BJA

British Journal of Anaesthesia, 133 (2): 416–423 (2024)

doi: 10.1016/j.bja.2024.04.051
Advance Access Publication Date: 10 June 2024
Clinical Investigation

REGIONAL ANAESTHESIA

Impact of spinal *versus* general anaesthesia on perioperative obstructive sleep apnoea severity in patients undergoing hip arthroplasty: a *post hoc* analysis of two randomised controlled trials

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Abstract

Background: Recommendations suggest favouring regional over general anaesthesia to reduce impact on postoperative sleep apnoea severity, but there is currently no evidence to support this. We compared the impact of general *vs* spinal anaesthesia on postoperative sleep apnoea severity and assessed the evolution of sleep apnoea severity up to the third postoperative night.

Methods: This *post hoc* analysis used pooled data from two previous randomised controlled trials in patients undergoing total hip arthroplasty under general or spinal anaesthesia (n=96), without performing a preliminary power analysis. All participants underwent respiratory polygraphy before surgery and on the first and third postoperative nights. The primary outcomes were the supine apnoea–hypopnea index on the first postoperative night and the evolution of the supine apnoea–hypopnea index up to the third postoperative night. Secondary outcomes included the oxygen desaturation index on the first and third postoperative nights.

Results: In the general and spinal anaesthesia groups, mean (95% confidence interval) values for the supine apnoea–hypopnoea index on the first postoperative night were 20 (16–25) and 21 (16–26) events h^{-1} (P=0.82), respectively; corresponding values on the third postoperative night were 34 (22–45) and 35 (20–49) events h^{-1} (P=0.91). The generalised estimating equations model showed a significant time effect. Secondary outcomes were similar in the two groups.

Conclusions: Use of spinal anaesthesia compared with general anaesthesia was not associated with a reduction in postoperative sleep apnoea severity, which was worse on the third postoperative night.

Clinical trial registration: NCT02717780 and NCT02566226.

Keywords: apnoea–hypopnea index; general anaesthesia; hip arthroplasty; obstructive sleep apnoea; perioperative medicine; spinal anaesthesia

Received: 14 October 2023; **Accepted:** 25 April 2024

Editor's key points

- Current recommendations suggest use of regional over general anaesthesia to reduce impact on postoperative sleep apnoea severity, but evidence to support this is lacking.
- The authors compared the impact of general *vs* spinal anaesthesia on postoperative sleep apnoea severity using sleep polygraphy in patients undergoing hip arthroplasty.
- Use of spinal anaesthesia compared with general anaesthesia was not associated with lower postoperative sleep apnoea severity, which was worse on the third postoperative night.
- These results do not support current recommendations for perioperative management of patients with sleep apnoea syndrome that favour use of regional anaesthesia and continuous monitoring on the first postoperative night.
- Additional research is needed to extend these findings to other procedures and to determine whether use of peripheral nerve blocks might improve sleep outcomes compared with surgery performed using general anaesthesia.

Individuals with sleep apnoea syndrome have increased morbidity after surgery.[1,2] For example, a retrospective analysis of more than 349,000 patients undergoing hip arthroplasty concluded that sleep apnoea syndrome was associated with higher rates of cardiovascular and pulmonary complications, hospital length of stay, and readmission.[1] Therefore, current recommendations suggest the use of short-acting agents rather than standard agents when providing general anaesthesia to individuals with sleep apnoea[3,4] or to carefully monitor patients for at least 24 h after the administration of contemporary doses of intrathecal morphine.[5] However, two randomised controlled trials published by our group failed to support these recommendations.[6,7] These two trials had an identical design; individuals undergoing total hip arthroplasty had three nights of respiratory polygraphy recording on the preoperative night and on postoperative nights 1 and 3. In the first trial, the supine apnoea–hypopnoea index (AHI) on postoperative night 1 (primary outcome) was similar when general anaesthesia was provided with desflurane and remifentanil or sevoflurane and fentanyl (19 *vs* 21 events h^{-1}, respectively; P=0.64).[6] In the second trial, the supine AHI on postoperative night 1 was identical whether the surgery was performed under spinal anaesthesia alone or with intrathecal morphine 100 μg (21 events h^{-1} in both groups; P=0.90).[7]

