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Review Article

REVIEW ARTICLES

Neuraxial *vs* general anaesthesia for total hip and total knee arthroplasty: a systematic review of comparative-effectiveness research

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Abstract

Background: This systematic review evaluated the evidence comparing patient-important outcomes in spinal or epidural *vs* general anaesthesia for total hip and total knee arthroplasty.
Methods: MEDLINE, Ovid EMBASE, EBSCO CINAHL, Thomson Reuters Web of Science, and the Cochrane Central Register of Controlled Trials from inception until March 2015 were searched. Eligible randomized controlled trials or prospective comparative studies investigating mortality, major morbidity, and patient-experience outcomes directly comparing neuraxial (spinal or epidural) with general anaesthesia for total hip arthroplasty, total knee arthroplasty, or both were included. Independent reviewers working in duplicate extracted study characteristics, validity, and outcomes data. Meta-analysis was conducted using the random-effects model.
Results: We included 29 studies involving 10 488 patients. Compared with general anaesthesia, neuraxial anaesthesia significantly reduced length of stay (weighted mean difference −0.40 days; 95% confidence interval −0.76 to −0.03; P=0.03; $I2$ 73%; 12 studies). No statistically significant differences were found between neuraxial and general anaesthesia for mortality, surgical duration, surgical site or chest infections, nerve palsies, postoperative nausea and vomiting, or thromboembolic disease when antithrombotic prophylaxis was used. Subgroup analyses failed to find statistically significant interactions (P>0.05) based on risk of bias, type of surgery, or type of neuraxial anaesthesia.
Conclusions: Neuraxial anaesthesia for total hip or total knee arthroplasty, or both appears equally effective without increased morbidity when compared with general anaesthesia. There is limited quantitative evidence to suggest that neuraxial anaesthesia is associated with improved perioperative outcomes. Future investigations should compare intermediate and long-term outcome differences to better inform anaesthesiologists, surgeons, and patients on importance of anaesthetic selection.

Key words: anaesthesia, general; anaesthesia, spinal; pain, postoperative; postoperative complications

Systematic evaluation of patient-important perioperative outcomes and economics is needed to assist patients and providers alike in making optimal decisions regarding the choice of anaesthesia for major orthopaedic surgery. The frequency of major hip and knee surgeries is forecasted to increase dramatically during the next 20 yr,[1 2] and anaesthetic options have become increasingly more complex and costly.[1] Unlike major abdominal or cardiac surgeries that require general anaesthesia, major lower extremity orthopaedic surgeries can be performed with either neuraxial or general anaesthesia. Several previous studies addressing possible differences in perioperative morbidity and mortality with neuraxial and general anaesthesia for total joint arthroplasty suggest largely equivalent results.[3 4]

Value in health-care delivery is directly proportional to perioperative outcomes and inversely proportional to cost.[5] Determining evidence-based practice for orthopaedic anaesthesia has been hindered by previous experimental and observational studies showing conflicting data on differences in major morbidity and mortality outcomes by anaesthesia type.[3 4 6–13] These studies were, however, limited in the ability to evaluate patient-important outcomes fully, largely because of the following factors: (i) there were few small studies specifically evaluating spinal or epidural anaesthesia *vs* general anaesthesia; and (ii) the low incidence of major complications, such as death, cardiovascular events, or permanent neurological injury cannot be investigated properly in small randomized controlled trials. Recently, Memtsoudis and colleagues,[4] in a large observational study of more than 500 000 patients, found that major morbidity and mortality may be significantly reduced among patients receiving neuraxial anaesthesia or neuraxial anaesthesia combined with general anaesthesia for total hip and knee arthroplasty when compared with general anaesthesia alone. However, retrospective studies based on large administrative databases are subject to bias because of lack of randomization; thus, such studies have limited internal validity and rarely accommodate straightforward comparisons between anaesthetic techniques. The aim of the present systematic review with meta-analysis, therefore, was to investigate differences in patient-important perioperative outcome between neuraxial and general anaesthesia in patients undergoing elective total hip arthroplasty (THA) or total knee arthroplasty (TKA) through qualitative and quantitative analysis of all available observational and experimental results, randomized and non-randomized, to guide an evidence-based recommendation more directly.

Methods

This protocol-driven systematic review addressing the intervention neuraxial (spinal or epidural) anaesthesia adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[14]

Eligibility criteria

Eligible studies included comparative studies, either randomized controlled (Level I) trials (RCTs) or prospective observational (Level II) studies, enrolling adult patients undergoing elective THA, TKA, or both. Only studies comparing neuraxial anaesthesia directly with general anaesthesia for primary anaesthesia type were eligible (combined general and regional anaesthesia was excluded). Only studies where outcome and exposure ascertainment was done using the clinical record were included, whereas studies in which outcome or exposure ascertainment was determined exclusively using administrative billing data were excluded. For the purposes of this review, neuraxial anaesthesia was differentiated from use of regional techniques (e.g. epidural or peripheral nerve infusions) for postoperative analgesia. Specific patient-important outcomes of interest included mortality, major morbidity [vascular events (e.g. deep vein thrombosis, cerebral vascular accidents, and myocardial infarction), infection (e.g. chest and wound), and nerve palsies] and any patient-centred/patient-experience outcomes available, including postoperative nausea and vomiting (PONV), postoperative pain persisting beyond 3 months, changes in mental status, and hospital length of stay. The duration of surgery and anaesthesia drug and supply costs were additional resource utilization outcomes of interest. All eligible studies were included regardless of size, language constraints, or quality assessment ratings. Strictly descriptive articles (e.g. reviews, commentaries, or letters) were excluded.

