BJA

British Journal of Anaesthesia, 123 (3): 269–287 (2019)

doi: 10.1016/j.bja.2019.05.042
Advance Access Publication Date: 24 July 2019
Review Article

CLINICAL PRACTICE

Anaesthetic care of patients undergoing primary hip and knee arthroplasty: consensus recommendations from the International Consensus on Anaesthesia-Related Outcomes after Surgery group (ICAROS) based on a systematic review and meta-analysis

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Accepted: 20 May 2019

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Abstract

Background: Evidence-based international expert consensus regarding anaesthetic practice in hip/knee arthroplasty surgery is needed for improved healthcare outcomes.
Methods: The International Consensus on Anaesthesia-Related Outcomes after Surgery group (ICAROS) systematic review, including randomised controlled and observational studies comparing neuraxial to general anaesthesia regarding major complications, including mortality, cardiac, pulmonary, gastrointestinal, renal, genitourinary, thromboembolic, neurological, infectious, and bleeding complications. Medline, PubMed, Embase, and Cochrane Library including Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, NHS Economic Evaluation Database, from 1946 to May 17, 2018 were queried. Meta-analysis and Grading of Recommendations Assessment, Development and Evaluation approach was utilised to assess evidence quality and to develop recommendations.
Results: The analysis of 94 studies revealed that neuraxial anaesthesia was associated with lower odds or no difference in virtually all reported complications, except for urinary retention. Excerpt of complications for neuraxial *vs* general anaesthesia in hip/knee arthroplasty, respectively: mortality odds ratio (OR): 0.67, 95% confidence interval (CI): 0.57–0.80/OR: 0.83, 95% CI: 0.60–1.15; pulmonary OR: 0.65, 95% CI: 0.52–0.80/OR: 0.69, 95% CI: 0.58–0.81; acute renal failure OR: 0.69, 95% CI: 0.59–0.81/OR: 0.73, 95% CI: 0.65–0.82; deep venous thrombosis OR: 0.52, 95% CI: 0.42–0.65/OR: 0.77, 95% CI: 0.64–0.93; infections OR: 0.73, 95% CI: 0.67–0.79/OR: 0.80, 95% CI: 0.76–0.85; and blood transfusion OR: 0.85, 95% CI: 0.82–0.89/OR: 0.84, 95% CI: 0.82–0.87.
Conclusions: Recommendation: primary neuraxial anaesthesia is preferred for knee arthroplasty, given several positive postoperative outcome benefits; evidence level: low, weak recommendation. Recommendation: neuraxial anaesthesia is recommended for hip arthroplasty given associated outcome benefits; evidence level: moderate-low, strong recommendation. Based on current evidence, the consensus group recommends neuraxial over general anaesthesia for hip/knee arthroplasty.
Trial registry number: PROSPERO CRD42018099935.

Keywords: anaesthesia, epidural; anaesthesia, general; anaesthesia, spinal; arthroplasty, replacement, hip; arthroplasty, replacement, knee; assessment, outcomes

Editor's key points

- In this state-of-the-art systematic review and analysis of the literature, a multinational expert group reached a consensus on the optimal anaesthetic approach for patients undergoing lower-limb arthroplasty.
- Considering multiple perioperative outcomes, the consensus was that neuraxial anaesthesia is the preferred anaesthetic technique (when no contraindications exist), and that this reduces the risk of most (but not all) complications.
- Neuraxial anaesthesia, which remains underutilised in many countries, may be used to improve perioperative outcomes, although limitations of the current literature may mandate the revision of these recommendations when new data become available.

Total joint arthroplasty (TJA) is amongst the most commonly performed surgical procedures in the developed world.[1] Globally, millions of patients receive total hip and knee arthroplasties every year with large projected increases as the population ages.[2] Despite the fact that TJA represents a value-based solution to end-stage arthritis of the hip and knee,[3] the procedure is associated with a moderate risk for complications. Complications affecting major organ systems have been reported to occur in approximately 8% of patients undergoing either hip or knee arthroplasty.[4] The identification of risk-modifying perioperative interventions represents an attractive target, given the large burden of resources required for the management of complications on a population-health level.

In this context, a number of recently published population-based studies have supported findings of earlier clinical trials, indicating that the type of anaesthetic technique may influence perioperative outcomes.[5,6] Whilst earlier RCTs suggested a potential benefit of neuraxial anaesthesia (NA) for outcomes, such as blood loss and thromboembolic events, these investigations were not sufficiently powered to study low-incidence outcomes, such as mortality, infectious, or cardiovascular complications.[7] Furthermore, earlier clinical trials were primarily conducted before the widespread use of chemical thromboembolic prophylaxis and contemporary blood-loss prevention practices.[8] The advent of population-based scientific approaches utilising large data sets that encompass healthcare information from hundreds of thousands of patients in actual practice environments has allowed researchers to add to the available knowledge in this field. Guided by a series of publications suggesting better outcomes with NA, a number of healthcare entities have developed policies encouraging the use of this anaesthetic type for TJA.[9]

Despite this development, definitive evidence in the form of large RCTs or pragmatic, multicentre trials is lacking. Moreover, it is questionable whether such studies will ever exist, given the challenges of feasibility and cost. As population-level data suggesting cost and outcome benefits of neuraxial approaches across a wide range of patient characteristics continue to emerge,[10–12] it is also unclear if the necessary pre-RCT condition of equipoise can exist to support an experimental trial design.

In light of these factors and given that the utilisation of NA remains low in many countries,[13] this international group of perioperative clinicians, researchers, quality experts, librarians, educators, and administrators assembled to (i) systematically investigate current published evidence to determine whether the type of anaesthesia technique can influence perioperative outcomes in patients undergoing total hip and knee arthroplasty; (ii) grade the level of evidence quality; and (iii) develop and formulate clinical practice recommendations, each with its own rating of strength.

The aim of the present consensus project was to systematically analyse and interpret current research evidence with regard to the impact of regional, and specifically neuraxial, anaesthesia in comparison to general anaesthesia (GA) on major perioperative outcomes for patients undergoing total hip or knee arthroplasties.

Methods

Consensus group

The International Consensus on Anaesthesia-Related Outcomes after Surgery (ICAROS) consensus group included 50 individuals with extensive expertise in the perioperative care of orthopaedic surgery patients. Included in this multidisciplinary group were anaesthesiologists, orthopaedic surgeons, healthcare outcomes and quality researchers, administrators, librarians, and methodologists from North America, Europe, and Oceania representing 19 nationalities, working in 10 countries. A 10-member steering committee was formed and tasked with overseeing day-to-day aspects of the project.

Study plan and healthcare question

A study plan was specified in advance, defining the healthcare questions and basic parameters, including intervention (NA) and alternative management strategy (GA), population, outcomes of interest, and inclusion and exclusion criteria. The detailed respective protocol, including analyses conducted for this project was registered on the International Prospective Register of Systematic Reviews (protocol number: CRD42018099935).[14] An institutional review board approval was not required because of the analysis of previously published data.

The healthcare questions posed to the group were:

(i) Does NA *vs* GA influence perioperative outcomes in patients undergoing total hip arthroplasty (THA)?
(ii) Does NA *vs* GA influence perioperative outcomes in patients undergoing total knee arthroplasty (TKA)?

The predefined outcomes of interest included the following major perioperative complications: mortality, cardiac (with and without myocardial infarction), pulmonary (including pneumonia), gastrointestinal, renal (including acute renal failure), genitourinary (including urinary retention and urinary tract infection), thromboembolic (DVT and pulmonary embolism [PE]), neurological (including CNS complications and stroke), infectious, and wound complications, as well as blood loss (in ml), transfusion requirements (both binary and in ml), and inpatient falls. To account for resource utilisation, the study plan also included outcomes, such as cost of care, length of hospitalisation, and admission to critical care settings. However, because of the lack of studies on cost of care, the outcome could *de facto* not be included in the quantitative meta-analysis.[15,16]

As specified in the study protocol, the consensus group will also address the impact of peripheral nerve block utilisation in patients undergoing total hip and knee arthroplasty. This healthcare question is currently being investigated and will be the focus of a subsequent analysis.