Large retrospective studies have shown that use of neuraxial anaesthesia when compared with general anaesthesia is associated with less deleterious outcomes in individuals with sleep apnoea.[1,8] Therefore, it is also recommended that regional anaesthetic techniques be favoured over general anaesthesia in this group.[3,9,10] However, there is a lack of data on the postoperative evolution of AHI after general *vs* neuraxial anaesthesia to support this recommendation. This analysis compared the impact of general *vs* spinal anaesthesia on postoperative sleep apnoea severity and assessed the evolution of sleep apnoea severity through the perioperative period up to the third postoperative night in individuals with obstructive sleep apnoea (OSA) undergoing total hip arthroplasty.

Methods

Study design

This *post hoc* analysis used pooled data from two randomised controlled trials that applied the same methodology on a homogenous sample of patients undergoing elective hip arthroplasty under either general anaesthesia (NCT02717780[6]) or spinal anaesthesia (NCT02566226[7]), using the same study design and preoperative and postoperative protocols. Both of these trials were conducted at the University Hospital of Lausanne between February 2016 and March 2019. The Swiss National Science Foundation sponsored the trials, which were approved by the Ethics Committee of the Lausanne University Hospital (Commission d'Ethique Romande, protocol number CER 2015/192; CER 265/15) and conducted according to Good Clinical Practice and Declaration of Helsinki 2002 principles. All participants provided written informed consent. Patients, all nursing staff, the research team, the sleep technician, the sleep physician, and the statistician were not aware of treatment allocation.

Study participants

Eligible individuals were age 18–85 yr and scheduled to undergo elective hip arthroplasty. Exclusion criteria included treatment of sleep apnoea with continuous positive airway pressure, presence of severe respiratory or cardiovascular disease, malignant hyperthermia susceptibility, preoperative use of benzodiazepines, chronic use of opioids at a dosage of 30 mg day^{-1} or more morphine equivalent, and pregnancy.

Perioperative procedure

After application of routine monitors in the operating theatre, general anaesthesia was induced with i.v. propofol 1.5–2 mg kg^{-1} and either remifentanil 0.5 μg kg^{-1} or fentanyl 1–2 μg kg^{-1}, and tracheal intubation was facilitated by i.v. rocuronium 0.6 mg kg^{-1}. Maintenance of anaesthesia involved either desflurane or sevoflurane in an air–oxygen mixture at a concentration of 0.8–1.2 minimum alveolar concentration (MAC). Any increase of >20% above preinduction values for heart rate or blood pressure was treated with a bolus of opioid. Positive pressure ventilation was initiated, and tidal volume and rate were adjusted to maintain end-tidal carbon dioxide pressure at 4.7 - 6.0 kPa (35–40 mm Hg). At the end of the surgery, paralysis was antagonised with neostigmine 50 μg kg^{-1} and glycopyrrolate 5–10 μg kg^{-1} in case of residual neuromuscular blockade defined as a train-of-four ratio <0.9. Spinal anaesthesia was performed with the patient in the lateral position. A pencil-point needle of 25-G was inserted through a 21-G introducer needle at L3–L4 or L4–L5 after sterile skin preparation. A mixture of isobaric bupivacaine 15 mg with morphine 100 μg or the equivalent volume of normal saline was injected.

