Regional Anesthesia and Pain

Best evidence in anesthetic practice

Prevention: intraoperative neuraxial blockade reduces some postoperative complications

Article appraised

Rodgers A, Walker N, Schmug S, et al. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials. BMJ 2000; 321: 1–12.

Structured abstract

Question: What are the effects of neuraxial blockade with epidural or spinal anesthesia on postoperative morbidity and mortality?

Data sources: Studies were identified by computerized searches of Current Contents (1995–6), EMBASE (1980–96), MEDLINE (1966–96), and the Cochrane Library (1988) using the keywords "regional anesthesia", "regional anaesthesia", "spinal", or "epidural" and the Cochrane Collaboration search terms for randomized trials. Citation review of reference lists and hand search of conference proceedings were also performed.

Study selection: Studies were selected if they were trials of patients randomized to intraoperative neuraxial blockade (epidural or spinal anesthesia) or general anesthesia. The neuraxial anesthesia group could also receive general anesthesia concurrently; the general anesthesia group could also receive postoperative neuraxial blockade.

Data extraction: Data were extracted on trial design, interventions, patient characteristics, and events. The main outcomes were all cause mortality, deep vein thrombosis (DVT), pulmonary embolism (PE), myocardial infarction (MI), transfusion requirements, pneumonia, other infections, respiratory depression, and renal failure.

Main results: One hundred forty-one trials with a total of 9559 patients met the inclusion criteria. Neuraxial blockade significantly reduced 30-day all cause mortality, DVT, PE, transfusion requirements, and respiratory depression (Table I). Reductions were noted in MI, stroke, wound infections, and renal failure, but these were not statistically significant. There were no differences in the number of deaths between 30 days and six months after surgery.

Conclusions: Intraoperative neuraxial blockade reduces 30-day all cause mortality, thromboembolic events, transfusion requirements, and respiratory depression.

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Commentary by S. Ganapathy

This report should be fascinating for clinical regional anesthesiologists and surgeons. Four of the 11 authors are well known regional anesthesiologists or surgeons. The authors have meticulously collected data from studies reported between 1966 and 1997 in which patients were randomized to have neuraxial block or general anesthesia. Two unblinded, objective reviewers and a mediator retrieved data and recorded critical events. They identified quasi-randomization, duplicate publications, adverse events that occurred after the publication of results as well as duration of follow-up with each study. They have selected and defined end points that are totally clinically relevant. They have accounted for all the patients and studies that they report on. The unique improvement in data collection is contacting the authors of relevant articles to gather additional data on study design and delayed mortality and to clarify ambiguities in reporting on 87% of patients reported in this study. This is as thorough as one can get for a retrospective meta-analysis.

Although the studies are reported over 30 years during which there were evolving changes in diagnostic criteria, management strategies, anesthesia techniques and surgery that could affect outcome, it is likely they are evenly distributed between the groups. This is particularly true for cardiovascular events, DVT and pul-

TABLE Effect of intraoperative neuraxial blockade on postoperative mortality and morbidity

Outcome	*Events*		*Odds ratio* (95% CI)*	*P-value*
	Neuraxial blockade	*Not neuraxial blockade*		
30-day mortality	103 / 4871	144 / 4688	0.70 (0.54; 0.90)	0.006
Deep vein thrombosis	145 / 4871	220 / 4688	0.56 (0.43; 0.72)	<0.001
Pulmonary embolus	30 / 4871	66 / 4688	0.45 (0.29; 0.69)	<0.001
Myocardial infarction	45 / 4871	59 / 4688	0.67 (0.45; 1.00)	not significant
Perioperative transfusion >2 units	193 / 4871	280 / 4688	0.50 (0.39; 0.66)	<0.001
Postoperative bleed requiring transfusion	31 / 4871	69 / 4688	0.45 (0.29; 0.70)	<0.001
Wound infection	29 / 4871	33 / 4688	0.79 (0.47; 1.33)	not significant
Pneumonia	149 / 4871	238 / 4688	0.61 (0.48; 0.76)	<0.001
Death from other infections	2 / 4871	10 / 4688	0.33 (0.10; 1.07)	not significant
Respiratory depression	26 / 4871	38 / 4688	0.41 (0.23; 0.73)	<0.001
Renal failure	18 / 4871	32 / 4688	0.57 (0.32; 1.00)	not significant

* Odds ratio less than 1 favours the neuraxial blockade group; odds ratio greater than 1 favours the non-neuraxial group.

monary embolism. The authors fail to comment on the important role of preoperative risk stratification on outcome. Studies included were from many countries but this only makes the report more valuable.