Study identification

Both electronic and hand-searching techniques were used to identify studies. Ovid MEDLINE, Ovid EMBASE, EBSCO CINAHL, Thomson Reuters Web of Science, and the Cochrane Central Register of Controlled Trials were all queried from database inception until March 2015. The search cross-referenced keywords and controlled vocabulary for each of the following areas of interest: arthroplasty, replacement, hip plus THA; arthroplasty, replacement, knee plus TKA; spinal, neuraxial, epidural, regional anaesthesia; and postoperative complications and outcomes, including specific problems, such as infection, nausea, transfusion, stroke, and paresthesias, in addition to the economic ramifications of complications, including cost and length of stay. The search yielded 1345 studies. A summary of the search strategies is available as Supplementary Appendix S1. Additional studies were identified by review of the reference sections of all eligible studies and review of previously published systematic reviews.[8–11 13 15–18]

Decisions for inclusion were based on independent review of each of the abstracts by four study investigators (R.L.J., C.M.D., C.M.B., and A.K.J.). Eligibility of potential studies (as determined by either reviewer) underwent full-text review by two reviewers working independently and in duplicate. Studies were excluded if the full-text review identified that they: (i) did not contain the population of interest (e.g. non-elective surgery for hip fractures was excluded); (ii) were not a direct comparative evaluation of spinal or epidural anaesthesia *vs* general anaesthesia (intervention); (iii) did not contain a patient-important outcome of interest; (iv) were not an original study; or (v) were a conference abstract without follow-up publication.

Data collection

Four reviewers (R.L.J., C.M.D., C.M.B., and A.K.J.) working independently and using replicate electronic data-collection tools extracted all data from the full-text versions of eligible studies. Study characteristics included author, publication year, sample size, study population (age), outcome data, primary anaesthesia type, type of major lower extremity surgery, study design, and quality ratings. Discrepancies in data collection between the two reviewers were resolved by consensus first, followed by verification by a third investigator (C.B.M.) not involved with the initial data-extraction process.

Risk of bias of the included studies was independently assessed by two reviewers (R.L.J. and S.L.K.). The Cochrane Collaboration Risk Assessment Tool[19] was adapted and used to evaluate risk of bias for RCT evidence. Allocation concealment, blinding of outcome assessors, incomplete outcome data, and loss to follow-up were critically assessed on included RCTs when determining the overall risk of bias as either high or low rating. The Newcastle–Ottawa quality assessment tool[20] was used to evaluate risk of bias amongst the observational studies. A study was rated overall as high risk for bias if there were important imbalances at baseline, if there was failure of blinding of outcome assessors, or if there was significant (>15%) loss to follow-up.

Statistical analysis

A qualitative synthesis was performed for studies that reported data not comparable by formal meta-analysis. To facilitate meta-analysis, standard deviations were imputed from reported ranges using guidelines outlined by Hozo and colleagues.[21] Forest plots were used to show point estimates and confidence intervals (CI) of individual included studies. Data analysis abided by the guidelines set out by the Cochrane Collaboration regarding statistical methods. In all instances, two-tailed P-values <0.05 were considered significant. Relative risks (RRs) and the weighted mean difference (WMD) for binary and continuous outcomes were also calculated. Considering the expected heterogeneity across studies, we decided *a priori* to use a random-effects model to evaluate outcomes.[22] We conducted subgroup analysis based on the risk of bias (high *vs* low), type of surgery (TKA, THA, or both) and type of anaesthesia (spinal, epidural, combined spinal and epidural anaesthesia, or general anaesthesia), and to address the influence of modern surgical and anaesthesia practice we analysed subgroups of articles published in 2006 or more recently compared with publications before 2006. Interaction testing between subgroups was conducted to determine whether differences between the effect sizes of subgroups was statistically significant.[23] Heterogeneity was assessed using the I^2 statistics, where values >50% are consistent with large heterogeneity.[24] Sensitivity analyses were performed on the results of the meta-analyses. Funnel plots were constructed to detect publication bias and statistically test for publication bias by using the Egger regression test. All analyses were conducted (by M.H.M.) using Comprehensive Meta-analysis V 2.0 (Biostat, Englewood, NJ, USA).

Results

Retrieved studies

After screening, 126 full-text articles were assessed for eligibility. The majority were excluded because of an inappropriate study design (19 studies),[3 4 18 25–40] population (seven studies),[16 41–46] intervention (44 studies),[47–90] or outcome measure (19 studies).[91–109] Nine conference abstracts were also excluded.[110–118] One study[119] was screened and added after review of the reference section. Another study[120] was published in Czech and was translated with the assistance of electronic translation software. In total, 29 studies published up to March 2015 met inclusion criteria.[6 7 12 104 119–143] Included studies date from 1989 to 2015. Neuraxial anaesthesia (epidural or spinal anaesthesia) was provided to 2776 patients (median age 68 yr), whereas 7712 patients (median age 67 yr) underwent general anaesthesia for total hip arthroplasty, total knee arthroplasty, or both. Supplementary Appendix S2 illustrates the process of study selection.