Selection criteria

Eligible studies included RCTs and observational prospective or retrospective studies in adult patients primarily undergoing elective total hip or knee arthroplasties. We included only studies directly comparing perioperative outcomes amongst patients who received NA *vs* those under GA. GA was defined as total intravenous, inhalational, or combination thereof, or when termed specifically as 'general anaesthesia' by the study authors. NA was defined as spinal, extradural, combined spinal and extradural, and caudal anaesthesia. Exclusion criteria encompassed patients under 18 yr, studies not reporting on postoperative outcomes of interest, case reports, and case series, and also studies without control groups.

Search strategy

A systematic literature search was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

The search strategy, including Medical Subject Headings (MeSH), keywords, and controlled vocabulary terms, was crafted and validated by the expert group in collaboration with two institutional librarians. Medline, PubMed, Embase, and Cochrane Library, including Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, Cochrane Central Register of Controlled Trials, Cochrane Methodology Register, Health Technology Assessment Database, and NHS Economic Evaluation Database, were queried from database inception (1946) to May 17, 2018. The search cross-referenced MeSH terms, keywords, and controlled vocabulary terms for the predefined areas of interest according to the healthcare question.

The following is the excerpt of respective search terms: arthroplasty, replacement, hip, total hip arthroplasty, total hip arthroplasties, hip prosthesis, total joint replacement, knee, knee replacement arthroplasty, knee replacement arthroplasties, total knee arthroplasty, knee prosthesis, total knee replacements, lower extremity, lower joints, anaesthesia, neuraxial, spinal, epidural, conduction, regional anaesthesia, intrathecal, peridural, and combined spinal epidural.

The full search strategy is reported in Supplementary materials and can be found in Supplementary Appendix A1. The search yielded 8985 studies. In addition to the electronic search, a manual search of previously published corresponding systematic reviews was performed for the purpose of completeness.

Study identification and data extraction

After deduplication, abstracts of 5553 studies were extracted and imported into the Covidence platform. Covidence is a web tool that provides a comprehensive framework for the complete process of a systematic literature review, including the steps of title and abstract screening, full-text review, data extraction, and quality assessment (risk of bias).[17] As required, each step was performed independently by two reviewers. In case of a disagreement, a third reviewer was consulted for resolution.

After the title and abstract screening, full-text articles of 956 studies were imported into Covidence for a detailed review and data extraction. Extracted data were categorised according to the predefined outcomes. Furthermore, within the Covidence platform, the risk of bias for each individual study was assessed and established as high, low, or unknown, according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) criteria for RCTs and observational studies.[18]

A flow chart describing the complete literature search process is depicted in Figure 1.

Quantitative analysis

To provide estimates of intervention effects for each outcome of interest,[19] RCT and observational data were pooled by meta-analysis. Review Manager software (Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) was utilised to facilitate data analysis and graphic presentation as is commonly used for preparing Cochrane reviews.[20] Summary estimates were calculated separately for each outcome (odds ratios [ORs] and 95% confidence intervals [CIs]), whilst heterogeneity utilising (I^2 statistic) was also determined in quantitative analysis. For binary outcomes, group-specific risk was presented in events per 1000, whilst the relative effect was presented in ORs. For continuous variables, risk was presented as mean difference.

The primary analysis was performed including all eligible studies for both types of surgery, respectively (n=27 for TKA; n=49 for THA). A separate analysis was performed amongst studies that reported on THA/TKA mixed populations (n=21).

Secondary analyses were performed to test the influence of combined NA+GA compared with GA on perioperative outcomes in THA and TKA separately (n=12 and n=4, respectively), and also in the mixed THA/TKA surgical cohort (n=8).

The following are the additional sensitivity analyses:

(i) Sensitivity analysis to investigate outcomes when only including evidence from RCTs (n=25 for THA; n=12 for TKA; n=2 for THA/TKA)
(ii) Sensitivity analysis to investigate outcomes when removing studies that did not explicitly exclude all revision/trauma-related surgery or bilateral arthroplasties

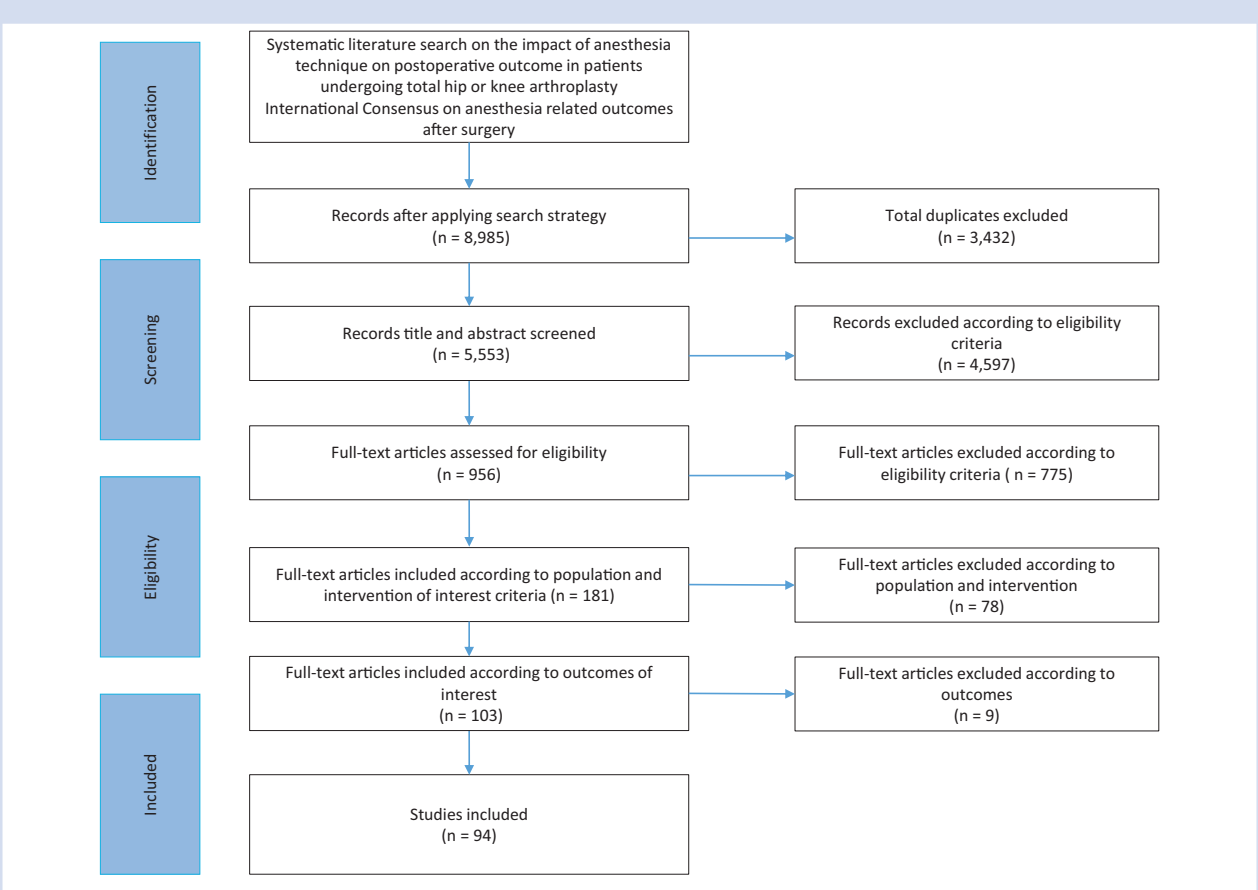

Fig 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

in their cohorts (n=46 for THA; n=25 for TKA; n=17 for THA/TKA)

(iii) Sensitivity analysis to investigate the potential impact of recent changes in utilisation of perioperative thromboembolic prophylaxis protocols on the outcome of thromboembolic complications (DVT+PE).

