Editorial

Randomized clinical trials

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The authors of this interesting paper1 reviewed the articles published in 6 neurosurgical journals and in the 3 most prestigious general medical journals (Journal of the American Medical Association, Lancet, and the New England Journal of Medicine) during the years 2006 and 2007 and found 27 reports of randomized clinical trials (RCTs) relevant to neurosurgery. They reviewed the instructions to authors to determine which journals endorsed the Consolidated Standards for Reporting of Trials (CONSORT) criteria that were constructed to improve the design and reporting of RCTs. These authors found that the 3 general medical journals endorse the criteria, whereas none of the neurosurgical journals do. They then judged the quality of those 27 RCTs using both the CONSORT criteria and the Jadad instrument, which is specifically designed to judge the quality of clinical trials. Not surprisingly, they found that the RCTs reported in the 3 general medical journals were of higher quality, as judged by these 2 criteria, than those reported in the neurosurgical journals. Based on these findings, Kiehna et al. suggest that the endorsement of the CONSORT criteria has been partially responsible for the higher quality of the trials reported in the general medical journals and recommend that neurosurgical journals adopt these criteria.

I will begin my comments on this paper with a disclaimer, admitting that I know very little about the design and execution of RCTs, although I have given much thought to the significance, interpretation, and application of the results of RCTs, both in the context of individual patient care and in the teaching of neurosurgical residents. As the authors state, RCTs have been “considered the gold standard of clinical research” and I agree with the authors that, when properly designed and reported, RCTs are the most influential ways of advancing clinical care. Therefore, any means of improving the quality of these trials is important. While agreeing in general with the overall conclusions of the authors, I will comment on some points of minor disagreement or criticism that mostly concern the emphasis rather than the substance of the authors’ study.

The authors state that they selected journals based on impact factor. Clearly, the impact factor of a journal is important in many respects; however, a comment is in order because it is my impression that many readers do not quite understand what this means. Briefly stated, the impact factor is the number of citations during 1 year of articles published in a journal during the 2 previous years divided by the total number of articles published in that journal during those 2 years. Although frequently used as a measure of the quality of the journal, the impact factor is only one of several metrics used to judge journals and there is frequently discordance between such metrics. For example, the impact factor of the Journal of Neurosurgery is slightly lower than that of Neurosurgery, but the Journal of Neurosurgery far exceeds Neurosurgery in the total number of citations and has a greater immediacy index and cited half-life, which indicates how long a journal’s articles are deemed important enough to cite (2009 Thompson Reuters Statistics). Furthermore, as reported in a recent study, the Journal of Neurosurgery has published the vast majority of the “most cited” and “classic” articles in our field.2,3

The authors chose to exclude trials concerning the treatment of spinal disorders and do not explain the reason for this. Although in several instances they state that they reviewed “all neurosurgical RCTs” I am sure they do not mean to imply that spine surgery is not neurosurgery. I am a bit sensitive about this subject because of my concern (perhaps paranoia) about what many of us perceive as a trend to separate spine surgery from mainstream neurosurgery. Although I did not specifically review the literature for the 2 years that the authors chose for the purpose of this study, I know that there have been several recent trials of variable quality that have been very influential in how neurosurgeons manage disorders of the spine. Although I do not believe that inclusion of spine trials would have substantially changed the results found by the authors, I think it would have been nice if they had included these trials that are clearly part of the spectrum of neurosurgery.

I believe that the authors’ findings would have been more robust had they studied a longer period of time. They found only 27 trials during the 2 years they reviewed and only 7 of those were published in the 3 general medical journals. Conceivably the results may have been somewhat different had their study encompassed a longer period of time.

The authors acknowledge the hurdles involved in conducting surgical trials such as small patient populations, use of multiple end points, and the difficulty of blinding surgical patients and their surgeons. There also exists the ethical concern of performing sham surgeries, which is the best way to properly randomize patients when studying the value of a particular surgical procedure. To this concern I would add the major ethical dilemma of insuring “equipoise” when we consider whether to randomize a particular patient. At least to me, this means that I could...
not randomize a patient for a particular surgical procedure versus a different one or for surgery versus no surgery if I had a reasonably well-founded opinion that, for that particular patient, one procedure is better than the other or that surgery is better than no surgery, or vice versa. The more experience there is with a particular procedure or specific treatment, the more difficult it is to achieve equipoise because hopefully we have learned from that experience. Likewise, the more experienced clinicians, who are the ones more likely to have more patients available for randomization, are less likely not to have formed an opinion about the value of a surgical procedure as compared to another, or of a surgical procedure as compared to no surgery for a particular patient. This problem significantly reduces the pool of patients available for randomization to those in whom we have no reasonably formed opinion as to which treatment, or lack of treatment, would be best for that patient. This limits randomization to only a fraction of eligible patients and leads to criticisms such as we have seen after the Extracranial-Intracranial (EC-IC) bypass trial and more recently the International Subarachnoid Aneurysm Trial (ISAT).