After prosthesis implantation, the surgical site was infiltrated with ropivacaine 0.2% 50 ml. Following routine institutional practice, all participants received i.v. paracetamol 1 g, ketorolac 30 mg, and ondansetron 4 mg at the end of surgery (as multimodal analgesic and antiemetic prophylactic medications).[11,12] In phase I recovery, pain was assessed on a visual analogue scale from 0 to 10. A score of ≥4, or patient request for analgesia, was managed with morphine 2 mg i.v. every 10 min as needed. After resumption of oral intake, patients received paracetamol 1000 mg every 6 h, ibuprofen 400 mg every 6 h, and oxycodone 5 mg every 3 h as needed. Ongoing

antiemetic medication included ondansetron 4 mg i.v. as needed. Subjects received oxygen at a rate of 2–4 L min^{-1} in phase I recovery but not after transfer to the ward.

Assessment of obstructive sleep apnoea

Sleep-related parameters and outcomes were measured using a portable respiratory polygraphy recorder (Embletta®; ResMed, Basel, Switzerland) on the night before surgery (preoperative baseline) and on the first and third nights after surgery. The polygraphy device has been validated against polysomnography[13] and allows noninvasive recording of nasal airflow via nasal cannula, oxygen saturation using finger pulse oximetry, respiratory effort using thoracic and abdominal belts, and body position. All recordings were scored by a specialised sleep technician and supervised and reviewed by a sleep physician, all of whom were unaware of treatment allocation. Apnoea was defined as breathing cessation lasting for 10 s or more, and hypopnea was defined as a decrease of 30% or more in the respiratory flow signal associated with a 3% or greater reduction in oxygen saturation. The AHI was defined as the number of apnoeas and hypopnoeas per hour of recording time, and the oxygen desaturation index reflected the number of oxygen desaturations of 3% or more per hour of recording time.

Outcomes

The primary outcome was the AHI in the supine position on the first postoperative night. Supine AHI was chosen rather than overall AHI because individuals had to sleep in the supine position after hip arthroplasty. The evolution of supine AHI through the perioperative period up to the third postoperative night was also determined. Secondary sleep-related outcomes were the global AHI, obstructive apnoea index, mixed apnoea index, central apnoea index, hypopnoea index, oxygen desaturation index, mean oxygen saturation, percentage of recording time with oxygen saturation below 90%, and percentage of time in the supine position; all were measured on the preoperative night and on the first and third postoperative nights.

Covariates

Among the covariates, we recorded age, sex, weight, height, body mass index, Epworth Sleepiness Scale (ESS) score, American Society of Anesthesiologists (ASA) physical status, duration of surgery, type of arthroplasty (primary *vs* secondary), comorbidities, NoSAS, STOP-BANG and Berlin scores, and preoperative AHI.

Statistical analysis

Categorical and continuous data are summarised as proportions and means with 95% confidence interval (CI) values, respectively. Categorical data were compared between groups (spinal *vs* general) using Fisher's exact test or the Pearson Chi-square test, as appropriate. Continuous variables were first compared between groups using Student *t*-tests. In a second step, generalised estimating equations were considered for each continuous outcome, with models including time, anaesthesia group, and interaction between time and anaesthesia groups. Based on these models, we could compute marginal differences not only between the type of anaesthesia, but also between the time points. To add some flexibility in the models, the three time points (preoperative, postoperative night 1, and postoperative night 3) were considered categorical variables instead of continuous. This allows several slopes in the evolution of respiratory parameters (e.g. a decrease until postoperative night 1 and then an increase until postoperative night 3).

Generalised estimating equations are extensions of general linear models to longitudinal or clustered data, where observations are no longer independent. The aim is to extend general linear models estimating equations to the multivariate setting by replacing the vector of responses and the vector of means by their corresponding multivariate counterparts and using a matrix of weights. Generalised estimating equations consider the dependence of observations by specifying a working correlation matrix.[14] This increases the efficiency of the estimators of the parameters compared with those arising under the assumption that repeated observations from a subject are independent of one another, as long as this assumption is true, and the resulting estimators remain consistent in the absence of missing data.[15] This method uses all the available information without excluding any individual even if they are missing data at some time points.

