EDITORIAL

A smoker’s paradox: does being a smoker really lead to a better outcome after aneurysmal SAH?

Kevin M. Cockroft, MD, MSc

Department of Neurosurgery, Penn State Hershey Medical Center, Hershey, Pennsylvania

In this paper from Dasenbrock et al., the authors assess the impact of tobacco smoking on outcome after aneurysmal subarachnoid hemorrhage (SAH) by analyzing data from the National Inpatient Sample (NIS) and the National Surgical Quality Improvement Program (NSQIP) registry. The central finding of the study was that smoking was associated with superior outcomes after rupture on several measures, including overall clinical outcome as indicated by the NIS-SAH outcome measure (NIS-SOM). This finding was present in both the entire study population, as well as in poor-grade patients when considered separately. The finding also remained true over a range of smoking frequencies.

With administrative databases possessing many well-known disadvantages, the authors took several steps to mitigate these limitations. Determining illness severity is often difficult and in this case the authors used the NIS-SAH severity scale, which correlates well with Hunt and Hess grade, to adjust for presenting severity. The score uses various related diagnostic and procedural codes, such as those for coma, hydrocephalus, hemiparesis, aphasia, and mechanical ventilation, to stratify patients. Similarly, the authors also used the NIS-SOM as their main clinical outcome measure. This externally validated end point defines outcome based on factors such as in-hospital mortality, discharge location, and tracheostomy/gastrostomy placement, with a poor NIS-SOM outcome closely mirroring a modified Rankin scale score of more than 3. By using their own hospital’s NSQIP data, the authors were also able to provide some verification of the accuracy of the data coding for smoking status. Finally, the authors used the statistical techniques of sensitivity analysis and propensity matching to assess the impact of a range of smoking frequencies on their outcome measures. While this analysis resulted in certain outcomes (such as in-hospital mortality, neurological complications, and delayed cerebral ischemia) no longer showing statistically significant differences, others measures remained significant, including extended hospitalization, discharge to institutional care, and poor NIS-SOM outcome.

The result is a robust, well-made case for a better outcome among smokers with aneurysmal SAH compared with nonsmokers. This is certainly a provocative and some might say paradoxical finding, but before we start encouraging all of our patients with aneurysms to take up smoking, there are some additional issues worth considering. As many know, the prior literature has been mixed with regard to smoking and intracranial aneurysms. Some retrospective studies have suggested higher rates of vasospasm/delayed neurological deficits (DNDs) in smokers, while a report based on the “Get With The Guidelines” prospective database found better outcomes among smokers. There is also good evidence to indicate that smoking increases the risk of developing an intracranial aneurysm, as well as the risk of experiencing a subsequent rupture. Perhaps most interestingly, though, are two relatively recent retrospective studies that demonstrated improved outcomes in smokers with SAH who received nicotine replacement. Both studies found similar rates of radiographic vasospasm, while one reported similar rates of clinical ischemic events in the experimental and control groups and the other showed a lower rate among those receiving nicotine replacement therapy. Of note here, the current study was not able to directly investigate vasospasm/DNDs and had no way of determining whether or not smokers received nicotine replacement during their hospitalization.

Smokers as recorded by the NIS are a diverse group, which includes long-term and short-term smokers, as well as noncigarette smokers, all with different levels of use. Patients may also receive nicotine through other means, such as chewing tobacco, electronic cigarettes, and smok-
ing cessation aids. As noted in the study, smokers tended to be much younger than nonsmokers. Although age was adjusted for in the multivariable analysis, the presence of additional unmeasured or unrecognized confounders potentially related to young age and or smoking status is always a concern in a retrospective study. Some potential covariates might include alcohol use (not abuse), nicotine replacement use, body mass index, and levels of physical activity.

Long-term outcome is another area to consider. As the authors point out, information on long-term outcome is lacking in the NIS, and discharge location may be a relatively crude measure of actual functional outcome. Will smoking hamper long-term brain recovery or will the comorbidities associated with smoking lead to other complications that impact long-term functional status?

From a practical standpoint, we are left with the question of where to go next. The finding that smokers may have a better outcome after aneurysmal SAH than nonsmokers may be interesting, but it still leaves us wondering what we as clinicians can do with this information in our treatment of such patients. An initial reaction might be to advocate for the use of nicotine supplementation. However, the present study does not really inform us in this regard. As the authors are quick to mention, tobacco smoke contains more than 4000 chemical components, of which nicotine may be the best studied, but arguably not necessarily the most important in this particular circumstance. With the rise in the use of electronic cigarettes, which have a more limited chemical composition, in the future it may be possible to perform a similar analysis to examine more directly the effects of nicotine itself. Importantly, the present study does not provide any information regarding the role of nicotine replacement in smokers, much less the role of nicotine supplementation in nonsmokers. If, as the present study suggests, smokers have better outcomes than nonsmokers, does adding nicotine supplementation further improve their outcome, as some other studies have suggested, or is their outcome already maximized by their prior exposure? Is this effect dose- or time-dependent? At present, the data do not appear to be sufficient to warrant a prospective randomized controlled trial (RCT) of nicotine therapy in aneurysmal SAH for nonsmokers and probably not even for smokers. However, multi-institutional retrospective or prospective registry studies may confirm the findings of Dasenbrock et al.3 and help better frame the questions and design requirements for a subsequent prospective RCT.

Disclosures
The author reports no conflict of interest.

Response
Hormuzdiyar H. Dasenbrock, MD, MPH, and Rose Du, MD, PhD
Department of Neurosurgery, Brigham and Women’s Hospital, Harvard Medical School, Boston, Massachusetts

Dr. Cockroft has written an insightful editorial about our article, and we appreciate his detailed analysis. As he has acknowledged, data were extracted in 5874 patients from across the US, and the goal of our study was to use a large national data set to evaluate the in-hospital outcomes of cigarette smokers who present with aneurysmal SAH, including mortality, neurological complications, tracheostomy or gastrostomy placement, length of hospital stay, discharge disposition, and poor outcome. However, Dr. Cockroft’s editorial emphasizes the importance of critically analyzing population-based publications, and raises 3 important questions: 1) are the findings valid; 2) are they biologically plausible; and 3) what are important future directions?

References