

# Benefits, Risks, and Best Practice in Regional Anesthesia

## *Do We Have the Evidence We Need?*

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**Abstract:** For more than 25 years, Regional Anesthesia has challenged anesthesiologists to determine whether it offers real benefits in terms of patient outcome from major surgery, compared with general anesthesia. Although there is good evidence that regional analgesia offers superior pain relief to systemic opioid analgesia, evidence to support improved outcome from surgery remains elusive. Although many publications appear to support the hypothesis, others show no benefit, and the lack of properly conducted, large studies makes it difficult to draw any evidence-based conclusions in favor of regional anesthesia. Given that all major regional techniques have the potential to cause significant risks to patient outcome, it is incumbent on all anesthesiologists to balance the intended benefits against the significant adverse events associated with regional techniques.

We are beginning to develop an evidence base for both the benefits and risks of regional anesthesia, when used for specific patient groups and for specific surgical procedures. This presentation looks at some of the evidence and examines how it can be used to develop guidelines for best practice.

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I was introduced to the mysteries and arts of regional anesthesia as a first-year anesthesia trainee in the Cornish city of Truro, over 35 years ago. Since then, I have remained convinced that safe and effective regional anesthesia offers benefits, which general anesthesia and systemic opioid analgesia cannot match. The superior quality of regional analgesia compared with opioid-based analgesia may be sufficient reason alone to offer a regional technique,<sup>1</sup> although others may dispute this. Relief from pain is a worthwhile humanitarian goal, but throughout my career, I have been convinced that, with a bit more effort, we should be able to prove that regional anesthesia offers more than just pain relief—reduction in surgical morbidity and mortality, shorter length of hospital stay, lower costs of treatment, and better functional outcome are all potential benefits. However, if better pain relief and improved outcome are the primary benefits of regional anesthesia, their achievement has to be balanced against the inevitable consequences of any associated risks.

Reliable evidence has been difficult to establish—for both sides of the regional anesthesia benefit-and-risk equation. Both require very large populations of patients in rigorously controlled prospective trials to detect subtle differences between regional anesthesia and alternative methods of anesthesia and

analgesia, and the published data are inconclusive. Through my membership of 2 separate study groups in recent years I have been privileged to explore, with others, important aspects of both sides of the equation. I hope that some of this new knowledge will help to set new standards of care to improve outcome and reduce risk.

On the benefit side, the Prospect group<sup>2</sup> is an international group of surgeons and anesthesiologists that produces evidence-based consensus recommendations for a range of specific surgical procedures by means of systematic reviews and, where possible, meta-analysis. Different surgical procedures result in postoperative pain that varies widely in intensity, duration, and character, something that is not always taken into account when studying the effectiveness of postoperative analgesic treatments.<sup>3</sup>

On the other (“darker?”) side of the equation, a lack of prospective data collection about the severe risks of central neuraxial blockade in the United Kingdom led to a National Audit Project by the Royal College of Anaesthetists (NAP3).<sup>4,5</sup> The results of this project, published in 2009, make an important contribution to our knowledge of risk and can help us to develop improved standards of practice and give our patients a more accurate understanding of the risks associated with aspects of their care.

### The Benefits

There is a large database of published studies claiming to show benefits in favor of regional techniques compared with other anesthetic and analgesic techniques. The problem is that when this database is interrogated to determine the benefits of regional anesthesia on overall outcome from surgery, the limitations of many of the studies become apparent (underpowered, lack of clarity about patient inclusion criteria, study design and end-point variables, failure to control other influences on outcome, etc), making it difficult to compare different studies.

The landmark CORTRA study,<sup>6</sup> which demonstrated a significant reduction in mortality in the central neuraxial group compared with the general anesthesia group, made the national news headlines in the United Kingdom when it was published—a very rare event for any anesthetic topic. But it was quickly followed by criticisms of the data analysis: mixed surgical populations undergoing a variety of surgical procedures, neither the anesthetic techniques nor the postoperative analgesia regimens were standardized; and many of the older papers included in the analysis did not reflect current surgical and anesthetic practice.

