoperative
AKI.4

Fourth, this study showed that a preoperative serum
albumin level of < 3.8 g/dl was independently associated
with postoperative mortality. We noted that the median
follow-up duration for the overall patient population was
4.1 years, and 36.5% of patients underwent glioma and
metastatic tumor operations. However, the types of brain
tumors were not included in the multivariate Cox propor-
tional hazards model identifying independent risk factors
for postoperative survival. In fact, patients with a preopera-
tive serum albumin level < 3.8 g/dl were older and were
more likely to have hypertension and diabetes mellitus, and
have a lower preoperative hemoglobin level than patients
with a preoperative serum albumin level ≥ 3.8 g/dl. In our
opinion, no matter how refined the adjustment is for dif-
ferences in health status and comorbid burden, it is never
possible to ensure a complete adjustment for differences
between patients with two preoperative serum albumin
levels. A preoperative serum albumin level < 3.8 g/dl may
be only an overall manifestation of worse health status and
greater comorbid burden that can markedly increase post-
operative morbidity and mortality. A “kitchen-sink” ap-
proach of adjusting for all available variables using multi-
variable analysis may lead to overadjustment and therefore
bias the true effects of a lower preoperative serum albumin
level itself on postoperative mortality. Thus, we argue that
great caution must be taken when interpreting the associa-
tion between a preoperative serum albumin level of < 3.8 g/
dl and postoperative mortality, as it has great inherent bias
that cannot be overcome by statistical adjustment.

 References

association of preoperative hypoalbuminemia with postopera-
tive acute kidney injury in patients undergoing brain tumor
surgery: a retrospective study. J Neurosurg [epub ahead of
print May 5, 2017. DOI: 10.3171/2016.11.JNS162237]
2. Kovacheva VP, Aglio LS, Boland TA, Mendu ML, Gibbons
FK, Christopher KB: Acute kidney injury after craniotomy is
associated with increased mortality: a cohort study. Neuro-
3. Onuigbo MAC, Agbas: The ignored role of intraoperative
hypotension in producing postoperative acute kidney injury
an obligatory appeal for more preventative nephrology. Curr
4. Sun LY, Wijeyasurya DN, Tait GA, Beattie WS: Associa-
tion of intraoperative hypotension with acute kidney injury
after elective noncardiac surgery. Anesthesiology 123:515–
523, 2015
5. Walsh M, Devereaux PJ, Garg AX, Kurz A, Turan A, Rods-
eth RN, et al: Relationship between intraoperative mean arte-
rial pressure and clinical outcomes after noncardiac surgery: a
6. Walsh M, Garg AX, Devereaux PJ, Argalious M, Honar H,
Sessler DI: The association between perioperative hemoglo-
bilin and acute kidney injury in patients having noncardiac