In our context, we decided to keep the models as simple and interpretable as possible by using additive models based on normal distribution and identity link functions. Moreover, within-subject dependencies were modelled with a first-order autoregressive correlation matrix. This means that for each outcome, the correlation between two consecutive time points (e.g. preoperative and postoperative night 1) has a value ρ, whereas the correlation between preoperative and postoperative night 3 is ρ^2.

Statistical analysis was performed using Stata 17 software (StataCorp 2021, Stata Statistical Software: Release 17, College Station, TX, USA). Significance was considered at $P<0.05$ based on a two-tailed probability, and Bonferroni correction was applied for three pairwise comparisons of the time points.

Results

Of 120 individuals recruited, 96 had available data for analysis of supine AHI (the first primary outcome) (Fig. 1). Participant characteristics are presented in Table 1. Of note, height, ESS score, duration of surgery, type of arthroplasty, and STOP-BANG score were significantly different between groups.

Mean [95% CI] supine AHI was similar in the general and spinal anaesthesia groups before the surgery (27 [21–33] and 20 [13–27] events h^{-1}; $P=0.13$) and on postoperative nights 1 (20 [16–25] and 21 [16–26] events h^{-1}; $P=0.82$) and 3 (34 [22–45] and 35 [20–49] events h^{-1}; $P=0.91$) (see Fig. 2). There were also no significant differences between the general and spinal anaesthesia groups in other postoperative respiratory parameters after the application of a Bonferroni correction (Table 2). The proportion of time spent in the supine position on the preoperative night and postoperative night 3 was significantly higher in the general *vs* spinal anaesthesia group (Table 2).

The generalised estimating equations model did not show any significant difference between groups and between groups over time, whereas a time effect was present for some