Qualitative analysis

To provide useful recommendations for the practice of evidence-based treatment at the point of care, we utilised the GRADE system.[15,16] This methodology for rating the quality of evidence and grading the strength of recommendations has been widely adopted for the purpose of providing high-quality summaries of research evidence in systematic reviews and for standardised guideline development. Subsequent to data collection and quantitative analysis, GRADE offers a comprehensive framework for assessing the quality of the body of evidence and for carrying out steps required for developing recommendations.[21] The concept of the certainty or quality of evidence represents the confidence in effect estimates and the extent to which they are sufficiently credible to support a particular recommendation. GRADE specifies four levels of certainty: high, moderate, low, and very low. This rating is determined for each relevant outcome by the systematic and transparent assessment of study design, limitations of the body of evidence, and special circumstances that increase the quality of evidence. Explicit criteria according to GRADE that were utilised for downgrading the quality of evidence included risk of bias according to study design and study conduct, inconsistency or heterogeneity (lack of similarity of point estimates and overlap of CIs; determination of I^2 statistic), imprecision (optimal information size for adequate power), indirectness (strength of association to the healthcare question), and publication bias (utilising funnel plots).[15] These criteria were assessed for each reported outcome of interest across informing studies. However, risk of bias was also assessed previously for each individual study, whilst in qualitative analysis the impact of risk of bias on cumulative evidence for each outcome was determined. The rationale for upgrading the quality of evidence, particularly for methodologically rigorous observational studies, includes large effect size, presence of a dose–response relationship, or when all plausible confounders or biases would decrease an apparent treatment effect.[22] Utilising the GRADEpro software (McMaster University and Evidence Prime Inc.),[23] final results, including the pooled estimates of effect and the quality of evidence, are presented in summary of findings (Tables 1 and 2 for THA and TKA, respectively).

Recommendations

The assessment of the quality of evidence, the formulation of recommendations, and the determination of their strength are separate processes. When moving from evidence to recommendations, the GRADE strategy focuses on integrating factors that are basic for the formulation of guidelines or recommendations.[19,24] Thus, critical factors beyond the quality of evidence include the balance between benefits and harms; patient values and preferences; resource considerations; and issues pertaining to feasibility, equity, and acceptability of recommendations.[19] GRADE distinguishes between strong and weak recommendations.

The balance between desirable and undesirable outcomes and the application of patients' values determine the direction of the recommendation. Moreover, these factors, along with the quality of evidence, resource implications, and clinical feasibility considerations, determine the strength or grade of recommendations.

Strong recommendations reflect a clear preference for one alternative and should apply to almost all eligible patients. Weak recommendations are appropriate when there is a close balance between desirable and undesirable consequences or alternative management strategies, uncertainty regarding the effects of the alternatives, uncertainty or variability in patient's values and preferences, or questionable cost-effectiveness. Weak recommendations usually require accessing the underlying evidence and a shared decision-making approach.[15,19,21] In certain circumstances, a strong recommendation is based on low-quality evidence.[16]

Modified Delphi process and consensus meeting

Subsequent to analyses completion, two pairs of participants were tasked with summarising the evidence, formulating conclusions, and suggesting recommendations. This work was distributed in the form of white papers for the THA and TKA cohorts separately. The white papers, together with detailed files and summary tables of analysis results, were distributed to the entire group with the request for anonymous edits and comments according to the modified Delphi process,[25] and repeated after revisions.[26]

Finally, the group met in person on December 8, 2018, in New York, NY, USA, to review the process; discuss results; and reach a consensus on conclusions, recommendations, and their strength. Approval was assessed in an anonymous vote after statements were finalised as facilitated by a group discussion.

Results

A summary of findings for patients undergoing THA and TKA, including the estimates of effect and the quality of evidence by outcomes, is found in Tables 1 and 2, respectively.

Additional in-depth quantitative and qualitative analysis data and figures are provided as Supplementary material.

Impact of the type of anaesthesia in total hip arthroplasties

Primary analyses (NA vs GA)

Amongst all hip arthroplasty patients, NA without GA was associated with fewer complications in most categories, except for urinary retention, when compared with patients who received GA (Table 3).

NA was associated with decreased odds for all-cause mortality (OR: 0.67, 95% CI: 0.57, 0.80; absolute effect: 2 per 1000 with GA *vs* 1 per 1000 with NA, 95% CI: 1, 2), pulmonary complications (OR: 0.65; 95% CI: 0.52, 0.80), pneumonia (OR: 0.69; 95% CI; 0.56, 0.84), and acute renal failure (OR: 0.69; 95% CI: 0.59, 0.81). NA was also associated with fewer thromboembolic events compared with GA, including DVT (OR: 0.52; 95% CI: 0.42, 0.65) and PE (OR: 0.63; 95% CI: 0.50–0.81). Furthermore, CNS complications (OR: 0.39; 95% CI: 0.23, 0.65), stroke (OR: 0.37; 95% CI: 0.22, 0.64), all-cause infections (OR:

Table 1 Grading of Recommendations Assessment, Development and Evaluation (GRADE) summary of findings for total hip arthroplasty (THA). CI, confidence interval; GA, general anaesthesia; MI, myocardial infarction; NA, neuraxial anaesthesia; OR, odds ratio. GRADE Working Group grades of evidence: high certainty (we are very confident that the true effect lies close to that of the estimate of the effect), moderate certainty (we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different), low certainty (our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect), and very low certainty (we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect). *The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). †Publication bias: funnel plot not symmetric. ‡Heterogeneity: widely differing estimates of effect.

Summary of findings

NA compared with GA for THA

Patient or population: THA
Setting: perioperative care
Intervention: NA
Comparison: GA

Outcomes/complications	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with GA	Risk with NA				
Mortality	2 per 1000	1 per 1000 (1–2)	OR: 0.67 (0.57–0.80)	(3 RCTs, 4 observational studies)	⊕⊕◯◯ Low	
Cardiac including MI	57 per 1000	53 per 1000 (50–58)	OR: 0.94 (0.88–1.02)	(3 RCTs, 3 observational studies)	⊕⊕◯◯ Low	
Cardiac excluding MI	48 per 1000	47 per 1000 (43–50)	OR: 0.96 (0.88–1.03)	(2 RCTs, 3 observational studies)	⊕◯◯◯ Very low†	
MI	3 per 1000	3 per 1000 (2–4)	OR: 0.94 (0.71–1.24)	(2 RCTs, 2 observational studies)	⊕⊕◯◯ Low	
Pulmonary	7 per 1000	4 per 1000 (3–5)	OR: 0.65 (0.52–0.80)	(3 observational studies)	⊕⊕⊕◯ Moderate	
Pneumonia	10 per 1000	7 per 1000 (5–8)	OR: 0.69 (0.56–0.84)	(2 RCTs, 2 observational studies)	⊕⊕⊕◯ Moderate	
Gastrointestinal	10 per 1000	8 per 1000 (7–10)	OR: 0.83 (0.67–1.02)	109 732 (1 observational study)	⊕⊕◯◯ Low	
Acute renal failure	15 per 1000	10 per 1000 (9–12)	OR: 0.69 (0.59–0.81)	(1 RCT, 5 observational studies)	⊕⊕◯◯ Low‡	
Urinary retention	111 per 1000	277 per 1000 (199–370)	OR: 3.05 (1.98–4.69)	(3 RCTs, 3 observational studies)	⊕⊕⊕◯ Moderate	
Urinary tract infection	15 per 1000	13 per 1000 (10–15)	OR: 0.86 (0.70–1.06)	(2 observational studies)	⊕⊕◯◯ Low	
DVT	15 per 1000	8 per 1000 (6–10)	OR: 0.52 (0.42–0.65)	(5 RCTs, 8 observational studies)	⊕⊕⊕◯ Moderate	
Pulmonary embolism (PE)	3 per 1000	2 per 1000 (2–2)	OR: 0.63 (0.50–0.81)	(7 RCTs, 6 observational studies)	⊕⊕◯◯ Low	
Thromboembolism (DVT+PE)	5 per 1000	3 per 1000 (3–4)	OR: 0.61 (0.53–0.71)	(15 RCTs, 16 observational studies)	⊕⊕⊕◯ Moderate	
CNS	2 per 1000	1 per 1000 (0–1)	OR: 0.39 (0.23–0.65)	(3 observational studies)	⊕⊕⊕◯ Moderate	
Stroke	2 per 1000	1 per 1000 (0–1)	OR: 0.37 (0.22–0.64)	(2 observational studies)	⊕⊕⊕◯ Moderate	
	25 per 1000	19 per 1000 (17–20)	OR: 0.73 (0.67–0.79)	(2 RCTs, 7 observational studies)		

