Can Neuraxial Anesthesia Reduce Perioperative Mortality?

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5.1 Introduction

Neuraxial anesthesia results from injection of local anesthetics into the subarachnoid space (spinal anesthesia) and/or into the epidural space (epidural anesthesia). According to two recent systematic reviews, neuraxial anesthesia compared with general anesthesia may reduce postoperative mortality in surgical procedures, especially in patients with intermediate-to-high cardiac risk [1, 2]. In the first analysis, Guay et al. summarized nine Cochrane systematic reviews in order to assess whether anesthetic technique influences mortality after surgery [1]. Compared with general anesthesia, neuraxial anesthesia alone reduced perioperative mortality up to 30 days after surgery (risk ratio 0.71; 95 % confidence interval 0.53–0.94: analysis of 20 studies with a cumulative $N = 3006$) [1]. Compared with general anesthesia alone, combined neuraxial and general anesthesia had no significant effect on perioperative mortality up to 30 days after surgery (relative risk 1.07; 95 % confidence interval 0.76–1.51: analysis of 18 studies with a cumulative $N = 3228$) [1]. In the second analysis, Pöpping et al. evaluated the impact on mortality of concomitant epidural analgesia, compared with systemic analgesia, in adults having surgery under general anesthesia (cumulative $N = 2201$: ten randomized controlled

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trials published up until July 2012) [2]. The results showed that there was a significant reduction in mortality risk associated with epidural analgesia (3.1 % vs 4.9 %; odds ratio 0.60; 95 % confidence interval 0.39–0.93) [2]. The results obtained in these two recent systematic reviews were in agreement with the findings from earlier analyses published in 2000 [3, 4]. Despite these recent publications, there is ongoing debate about whether neuraxial blockade can reduce perioperative mortality. Recent large high-quality trials have focused on this important question. This chapter will review the main recent trials in this area and develop an evidence-based answer to this debate.

5.2 Main Evidence

5.2.1 Orthopedic Surgery

The principal paper on this field was published by Urwin et al. [4]. They performed a meta-analysis of 15 randomized trials that compared mortality associated with general versus regional anesthesia for hip fracture patients and found a reduced 1-month mortality in the regional anesthesia group (odds ratio 0.66; 95 % confidence interval 0.47–0.96) [4]. A subsequent Cochrane systematic review published in 2004 ($N = 2567$: 22 trials) demonstrated that there was insufficient evidence to rule out clinically important effects on perioperative mortality due to neuraxial blockade in the setting of adult hip fracture surgery [5]. A single-center study ($N = 298$) also failed to demonstrate any survival advantage associated with anesthetic technique in geriatric patients undergoing surgery for hip fracture [6]. A recent large database analysis ($N = 18{,}158$; 126 medical centers during 2007 and 2008 throughout New York State, USA) found that neuraxial anesthesia significantly reduced mortality in adult hip fracture surgery (odds ratio 0.710; 95 % confidence interval 0.541–0.932; $P = 0.014$) [7]. In primary adult lower-extremity joint arthroplasty, general anesthesia as compared with neuraxial anesthesia also has recently been associated with increased mortality in multivariate analysis (odds ratio 1.83; 95 % confidence interval 1.08–3.1; $P = 0.02$) in a massive observational cohort ($N = 382{,}236$ in 400 medical centers around the USA from 2006 to 2010) [8]. The increased mortality risk associated with general anesthesia in this clinical setting persisted when compared to patients undergoing neuraxial blockade combined with general anesthesia (odds ratio 1.70; 95 % confidence interval 1.06–2.74; $P = 0.02$) [8]. In a large observational cohort of adult primary knee arthroplasty ($N = 14{,}052$ from 2005 to 2010), neuraxial anesthesia significantly reduced perioperative complications, including mortality [9].

In summary, the current evidence base suggests that there may be a survival advantage associated with neuraxial anesthesia in lower-extremity major joint procedures [4–9]. Although these data are suggestive, they are not conclusive [10, 11]. They serve as hypothesis generating in the planning and execution of appropriately powered randomized clinical trials to test whether anesthetic technique reduces mortality in this clinical setting.