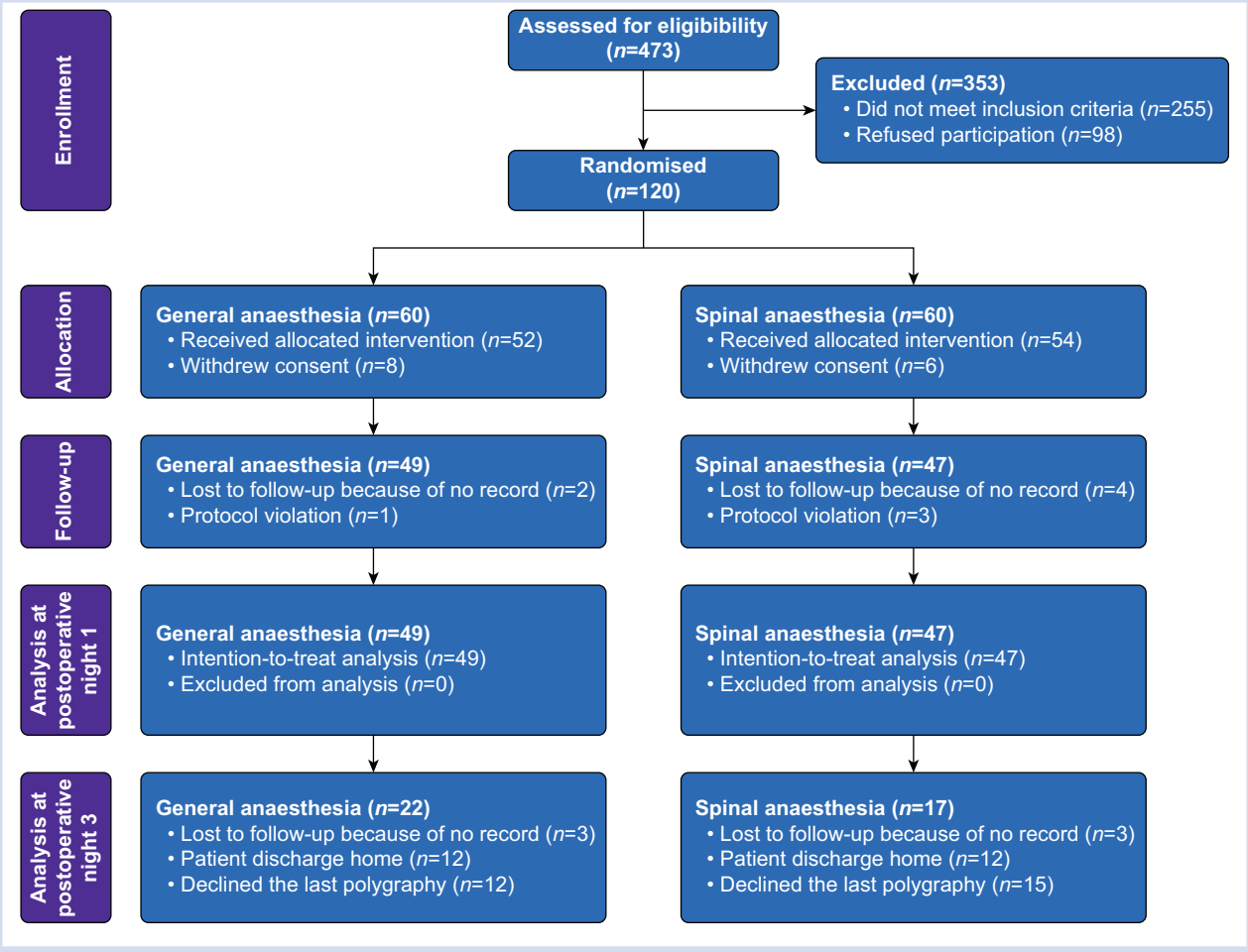

Fig 1. Flowchart of the study population.

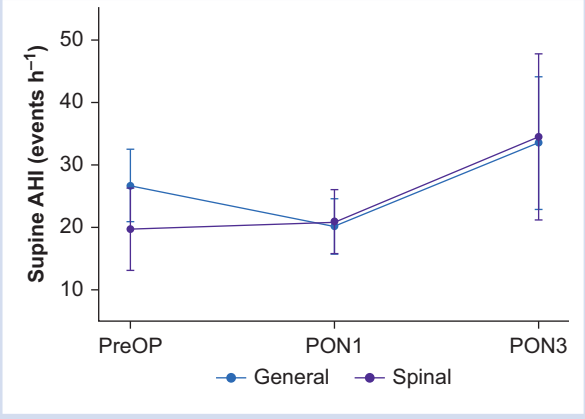

Fig 2. Change in the AHI in the supine position over time (data are shown as mean with 95% confidence interval). AHI, apnoea–hypopnoea index; PON1, postoperative night 1; PON3, postoperative night 3; PreOP, preoperative.

outcomes when analysing the three nights in all subjects (Table 3). For example, supine AHI was similar on postoperative night 1 compared with preoperative baseline ($P=0.17$) but significantly higher on postoperative night 3 compared with preoperative baseline ($P=0.002$) or postoperative night 1 ($P<0.001$) (Table 3).

Discussion

This *post hoc* analysis of pooled data from two randomised controlled trials found that the severity of sleep apnoea in the postoperative period was not different with use of spinal anaesthesia compared with general anaesthesia. The current findings also showed that sleep apnoea is not worse on the first postoperative night but instead becomes more severe in subsequent days. These results do not support current recommendations relating to the perioperative management of individuals with sleep apnoea syndrome, which favour use of regional anaesthetic techniques and continuous monitoring on the first postoperative night.[9] However, additional research is needed to determine whether surgery performed using peripheral nerve block only would improve sleep

Table 1 Baseline characteristics of study participants. Data are mean (95% confidence interval) or *n* (%) as appropriate. AHI, apnoea–hypopnoea index; ASA, American Society of Anesthesiologists; ESS, Epworth Sleepiness Scale.

