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RE: Hadley et al. [2017 Nov 1;81(5):713-732].

Dear Dr. Oyesiku:

My colleagues and I are writing to you as members of the Board of Directors of the American Society of Neurophysiological Monitoring (ASNM), and on behalf of our membership. We wish to express grave concern over a recent publication in *Neurosurgery* authored by Hadley et al. (2017 Nov 1;81(5):713-732).

As detailed in the attached Letter to the Editor, we have identified highly significant flaws in this paper to which we'd like to draw your attention. Please consider the following examples:

- The manuscript erroneously claims to be a guideline when, in fact, it is most accurately classified as a systematic review.
- The manner in which the authors have chosen to include vs exclude and acknowledge vs ignore specific studies among the available literature, combined with the authors' conclusions, suggests a bias against neuromonitoring.
- There is both inconsistency and inaccuracy in the classification of studies according to levels of evidence.
- The authors combine surgical procedures with different risks and opportunities for intraoperative interventions following an alert (*e.g.* cervical surgeries and intramedullary tumors).
- Studies are summarized incorrectly as the authors repeatedly make the common mistake of reporting *no evidence of a significant difference* as if it were equivalent to *evidence for no effect*.
- The authors confuse the term "gold standard" with "standard of care".
- Finally, and critically, the authors largely overlook the value of performing interventions in response to intraoperative alerts when they report diagnostic value.

Based on these methodological flaws and others, upon which we've expanded in our attached Letter to the Editor, we submit that this paper has the potential to do significant harm because it provided erroneous information to patients and surgeons who may benefit from IONM.

According to the Institute of Medicine, authorship of clinical practice guidelines should consist of individuals representing multiple relevant disciplines. The paper written by Hadley and colleagues is written exclusively by neurosurgeons. Intraoperative neurophysiological monitoring is a niche profession with methods, techniques and data that vary significantly with context and require extensive training and expertise to utilize and interpret. It is our perspective that guideline statements regarding neuromonitoring, and systematic reviews of the neuromonitoring literature, should contain at least one author who is an expert in the field. This kind of multidisciplinary approach will ensure that utility and value of neuromonitoring are assessed objectively, accurately and thoroughly. We hope that you, as Editor-in-Chief, will agree with this perspective and consider publishing our letter.

Disclosure: the authors have no conflicts of interest to report and no financial interests to disclose.

Sincerely,

The American Society of Neurophysiological Monitoring

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To the Editor:

RE: Guidelines for the Use of Electrophysiological Monitoring for Surgery of the Human Spinal Column and Spinal Cord

We read with great interest the article recently published by Hadley et al.[1], which purports to be a guideline on the use of intraoperative neurophysiological monitoring (IONM) in spine surgery, and would like to express our concerns regarding serious methodological flaws and systematic errors that substantially limit confidence in its recommendations.

In this paper, the authors review and grade the literature on IONM in spine surgery and make recommendations regarding the diagnostic value, therapeutic value and cost effectiveness of IONM according to modified North American Spine Society (NASS) criteria. Broadly speaking, the authors conclude that IONM has diagnostic value in spine surgery, but the therapeutic value has not been shown; therefore, the expense of IONM does not justify its use in spine surgery.

The work of Hadley et al.[1] claims to be a guideline yet lacks the critical components of a guideline. Clinical practice guidelines are statements that include recommendations intended to optimize patient care, and usually are created by multidisciplinary societal committees as opposed to single institutions[2]. These statements are informed by a systematic review of evidence *and* an assessment of the benefits and costs of alternative care options[2,3]. Additionally, a guideline considers the risks of each procedure, how patients value those risks, and the cost of not using IONM during high risk surgery[2,3]. Aside from increasing the cost of surgery, the harms associated with IONM are minor, and the only alternative to IONM for intraoperative assessment of neurologic function is the wakeup test with its limitations[4]. The potential benefits of IONM are specific to different surgical procedures which vary considerably both in baseline risks and available interventions that can potentially be used to avoid or limit iatrogenic injury[4]. Unfortunately, due to a biased interpretation of the existing literature as we will describe below, the authors neglected to consider all of these points and the paper is more accurately classified as a systematic review.

