Original Article

Impact of short-acting vs. standard anaesthetic agents on obstructive sleep apnoea: a randomised, controlled, triple-blind trial

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Summary

Sleep apnoea is associated with negative outcomes following general anaesthesia. Current recommendations suggest using short-acting anaesthetic agents in preference to standard agents to reduce this risk, but there is currently no evidence to support this. This randomised controlled triple-blind trial tested the hypothesis that a combination of short-acting agents (desflurane-remifentanil) would reduce the postoperative impact of general anaesthesia on sleep apnoea severity compared with standard agents (sevoflurane-fentanyl). Sixty patients undergoing hip arthroplasty under general anaesthesia were randomised to anaesthesia with desflurane-remifentanil or sevoflurane-fentanyl. Respiratory polygraphy was performed before surgery and on the first and third postoperative nights. The primary outcome was the supine apnoea-hypopnoea index on the first postoperative night. Secondary outcomes were the supine apnoea-hypopnoea index on the third postoperative night, and the oxygen desaturation index on the first and third postoperative nights. Additional outcomes included intravenous morphine equivalent consumption and pain scores on postoperative days 1, 2 and 3. Pre-operative sleep study data were similar between groups. Mean (95%CI) values for the supine apnoea-hypopnoea index on the first postoperative night were 18.9 (12.7–25.0) and 21.4 (14.2–28.7) events.h^{-1}, respectively, in the short-acting and standard anaesthesia groups (p = 0.64). Corresponding values on the third postoperative night were 28.1 (15.8–40.3) and 38.0 (18.3–57.6) events.h^{-1} (p = 0.34). Secondary sleep- and pain-related outcomes were generally similar in the two groups. In conclusion, short-acting anaesthetic agents did not reduce the impact of general anaesthesia on sleep apnoea severity compared with standard agents. These data should prompt an update of current recommendations.

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Introduction

Obstructive sleep apnoea (OSA) is characterised by intermittent and recurrent episodes of apnoea due to partial or complete obstruction of the upper airway during sleep following a reduction in pharyngeal muscle tone [1]. The prevalence of sleep apnoea is high; 49% of men and 23% of women aged > 40 years in a Swiss population-based cohort [2], and the condition is an important public health issue due to its association with hypertension [3]; metabolic syndrome [4]; acute coronary syndrome [5]; stroke [6]; and mortality [7, 8].

In patients with OSA, volatile anaesthetics and opioids increase the incidence of upper airway obstruction secondary to a reduction in pharyngeal muscle tone [9]. In

addition, opioids aggravate the risk of prolonged apnoea by decreasing central respiratory drive [10]. Therefore, patients with OSA are at an increased risk of developing respiratory and cardiovascular complications after general anaesthesia [11–13].

Current recommendations for anaesthetic management of patients with OSA suggest that short-acting agents such as desflurane and remifentanil should be used for general anaesthesia [14, 15]. These agents have been shown to be associated with an improved recovery profile, oxygen saturation and respiratory rate 2 h after surgery compared with sevoflurane or alfentanil in patients without OSA [16, 17]. Furthermore, morbidly obese patients who received general anaesthesia with desflurane had earlier extubation times, earlier verbal contact, and were more awake on arrival at the recovery area, compared with morbidly obese patients who received sevoflurane [18]. However, there is still uncertainty about the benefits of short-acting anaesthetic agents in patients with OSA because they have not yet been compared with standard agents in a randomised controlled clinical trial.

This study was designed to test the hypothesis that a combination of desflurane and remifentanil (short-acting agents) would reduce the impact of general anaesthesia on postoperative OSA severity compared with a combination of sevoflurane and fentanyl (standard agents).

Methods

This randomised, triple-blind, parallel-group trial was conducted at the University Hospital of Lausanne between February 2016 and May 2018. Randomisation was undertaken using a computer-generated randomisation table in aggregates of 10. Assignments were concealed in a sealed opaque envelope. The patients, nursing staff, research team, the sleep technician and the sleep physician were not aware of treatment allocation. The trial was sponsored by the Swiss National Science Foundation. The study was approved by the hospital ethical committee and all patients provided written informed consent.