Study characteristics

Table 1 presents highlighted study features. Nineteen studies[6 7 12 119 123 125 127–129 131–135 137 139–141 143] were RCTs, and 10 studies[104 120–122 124 126 130 136 138 142] were observational studies. Surgical data for THA was included in 14 studies[6 118 119 124–126 130 136–142] [median study size 78 patients (range 22–140)] and for TKA in 10 studies[7 122 123 127 128 131–134 144] [median study size 68 patients (range 20–377)]. Two studies[120 129] provided separate outcomes data from THA and TKA populations. Three studies [median study size 146 patients (range 40–7704)][12 121 135] provided data on a mixed total hip and knee arthroplasty population.

A majority of included studies, 16, used epidural anaesthesia as the primary type of neuraxial anaesthesia.[104 119 125–134 139–143] Spinal anaesthesia was used in 10 studies[6 7 12 121 122 124 133 135 137 138] and combined spinal and epidural anaesthesia (CSE) in two studies.[120 123] One study reported data on both spinal and epidural anaesthesia use together.[136] Epidural infusions were reported to be continued for postoperative analgesia in 10 included studies.[119–123 125 132–134 139–141] There was a noticeable change in preferences for neuraxial anaesthesia over time. Recent studies (from 2003 to the present)[6 7 12 120–124] reported use of spinal or CSE anaesthesia (eight of eight studies), whereas studies from 1980 to 2003 reported mainly epidural anaesthesia usage (15 of 20 studies).

Qualitative synthesis: comparative effectiveness of spinal or epidural *vs* general anaesthesia

Each study reported one or more patient-important perioperative outcome (Table 1). Assorted differences relating to short-term, within-hospital, patient-centred/patient-experience perioperative outcome were available among the included studies (Table 1), such as pain at rest and with movement at various time points, opioid consumption, PONV, ambulation distance/rehabilitation goals, use of urinary catheters, patient satisfaction, postdural puncture headache, and inpatient falls. Differences in perioperative outcome relating to short-term resource allocation were examined in a few studies, including postoperative anaesthesia care unit (PACU) length of stay, hospital length of stay, and anaesthesia drug and supply costs. No study reported on postoperative pain persistent beyond 3 months, measures of health-related quality of life, functional capacity, resource utilization, or long-term outcomes after hospital discharge. Differences in short- and long-term cognitive outcome were discussed within five studies (Table 2).[128 133 135 138 143]

Assessment of risk of bias

Thirteen of the included RCTs were rated with overall low risk of bias,[6 7 12 119 123 124 127 131 135 137 140 141 143] and seven as high risk of bias[125 128 129 132–134 139] (Supplementary Appendix S3) based on criteria adapted from the Cochrane 'Risk of Bias' assessment tool.[19] There were no important imbalances at baseline in any trial. None of the RCTs reported loss to follow-up >15%. Overall ratings were decided as low risk of bias primarily as a result of 'blinding of outcome assessors', the presence of 'incomplete outcome data' within the included trials, or both.

Supplementary Appendix S4 presents the quality ratings of the nine cohort studies, as determined using the Newcastle–Ottawa Assessment Scale.[20] Four cohort studies were rated low risk of bias[77 121 122 126] and the remaining five studies were judged high risk of bias based on imbalances between neuraxial and general anaesthesia groups at baseline, failure to blind outcome assessors, inadequate follow-up of patients, or a combination of these factors.[39 120 130 138 142]

Meta-analysis: effectiveness of neuraxial anaesthesia compared with general anaesthesia

Compared with general anaesthesia, neuraxial anaesthesia was associated with lower risk of deep vein thrombosis (RR 0.51; 95% CI 0.41–0.62, nine studies) and pulmonary embolism (RR 0.36; 95% CI 0.22–0.60, seven studies) in patients who did not receive chemical antithrombotic prophylaxis. However, in those studies that included chemical antithrombotic prophylaxis in

Table 1 Detailed information on study features. CSE, combined spinal epidural anaesthesia; LOS, length of stay; OBS, observational study; PACU, postanaesthesia care unit; PON, postoperative nausea; POV, postoperative vomiting; PONV, postoperative nausea and vomiting; RCT, randomized controlled trial; THA, total hip arthroplasty; TKA, total knee arthroplasty; 'THA and TKA', mixed total hip and total knee outcomes data; 'THA; TKA', separated outcomes from total hip and total knee arthroplasty