Continued

Table 1 Continued

Summary of findings

NA compared with GA for THA

Patient or population: THA
Setting: perioperative care
Intervention: NA
Comparison: GA

Outcomes/complications	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with GA	Risk with NA				
All infections (including pneumonia and sepsis)					⊕⊕◯◯ Low	
Wound superficial infection	8 per 1000	9 per 1000 (7–12)	OR: 1.21 (0.93–1.56)	(1 RCT, 2 observational studies)	⊕⊕◯◯ Low	
Wound deep infection	7 per 1000	6 per 1000 (5–7)	OR: 0.86 (0.70–1.06)	(3 observational studies)	⊕⊕◯◯ Low	
Blood transfusion	224 per 1000	197 per 1000 (192–205)	OR: 0.85 (0.82–0.89)	(8 RCTs, 9 observational studies)	⊕◯◯◯ Very low†	
Critical care admission	2 per 1000	1 per 1000 (1–2)	OR: 0.80 (0.49–1.32)	(2 observational studies)	⊕⊕◯◯ Low	
Readmission	38 per 1000	34 per 1000 (30–39)	OR: 0.91 (0.80–1.04)	28 857 (1 observational study)	⊕⊕◯◯ Low	
Nerve injury	2 per 1000	2 per 1000 (1–3)	OR: 0.81 (0.56–1.18)	(1 RCT, 4 observational studies)	⊕⊕◯◯ Low	
Falls	16 per 1000	13 per 1000 (12–15)	OR: 0.81 (0.72–0.92)	166 871 (1 observational study)	⊕⊕◯◯ Low	
Blood loss (ml)	The mean blood loss was 0.	The mean blood loss in the intervention group was 146.12 lower (173.73 lower to 118.51 lower).	—	1546 (12 RCTs, 4 observational studies)	⊕⊕⊕◯ Moderate‡	
Length of stay (days)	The mean length of hospital stay (LOS) was 0.	The mean LOS in the intervention group was 0.16 lower (0.22 lower to 0.1 lower).	—	(1 RCT, 1 observational study)	⊕⊕◯◯ Low	
Blood transfusion (ml)	The mean blood transfusion was 0.	The mean blood transfusion in the intervention group was 187.83 lower (272.29 lower to 103.38 lower).	—	(2 RCTs, 3 observational studies)	⊕⊕◯◯ Low	

Table 2 GRADE summary of findings for total knee arthroplasty (TKA). CI, confidence interval; GA, general anaesthesia; GRADE, Grading of Recommendations Assessment, Development and Evaluation; MI, myocardial infarction; NA, neuraxial anaesthesia; OR, odds ratio. GRADE Working Group grades of evidence: high certainty (we are very confident that the true effect lies close to that of the estimate of the effect), moderate certainty (we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different), low certainty (our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect), and very low certainty (we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect). *The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). †Imprecision. ‡Risk of bias: random sequence generation.

Summary of findings:

NA compared with GA for TKA

Patient or population: TKA
Setting: perioperative care
Intervention: NA
Comparison: GA

Outcomes/complications	Absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with GA	Risk with NA				
Mortality	1 per 1000	1 per 1000 (1–1)	OR: 0.83 (0.60–1.15)	259 847 (2 RCTs, 4 observational studies)	⊕⊕◯◯ Low	
Cardiac including MI	59 per 1000	60 per 1000 (58–63)	OR: 1.03 (0.98–1.08)	261 695 (1 RCT, 6 observational studies)	⊕⊕◯◯ Low	
Cardiac excluding MI	57 per 1000	58 per 1000 (55–61)	OR: 1.02 (0.97–1.08)	259 332 (4 observational studies)	⊕⊕◯◯ Low	
MI	2 per 1000	2 per 1000 (2–3)	OR: 0.99 (0.80–1.22)	261 695 (1 RCT, 6 observational studies)	⊕⊕◯◯ Low	
Pulmonary	6 per 1000	4 per 1000 (4–5)	OR: 0.69 (0.58–0.81)	259 392 (1 RCT, 4 observational studies)	⊕⊕⊕◯ Moderate	
Pneumonia	8 per 1000	6 per 1000 (6–7)	OR: 0.82 (0.72–0.94)	275 947 (1 RCT, 5 observational studies)	⊕⊕◯◯ Low	
Gastrointestinal	7 per 1000	7 per 1000 (6–8)	OR: 0.99 (0.85–1.15)	223 108 (1 observational study)	⊕⊕◯◯ Low	
Acute renal failure	14 per 1000	10 per 1000 (9–11)	OR: 0.73 (0.65–0.82)	273 384 (5 observational studies)	⊕⊕◯◯ Low	
Urinary retention	235 per 1000	203 per 1000 (121–317)	OR: 0.83 (0.45–1.51)	277 (2 RCTs, 1 observational study)	⊕⊕⊕◯ Moderate†	
Urinary tract infection	15 per 1000	12 per 1000 (11–14)	OR: 0.82 (0.71–0.96)	52 779 (4 observational studies)	⊕⊕◯◯ Low	
DVT	36 per 1000	27 per 1000 (22–32)	OR: 0.77 (0.64–0.93)	19 756 (6 RCTs, 6 observational studies)	⊕⊕◯◯ Low	
Pulmonary embolism (PE)	6 per 1000	4 per 1000 (4–5)	OR: 0.79 (0.67–0.94)	238 066 (3 RCTs, 4 observational studies)	⊕⊕◯◯ Low	
Thromboembolism (DVT+PE)	7 per 1000	5 per 1000 (5–6)	OR: 0.77 (0.68–0.88)	257 793 (8 RCTs, 10 observational studies)	⊕⊕◯◯ Low	
CNS	1 per 1000	1 per 1000 (1–1)	OR: 0.77 (0.55–1.08)	259 594 (1 RCT, 3 observational studies)	⊕⊕◯◯ Low	
Stroke	1 per 1000	1 per 1000 (1–1)	OR: 0.70 (0.49–1.01)	259 585 (1 RCT, 4 observational studies)	⊕⊕◯◯ Low	
All infections	22 per 1000	17 per 1000 (16–18)	OR: 0.80 (0.76–0.85)			

Continued

Table 2 Continued

Summary of findings:

NA compared with GA for TKA

Patient or population: TKA
Setting: perioperative care
Intervention: NA
Comparison: GA

Outcomes/complications	Absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with GA	Risk with NA				
				571 503 (1 RCT, 12 observational studies)	⊕⊕◯◯ Low	
Wound superficial infection	6 per 1000	4 per 1000 (3–6)	OR: 0.77 (0.60–0.98)	52 839 (1 RCT, 4 observational studies)	⊕⊕◯◯ Low	
Wound deep infection	2 per 1000	2 per 1000 (1–3)	OR: 1.01 (0.60–1.69)	31 843 (3 observational studies)	⊕⊕◯◯ Low	
Blood transfusion	165 per 1000	142 per 1000 (139–146)	OR: 0.84 (0.82–0.87)	259 332 (4 observational studies)	⊕⊕◯◯ Low	
Critical care admission	1 per 1000	0 per 1000 (0–1)	OR: 0.17 (0.04–0.75)	20 936 (1 observational study)	⊕⊕⊕◯ Moderate†	
Readmission	76 per 1000	38 per 1000 (23–59)	OR: 0.48 (0.29–0.77)	1629 (1 observational study)	⊕⊕⊕◯ Moderate	
Nerve injury	4 per 1000	5 per 1000 (2–10)	OR: 1.16 (0.58–2.32)	25 243 (4 observational studies)	⊕⊕◯◯ Low	
Falls	0 per 1000	0 per 1000 (0–0)	OR: 0.00 (–0.03 to 0.03)	118 (1 observational study)	⊕⊕◯◯ Low	Not estimable
Blood loss (ml)	The mean blood loss was 0.	The mean blood loss in the intervention group was 13.54 higher (25.75 lower to 52.83 higher).	—	130 (1 RCT)	⊕⊕⊕◯ Moderate‡	
Length of stay (days)	The mean length of hospital stay (LOS) was 0.	The mean LOS in the intervention group was 0.09 lower (0.15 lower to 0.02 lower).	—	36 956 (3 RCTs, 5 observational studies)	⊕⊕◯◯ Low	

Table 3 Influence of anaesthesia type on perioperative outcomes in total hip arthroplasty. CI, confidence interval; GA, general anaesthesia; MI, myocardial infarction; NA, neuraxial anaesthesia; OR, odds ratio; PE, pulmonary embolism. All infections, including pneumonia and sepsis; pulmonary complications, excluding pneumonia; *n* (NA/GA): total number of patients with NA/GA.