Patients were eligible for participation in the study if they were aged between 18 and 85 years and scheduled to undergo hip arthroplasty. Exclusion criteria included: treatment of sleep apnoea with continuous positive airway pressure; presence of severe respiratory or cardiovascular disease; malignant hyperthermia; pre-operative consumption of benzodiazepines; chronic use of opioids at a dosage of 30 mg.day^{-1} or more morphine equivalents; and pregnancy. On the day of surgery, patients were randomised to general anaesthesia with desflurane and remifentanil (short-acting group), or sevoflurane and fentanyl (standard group).

Anaesthesia was induced using intravenous propofol 1.5–2.0 mg.kg^{-1} and either remifentanil 0.5 µg.kg^{-1} (short-acting) or fentanyl 1–2 µg.kg^{-1} (standard), with tracheal intubation facilitated by intravenous rocuronium 0.6 mg.kg^{-1}. Anaesthesia was maintained using desflurane (short-acting) or sevoflurane (standard) in an air-oxygen mixture at a concentration of 0.8–1.2 minimum alveolar concentration (MAC) to achieve a bispectral index (Aspect Medical Systems, Norwood, MA, USA) of between 40 and 60. Analgesia to manage increases in heart rate or blood pressure of more than 20% above pre-operative values was provided with an infusion of remifentanil 0.1 µg.kg^{-1}.min^{-1} (short-acting) or 25 µg bolus doses of fentanyl (standard) [19]. Positive pressure ventilation was initiated, and tidal volume and rate adjusted to maintain EtCO$_2$ between 4.7 and 5.3 kPa.

After prosthesis implantation, the surgical site was infiltrated with 50 ml of ropivacaine 0.2%. As per routine institutional practice, at the end of surgery all patients received intravenous acetaminophen 1000 mg and intravenous ketorolac 30 mg for multimodal analgesia and intravenous ondansetron 4 mg for anti-emetic prophylaxis [20, 21]. In case of residual neuromuscular blockade (defined as a train-of-four ratio < 0.9), muscle relaxation was antagonised with neostigmine 50 µg.kg^{-1} and glycopyrrolate 5–10 µg.kg^{-1} [22]. In Phase 1 recovery, pain was assessed on a visual analogue scale with a range of 0–10. A score of 4 or more or patient request for analgesia was managed with morphine 2 mg every 10 min as needed. After resumption of oral intake, patients received acetaminophen 1000 mg every 6 h, ibuprofen 400 mg every 6 h, and oxycodone 5 mg every 3 h as needed. Ongoing anti-emetic medication included intravenous ondansetron 4 mg as needed. Patients received oxygen at a rate of 2–4 l.min^{-1} in Phase 1 recovery, but not after transfer to the ward.