Characteristics	General anaesthesia (*n*=49)	Spinal anaesthesia (*n*=47)	*P*-value
Age (yr)	65 (61–68)	70 (66–73)	0.07
Male sex, *n* (%)	33 (67.3)	26 (55.3)	0.30
Weight (kg)	83 (78–89)	77 (72–82)	0.09
Height (cm)	172 (170–175)	167 (165–170)	0.008
Body mass index (kg m^{-2})	28 (27–30)	27 (26–29)	0.55
ESS score ≥ 11	8 (16.3)	0 (0)	0.006
ASA physical status, *n* (%)			0.71
1	6 (12.2)	3 (6.4)	
2	34 (69.4)	35 (74.5)	
3	9 (18.4)	9 (19.1)	
Duration of surgery (min)	143 (128–157)	124 (115–132)	0.03
Hip arthroplasty, *n* (%)			<0.001
Primary	26 (53.1)	4 (8.5)	
Secondary	23 (46.9)	43 (91.5)	
Comorbidities, *n* (%)			
Coronary artery disease	2 (4.1)	3 (6.4)	0.67
Hypertension	20 (40.8)	23 (48.9)	0.54
Renal failure	2 (4.1)	1 (2.1)	1.00
Diabetes mellitus	2 (4.1)	4 (8.5)	0.43
Hyperlipidaemia	5 (10.2)	9 (19.1)	0.25
Sleep apnoea scores, *n* (%)			
NoSAS score ≥8	35 (71.4)	30 (63.8)	0.38
STOP-BANG score ≥3	42 (85.7)	25 (53.2)	<0.001
Berlin score ≥2	23 (46.9)	13 (27.7)	0.06
Preoperative AHI (events h^{-1}), *n* (%)			0.44
<5	7 (14.3)	10/36 (27.8)	
5–14.9	19 (38.8)	11/36 (30.6)	
15–29.9	15 (30.6)	11/36 (30.6)	
≥30	8 (16.3)	4/36 (11.1)	
Missing	*0*	*11*	

Table 2 Sleep study data. Data are presented as mean (95% confidence interval) or *n* (%). SpO_2, pulse oxygen saturation.

	Preoperative night			Postoperative night 1			Postoperative night 3		
	General anaesthesia	Spinal anaesthesia	*P*-value	General anaesthesia	Spinal anaesthesia	*P*-value	General anaesthesia	Spinal anaesthesia	*P*-value
n	49	36		49	47		22	17	
Apnoea–hypopnoea index (events h^{-1})	19 (14–23)	14 (10–18)	0.14	20 (15–24)	20 (15–25)	0.92	33 (22–44)	27 (15–39)	0.48
Obstructive apnoea index (events h^{-1})	4 (2–7)	2 (1–3)	0.14	3 (0–6)	6 (3–8)	0.16	12 (3–20)	10 (2–17)	0.68
Central apnoea index (events h^{-1})	2 (1–3)	2 (0–3)	0.43	2 (1–3)	2 (0–4)	0.94	4 (2–6)	2 (1–4)	0.26
Mixed apnoea index (events h^{-1})	1 (1–3)	1 (0–2)	0.59	1 (0–1)	2 (0–4)	0.25	3 (1–5)	3 (1–5)	0.97
Hypopnoea index (events h^{-1})	11 (8–13)	9 (6–12)	0.41	14 (11–17)	11 (8–13)	0.09	15 (10–20)	13 (7–19)	0.61
Oxygen desaturation index (events h^{-1})	22 (17–27)	17 (12–21)	0.13	29 (23–34)	21 (16–26)	0.05	38 (26–50)	33 (20–46)	0.52
Mean SpO_2 (%)	93 (92–93)	92 (92–93)	0.48	91 (90–92)	91 (90–92)	0.45	92 (91–94)	92 (90–93)	0.52
Proportion of time with SpO_2 <90% (%)	12 (6–19)	16 (18–24)	0.50	25 (15–35)	29 (19–39)	0.58	17 (6–29)	25 (9–42)	0.37
Proportion of time spent in the supine position (%)	53 (45–62)	32 (23–41)	0.001	96 (93–99)	94 (90–98)	0.39	99 (97–100)	83 (66–99)	0.02

outcomes compared with surgery performed using general anaesthesia.