Complication	NA *vs* GA					NA+GA *vs* GA				
	Studies	OR (95% CI)	*n* (NA)	*n* (GA)	*P*-value	Studies	OR (95% CI)	*n* (NA)	*n* (GA)	*P*-value
Mortality	Various authors[5,27–36]	0.67 (0.57–0.80)	60 499	148 583	<0.0001	Various authors[5,30]	0.58 (0.38–0.89)	15 331	98 230	0.014
Cardiac including MI	Various authors[5,28,32–34,37]	0.94 (0.88–1.02)	28 182	121 215	0.135	Various authors[5,38]	0.76 (0.54–1.07)	15 281	98 139	0.113
Cardiac excluding MI	Various authors[5,27,32–34]	0.96 (0.88–1.03)	32 639	133 832	0.255	Memtsoudis and colleagues[5]	1.01 (0.95–1.09)	15 261	98 122	0.689
MI	Various authors[5,33,34,37]	0.94 (0.71–1.24)	23 022	115 759	0.647	Various authors[5,38]	0.76 (0.54–1.07)	15 281	98 139	0.113
Pulmonary	Various authors[5,28,33]	0.65 (0.52–0.80)	28 029	121 058	<0.0001	Memtsoudis and colleagues[5]	0.66 (0.52–0.84)	15 261	98 122	0.001
Pneumonia	Various authors[5,33,34,37]	0.69 (0.56–0.84)	23 022	115 759	<0.0001	Memtsoudis and colleagues[5]	0.88 (0.74–1.05)	15 261	98 122	0.165
Gastrointestinal	Memtsoudis and colleagues[5]	0.83 (0.67–1.02)	11 610	98 122	0.078	Memtsoudis and colleagues[5]	0.79 (0.65–0.95)	15 261	98 122	0.013
Acute renal failure	Various authors[5,33,37,39,40]	0.69 (0.59–0.81)	34 366	133 687	<0.0001	Memtsoudis and colleagues[5]	0.75 (0.65–0.86)	15 261	98 122	<0.0001
Urinary retention	Various authors[34,39–43]	3.05 (1.98–4.69)	252	628	<0.0001	Various authors[44,45]	1.91 (1.05–3.48)	123	163	0.035
Urinary tract infection	Various authors[30,33]	0.86 (0.70–1.06)	11 334	17 648	0.164	Brinker and colleagues[30]	1.14 (0.43–2.99)	70	108	0.793
DVT	Various authors[30,33,36,41,43,46–53]	0.52 (0.42–0.65)	15 688	20 477	<0.0001	Various authors[30,38]	0.81 (0.17–3.89)	90	125	0.795
PE	Various authors[5,33–37,41,48–53]	0.63 (0.50–0.81)	34 875	123 934	<0.0001	Memtsoudis and colleagues[5]	0.68 (0.46–1.03)	15 261	98 122	0.066
DVT+PE	Various authors[5,30,33–37,41,43,46–57]	0.61 (0.53–0.71)	59 573	157 731	<0.0001	Various authors[5,30,38]	0.69 (0.47–1.02)	15 351	98 247	0.065
CNS	Various authors[5,33,58]	0.39 (0.23–0.65)	22 977	115 712	<0.0001	Various authors[5,34,59]	0.68 (0.42–1.09)	15 306	98 162	0.112
Stroke	Various authors[5,33]	0.37 (0.22–0.64)	22 927	115 662	<0.0001	Memtsoudis and colleagues[5]	0.71 (0.44–1.16)	15 261	98 122	0.176
All infections	Various authors[5,28,30,33,34,37]	0.73 (0.67–0.79)	62 385	254 465	<0.0001	Various authors[5,30]	0.86 (0.79–0.92)	30 592	196 352	<0.0001
Wound (superficial)	Various authors[30,33,34]	1.21 (0.93–1.56)	11 363	17 679	0.152	Brinker and colleagues[30]	1.56 (0.21–11.33)	70	108	0.661
Wound (deep)	Various authors[28,33,54]	0.86 (0.70–1.06)	24 603	35 688	0.159					
Blood transfusion	Various authors[5,30,33,34,37,41,43,60–69]	0.85 (0.82–0.89)	25 033	117 443	<0.0001	Various authors[5,30,38,61]	0.78 (0.75–0.82)	15 421	98 317	<0.0001
Critical care	Various authors[27,33]	0.80 (0.49–1.32)	20 690	33 125	0.387					
Readmission	Haughom and colleagues[33]	0.91 (0.80–1.04)	11 317	17 540	0.161					
Nerve injury	Various authors[30,33,34,69]	0.81 (0.56–1.18)	19 842	27 106	0.278	Brinker and colleagues[30]	0.30 (0.01–6.39)	70	108	0.442
Falls	Kendrišić and colleagues[71]	0.81 (0.72–0.92)	20 985	145 886	0.001					
Blood loss (ml)	Various authors[36,43,50–52,60–62,66,68,72–77]	−146.12 (−173.73 to −118.51)	902	644	<0.0001	Various authors[38,59,61,74,77–79]	−20.13 (−50.10 to 9.83)	226	216	0.188
Length of stay (days)	Various authors[28,80]	−0.16 (−0.22 to −0.10)	5146	5442	<0.0001	Benson and colleagues[59]	−6.00 (−14.77 to 2.77)	16	9	0.18
Blood transfusion (ml)	Various authors[43,50,51,60,66]	−187.83 (−272.29 to −103.38)	310	195	<0.0001					

0.73; 95% CI: 0.67, 0.79), blood transfusion requirements (OR: 0.85; 95% CI: 0.82, 0.89), and postoperative falls (OR: 0.81; 95% CI: 0.72, 0.92) were reduced with NA *vs* GA.

We did not identify any differences in cardiac, gastrointestinal, or wound complications; critical care admissions; readmissions; and nerve injuries between NA and GA amongst hip arthroplasty patients.

Impact of the type of anaesthesia in total knee arthroplasties

Primary analyses (NA vs GA)

Amongst patients undergoing total knee arthroplasties, the utilisation of NA in comparison to GA was associated with improved outcomes with regard to multiple complications (Table 4). Amongst patients who received NA, reduced odds were observed for pulmonary complications (OR: 0.69; 95% CI: 0.58–0.81), pneumonia (OR: 0.82; 95% CI: 0.72, 0.94), acute renal failure (OR: 0.73; 95% CI: 0.65, 0.82), urinary tract infection (OR: 0.82; 95% CI: 0.71, 0.96), DVT (OR: 0.77; 95% CI: 0.64, 0.93), PE (OR: 0.79; 95% CI: 0.67, 0.94), all-cause infections (OR: 0.80; 95% CI: 0.76, 0.85), superficial wound infections (OR: 0.77; 95% CI: 0.60, 0.98), blood transfusions (OR: 0.84; 95% CI: 0.82, 0.87), critical care admissions (OR: 0.17; 95% CI: 0.04, 0.75), and readmissions (OR: 0.48; 95% CI: 0.29, 0.77).