Sleep-related parameters and outcomes were measured on the night before surgery (pre-operative baseline) and on the first and third nights after surgery using a portable respiratory polygraph recorder (Embletta$^{®}$, ResMed, San Diego, CA, USA). This system, previously validated against polysomnography [23], allows non-invasive recording of nasal airflow via nasal cannula, oxygen saturation using finger pulse oximetry, respiratory efforts using thoracic and abdominal belts, and body position. All recordings were scored by a specialised sleep technician, supervised and reviewed by a sleep specialist, and both were unaware of treatment allocation. Apnoea was defined as breathing cessation lasting for 10 s or more, and hypopnoea was defined as a fall of 30% or more in the
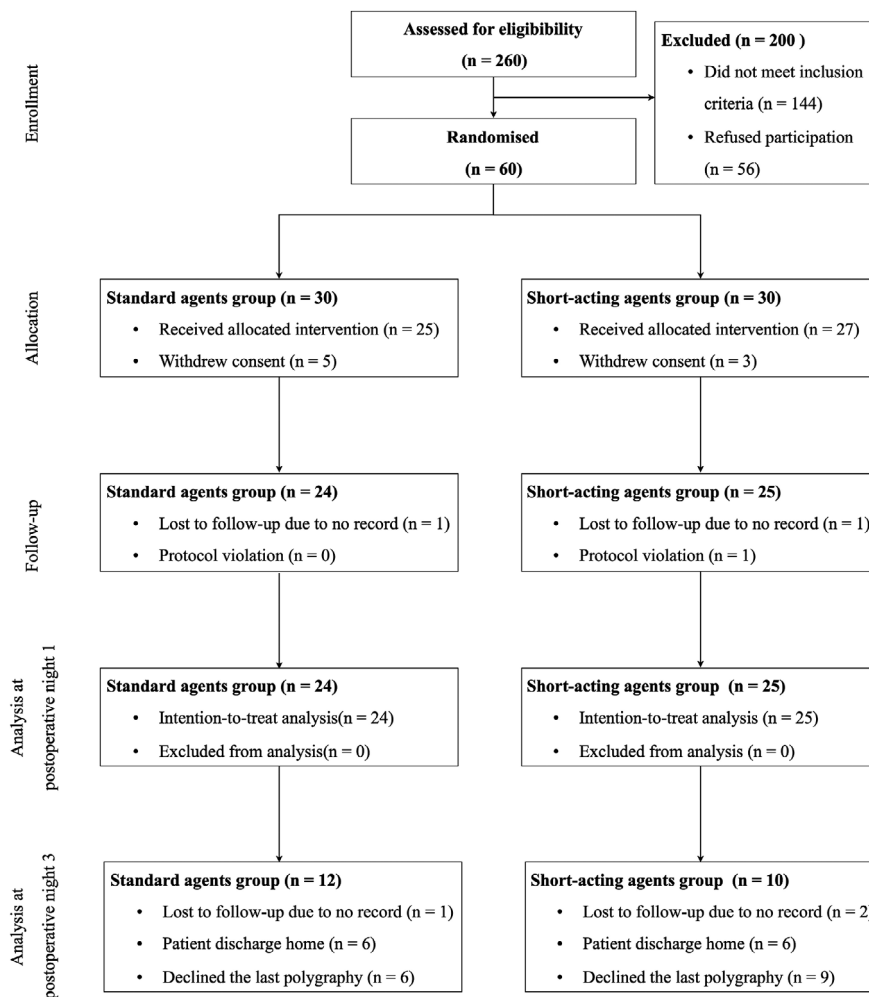
Figure 1 Study flow diagram.

respiratory flow signal associated with a 3% or greater drop in oxygen saturation. The apnoea-hypopnoea index (AHI) was defined as the number of apnoeic and hypopnoeic events 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. Central apnoea was defined as the presence of > 50% of events without abdominal or thoracic movements.

The primary outcome was the AHI in the supine position on the first postoperative night. Secondary sleep-related outcomes were: supine AHI on the third postoperative night; AHI; obstructive apnoea index; mixed apnoea index; central apnoea index; hypopnoea index; oxygen desaturation index; percentage of recording time with oxygen saturation below 90%; and proportion of time in the supine position on the first and third postoperative nights. Secondary pain-related outcomes were: intravenous morphine AHI equivalent consumption in the recovery area

and on postoperative days 1, 2 and 3; pain scores at rest on arrival and at departure and on postoperative days 1, 2 and 3; rates of postoperative nausea and vomiting or pruritus on postoperative days 1, 2 and 3; and satisfaction score (rated on a visual analogue scale from 0 to 10).

It was calculated that 22 patients were required in each treatment group to detect a difference in supine AHI of 5 events.h^{-1} with a standard deviation of 5, 90% power and a two-sided alpha error of 0.05. Based on an estimated drop-out rate of 30%, the recruitment target was set at 60 subjects (30 per group). A between-group difference in AHI of 5 events.h^{-1} was chosen because this has previously been defined as clinically relevant [3, 24].

Statistical analysis was performed using SPSS Statistics for Windows Version 25.0 (IBM, Armonk, NY, USA). Categorical data were summarised as rates and continuous data were summarised as mean with 95%CI. Categorical data were compared using the Fisher's exact

test or Pearson Chi-square test with Yates' correction as appropriate. Continuous independent variables were analysed using general linear models, while categorical and continuous repeated measurements were analysed using generalised estimating equations according to time, anaesthesia group, and interaction between time and anaesthesia effects. When more than one distribution fitted the model, the best was chosen based on the lowest quasi-likelihood under independence model criterion for generalised estimating equations and lowest Akaike information criterion for general linear models.