Author	Year	Volume	Design	Type of surgery	Type of neuraxial anaesthesia	Risk of bias	Outcomes measured
Harsten[6]	2015		RCT	THA	Spinal	Low	Surgery duration, PACU LOS, LOS, discharge criteria, ambulation tests, dizziness scores, pain (at rest and movement), morphine consumption, PON, POV, patient satisfaction, falls, mortality
Curry[121]	2014		OBS	THA and TKA	Spinal	Low	30 day surgical site infection
Harsten[7]	2013		RCT	TKA	Spinal	Low	Surgery duration, PACU LOS, LOS, discharge criteria, ambulation tests, dizziness scores, pain (at rest and movement), morphine consumption, PONV, urinary catheterization, patient satisfaction, anaesthesia duration, pulmonary embolism, mortality
Fořtová[120]	2010		OBS	THA; TKA	CSE	High	Operative time, pain (at rest), patient satisfaction
Napier[122]	2007		OBS	TKA	Spinal	Low	LOS, ambulation distance, pain at rest at: pain at PACU discharge, 12, 18, 36, and 48 h
Gonano[12]	2006		RCT	THA and TKA	Spinal	Low	Anaesthesia drug and supply costs, anaesthesia duration, PACU LOS, pain at rest, pain at admission to PACU, piritramide consumption, PACU PONV
Chu[123]	2006		RCT	TKA	CSE	Low	Pain scores, PON, POV, pruritus, pulse oximetry (1, 8, 12, 24, and 48 h), time to first ambulation, time to first drink and meal, discharge, deep vein thrombosis, infection
Brueckner[124]	2003		OBS	THA	Spinal	Low	Surgery duration, deep vein thrombosis
Wulf[125]	1999		RCT	THA	Epidural	High	PACU LOS, LOS, discharge criteria, degree of motor block, pain (at rest and movement), PON, POV,
Brinker[126]	1997		OBS	THA	Epidural	Low	Total operating room time, surgery duration, LOS, deep vein thrombosis, deep infections, mortality, urinary tract infections
Williams-Russo[127]	1996		RCT	TKA	Epidural	Low	Surgery duration, LOS, rehabilitation goals, deep vein thrombosis, mortality
Williams-Russo[128]	1995		RCT	TKA	Epidural	High	Cognitive effects (delirium, long-term 6 months), LOS, surgery duration, mortality, myocardial infarction or pulmonary oedema, or both
Moiniche[129]	1994		RCT	THA; TKA	Epidural	High	Pain at rest (4, 8, 12, 24, 30, 48, and 54 h); pain on movement (24 h), fatigue, opioid consumption, activity of patients, need for nursing assistance with everyday functions, surgery duration
Dalldorf[130]	1994		OBS	THA	Epidural	High	Deep vein thrombosis, operative time, LOS
Sharrock[144]	1991		OBS	TKA	Epidural	Low	Deep vein thrombosis, pulmonary embolism, tourniquet time
Mitchell[131]	1991		RCT	TKA	Epidural	Low	Operative time, LOS, thromboembolic disease (deep vein thrombosis and pulmonary embolism)
Jørgensen[132]	1991		RCT	TKA	Epidural	High	Deep vein thrombosis, pulmonary embolism, tourniquet time
Nielson[133]	1990	73	RCT	TKA	Spinal	High	Neuropsychological functions
Nielson[134]	1990	61	RCT	TKA	Epidural	High	Operative time, deep vein thrombosis
Jones[135]	1990		RCT	THA and TKA	Spinal	Low	Neuropsychological functions, surgical duration, morphine consumption, LOS, deep vein thrombosis, pulmonary embolism, chest infection, wound infection, mortality
Wille-Jørgensen[136]	1989		OBS	THA	Epidural or spinal	High	Deep vein thrombosis, pulmonary embolism
Davis[137]	1989	71	RCT	THA	Spinal	Low	Surgery duration, deep vein thrombosis, pulmonary embolism, mortality

Continued

Table 1 *Continued*

Author	Year	Volume	Design	Type of surgery	Type of neuraxial anaesthesia	Risk of bias	Outcomes measured
Hughes[138]	1988		OBS	THA	Spinal	High	Memory (recall and recognition)
Fredin[139]	1986		RCT	THA	Epidural	High	Deep vein thrombosis, pulmonary embolism
Modig[119]	1986		RCT	THA	Epidural	Low	Operative time, deep vein thrombosis, pulmonary embolism
Modig[140]	1983		RCT	THA	Epidural	Low	Operative time, deep vein thrombosis, pulmonary embolism
Modig[141]	1981		RCT	THA	Epidural	Low	Operative time, deep vein thrombosis
Thorburn[142]	1980		OBS	THA	Epidural	High	Deep vein thrombosis
Hole[143]	1980	24	RCT	THA	Epidural	Low	Operative time, myocardial infarction and death, pulmonary embolism, pneumonia, mental changes, wound infection, neurological sequelae, PONV, headache, morphine consumption

patient-care protocols, there were no statistically significant differences in either deep vein thrombosis or pulmonary embolism rates. Figure 1 shows that patients who received neuraxial anaesthesia had statistically significant shorter hospital stay (WMD −0.40 days; 95% CI −0.76 to −0.03; I^2 73%; 12 studies, 1240 patients). Although neuraxial anaesthesia resulted in up to a 10 min shorter operative time (WMD −5.13 min; 95% CI −10.96 to −0.70; I^2 94%; 21 studies, 9382 patients; Fig. 2), overall this difference in outcome failed to achieve statistical significance (P=0.08). There was no statistically significant difference in other outcomes, including mortality, chest infection, surgical site infection, nerve palsies, or PONV. The results of meta-analysis of all outcomes are contained in Table 3. All subgroup analyses failed to show statistically significant interactions (P>0.05) based on risk of bias, type of surgery, year of publication (2006 and newer *vs* publication before 2006), and type of neuraxial anaesthesia. Sensitivity analysis for mortality was performed by adding 378 patients from three trials with no events,[6 7 137] which resulted in no meaningful change in mortality results (RR 0.85; 95% CI 0.30–2.46; I^2 0%; seven studies). We were unable to detect a statistically significant publication bias; however, the number of studies included in each analysis was small, making tests for publication bias unreliable.