Impact of the type of anaesthesia in studies reporting outcomes in mixed total knee/hip arthroplasties

Primary analyses (NA vs GA)

The results are presented in Supplementary Table A5. Overall, improved outcomes were seen in association with the use of NA *vs* GA in this cohort of studies.

Secondary analyses (NA+GA vs GA)

In a secondary analysis, we compared the utilisation of combined NA+GA *vs* GA only to assess the impact on studied outcomes in patients undergoing THA and TKA (Tables 3 and 4, and Supplementary Table A5). The output indicated a similar trend as observed in the NA *vs* GA analysis. The outcomes with significantly reduced odds for combined NA+GA *vs* GA included mortality, pulmonary complications, gastrointestinal complications, acute renal failure, all-cause infections, and blood transfusions, whilst the odds for urinary retention were increased as seen in the NA *vs* GA comparison.

Sensitivity analyses

Randomised clinical trials only

The first sensitivity analysis focused on RCTs only and verified that NA was associated with fewer thromboembolic events than GA (Tables 5 and 6, and Supplementary Table A6). NA patients also had less blood loss and received lower blood transfusion volumes (Table 5). This analysis did not present statistically significant differences in other complications, which may be attributable to the much smaller sample size in RCTs compared with population-based analyses.

Exclusion of studies likely containing a minority of revision/trauma surgery or bilateral arthroplasty cases

Our primary analysis included all patients from all candidate studies, which encompassed RCTs and observational studies. In some of these investigations, revision/trauma-related arthroplasty patients could not be excluded with certainty. To test the potential effect that this patient population may have on outcomes, we excluded them in a sensitivity analysis. The relationship between anaesthetic type and outcomes when excluding revision/trauma arthroplasty was nearly identical compared with the primary inclusive analysis (Supplementary Tables A2–A4).

Sensitivity analysis: thromboembolic complications (DVT+PE)

To account for potential prognostic imbalance as a result of recent emerging differences in perioperative care with regard to the implementation of thrombosis prophylaxis in recent years, we performed a further sensitivity analysis. Estimates of intervention effects were established for the outcome of thromboembolic complications (DVT+PE) when including all eligible studies, when excluding studies without thrombosis prophylaxis, and when excluding studies published before 1995.

NA was associated with a 24% reduction in thromboembolic events when including all studies (n=37; OR: 0.76; 95% CI: 0.71, 0.83), a 14% reduction when excluding studies lacking thromboembolic prophylaxis (n=9; OR: 0.86; 95% CI: 0.79, 0.92), and a 16% reduction when excluding studies before 1995 (n=14; OR: 0.84; 95% CI: 0.78, 0.90).

Discussion

Recommendations and comments

Does type of anaesthesia influence perioperative outcomes in THA?

The utilisation of NA over GA for THA was associated with lower complication odds for most studied outcomes. The utilisation of combined NA and GA was also associated with better perioperative outcomes compared with GA alone, although the magnitude and diversity of benefits were decreased compared with using NA alone (Tables 1 and 3).

(i) Level of evidence: low to moderate
(ii) Recommendation: NA is recommended for primary unilateral THA when there is no significant contraindication or special circumstance to preclude its use.
(iii) Strength of recommendation: strong
(iv) Rationale: Based on the findings of our analysis and the grading of evidence, the group reached a unanimous decision on the aforementioned recommendation. The results of all analyses showed improvement in outcomes with NA compared with GA in most cases, or no impact, with the sole exception of urinary retention, albeit the latter is a known, expected side-effect of NA.[101]

The level of evidence underlying the individual analyses by outcome was low to moderate. When considering the factors integrated by the GRADE approach for the development of recommendations,[19] the majority of the group (n=33 out of 43 votes) determined it to be overall strong.

The latter conclusion was based on the observations that: (i) the evidence was largely in favour of the intervention, (ii)

Table 4 Influence of anaesthesia type on perioperative outcomes in total knee arthroplasty. CI, confidence interval; GA, general anaesthesia; MI, myocardial infarction; NA, neuraxial anaesthesia; OR, odds ratio; PE, pulmonary embolism. All infections, including pneumonia and sepsis; pulmonary complications, excluding pneumonia; *n* (NA/GA): total number of patients with NA/GA.

Complication	NA *vs* GA					NA+GA *vs* GA				
	Studies	OR (95% CI)	*n* (NA)	*n* (GA)	*P*-value	Studies	OR (95% CI)	*n* (NA)	*n* (GA)	*P*-value
Mortality	Various authors[5,6,54,57,81,82]	0.83 (0.60–1.15)	43 653	216 194	0.261	Memtsoudis and colleagues[5]	0.73 (0.51–1.05)	34 135	194 682	0.094
Cardiac including MI	Various authors[5,6,54,57,81,83,84]	1.03 (0.98–1.08)	44 831	216 864	0.324	Various authors[5,85]	1.07 (0.85–1.34)	34 165	194 715	0.553
Cardiac excluding MI	Various authors[5,6,54,57]	1.02 (0.97–1.08)	43 386	215 946	0.349	Memtsoudis and colleagues[5]	1.07 (1.02–1.12)	34 135	194 682	0.007
MI	Various authors[5,6,54,57,81,83,84]	0.99 (0.80–1.22)	44 831	216 864	0.896	Various authors[5,85]	1.07 (0.85–1.34)	34 165	194 715	0.553
Pulmonary	Various authors[5,6,54,57,86]	0.69 (0.58–0.81)	43 416	215 976	<0.0001	Various authors[5,85]	0.89 (0.77–1.03)	34 165	194 715	0.132
Pneumonia	Various authors[5,6,54,57,86,87]	0.82 (0.72–0.94)	50 804	225 143	0.003	Memtsoudis and colleagues[5]	1.02 (0.90–1.16)	34 135	194 682	0.727
Gastrointestinal	Memtsoudis and colleagues[5]	0.99 (0.85–1.15)	28 426	194 682	0.855	Various authors[5,85]	1.07 (0.93–1.22)	34 165	194 715	0.344
Acute renal failure	Various authors[5,6,54,57]	0.73 (0.65–0.82)	49 416	223 968	<0.0001	Memtsoudis and colleagues[5]	0.96 (0.87–1.05)	34 135	194 682	0.377
Urinary retention	Various authors[32,86,88]	0.83 (0.45–1.51)	111	166	0.537					
Urinary tract infection	Various authors[6,54,57,87]	0.82 (0.71–0.96)	22 348	30 431	0.011					
DVT	Various authors[6,47,56,82,83,89–95]	0.77 (0.64–0.93)	9466	10 222	0.005	[85]	0.53 (0.05–6.21)	30	33	0.617
PE	Various authors[5,6,42,82,90,92,94]	0.79 (0.67–0.94)	34 890	203 176	0.007	Memtsoudis and colleagues[5]	0.78 (0.66–0.93)	34 135	194 682	0.006
DVT+PE	Various authors[5,6,42,47,56,82,83,89,90,92–95]	0.77 (0.68–0.88)	44 373	213 420	<0.0001	Various authors[5,85]	0.78 (0.66–0.93)	34 165	194 715	0.005
CNS	Various authors[5,6,54,57,81]	0.77 (0.55–1.08)	43 520	216 074	0.133	Various authors[5,85,96]	1.03 (0.75–1.43)	34 270	194 823	0.84
Stroke	Various authors[5,6,54,57,82]	0.70 (0.49–1.01)	43 519	216 066	0.059	Various authors[5,85]	1.06 (0.76–1.49)	34 165	194 715	0.72
All infections	Various authors[5,6,54,57,86,87]	0.80 (0.76–0.85)	109 150	462 353	<0.0001	Memtsoudis and colleagues[5]	0.98 (0.93–1.03)	68 270	389 364	0.464
Wound (superficial)	Various authors[6,54,57,86,87]	0.77 (0.60–0.98)	22 378	30 461	0.034					
Wound (deep)	Various authors[6,57,87]	1.01 (0.60–1.69)	14 164	17 679	0.982					
Blood transfusion	Various authors[5,6,54,57]	0.84 (0.82–0.87)	43 386	215 946	<0.0001	Memtsoudis and colleagues[5]	1.02 (0.99–1.05)	34 135	194 682	0.197
Critical care	Basques and colleagues[54]	0.17 (0.04–0.75)	8184	12 752	0.019					
Readmission	Belmont and colleagues[97]	0.48 (0.29–0.77)	586	1043	0.003					
Nerve injury	Various authors[6,57,70]	1.16 (0.58–2.32)	7304	17 939	0.665					
Falls	Harsten and colleagues[32]	0.00 (0.00–0.00)	58	60	<0.0001	Kendrišić and colleagues[71]	0.91 (0.81–1.02)	24 699	145 886	0.092
Blood loss (ml)	Zhou and colleagues[95]	13.54 (−25.75 to 52.83)	63	67	0.499	Kudoh and colleagues[96]	13.10 (−18.99 to 45.19)	75	75	0.424
Length of stay (days)	Various authors[6,54,57,81,82,98–100]	−0.09 (−0.15 to −0.02)	15 326	21 630	0.009					