Briefly, generalised estimating equations are an extension of general linear models to longitudinal or clustered data, where observations are no longer independent. The aim was to extend the 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 take into account the dependence of observations by specifying a working correlation matrix [25]. 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 [26]. This method uses all the available information without

Table 1 Baseline and clinical characteristics of patients. Values are mean (SD), median (IQR [range]) or number (proportion) as appropriate.

Characteristic	Standard agents n = 24	Short-acting agents n = 25
Age; y	64 (15)	66 (10)
Men; n	17 (71%)	16 (64%)
Weight; kg	81 (71–93 [58–130])	82 (69–90 [62–135])
Height; cm	174 (9)	170 (9)
BMI; kg.m^{-2}	27.1 (24.3–29.6 [19.5–41.0])	27.0 (24.6–31.0 [22.1–43.9])
ESS score ≥ 11	4 (17%)	4 (17%)
ASA physical status		
1	6 (25%)*	0
2	12 (50%)	22 (88%)*
3	6 (25%)	3 (12%)
Duration of surgery; min	132 (106–162 [80–360])	136 (112–165 [76–252])
Hip arthroplasty		
Primary	12 (50%)	11 (44%)
Secondary	12 (50%)	14 (56%)
Comorbidities		
Coronary artery disease	0	2 (8%)
Hypertension	10 (42%)	10 (40%)
Renal failure	0	2 (8%)
Diabetes	1 (4%)	1 (4%)
Hyperlipidaemia	2 (8%)	3 (12%)
Sleep apnoea scores		
NoSAS score ≥ 8	16 (67%)	19 (79%)
STOP-BANG score ≥ 3	22 (92%)	20 (83%)
Berlin score ≥ 2	13 (54%)	10 (42%)
Pre-operative AHI		
< 5 events.h^{-1}	4 (17%)	3 (12%)
5–14.9 events.h^{-1}	10 (42%)	9 (36%)
15–29.9 events.h^{-1}	6 (25%)	9 (36%)
≥ 30 events.h^{-1}	4 (17%)	4 (16%)

AHI, apnoea-hypopnoea index; ESS, Epworth Sleepiness Scale.
*Observed frequency significantly different from overall frequency (adjusted residual > |2|).
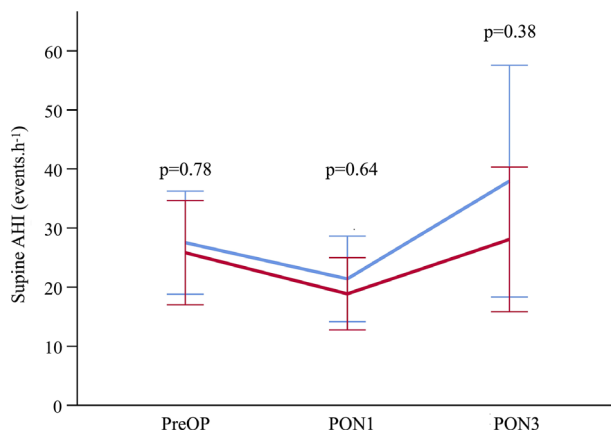
Figure 2 Change in the apnoea-hypopnoea index (AHI) in the supine position over time (values are shown as mean with 95%CI). PreOP, pre-operative; PON1, postoperative night 1; PON3, postoperative night 3. Blue line, standard agents; red line, short-acting agents.

excluding any individual, even if they are missing data at some time-points.

To assess the generalisability of our findings, sensitivity analyses were performed on sub-groups of patients with OSA (AHI $\geq$ 5 events.h^{-1} or $\geq$ 15 event.h^{-1}) or at high risk of OSA (NoSAS score $\geq$ 8, STOP-BANG score $\geq$ 3, or Berlin score $\geq$ 2). Multiple comparisons (for time or interaction effects) were performed using Bonferroni's post-hoc test.

Results

Sixty patients were recruited and 49 completed the study for the primary outcome (Fig. 1). Twelve and 15 patients did not perform the last polygraphy in the standard and short-acting groups respectively (p = 0.48). Patient characteristics were similar in the two treatment groups (Table 1) and between those who did vs. did not complete the last polygraphy (online Supporting Information, Table S1). Only one patient in the standard agents group had central apnoea (58% of all apnoea events were not accompanied by thoracic or abdominal effort).