As a systematic review, the manuscript appears to suffer from bias in the inclusion and/or acknowledgement of available research. As just one representative example among many, consider the review of literature related to IONM for intramedullary spinal cord tumor (IMSCT) resection. Perhaps the strongest study ever published on the use of IONM during IMSCT surgery is that of Sala et al.[5]. Their historically controlled study, using a single, experienced surgeon, compared monitored and unmonitored groups using McCormick Scale scores *relative to baseline,* and found significant, statistically better outcomes with IONM. By comparison, a careful reading of Choi et al.[6] shows that they did not take into consideration the patients' baseline neurologic function, and simply compared McCormick Scale scores between the groups. While both studies used the same research design (retrospective comparative), Sala et al.[5] took the additional step of matching comparison groups for prognostic characteristics. It is thus unclear why Choi et al.[6] is classified as Level II evidence and Sala et al.[5] is classified as Level III evidence. Additionally, the Sala et al.[5] study is listed in a table but curiously missing from the results text for therapeutic studies where Choi et al.[6] is highlighted. Finally, the authors omitted two IMSCT studies evaluating IONM against unmonitored controls, both of which demonstrated significantly better outcomes with IONM.[7,8] In their omission of controlled studies in this review, and in opting to highlight studies that support their position, the authors demonstrate bias which skews the reader's perception toward an unfavorable view of the utility and value of IONM.

In summarizing the literature, the authors make the common mistake of repackaging *no evidence for improvement with IONM* as if it were equal to *evidence against improvement with IONM*. In making this mistake, the authors suggest that failure to reject the null hypothesis provides evidence equal and opposite to a rejection of the null hypothesis. For example, in their summary of Choi et al.[6], the authors state, "The use of IOM did not result in improvement in rate of gross total resection or in neurological outcome. Not an effective therapeutic adjunct." Statements such as this may actually misinform the reader. Absence of effect for a therapy or intervention can result from flawed methods or small samples which can render the study inadequately powered. Indeed, small sample sizes are common in the surgical literature.

A perplexing action taken by Hadley and colleagues is their reclassification of the true positive data as false positive data in Nuwer et al.[9] Ironically, Nuwer et al.'s original, societal-approved classification strategy illustrates a fundamental concept regarding IONM in spine surgery: a significant loss of data followed by a timely intervention which returns the data to baseline lends just as favorable a prognosis as no change in data from baseline. Thus, when evoked potential changes are resolved and associated with preserved neurologic status, they are most accurately classified as true positives in the literature[10,11]. The reclassification by Hadley et al.[1] misses the main point: both methods for scoring diagnostic test results are susceptible to bias in the "flow and timing" domain because an intervention by the surgeon is often inserted between the IONM test result and postoperative neurologic assessments[12].

Throughout their review of the literature, the authors make incongruous statements regarding the diagnostic value of different IONM tests. For example, the authors correctly state that somatosensory evoked potentials (SSEPs) monitor *somatosensory* function (*i.e.,* vibration and proprioception), and motor evoked potentials (MEPs) monitor *motor* function (*i.e.,* voluntary muscle strength); then, they continuously report on the independent sensitivity and specificity of SSEPs in diagnosing *motor dysfunction*. This conflation of surrogate tests for specific clinical end points is a vexing residuum of an era in which SSEPs were the only test available to monitor "spinal cord function". Contemporary techniques allow for specific functions to be monitored and therein lies the benefit of multimodality monitoring. This basic concept is common knowledge among neurophysiologists, but rarely discussed in the neurosurgical literature. It is rather unfortunate, thus, that Hadley and colleagues failed to clarify these issues.

The authors repeatedly take issue with application of the phrase "gold standard" to describe IONM in spine surgery, but they fail to recognize that there is no other method available to monitor spinal cord function under general anesthesia. In this way, the authors appear to confuse "gold standard" with "standard of care". In our view, IONM is the gold standard because there are no alternatives to IONM, but this does not translate to required use of IONM. Whether IONM is the *standard of care* in spine surgery is a different question altogether and beyond the scope of this "guideline" and our commentary.

In summary, IONM is a niche profession with methods, techniques and data that vary significantly with context and require extensive training and expertise to utilize and interpret. It is our perspective that guideline statements regarding IONM, and systematic reviews of the IONM literature, should contain at least one author who is an expert in the field of IONM. The real disappointment of this work lies in the authors' failure to procure a meaningful guideline on IONM in spine surgery when one is needed. Guideline recommendations that engender confidence use best scholarship and evidence for the risks and benefits of treatment effects and how these are valued by patients. These standards, described by the Institute of Medicine[2], provide a foundation as we work together to improve patient care. Unfortunately, Hadley et al. produced a rather biased review that failed to meet these standards. In doing so, their publication does irreparable harm because it provides erroneous information to patients and surgeons who may benefit from IONM. For all of the reasons indicated above, we recommend that the authors publish an *erratum* to both enhance objectivity and reclassify their paper as a systematic review.

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