Table 5 Subgroup RCTs: influence of anaesthesia type on perioperative outcomes in total hip arthroplasty. CI, confidence interval; GA, general anaesthesia; MI, myocardial infarction; NA, neuraxial anaesthesia; OR, odds ratio; PE, pulmonary embolism. All infections, including pneumonia and sepsis; pulmonary complications, excluding pneumonia; *n* (NA/GA): total number of patients with NA/GA.

Complication	NA *vs* GA					NA+GA *vs* GA				
	Studies	OR (95% CI)	*n* (NA)	*n* (GA)	*P*-value	Studies	OR (95% CI)	*n* (NA)	*n* (GA)	*P*-value
Mortality	Various authors[32,34,36]	0.34 (0.01–8.80)	135	137	0.519					
Cardiac including MI	Various authors[32,34,37]	0.82 (0.19–3.48)	153	157	0.783	Dauphin and colleagues[38]	1.78 (0.15–21.51)	20	17	0.651
Cardiac excluding MI	Various authors[32,34]	0.65 (0.08–5.38)	87	91	0.687					
MI	Various authors[34,37]	0.75 (0.14–4.07)	95	97	0.736	Dauphin and colleagues[38]	1.78 (0.15–21.51)	20	17	0.651
Pneumonia	Various authors[34,37]	1.03 (0.14–7.53)	95	97	0.973					
Acute renal failure	Liang and colleagues[37]	0.33 (0.01–8.21)	66	66	0.498					
Urinary retention	Various authors[34,41,42]	1.65 (0.89–3.05)	158	162	0.113					
DVT	Various authors[36,41,50,51]	0.33 (0.20–0.55)	177	174	<0.0001	Dauphin and colleagues[38]	0.81 (0.17–3.89)	20	17	0.795
PE	Various authors[34,36,37,41,50,51]	0.40 (0.20–0.79)	255	257	0.008					
DVT+PE	Various authors[34,36,37,41,50,51,55,56]	0.43 (0.30–0.63)	482	479	<0.0001	Dauphin and colleagues[38]	0.81 (0.17–3.89)	20	17	0.795
CNS						Various authors[34,59]	0.26 (0.03–2.28)	45	40	0.222
All infections	Various authors[34,37]	1.03 (0.14–7.53)	95	97	0.973					
Wound (superficial)	34	0.33 (0.03–3.40)	29	31	0.354					
Blood transfusion	Various authors[34,37,41,61–63,67,68]	0.43 (0.28–0.65)	357	364	<0.0001	Various authors[38,61]	0.50 (0.24–1.05)	90	87	0.067
Nerve injury	Hole and colleagues[34]	0.34 (0.01–8.80)	29	31	0.519					
Blood loss (ml)	Various authors[36,50,51,61,62,68,72–75,77]	−121.82 (−152.22 to −91.42)	334	335	<0.0001	Various authors[38,59,61,74,77–79]	−20.13 (−50.10 to 9.83)	226	216	0.188
Length of stay (days)	Williams-Russo and colleagues[80]	−3.00 (−6.25 to 0.25)	44	46	0.07	Benson and colleagues[59]	−6.00 (−14.77 to 2.77)	16	9	0.18
Blood transfusion (ml)	Various authors[50,51]	−542.64 (−771.95 to −313.32)	45	45	<0.0001					

Table 6 Subgroup RCTs: influence of anaesthesia type on perioperative outcomes in total knee arthroplasty. CI, confidence interval; GA, general anaesthesia; MI, myocardial infarction; NA, neuraxial anaesthesia; OR, odds ratio; PE, pulmonary embolism. All infections, including pneumonia and sepsis; pulmonary complications, excluding pneumonia; *n* (NA/GA): total number of patients with NA/GA.

Complication	NA *vs* GA					NA+GA *vs* GA				
	Studies	OR (95% CI)	*n* (NA)	*n* (GA)	*P*-value	Studies	OR (95% CI)	*n* (NA)	*n* (GA)	*P*-value
Mortality	Various authors[81,82]	0.93 (0.13–6.64)	267	248	0.941					
Cardiac including MI	Williams-Russo and colleagues[81]	1.28 (0.28–5.84)	134	128	0.748					
MI	Williams-Russo and colleagues[81]	0.95 (0.19–4.82)	134	128	0.955					
Pulmonary	Chu and colleagues[86]	0.48 (0.04–5.63)	30	30	0.561					
Pneumonia	Chu and colleagues[86]	0.19 (0.01–4.06)	30	30	0.286					
Urinary retention	Various authors[32,86]	0.86 (0.47–1.59)	88	90	0.628					
DVT	Various authors[56,82,89–91,95]	0.82 (0.56–1.18)	256	327	0.283					
PE	Various authors[42,82,90]	1.17 (0.45–3.03)	163	149	0.748					
DVT+PE	Various authors[42,56,82,89,90,95]	0.78 (0.56–1.10)	436	498	0.157					
CNS	Williams-Russo and colleagues[81]	1.31 (0.59–2.89)	134	128	0.503	Kudoh and colleagues[96]	0.74 (0.16–3.42)	75	75	0.7
Stroke	Williams-Russo and colleagues[82]	2.73 (0.11–67.61)	133	120	0.54					
All infections	Chu and colleagues[86]	0.19 (0.01–4.06)	30	30	0.286					
Wound (superficial)	Chu and colleagues[86]	0.48 (0.04–5.63)	30	30	0.561					
Falls	Harsten and colleagues[32]	0.00 (0.00–0.00)	58	60	<0.0001					
Blood loss (ml)	Zhou and colleagues[95]	13.54 (−25.75 to 52.83)	63	67	0.499	Kudoh and colleagues[96]	13.10 (−18.99 to 45.19)	75	75	0.424
Length of stay (days)	Various authors[81,82,98]	−0.14 (−0.56 to 0.28)	308	295	0.512					

the desirable effects of the intervention outweigh the undesirable ones, (iii) the intervention was associated with neutral to beneficial resource utilisation, (iv) the intervention is acceptable to stakeholders, and (v) the intervention is feasible.

Does type of anaesthesia influence perioperative outcomes in TKA?

Compared with GA, NA was associated with fewer complications or no difference in complications in all reported outcomes after TKA (Tables 2 and 4).

NA was associated with lower odds of thromboembolic events and blood transfusion, and also infectious complications, including pneumonia and all-cause infections. Furthermore, lower odds for acute renal failure and respiratory complications were found amongst patients receiving NA for TKA. With regard to outcomes of resource utilisation, NA was associated with fewer admissions to critical care units, lower rates of hospital readmissions, and a shorter length of hospital stay (mean difference: −0.08; 95% CI: −0.15 to 0.01 days).

Our analysis failed to find any significant differences in the odds for mortality, composite CNS complications, or stroke. There was also no effect of anaesthetic type on cardiac or gastrointestinal complications.

(i) Level of evidence: low
(ii) Recommendation: Provided no contraindication, a primary neuraxial anaesthetic technique is preferred for TKA, given several positive benefits of NA on important post-TKA outcomes, together with no evidence of worse outcomes.
(iii) Strength of recommendation: weak
(iv) Rationale: Based on the findings of our analysis and the grading of the level of evidence, the group reached a majority (n=42 out of 43 votes) decision on the aforementioned recommendation. The results of all analyses showed improvement with NA for outcomes compared with GA for some but not all outcomes. The effect was smaller than that seen in the larger THA cohort.