Several studies have reported that neuraxial anaesthesia was associated with lower postoperative morbidity compared with other types of analgesia in individuals with sleep apnoea.[1,2,16] One potential explanation would be better pain control with neuraxial techniques, resulting in less activation of the sympathetic nervous system and therefore a lower

Table 3 Estimates of means from the generalised estimating equations model for primary and secondary sleep-related outcomes with 95% confidence intervals, by time points. The *P*-values from two-by-two comparisons of these time points are also shown. Generalised estimating equations were used for each outcome, with models including time, anaesthesia group, and interaction between time and anaesthesia groups. The three time points (preoperative, postoperative night 1, and postoperative night 3) were considered categorical variables instead of continuous. This allows several slopes in the evolution of respiratory parameters (e.g. a decrease until postoperative night 1 and then an increase until postoperative night 3). PON1, postoperative night 1; PON3, postoperative night 3; PreOP, preoperative night; SpO_2, pulse oxygen saturation.

	Preoperative night	Postoperative night 1	Postoperative night 3	P-value		
				PreOP *vs* PON1	PreOP *vs* PON3	PON1 *vs* PON3
Supine apnoea–hypopnoea index (events h^{-1})	24 (20–28)	21 (17–25)	34 (28–39)	0.17	0.002	<0.001
Apnoea-hypopnoea index (events h^{-1})	17 (13–20)	20 (17–24)	30 (25–35)	0.03	<0.001	<0.001
Obstructive apnoea index (events h^{-1})	4 (1–6)	4 (2–7)	10 (7–13)	0.38	<0.001	<0.001
Central apnoea index (events h^{-1})	2 (1–3)	2 (1–3)	3 (2–4)	0.88	0.08	0.04
Mixed apnoea index (events h^{-1})	1 (1–2)	1 (1–2)	3 (2–4)	1.00	0.03	0.01
Hypopnoea index (events h^{-1})	10 (8–12)	13 (11–15)	14 (11–17)	0.02	0.01	0.34
Oxygen desaturation index (events h^{-1})	20 (15–24)	26 (22–30)	36 (30–41)	<0.001	<0.001	<0.001
Mean SpO_2 (%)	92 (92–93)	91 (91–92)	92 (91–93)	<0.001	0.16	0.04
Proportion of time with SpO_2 <90% (%)	14 (8–20)	26 (20–32)	21 (13–29)	<0.001	0.12	0.20
Proportion of time spent in the supine position (%)	44 (40–49)	95 (91–99)	92 (85–98)	<0.001	<0.001	0.41

burden for the cardiovascular system.[17,18] Unfortunately, our findings did not confirm this explanation as they did not show improvement in the AHI or blood oxygenation in the postoperative period after spinal anaesthesia. However, we cannot exclude that the absence of differences between groups in this report might be attributable to different anaesthetic regimens used in the two included trials. Indeed, patients undergoing the surgery under general anaesthesia received either sevoflurane and fentanyl or desflurane and remifentanil,[6] whereas half of the patients having spinal anaesthesia received intrathecal morphine.[7]

One might argue that the sample size was inadequate in this study. Notably, a *post hoc* power analysis with an alpha error of 0.05 and a power of 80% showed that 4020 patients per group would be needed (total 8040) to detect a between-group difference in supine AHI of 1 event h^{-1}, with a standard deviation of 16, highlighting the futility of performing a randomised controlled trial. That said, these results should be considered exploratory and useful for hypothesis generation. As an example, the absence of difference in AHI on postoperative night 1 might be the result of a reduction of rapid eye movement (REM) sleep in both groups, where most events occur, as explained below. Researchers are encouraged to seek confirmation of absence of difference between both anaesthetic strategies with an equivalence trial, using homogeneous anaesthetic regimen for general and spinal anaesthesia, and using an AHI difference of 5 events h^{-1}.