A large, prospective, randomized trial (MASTER) comparing postoperative epidural infusion with intravenous patient-controlled analgesia came to a largely negative conclusion, contrary to the CORTRA study, showing only that epidural infusions offered good analgesia and some respiratory protection.<sup>7</sup>

Study design is easier to control when the effects of regional anesthesia on a single postoperative outcome are investigated. It is not surprising, therefore, that more positive data exist for the benefits of regional anesthesia in reducing postoperative risks of pulmonary, cardiovascular, and gastrointestinal complications,<sup>6–9</sup> but even the simplest of comparators is subject to uncertainty. Reduction in pain scores is one of the easier, more objective ways

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of comparing regional and systemic analgesia techniques, but there are difficulties in interpreting the significance of the results. A statistical significance does not always translate into clinical significance; a decline of 20-mm visual analog scale within patients or more than 33% between groups is generally accepted as clinically (as opposed to statistically) relevant.<sup>10,11</sup>

In the face of uncertainty, debate continues, and as the tendency of patients and lawyers to seek compensation grows, many anesthesiologists have become reluctant to continue to offer epidural analgesia, even to those patients who would benefit from them, based on our current understanding. In the United Kingdom, a case series showing a raised incidence of epidural complications<sup>12</sup> accelerated the decline in popularity of epidurals, despite the lack of data about the incidence of both usage and complications. The same is reported from other countries (Canada, United States, and Australia). Thus, after some 30 years of concerted effort, we still lack the evidence to define the role of regional anesthesia in optimizing the patient's outcome from surgery, largely because even the best randomized studies do not have large-enough patient numbers to demonstrate a clear difference in mortality and morbidity,<sup>13</sup> and there are too many confounding variables. In a major review, Liu and Wu<sup>14</sup> confirm that, although regional anesthesia provides superior analgesia compared with opioids, improvement in specific outcome parameters (cardiovascular and respiratory) is restricted to particular patient subsets, and overall, there is no convincing evidence of improvement in outcome.

The risks of severe adverse events have to be balanced against benefits when constructing clinical guidelines and obtaining properly informed consent. All major regional anesthesia techniques are associated with rare but potentially very severe complications, yet currently, we cannot offer our patients a realistic estimate of risk to balance against any potential benefits with any certainty. All of this begs the question: Where are the data we need to inform our highest standards of clinical practice?

### Development of Specific Criteria

If the broad overview of benefits is uncertain, it makes sense to evaluate the role of regional anesthesia using more specific criteria and the current evidence-based data to produce best practice guidelines. Systematic review and meta-analysis are the usual method of interrogating data when the size of individual trials prevents definitive analysis. Although these techniques have their limitations,<sup>15</sup> they do allow us to search for subtle or rare events, the significance of which may be apparent only when using such techniques.

Since 2003, a number of evidence-based resources have been published in print and online. They make a valuable contribution to the development of a more rational approach to the overall management of postoperative pain and the specific role of regional anesthesia/analgesia. Rosenquist and Rosenburg<sup>16</sup> developed an algorithm-based decision process based on evidence-based, site-specific, pain management interventions. Bonnet and Marret<sup>17</sup> reviewed the role of regional anesthesia in influencing outcome and found no convincing evidence that the superior quality of regional analgesia compared with systemic opioids had yet translated into improved outcome, although positive data from some studies gave some direction to future studies. Other work, particularly looking at lower-limb joint replacement, also showed positive results and suggested how we might target future research.<sup>18,19</sup> The American Society of Regional Anesthesia and Pain Medicine carried out a critical analysis of the available evidence for 10 new and emerging techniques of postoperative analgesia in 2006, summarizing the strengths and weaknesses for each procedure and comparing the data with a

survey of the accepted standards of clinical practice of American Society for Regional Anesthesia and Pain Medicine members.<sup>20</sup> The Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine have conducted a detailed review of the available evidence for their authoritative publication, "Acute Pain Management: Scientific Evidence," now in its third edition.<sup>21</sup>

Prospect performs its systematic reviews according to the Cochrane methodology and then, using the Delphi consensus process, formulates recommendations for both anesthetic and analgesic regimens where there is clear evidence that they improve analgesia in specific surgical procedures.<sup>22</sup> To date, the Web site contains detailed systematic reviews of 9 surgical procedures, and local and regional anesthesia has a prominent role in providing evidence-based, effective analgesia in all except one of these procedures. As well as recommending analgesic modalities, Prospect is also able to advise against the use of regional anesthesia in those surgical procedures where, although the analgesia may be effective, the evidence of risk versus benefit does not justify its use in routine cases (epidural for abdominal hysterectomy, for example). The full methodology, search terms, and criteria for inclusion and exclusion of papers for each systematic review, together with all the recommended and excluded analgesic regimens, are available on the Prospect Web site.<sup>2</sup> Some procedures have generated published reviews in the peer-reviewed literature,<sup>23–25</sup> and other data revealed by the systematic review on analgesia for thoracotomy were robust enough to generate a further contribution to what is already known about the role of regional analgesia for this procedure.<sup>26</sup>