The authors state “...we need to overcome these hurdles to advance the care of our patients.” I am not sure that we could or should necessarily overcome these hurdles, particularly the issue of insistence on equipoise as a prerequisite for randomization. I hope that the readership does not interpret the authors’ comments as indicating that RCTs are the only way “to advance the care of our patients.” Clearly, the care of our patients has been advanced in major ways by, for example, the description of new surgical procedures, the careful retrospective review of large series of patients, and even anecdotal case reports describing a particular complication and ways to avoid it in the future.

The authors discuss well the fact that there may be reasons other than whether a particular journal endorses the CONSORT criteria to explain why certain trials are reported in general medical journals that reach wider audiences as opposed to neurosurgical journals that have a considerably narrower readership. However, Kiehna et al. are emphatic in their recommendation that neurosurgical journals should adopt the CONSORT criteria and they predict that this would increase the quality of RCTs reported in neurosurgical journals. Incidentally, for the last 2 years the Journal of Neurosurgery has recommended in its author instructions that authors follow the CONSORT guidelines when reporting RCTs. I personally believe that while these criteria should be used as a checklist or as guidelines to improve the design and reporting of RCTs, strict adherence to them as a condition for publication may discourage the submission of reports of important neurosurgical trials to our journals. For example, insisting on binding of the subject and the treating physician and on external validity (generalizability) of the findings of the trials may exclude some important trials from publication in our journals.

We are indebted to the authors for bringing this important issue to general neurosurgical attention. Unquestionably, the design and publication of neurosurgical RCTs can be improved and more general awareness of these criteria cannot but help in this respect.

References


Response

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We would like to thank Dr. Heros for his review of our paper and we appreciate his insightful editorial comments. Dr. Heros’ clarification of the impact factor is important. We did select the general medical journals based, in part, on impact factor, but also based on previous validation for inclusion as index journals. Other parameters, such as total number of citations, immediacy index, and cited half-life are also important in the evaluation of academic journals.

We would also like to emphasize that we did not mean to imply that spine surgery is not neurosurgery. We unequivocally agree that spine surgery is a critically important component of neurosurgery. We spent considerable time deciding whether or not to include spine clinical trials in the present study. However, we decided to focus on the cranial subcomponent of neurosurgery. As a result of the interdisciplinary nature of spine surgery and the heterogeneous nature of the journals in which such studies are published, our intent was to conduct a separate such analysis for spine studies. To include spine-related RCTs only from neurosurgical journals in the current analysis would result in an incomplete evaluation of the quality and broader impact of RCTs on the practice of spine surgery.

Randomized clinical trials have clearly had an enormous impact on the care of patients across almost all disciplines of medicine including neurosurgery. However, as Dr. Heros eloquently adds, so many important advances in the care of our patients have been made through other types of studies including technical notes, retrospective case series, case reports, and observational studies, among others. Our intent was not to imply that RCTs are the only means by which to advance care. Moreover, we acknowledge the limitations and difficulties of implementing clinical trials in our patient population, especially as it relates to clinical equipoise and enrollment. We wanted to emphasize, however, that when it is possible to conduct clinical trials, it is important that we encourage our community to conduct such studies in accordance with CONSORT criteria such that they are conducted in the best manner possible.
Otherwise, studies may be of inferior quality, the resources invested in such clinical trials may be wasted, and the findings may not be as generalizable. Again, our point is not that neurosurgery can only progress through clinical trials, but that when clinical trials are conducted, we need to encourage means to ensure that they be of the highest quality.

Finally, we agree with many of the points raised in Dr. Heros’ comments concerning the potential limitations of strict adherence to the CONSORT criteria. The purpose of this study was to raise awareness of the CONSORT criteria amongst the neurosurgical community in hopes that these criteria may be of utility in the future planning, execution, and reporting of RCTs in neurosurgery. Other subspecialty journals have begun to adopt these same criteria.

References


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