A key finding of this study was that sleep apnoea severity was significantly higher on the third postoperative night compared with the preoperative night and the first postoperative night, confirming the findings of two previous studies.[19,20] Similar to our findings, one of these studies showed a higher AHI on postoperative night 3 *vs* postoperative night 1 or before surgery in individuals with mild-to-severe OSA (n=174) who were undergoing different types of surgery under different anaesthetic strategies.[19] In the other trial, 21 individuals with OSA underwent portable polysomnography before surgery and then on postoperative nights 1, 3, 5, and 7.[20] The AHI peaked on postoperative night 3 before progressively declining on postoperative nights 5 and 7.[20] One possible explanation for these findings could be a rebound in REM sleep after the first postoperative night, and this sleep stage is where most apnoeic and hypopnoeic episodes occur.[19,21]

The peak in sleep apnoea severity on the third postoperative night after both types of anaesthesia in the current study could be problematic because most individuals scheduled for minor to intermediate surgical procedures have already been discharged home by this point, especially in the current context of more ambulatory surgery and a desire to reduce the overall length of hospital stay. This suggests that a prescription for temporary continuous positive airway pressure therapy[22,23] or a mandibular advancement device[24] could be interesting and cost-effective options for perioperative management of at-risk individuals, such as those with severe sleep apnoea or advanced cardiovascular or cerebrovascular disease.

Several limitations inherent to the design of this study should be mentioned. Firstly, this was a *post hoc* analysis of data from two randomised controlled trials that were not designed to evaluate the endpoints used in the current analysis. However, all subjects included in the analysis had the same surgery performed by the same surgical team with homogenous perioperative management. Moreover, some covariates such as the height, duration of surgery, or STOP-BANG score were not included in our model, following our initial statistical analysis plan, and could therefore impact our results. That said, we believe these results are of interest because of the paucity of data in this area and can also be considered hypothesis-generating for future research. Secondly, we chose to use a portable polygraphy device that has been validated against polysomnography[13] to reduce the number of sensors that could further disturb the sleep quality of study participants, especially in the postoperative setting. However, although portable respiratory polygraphy is recommended for sleep apnoea diagnosis in clinical practice, unlike full polysomnography it does not provide data on sleep structure. As the mean BMI in our patients was just above normal, between 27 and 28 kg m^{-2}, and as patient care was

protocolised, generalisation of our results to populations with much higher BMI requires caution and might not be translatable. Finally, there was a limited number of subjects having the third respiratory polygraphy.

In conclusion, use of spinal anaesthesia was not associated with a reduction in postoperative sleep apnoea severity compared with general anaesthesia in individuals with OSA undergoing total hip arthroplasty. In addition, postoperative sleep apnoea severity was found to peak on the third postoperative night.

Authors' contributions

Study design: EA
Primary manuscript preparation: EA
Data interpretation: EA, VB, RH
Manuscript editing: JW, JBR, VB, RH
Statistical analysis: JBR

Acknowledgements

English language editing assistance was provided by Nicola Ryan, an independent medical writer.

Declarations of interest

EA received grants from the Swiss Academy for Anesthesia Research (SACAR), Lausanne, Switzerland; B. Braun Medical AG, Sempach, Switzerland; and the Swiss National Science Foundation, Bern, Switzerland to support his clinical research. EA also received an honorarium from B. Braun Medical AG Switzerland, Sintetica Ltd UK, and MSD AG Switzerland. SG received a research grant and an honorarium from MSD AG Switzerland. All other authors have no conflict of interest to disclose.

Funding

Swiss National Science Foundation to EA (353,408 CHF, 32003B_169974/1).

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Handling Editor: Hugh C Hemmings Jr