Why did we not see these benefits of regional anesthesia in individual studies? This article clearly demonstrates the role of sample size in clinical trials. For a rate of event of 0.08 (=0.05 and ß=0.8), the number of patients required per group to show a 25% difference in outcome is 2,521 and for a 50% difference is 534.[1] The largest studies addressing this issue had randomized only a tenth of this number.[2–4]

Although the authors comment that there was no clear difference between different surgical groups on total mortality, Table II in their paper reveals that orthopedic and vascular patients contribute the entire mortality difference of 30%. Vascular patients contributed little to the benefits seen with reduction in DVT, pulmonary emboli, myocardial infarction and perioperative transfusion requirements and therefore the reduction in their mortality could be attributed to reduction in infective and respiratory complications. The intraoperative death risk is 3 times higher in this group with general anesthesia.

Finally, the lack of benefit seen in general surgical and urological patients and lumbar epidurals may be interlinked. Perhaps the use of lumbar epidurals for general or abdominal surgery may be detrimental to outcome. A subgroup analysis of this factor is lacking in this paper. It will be difficult, if not impossible, not to combine light general anesthesia with neuraxial blocks for abdominal surgery. As per Rodgers *et al*'s paper, addition of general anesthesia seems to take away the benefits of regional anesthesia.

This meta-analysis is much awaited preliminary evidence in favour of regional anesthesia and indicates the need for large multicentre randomized prospective trials.

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Commentary by D.N. Buckley

I may yet be convinced of the utility of meta-analysis. Thus far I have been somewhat coloured by an exchange in Isaac Asimov's Foundation Trilogy.[1] In this interaction an "archeological expert" describes his work to another character. His method is to read the work of the "experts" and then develop his own "opinion", scorning the need to sully himself with the trials and inconvenience of field research. I admit that I have viewed some meta-analytic work in this same light – that is, it is a substitute, from the safety and relative control of an office, for the necessary travails of primary research of sufficient quality and power to adequately answer the question posed.

The systematic review reported by Rodgers *et al* goes some considerable way in dispelling my skepticism. It addresses one of the most pressing issues in current anesthetic practice – whether or not our individual choices in anesthetic technique have important effects upon patient outcome. It should have a major effect on perioperative medical practice. It provides information that probably would not have been gathered in any other way, and which is useful to the work-a-day anesthesiologist. It is intellectually rigorous. This is the information that we require daily to support and guide our practice. We not only face budgetary constraints and the never-ending drive of the surgeon to start sooner ("Why do we always have to wait for anesthesia? Those epidurals take so long!"), but we also interact with other elements of perioperative care such as prophylaxis of deep vein thromboembolism (DVT). The US Food and Drug Administration Public Health Advisory concerning low molecular weight heparins (LMWH)[2] states, in part, that "practitioners should consider fully the potential benefit versus risk before neuraxial intervention in patients anticoagulated *or to be anticoagulated for thromboprophylaxis*"[2] (italics mine). The American Society of Regional Anesthesia consensus conference[3] similarly advises careful consideration of risks versus benefits of regional anesthesia in conjunction with LMWH. A major problem, to date, has been that we have "*believed*" that a benefit existed, but we have had no *evidence* that such benefit existed because hard clinical outcomes such as all- cause mortality or major morbidity are just too rare in current anesthetic practice to appear in manageable clinical trials. Trials that support the use of low molecular weight heparins for DVT prophylaxis, on the other hand, have consistently been of sufficient power (in part because of the financial stakes) to support their use as effective "state of the art" thromboprophylactic agents. Thus one component of perioperative management directs another on the basis of superior quality evidence. With the information presented by Rodgers *et al*, the discussion of perioperative risk and benefit for patients can be carried out with a better perspective on the total picture; rational discussions can be had with other perioperative physicians. All anesthesiologists should become familiar with this work in its description of our practice and its implications for perioperative management.

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