5.2.2 Vascular Surgery

A recent multicenter observational trial ($N=6009$ in medical centers around the USA from 2005 to 2008) compared neuraxial anesthetic techniques with general anesthesia and monitored anesthesia care in elective endovascular aortic aneurysm repair [12]. Although general anesthesia compared to neuraxial blockade was significantly associated with pulmonary morbidity (odds ratio 4.0; 95 % confidence interval 1.3–12.5; $P=0.020$) and a 10 % increase in hospital length of stay (95 % confidence interval 4.8–15.5 %; $P=0.001$), neuraxial blockade did not offer any survival advantage in this setting [12]. A large international observational study ($N=1271$: 79 medical centers in 30 countries) also demonstrated no survival advantage related to anesthetic technique, although neuraxial anesthesia significantly reduced the risk of admission to the intensive care unit (odds ratio 0.71; 95 % confidence interval 0.53–0.97; $P=0.030$) and the duration of hospital stay ($P=0.003$) [13]. A recent meta-analysis highlighted the lack of high-quality randomized data to guide decision-making about which anesthetic technique reduces perioperative mortality in this major vascular surgical procedure [14].

In lower-extremity vascular surgery, recent observational database analysis ($N=5462$ in multiple medical centers across the USA from 2005 to 2008) documented a perioperative mortality rate of 3 %: multivariate analysis demonstrated no significant effect of neuraxial anesthesia on mortality [15]. Contemporary meta-analysis from the Cochrane group on this question ($N=696$: four studies) demonstrated no conclusive effect on mortality from neuraxial anesthetic techniques, but also noted that that insufficient high-quality evidence was available [16]. A recent review has noted that while neuraxial blockade has significant clinical application in vascular surgical patients, the current evidence base does not permit a definite conclusion about its effects on perioperative mortality [17]. In summary, future appropriately powered randomized trials should evaluate this question, as has already been done for local anesthesia in carotid endarterectomy [18].

5.2.3 Cardiac Surgery

A recent series of three meta-analyses have explored the effects of neuraxial anesthetic techniques on outcomes after cardiac surgery, including perioperative mortality [19–21]. The first two demonstrated no beneficial effect on mortality due to neuraxial blockade [19, 20]. The third meta-analysis ($N=2366$: 33 trials) suggested that epidural anesthesia in cardiac surgery reduces the composite endpoint of mortality and myocardial infarction (odds ratio = 0.61; 95 % confidence interval 0.40–0.95; $p=0.03$ number needed to treat = 40) [21]. Recent randomized trials of neuraxial blockade in cardiac surgery have been underpowered to rule out a clinically meaningful beneficial effect on perioperative mortality in cardiac surgery [22–24]. The clinical concern about the risk of neuraxial hematoma in this anticoagulated surgical patient cohort will likely remain a significant barrier to recruitment for large adequately powered clinical trials to effectively address this question.

5.2.4 Cancer Surgery

A recent meta-analysis has suggested that neuraxial anesthesia may significantly improve survival after surgery for urologic and colorectal cancer [25, 26]. Although the evidence favors a reduction in mortality associated with neuraxial anesthesia in these settings, it appears inadequate to ascertain whether the risk of tumor recurrence is also reduced [27]. In summary, appropriately powered randomized trials are indicated to test these associations detected in meta-analysis yet further.

Conclusion

The current evidence base suggests that the real effect of neuraxial blockade on perioperative mortality, despite extensive meta-analyses both in cardiac and non-cardiac surgery, is still uncertain. Nevertheless, the Consensus Conference by Landoni et al. included neuraxial anesthesia among the interventions which may provide a survival benefit in the perioperative period [28, 29]. Future trials should explore this enduring question with adequate power, ideally in the setting of high-quality multicenter randomized trials.

Summary Table

Clinical summary			
Technique	Indications	Cautions	Notes
Neuraxial anesthesia	Lower-extremity major joint procedures	Neuraxial hematoma	Suggestive reduction in mortality
Neuraxial anesthesia/ analgesia	Cardiac surgery	Neuraxial hematoma	No conclusive effect on mortality
Neuraxial anesthesia	Lower-extremity vascular surgery	Neuraxial hematoma	No conclusive effect on mortality
Neuraxial anesthesia	Elective endovascular aortic aneurysm repair	Neuraxial hematoma	No conclusive effect on mortality
Neuraxial anesthesia	Cancer surgery	Neuraxial hematoma	Suggestive reduction in mortality

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