Understanding outcomes after neuraxial anaesthesia: time to turn the page

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For most of the last century, anaesthetists have debated the advantages and disadvantages of neuraxial block for patients undergoing major surgical procedures.\textsuperscript{1} While major clinical trials comparing outcomes with and without such techniques have not been carried out since the early 2000s,\textsuperscript{2,3} the anaesthesia literature has seen a proliferation of interest in this subject over the past 10 yr, as epitomized by a flurry of non-randomized studies comparing outcomes among patients undergoing surgical procedures with and without neuraxial block.\textsuperscript{4–14} In this issue of the BJA, Kate Leslie and colleagues\textsuperscript{15} present an insightful new analysis that adds to the growing knowledge base regarding potential associations between the use of neuraxial techniques and patient outcomes, while also highlighting the vital need for high-quality randomized controlled trials to move this dialogue forward.

Using data from the POISE-2 trial, a large multicentre study that randomized high-risk surgical patients to aspirin or placebo and to clonidine or placebo, Leslie and colleagues\textsuperscript{15} compared outcomes among study patients who did and did not receive neuraxial blocks as part of their anaesthesia care. Leslie and colleagues\textsuperscript{15} found no statistically significant association between the receipt of any intraoperative neuraxial block and the odds of death, myocardial infarction, or stroke at 30 days, although a subgroup analysis did find spinal anaesthesia alone to be associated with lower odds of death or non-fatal myocardial infarction than general anaesthesia alone. A smaller accompanying analysis found no statistically significant association between postoperative epidural analgesia and death, myocardial infarction, or stroke.

The work of Leslie and colleagues\textsuperscript{15} took advantage of rich research data collected prospectively across a large sample of patients. As such, the investigators were able to adjust for potential confounding as a result of certain clinical factors, such as baseline co-morbidities and medication use, beyond the degree typically permitted by administrative or registry-based data sources. The authors used rigorous propensity-score weighting methods to balance observable patient factors for patients who did and did not receive neuraxial techniques. The results presented, most notably the authors’ findings on outcomes with spinal vs general anaesthesia, align with the findings of several other recent observational studies.\textsuperscript{5–7,13,14,16}

Nevertheless, the paper demands careful interpretation. As with any non-randomized study, the authors’ findings are limited by the possibility of residual confounding as a result of variables not included in their risk-adjustment models. In the present instance, residual confounding could exist because of differences between groups in terms of the specific surgical procedures received, the severity of patients’ chronic illnesses, or variations in the quality of care delivered at hospitals that tended to use neuraxial anaesthesia more or less frequently. As the authors acknowledge, such limitations preclude a causal interpretation of their results and demand that any application of these findings to clinical practice take place with recognition of the potential biases inherent in non-randomized studies.

The overall findings of Leslie and colleagues\textsuperscript{15} also diverge in important ways from the group’s previous analysis of data from the POISE-1 trial,\textsuperscript{16} which found intraoperative neuraxial block to be associated with increased odds of 30 day cardiovascular death, myocardial infarction, or cardiac arrest. While such differences between studies may have occurred because of random error as the authors point out, they could also relate to observed or unobserved differences between studies in terms of the overall health of patients who were and were not treated with neuraxial anaesthesia, or in terms of the specific surgeries they received. Likewise, such divergent findings could also stem from differences between studies in the proportion of patients who received...
spinal vs epidural blocks or more subtle variations across studies in providers’ approaches to the intraoperative management of general vs neuraxial anaesthesia.

Such considerations not only highlight the challenges of drawing conclusions about the relative advantages and disadvantages of neuraxial block from retrospective, observational studies; furthermore, they emphasize the vital need for high-quality large randomized trials to help begin to fill in persistent gaps in knowledge related to this area of anaesthesia care. On a certain level, all available observational studies that compare neuraxial approaches with other anaesthetic modalities share a common limitation in their inability to account fully for selection bias; as such, thoughtfully designed and conducted randomized trials may offer a type of insight into the potential relationships between anaesthesia technique and outcomes not available from non-randomized comparisons.

Beyond this, even apparently uniform categories such as ‘spinal block’ or ‘epidural block’ may in practice encompass a variety of techniques and management approaches, with potentially different consequences for patient outcomes when applied in distinct populations or surgical contexts. In observational studies, it may be difficult or even impossible to assess the extent and impact of such heterogeneity, depending on the nature and granularity of the available data; in contrast, clinical trials offer investigators the opportunity to be explicit about what is being compared by forcing them to make active choices about study design related to which patients and surgeries to include or exclude, which types of anaesthesia regimens to compare, and what degree of permissiveness or control to build into those regimens.

Looking forward, practitioners and policy-makers may be optimistic that such randomized trial evidence will become available over time to guide clinical decisions regarding the use of neuraxial techniques. In the context of hip fracture care, both the UK National Institute for Health and Care Excellence17 and the US Academy of Orthopedic Surgeons18 have called for randomized studies to evaluate the risks and benefits of neuraxial vs general anaesthesia. With funding from the US Patient Centered Outcomes Research Institute, the REGAIN Trial (Regional vs General Anaesthesia for Promoting Independence after Hip Fracture)19 will seek to meet this challenge, beginning in September 2015, through a planned 1600-patient, multicentre pragmatic randomized controlled trial comparing outcomes among hip fracture patients randomized to receive spinal vs general anaesthesia. This study will seek to build on the experiences and insights of researchers who have evaluated the risks and benefits of neuraxial techniques for patients with hip fracture20 and other conditions,2 3 21 while also seeking to serve as a potential starting point for future randomized comparisons.

Ultimately, the work presented here by Leslie and colleagues15 is important both as a source of insight regarding the potential risks and benefits of neuraxial techniques and as an occasion to consider the types of insights that available research in this area has yet to provide. As such, it should prompt us not only to debate the implications of their findings for clinical practice and policy, but also to engage in mapping out the key questions in this area that remain to be answered by randomized trials, and to start to think through the advantages and disadvantages of different trial designs for answering these questions. In so doing, it serves both as a useful exploration of outcomes associated with a key type of clinical decision within perioperative medicine as it is now practised and as an occasion to turn the page in research on neuraxial techniques in anaesthesia towards building the base of evidence needed to shape practice going forward.

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### References