The level of evidence underlying the individual analyses by outcome was low.

When considering the factors integrated by the GRADE approach for the development of recommendations, the majority of the group (n=31 out of 43 votes) determined it to be overall weak.

The latter conclusion was based on the observations that the evidence was in favour of the intervention, but to a lesser extent than that observed in the THA cohort. However, the group believed that the desirable effects of the intervention outweigh the undesirable effects, and that the intervention was associated with beneficial resource utilisation. Further, the intervention is acceptable to stakeholders and is clinically feasible.

Comments

Several limitations to our consensus approach have to be considered. Perioperative care has evolved significantly over years and decades, including surgical techniques. This may be a source of unmeasured or unknown confounding that is not adequately balanced by randomisation.

Further, the group discussed extensively the lack of detailed information regarding the potentially wide variability in the conduct of GA and the potential influence of GA technique on outcomes. Whilst NA as a technique may vary to certain degrees (type of local anaesthetic used, use of spinal *vs* extradural *vs* combined spinal/extradural, and level of neuraxial block), the group agreed that the conduct of the technique and its major characteristics are standardised and have been in place for many decades. In contrast, the conduct of GA has evolved significantly over time with changes in pharmacological agents (both intravenous and inhalational), assistive technology (target-controlled infusion), airway devices, monitoring, and ventilation equipment, and also care strategies.

Therefore, it seems appropriate to re-evaluate the differential impact of modern general anaesthetic techniques in this context once such granular information becomes reliably available in the future.

Additional factors that may influence outcomes include the use of procedural sedation and its depth, which may, in practice, approach levels seen with GA.[102] However, at this time, such an analysis is not feasible because of the lack of adequate data. In addition, the inherent anaesthetic-related risks of each technique (GA or NA) were not considered in this analysis, but are rare for either approach.

In the last decade, advances in regional anaesthesia, such as the utilisation of ultrasound-guided peripheral nerve block techniques, have gained significant popularity in the clinical setting. Thus, our research group is currently reviewing evidence regarding the perioperative impact of peripheral nerve blocks. However, given the numerous options and combinations of various anaesthesia-related procedures, further studies are needed to address specifically the impact of peripheral nerve blocks as adjuncts to GA when compared with NA.

Further, the group discussed what future research would be needed to derive definitive data on the questions addressed in this consensus article. Whilst large, multicentre RCTs or pragmatic trials may provide definitive evidence, they are not and may never be available. Future studies are indicated to better evaluate the mechanisms by which the observed beneficial effects associated with NA are realised. The group acknowledged that, whilst a plausible mechanism for improved outcomes is likely related to NA-associated reductions in stress response, the body of evidence establishing this link is scarce.[103] Further, it was determined that future research is needed to elucidate the relationship between anaesthetic type and outcomes in the ever-increasing commonality of high-risk patient populations presenting for joint arthroplasty. Moreover, comparative literature for some complications, such as postoperative cognitive dysfunction, is rare, and these topics require more scientific investigations to allow robust analysis and conclusions in the context of anaesthesia practice.[58,81] Finally, the group commented that, given the potential benefits and relative underutilisation of NA, research with focus on identification and amelioration of barriers to the widespread implementation of NA techniques is needed.

Executive summary

Does type of anaesthesia influence perioperative outcomes in THA?

The utilisation of NA over GA for THA was associated with lower complication risk for most studied outcomes. Furthermore, the utilisation of combined NA and GA was also associated with better perioperative outcomes compared with GA alone, although the magnitude and diversity of benefits were decreased compared with using NA alone (Tables 1 and 3).

(i) Level of evidence: low to moderate
(ii) Recommendation: NA is recommended for primary unilateral THA when there is no significant contraindication or special circumstance to preclude its use.
(iii) Strength of recommendation: strong

Does type of anaesthesia influence perioperative outcomes in TKA?

(i) Level of evidence: low
(ii) Recommendation: Provided no contraindication, a primary neuraxial anaesthetic technique is preferred for TKA, given several positive benefits of NA on important post-TKA outcomes, together with no evidence of worse outcomes.
(iii) Strength of recommendation: weak

Authors' contributions

Study conception: SGM
Study design/planning/execution: SGM, NES, CC, JB, JL, EMS, ERM, RLJ, MJH, GG
Reviewing/expanding study plan: EA, MJB, AB, JDA, NE, PEG, PG, AGDV, EG, PK, SLK, PL'H, CHML, CBM, DM, AM, JMN, MP, JPa, LP, JPo, LAP, BDS, OS, ECS, ERV, EGV-V, CW, JTYD
Literature search: CC, RG, BJ, LP, BHL, PW, MB, GG, SJK, LB, DW, GH
Data extraction: JB, DB, CC, BHL, PW, MB, GG, SJK, LB, DW, GH, JL, SGM
Data analysis: CC, SGM, NES, JPo, JB, JL, ES, ERM, RLJ, MJH, GG
Reviewing results of data analysis: EA, MJB, AB, JDA, NE, PEG, PG, AGDV, EG, PK, SLK, PL'H, CHML, CBM, DM, AM, JMN, MP, JPa, LP, JPo, LAP, BDS, OS, ECS, ERV, EGV-V, CLW, JTYD
Interpreting results: CC, SGM, NES, JPo, JB, JL, ES, ERM, RLJ, MJH, GG
Reviewing/editing white papers: EA, MJB, AB, JDA, NE, PEG, PG, AGDV, EG, PK, SLK, PL'H, CHML, CBM, DM, AM, JMN, MP, JPa, LP, JPo, LAP, BDS, OS, ECS, ERV, EGV-V, CLW, JTYD
Writing paper: SGM, CC, NES, JB, JL, EMS, ERM, RLJ, MJH, GG
All authors reviewed, commented on, and approved the study plan; reviewed the data and the analysis results; commented on and gave feedback to the interpretation of results, including quantitative and qualitative analyses; and convened in person or were given the opportunity to join remotely in an all-day consensus conference held on December 8, 2018 at the Hospital for Special Surgery, New York, NY, USA, where the entire analysis steps and results were presented, and the GRADE approach was utilised for the interpretation of the body of evidence and the formation of recommendations.
SGM had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declarations of interest

SGM is a director of the boards of the American Society of Regional Anesthesia and Pain Medicine and the president of the Society of Anesthesia and Sleep Medicine. He is a one-time consultant for Teikoku, Sandoz Inc. and a consultant/investor for HATH. Furthermore, SGM has a US Patent application pending for a Multicatheter Infusion System (US-2017-0361063). He is the owner of SGM Consulting, LLC, and co-owner of FC Monmouth, LLC. None of these relations influenced the conduct of the present project. ERM is a director of the board of the American Society of Regional Anesthesia and Pain Medicine and an officer of the California Society of Anesthesiologists. ERM is also an employee of the United States government, and his contribution to this project is supported with resources based at the Veterans Affairs (VA) Palo Alto Health Care System (Palo Alto, CA, USA). The contents do not represent the views of VA or the United States Government. NE is a board member of the American Society of Regional Anesthesia and Pain Medicine. NE is also a consultant for Foundry Therapeutics, but declared no conflict of interest. ECS reports consulting fees from Egalet, Inc. and the Mission Lisa foundation and acknowledges funding from the National Institute on Drug Abuse (K08DA042314). which are unrelated to this work. The other authors declare that they have no conflicts of interest.

Funding

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Disclaimer

The conclusions and recommendations resulting from this project are not intended to establish practice guidelines or standards, nor can they—if followed—guarantee successful outcomes. Many adequate reasons exist why a clinician or patient may deviate from the recommendations in this article, including, but not limited to, medical circumstances, individual patient and clinician preferences, and the availability of resources. The present conclusions and recommendations are based on the currently available literature, established in a systematic review process; thus, reassessment and revisions are required as new or different evidence emerges.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2019.05.042.

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Handling editor: J.G. Hardman