### The Risks

As with the benefits, the database concerning the risks of regional anesthesia is large but confusing. The quoted ranges of complications for severe adverse events vary widely because the study methodologies vary, much of the data are retrospective, and the distinction between temporary and permanent disability is not always clear. Most of the data come from retrospective, observational studies, many of which lack a control group, making it difficult to calculate an accurate incidence of risk. Moen et al<sup>27</sup> offer some important retrospective data from the Swedish study of neurologic complications as it distinguishes between spinals (1:20–30,000), obstetric (1:25,000), and non-obstetric epidurals (1:3600), suggesting that epidurals have a higher risk of complications than spinals. By contrast, a large, prospective, voluntary reporting survey in France showed a higher rate of complications for spinals than epidurals and peripheral nerve blocks.<sup>28</sup>

As with the assessment of benefits, attempts to accurately calculate the incidence of adverse events are also associated with uncertainty and confusion. Published rates of severe adverse events associated with epidurals for major surgery range from 1:875 (Christie and McCabe<sup>12</sup>) to 1:19,000 (Aromaa et al<sup>29</sup>), and different subsets of patients are subject to differing risk, making it difficult to offer detailed information to patients. Recent guidelines in how to limit the risks of, investigate, and treat neurologic injury are helpful but also recognize the difficulty of accurately estimating the incidence of those risks.<sup>30</sup>

The NAP3 project was a yearlong prospective study of risks associated with central neuraxial block in 5 predefined patient groups (pediatric, obstetric, perioperative, chronic pain, and nonanesthetic). The project working party performed a national (United Kingdom) snapshot census of activity to provide an accurate figure for the numerator and then prospectively collected all the severe complications notified nationally during the 12-month data collection period. The study was extended for a further 6 months to allow for late presentation of cases that had

occurred during the data collection period and to monitor any changes and improvements in patient symptoms, so that the incidence of permanent harm could be calculated with more certainty. The national census revealed a total of 707,425 central blocks as the numerator (spinal = 46%, epidural = 41%, caudal = 11%), of which 45% were performed for obstetric indications and 44% for perioperative indications. Eighty-four severe adverse events were reported, with 52 meeting the inclusion criteria. All cases were investigated in detail to examine the role of the regional technique and whether other factors unrelated to the block were implicated; a further 22 were excluded from the final analysis. In the remaining 30 cases, the working group considered there to be a direct link between the block and the causation of the injury, and for the purposes of calculating an incidence of injury, a “pessimistic” outcome was assumed for all 30 cases (no improvement likely to occur and a strong likelihood of causation due to suboptimal or poor case selection, performance of the block, subsequent patient management, etc). Sixteen of the 30 cases subsequently made a full recovery before the end of the extended monitoring period, or the link between the block and the injury was considered tenuous or uncertain, which left 14 cases to calculate the “optimistic” incidence of injury.

Epidurals and combined spinals/epidurals were associated with higher risks of injury than spinals and caudals, and perioperative epidurals produced more than half of all the complications, with an incidence of between 1:5700 (pessimistic) and 1:12,200 (optimistic), with very low incidences for pediatric, obstetric, and other uses. These prospective figures are reassuring and compare well with those of other large studies. A wealth of other NAP3 data means that we can now offer patients a validated source of information regarding risks associated with central neuraxial block in a variety of clinical settings and separated into different categories of complication.

### Best Practice

With access to better information about both the beneficial role of regional anesthesia in different procedures and the attendant risks, it is possible to establish standards of best practice, the aims of which are 3-fold:

- (1) optimal quality postoperative analgesia, with a minimum incidence of adverse events;
- (2) the use of active rehabilitation programs to accelerate recovery, improve mobility, achieve targets of functional recovery, and reduce duration of hospital admission; and
- (3) improve long-term outcome and reduce the risk of chronic pain and poor functional results due to the inadequate management of high-intensity pain in the early postoperative period.