Discussion

This systematic review and meta-analysis confirms that neuraxial anaesthesia was either equivalent or favoured over general anaesthesia for patient-important outcomes of total hip or total knee arthroplasty. Surgical durations were not lengthened, yet hospital length of stay was reduced when neuraxial techniques were used. Although the evidence is limited to suggest that use of neuraxial anaesthesia is associated with improved perioperative outcomes, there are no meta-analysis results supporting that outcomes are better when general anaesthesia is used.

Comparison with previous literature

There are previous systematic reviews and meta-analyses[8–11 18] and recent population-based studies using administrative billing data[3 4 27 30 35 145] that have analysed differences in mortality and major morbidity outcomes by anaesthesia type. Not unlike our review, previous literature on this topic also reports results for a superior anaesthesia technique (e.g. neuraxial) for some, but often not all included outcomes. In the last several years, administrative billing data studies have dominated the literature on this topic, and despite larger sample sizes within these papers, the results have yet to be definitive enough to transform clinical practice to default to neuraxial anaesthesia. The most recent population-based studies are summarized in Table 4. Additionally, past studies have been indirect for anaesthesia comparisons, lacking head-to-head examination, and imprecise in the estimation of the effect size. For instance, Rodgers and colleagues[13] were among the first to synthesize the evidence for benefits of neuraxial techniques, yet their systematic review was highly criticized for its wide confidence intervals among outcomes, which probably resulted from inclusion of a broad range of surgical populations. In contrast to most previous studies, we focused our systematic review and meta-analysis to compare directly the primary types of anaesthesia specifically used for total hip and knee arthroplasty.

Total hip and knee arthroplasty rarely require the combination of both general and neuraxial anaesthesia during the same procedure. Previous studies using administrative billing data are often restricted by coding limitations and thus include both neuraxial and general anaesthesia interventions during analysis. Consequently, results from this research, in particular for orthopaedic procedures that do not require combined anaesthesia techniques, do little to inform decisions. For instance, Memtsoudis and colleagues[4] grouped patients undergoing orthopaedic procedures under broad categories of anaesthesia type that included neuraxial, general plus neuraxial, and general alone. As our investigation was not restricted to billing data, we were able to make a more direct comparison of neuraxial and general anaesthesia types.

Implications

Unfortunately, disparities exist in the availability of neuraxial anaesthesia and anaesthesia practice utilization has been understudied.[146] An analysis from the Anaesthesia Quality Institute found that neuraxial anaesthesia was accessible disproportionately less often (31.3 *vs* 57.9%) than general anaesthesia to patients undergoing TKA.[146] Neuraxial anaesthesia, in this study by

Table 2 Studies comparing cognitive outcomes with neuraxial *vs* general anaesthesia. GA, general anaesthesia; NA, neuraxial anaesthesia; OBS, observational study; RCT, randomized controlled trial; THA, total hip arthroplasty; TKA, total knee arthroplasty; 'THA and TKA', mixed total hip and total knee outcomes data

Author (year; volume if needed)	Type of surgery	Type of neuraxial anaesthesia	Design	Cognitive domains evaluated	Assessment time	Findings
Williams-Russo (1995)[128]	TKA	Epidural	RCT	Linguistic, psychomotor skills, memory, delirium	Preoperative, 1 week and 6 months postoperative	No significant within-subject change in score for any neuropsychological test. Delirium rates did not differ. No significant differences in cognitive morbidity exist between general and epidural anaesthesia
Nielson (1990; 73)[133]	TKA	Spinal	RCT	Linguistic, general intelligence, psychomotor skills, memory, sensation, impact of illness on activity	Preoperative, 3 months postoperative	No significant differences in neuropsychological testing exist between general and epidural anaesthesia
Jones (1990)[135]	THA and TKA	Spinal	RCT	General intelligence, psychomotor skills, memory, activities of daily living, subjective complaints	Preoperative, 3 months postoperative	No significant differences in neuropsychological testing exist between general and epidural anaesthesia, except that reaction time test improved at 3 months for those patients receiving general anaesthesia ($P<0.05$)
Hughes (1988)[138]	THA	Spinal	OBS	Memory	Preoperative, 24 and 48 h and 1 week postoperative	Word recognition was worse 24 h after operation with spinal anaesthesia; the difference in memory between groups was not statistically significant at 1 week
Hole (1980)[143]	THA	Epidural	RCT	Mental status (amnesia of personal data, orientation deficits, states of confusion with or without restlessness or aggressiveness)	1–14 days and 4–10 months postoperative	Statistically significant persistent changes in mental status in patients receiving general anaesthesia; 7/31 GA patients compared with 0/29 NA patients ($P<0.01$)

Fleischut and colleagues,[146] was provided less often, and despite this, appears to be preferentially more available to older patients and those with more co-morbidities (higher ASA physical class score ≥III). Likewise, our review found disproportionate use of anaesthesia types even in randomized trials such that neuraxial anaesthesia was provided to only about one-third of the overall sample. Regardless, meta-analysis indicates equivalent results when neuraxial anaesthesia is used. Future research should focus study on patient, surgeon, and anaesthetist preferences in choosing neuraxial techniques, including use in specific subpopulations, such as the elderly and sick, where the benefits may be more apparent.