The Prospect procedure-specific reviews highlight where the available data lack sufficient detail to make robust recommendations and suggest new areas for future research to address the current weaknesses of our knowledge. Hip and knee arthroplasties serve as examples; despite being common surgical procedures, uncertainty remains about the best means of providing both anesthesia and postoperative analgesia. In developing the procedure-specific recommendations, it became clear that the published literature could not answer many questions. Other major reviews express similar concerns; a systematic review comparing epidural analgesia with peripheral nerve blocks for major knee joint surgery was unable to reach a positive conclusion because of an insufficient number of studies that met the inclusion criteria and their widely differing methodologies.<sup>31</sup> Perineural catheters are widely used to provide prolonged regional

analgesia for lower-limb joint surgery, but can their use be justified? Their use is associated with improved postoperative analgesia but, in turn, produces prolonged motor weakness and delayed mobility,<sup>32</sup> and the prolonged analgesia does not translate into any improvement in functional recovery.<sup>33</sup> More encouraging outcome studies are beginning to point us in the direction of goal-directed pathways, using multimodal analgesia regimens as part of a very structured approach to postoperative rehabilitation,<sup>34</sup> although the authors recognize that this retrospective study has several limitations and may not be reproducible elsewhere. Nevertheless, it does offer some pointers for future research. Very dilute concentrations of levobupivacaine can minimize motor weakness to improve mobility while still providing satisfactory analgesia after knee replacement<sup>35</sup> and may prove to be a useful addition to postoperative analgesia. However, such targeted studies need to be confirmed by other research groups, and a number of important questions still need to be addressed; future research in regional anesthesia should be focused to address these uncertainties and concentrate on identifying the role of regional anesthesia in optimizing the functional outcome for specific surgical procedures with the minimum of adverse events (Table 1).

Even if the most effective anesthetic and analgesic combinations can be identified by systematic review and consensus recommendation, best practice remains difficult to achieve. It is a complex concept and is subject to significant influence by surgical as well as anesthetic factors. Ward routines and physiotherapy regimens, as well as local medical custom and practice, all influence best practice; it is not simply the optimal, evidence-based anesthesia or analgesia technique. Good analgesia is a means to an end, not the end in itself, and although it makes fast-track surgery possible, there are many other factors that influence patient satisfaction and length of stay.<sup>36</sup>

**TABLE 1.** Regional Anesthesia and Optimal Functional Outcome: Some of the Questions That Still Need to Be Answered

- Do single-shot perineural injections provide sufficient duration of analgesia, for major joint surgery, in combination with other supportive analgesia?
- If perineural catheter infusions are better than single injections, what is the optimal duration of infusion and concentration of the infusate?
- Is a femoral nerve block sufficient, or does the addition of a sciatic nerve block improve functional outcome as well as analgesia for total knee replacement?
- Does epidural anesthesia/analgesia have any value in functional recovery other than in colorectal and thoracic surgery?
- Should we still be using epidurals for primary lower-limb arthroplasty?
- Does effective management of high-intensity acute pain reduce the incidence of postoperative chronic pain syndromes? If so, is regional anesthesia an essential component of the pain management?
- Is total regional analgesia the ultimate goal? Complete analgesia may mean complete immobility. How best can we ensure early mobility?
- Should analgesia be sufficient only to ensure compliance with active rehabilitation?
- Is opioid-free multimodal analgesia achievable, and what is the optimal role of regional analgesia within a multimodal analgesia regimen?
- What are the key elements of an active rehabilitation program, and how do they vary for different surgical procedures?

## CONCLUSIONS

The hypothesis that regional anesthesia might have a beneficial effect on patient outcome from surgery remains difficult to prove, despite some early evidence in its favor. As regional anesthesia becomes more widely practiced, there is an increased awareness of its rare but very serious adverse events, and we need to balance the intended benefits of regional anesthesia against the potential risks, with both sides of the equation supported by good-quality scientific evidence as well as accepted clinical custom and practice. Regional anesthesia and analgesia guidelines need to show demonstrable benefit for a specific surgical procedure and/or a specific patient population. We have now made a start; we have good answers to some questions, and we now know some of the questions we still need to answer.

Surgical and regional anesthetic techniques will continue to evolve and set new challenges for us to focus our research on. There remains much work to be done!

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