Current expert opinions on the overall importance of primary anaesthesia choice on differences in outcome are varied. The results from our review do support choosing neuraxial anaesthesia over general anaesthesia for the outcome of hospital stay. However, as with other retrospective studies, we are unable to draw a causal link between the choice of anaesthetic and the differences in outcome. Systematic reviews are also retrospective in design and inherently limited by the quality of the available literature. It is possible that our protocol may have missed eligible studies, our inclusion criteria could have been too narrow, or exclusion of articles may have affected our results. We emphasize that our review directly compared spinal or epidural anaesthesia with general anaesthesia rather than evaluating the effects of multimodal analgesia protocols that include regional anaesthesia for postoperative analgesia. As such, the present review does not elucidate possible effects of regional analgesia techniques, including neuraxial or peripheral nerve block, on perioperative outcomes. Nevertheless, the strengths of our study relate to the thoroughness of our rigorous protocol determined *a priori* with sensitivity analyses performed to test the robustness of the results. Consequently, this systematic review and meta-analysis summarizes the best available evidence to inform providers on the comparative effectiveness of neuraxial block compared with general anaesthesia for total hip and total knee arthroplasty.

Length of stay (days)

Study name		Difference in means	Lower limit	Upper limit
Jones	Spinal	1.50	–1.23	4.23
Mitchell	Epidural	–0.60	–2.98	1.78
Dalldorf	Epidural	–1.70	–3.53	0.13
Moiniche	Epidural	0.00	–4.28	4.28
Moiniche TKA	Epidural	–1.00	–5.49	3.49
Williams-Russo	Epidural	0.00	–1.17	1.17
Brinker	Epidural	–0.70	–3.50	2.10
Wulf	Epidural	–3.00	–6.29	0.29
Chu	CSE	–1.50	–1.98	–1.01
Napier	Spinal	–0.20	–0.43	0.03
Harsten	Spinal	0.00	–0.28	0.28
Harsten THA	Spinal	0.00	–0.10	0.10
		–0.39	–0.75	–0.02

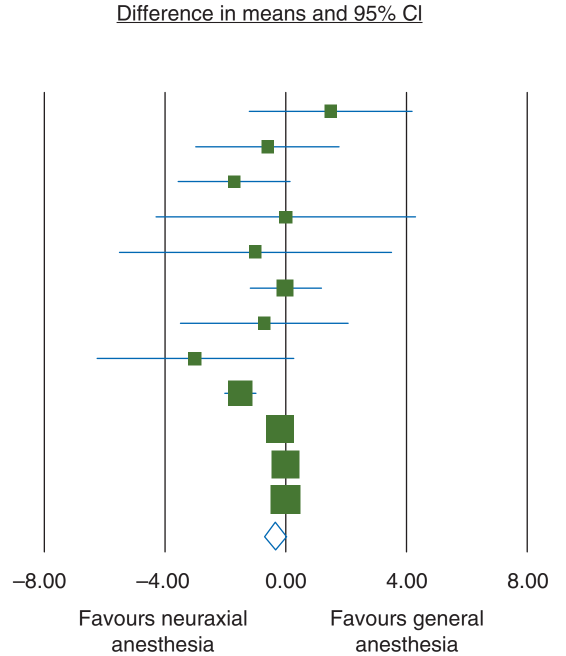

Fig 1 Forest plot comparison of neuraxial anaesthesia *vs* general anaesthesia for length of stay.

The most significant confounder or effect modifier of outcome results may still be unknown. Depth of sedation, for instance, is once such variable. The fact that depth of sedation was unknown in all studies leaves us to wonder whether a deep sedation with spinal anaesthesia compared with general anaesthesia is different enough for comparison. With a majority of our patients requesting to 'hear nothing', practitioners often 'over-' rather than 'undersedate' a patient. This may further disambiguate relationships between anaesthesia type and outcome measurement. Also, the use of an enhanced recovery programme needs to be considered in isolation because influences of multimodal analgesia apart from the choice of primary anaesthesia type still require study. Without an ability to control for confounding variables, solid conclusions comparing anaesthetic options for total hip and knee arthroplasty may never be made through retrospective study. In the end, only a valid randomized trial may control adequately for these observed inequities in the use of anaesthesia type and control for the resultant confounding effects. Our systematic review results suggest that it may be of economic interest to pursue a large, multicentre randomized trial based on the evidence of length-of-stay reduction alone. Even the reported half-day difference on a population level makes significant argument for funding such a costly trial.

We intended to report on major differences in morbidity and mortality and on variation in patient-experience outcome between neuraxial and general anaesthesia for total joint arthroplasty. However, our efforts were limited by the lack of comparative-effectiveness research evaluating most patient-important outcomes. Intermediate-term outcomes for pain, including persistent pain beyond the immediate postoperative period or conversion from acute to chronic pain syndromes, are also lacking. Scoring of subjective pain rating (at rest or with movement) and opioid consumption were the lone descriptors of pain outcomes, and for a majority of studies were used as a primary outcome to achieve individual study power calculations. Likewise, we were unable to comment directly on differences in either patient satisfaction or rehabilitation milestones (e.g. ambulation) between neuraxial and general anaesthesia because too few studies included these patient-important outcomes. Lastly, differences in long-term outcome in activities of daily living and quality of life according to type of anaesthesia are unavailable for synthesis. Considering the emerging importance of 'the patient experience' within healthcare delivery, future researchers may wish to consider including more patient-experience outcomes, intermediate and long-term outcome assessments, or both in future study designs.

Conclusion

Neuraxial anaesthesia appears equally effective with no more adverse events compared with general anaesthesia among the comparative-effectiveness research studies to date on patients undergoing total hip arthroplasty, total knee arthroplasty, or both. We did, however, find that patients receiving neuraxial anaesthesia have a shorter hospital length of stay than patients undergoing general anaesthesia. There is evidence to suggest that neuraxial anaesthesia takes no more time to perform and may even be responsible for shorter surgical durations (up to 11 min less), although these time differences have indeterminate clinical significance. Genuine uncertainty, clinical equipoise, remains when it comes to differences in patient-important outcome by anaesthesia type for total hip and knee arthroplasty amongst studies directly comparing

Surgery duration (min)

Study name		Difference in means	Lower limit	Upper limit
Hole	Epidural	−17.00	−20.03	−13.96
Modig 1981	Epidural	−14.30	−36.75	8.15
Modig 1983	Epidural	−10.00	−22.33	2.33
Modig 1986	Epidural	2.00	−8.43	12.43
Davis	Spinal	−6.00	−11.80	−0.19
Nielson	Epidural	0.00	−8.16	8.16
Jones	Spinal	−5.00	−13.45	3.45
Mitchell	Epidural	1.00	−9.07	11.07
Dalldorf	Epidural	−8.20	−15.95	−0.44
Moiniche	Epidural	−5.00	−20.91	10.91
Moiniche THA	Epidural	0.00	−9.44	9.44
Williams-Russo	Epidural	−3.00	−10.87	4.87
Brinker	Epidural	−35.00	−46.74	−23.25
Brueckner	Spinal	−12.00	−35.71	11.71
Chu	CSE	−11.00	−17.19	−4.80
Gonado	Spinal	−4.00	−23.75	15.75
Fortova THA	CSE	−10.00	−20.45	0.45
Fortova TKA	CSE	1.90	−10.58	14.38
Harsten	Spinal	5.00	1.70	8.29
Curry	Spinal	12.10	10.12	14.07
Harsten THA	Spinal	1.00	−5.68	7.68
		−5.10	−10.96	0.96

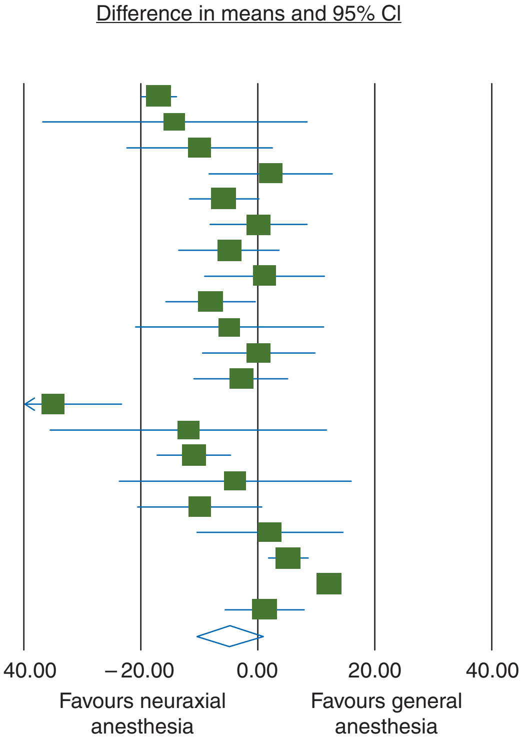

Fig 2 Forest plot comparison of neuraxial anaesthesia *vs* general anaesthesia for duration of surgery.

Table 3 Results of the meta-analysis for all outcomes of neuraxial *vs* general anaesthesia. *Chest infection included pneumonia; 'DVT, none', deep vein thrombosis without chemical antithrombotic prophylaxis; 'DVT, Rx', deep vein thrombosis with chemical antithrombotic prophylaxis; 'PE, none', pulmonary embolism without chemical antithrombotic prophylaxis; 'PE, Rx', pulmonary embolism with chemical antithrombotic prophylaxis; PONV, postoperative nausea, vomiting, or both combined; surgical site infection included superficial and deep wound infection. †Inconsistency value, marker for heterogeneity. 95% CI, 95% confidence interval; RR, relative risk ratio; WMD, weighted mean difference

Outcome*	Studies (*n*)	Patients (*n*)	WMD or RR (95% CI)	P-value	I^2 (%)†
Surgery duration (min)	21	9382	WMD −5.13 (−10.96 to 0.70)	0.08	94
Length of stay (days)	12	1240	WMD −0.40 (−0.76 to −0.03)	0.03	73
DVT, none	9	721	RR 0.51 (0.41–0.62)	0.00	0
PE, none	7	607	RR 0.36 (0.22–0.60)	0.00	0
DVT, Rx	6	949	RR 0.82 (0.65–1.04)	0.10	34
PE, Rx	4	613	RR 0.83 (0.48–1.43)	0.50	0
Mortality	7	1149	RR 0.85 (0.30–2.46)	0.77	0
PONV	5	328	RR 1.33 (0.69–2.57)	0.40	86
Surgical site infection	5	8095	RR 0.91 (0.56–1.47)	0.69	0
Chest infection	3	266	RR 0.88 (0.19–4.11)	0.87	0
Nerve palsies	2	185	RR 0.68 (0.08–5.97)	0.73	0

neuraxial with general anaesthesia. It is thus essential to conduct prospective studies on differences in patient-important perioperative outcome of anaesthetic choice for total hip and total knee arthroplasty. We call for the funding of a large, multicentre study that directly compares general anaesthesia with neuraxial anaesthesia, barring contraindications, while controlling for depth of sedation in order to inform shared decision-making between patients, anaesthetists, and surgeons.

Table 4 Recent administrative data studies comparing outcomes by neuraxial *vs* general anaesthesia. ACS NSQIP, American College of Surgeons National Surgical Quality Improvement Program; Combined, combined neuraxial and general anaesthesia; GA, general anaesthesia; MV, mechanical ventilation or ventilator-dependent patients; NA, neuraxial anaesthesia (spinal or epidural); THA, total hip arthroplasty; TKA, total knee arthroplasty; 'THA and TKA', mixed total hip and total knee outcomes data

Author (year; volume if needed)	Inclusion	Exclusion	Time frame	Findings
Chen (2015)[145]	Taiwan Longitudinal Health Insurance Database 2847 GA 2847 NA (propensity matched) Primary THA or TKA	Excluded more than the initial THA or TKA index hospitalization. Type of anaesthesia (NA or GA) unknown	1997–2010	Adjusted odds (propensity matched) were significantly lower in the NA group than in the GA group for: • hospital length of stay (days) • hospital treatment charges (dollars) • overall survival (beginning at 5 yr after surgery and throughout 14 yr follow-up period) No significant differences in short-term mortality (1–3 months) between general and epidural anaesthesia
Helwani (2015)[3]	ACS NSQIP database 5396 GA 5102 NA (propensity matched) primary or revision THA	Age <16 yr, preoperative MV or coma, use of type of anaesthesia other than NA or GA	2007–2011	Adjusted odds (propensity matched) were significantly lower in the NA group than in the GA group for: • deep surgical site infections • hospital length of stay (days) • cardiovascular complications • respiratory complications No significant differences in mortality exist between general and epidural anaesthesia
Pugely (2013)[27]	ACS NSQIP database 8022 GA 6030 NA Primary TKA	Use of type of anaesthesia other than NA or GA	2005–2010	Complication rates (adjusted odds ratio, propensity stratification, and logistic regression) were significantly lower in the NA group than in the GA group. Overall statistical differences between NA and GA were <1% in many comparisons with unknown to low clinical significance. However, observed differences were greatest in patients with more co-morbidities, suggesting that the benefits to NA may be more pronounced in sicker patients
Liu (2013)[30]	ACS NSQIP database 9167 GA 7388 NA Partial knee arthroplasty or TKA	Bilateral knee arthroplasty, pre-existing infections, MV, or contaminated wound classifications, use of type of anaesthesia other than NA or GA	2005–2010	Significantly lower incidences of 30 day postoperative complications in the NA group than in the GA group for: • pneumonia • composite systematic infection No significant differences in superficial or deep surgical wound or organ space infection, surgical wound disruptions, sepsis or septic shock, or urinary tract infection occurrences exist between general and epidural anaesthesia

Continued

Table 4 *Continued*

Author (year; volume if needed)	Inclusion	Exclusion	Time frame	Findings
Memtsoudis (2013)[4]	Premier Perspective Database 292 804 GA 40 036 NA 49 396 combined Primary THA and TKA	Type of anaesthesia unknown or missing	2006–2010	NA *vs* GA results were statistically significantly lower in the NA group than in the GA group for: • 30 day mortality • incidence rates of in-hospital systemic complications • resource utilization (blood product transfusion and MV) • hospital length of stay (days) No significant differences in gastrointestinal, acute myocardial infarction, and other non-myocardial cardiac complications exist between general and epidural anaesthesia
Chang (2010)[35]	Taiwan Longitudinal Health Insurance Database 1191 GA 1890 NA Primary THA or TKA	Excluded more than the initial THA or TKA index hospitalization	2002–2006	Adjusted odds (logistic regression) showed significantly higher odds of 30 day postoperative surgical site infections for patients receiving THA or TKA under general anaesthesia (odds ratio 2.21, 95% confidence interval 1.25–3.90; P=0.007)

Authors' contributions

Principal investigator responsible for designing the protocol, collecting data, analysing data, and preparing the manuscript: R.L.J.
Assisted with protocol development: M.H.M., C.B.M.
Executed the search strategy: P.J.E.
Collected data: S.L.K., C.M.B., C.M.D., A.K.J., C.B.M.
Analysed data: S.L.K., C.M.B., M.H.M., C.B.M.
Prepared the manuscript: S.L.K., C.M.B., P.J.E., M.H.M., C.B.M.
Approved the manuscript: S.L.K., C.M.B., C.M.D., A.K.J., P.J.E., M.H. M., C.B.M.

Supplementary material

Supplementary material is available at *British Journal of Anaesthesia* online.

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Declaration of interest

None declared.

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