The supine AHI did not differ significantly between the short-acting and standard groups at baseline, or on the first or third night after surgery (Fig. 2). The other secondary sleep-related outcomes were comparable between groups (Table 2). Changes from pre-operative baseline to the first postoperative night were similar in those who did vs. did not complete the final polygraphy (online Supporting Information, Table S2).

The generalised estimating equations model did not show any significant interaction (p = 0.63) or group effect

(p = 0.43), whereas a time effect was present (p < 0.0001) when analysing the three nights in all patients (Table 3). The supine AHI was significantly lower on postoperative night 1 compared with the pre-operative baseline (p = 0.03) and postoperative night 3 (p = 0.003). There was no significant difference between pre-operative baseline and the third postoperative night (p = 0.41) (Table 3).

Overall, the prevalence of severe OSA (defined as an AHI > 30 events.h^{-1}) on the third postoperative night was significantly higher than on the pre-operative night (OR 7.00, 95%CI 2.07–23.60; p < 0.0001). The prevalence of severe OSA on the first postoperative night did not differ significantly from the pre-operative baseline (OR 2.50, 95% CI 0.86–7.31; p = 0.09). Sensitivity analyses showed that the study findings were consistent across patient sub-groups based on OSA definition and in patients at high risk of OSA.

Pain scores were similar between groups during the course of the study (online Supporting Information, Figure S1). Other pain-related outcomes did not differ significantly between treatment groups (Table 4), apart from intravenous morphine equivalent consumption in the recovery area, which was significantly higher in the short-acting group (Table 4).

Discussion

The results of this randomised controlled trial suggest that short-acting anaesthetic agents do not reduce the impact of general anaesthesia on OSA severity on the first and third postoperative nights, compared with standard agents. In that context, given that both desflurane and remifentanil are expensive agents [27], desflurane releases more carbon dioxide into the atmosphere than other inhaled anaesthetics [28] and that remifentanil is associated with secondary hyperalgesia [29], we suggest that current recommendations for the use of short-acting anaesthetics in patients with OSA should probably be revised. Furthermore, our results do not support existing recommendations that encourage monitoring of patients on the first postoperative night only [14, 15]. Our data suggest that monitoring should be continued up to at least the third postoperative night. However, this may not be feasible given the expansion of ambulatory surgery and overall reductions in length of hospital stay. Therefore, a temporary prescription for continuous positive airway pressure therapy or a mandibular advancement device might represent satisfactory and cost-effective alternative measures for postoperative management of patients with OSA [30].

There are a number of potential explanations for the lack of difference seen between short-acting and standard

Table 2 Sleep study data. Values are mean (95%CI).

	Standard agents	Short-acting agents	p value
Pre-operative baseline	(n = 24)	(n = 25)	
AHI; events.h^{-1}	17.6 (11.0–24.1)	19.4 (11.7–27.1)	0.68
OAI; events.h^{-1}	4.1 (1.2–7.0)	4.7 (0–9.4)	0.68
CAI; events.h^{-1}	1.5 (0.1–2.9)	2.6 (1.3–3.9)	0.12
MAI; events.h^{-1}	8.3 (0.5–16.0)	10.8 (1.2–20.5)	0.42
HI; events.h^{-1}	10.8 (7.0–14.7)	10.5 (7.3–13.7)	0.86
ODI; events.h^{-1}	21.0 (13.6–28.3)	22.9 (15.7–30.1)	0.67
Mean S_pO_2; %	92.2 (91.0–93.3)	92.8 (92.1–93.5)	0.35
Time with S_pO_2 < 90%; %	16.1 (4.5–27.6)	8.7 (2.1–15.3)	0.09
Supine time; %	52.6 (39.8–65.4)	53.5 (41.7–65.4)	0.92
Postoperative night 1	(n = 24)	(n = 25)	
AHI; events.h^{-1}	20.7 (13.4–28.0)	18.8 (12.7–25.0)	0.73
OAI; events.h^{-1}	4.4 (−1.1–9.9)	1.9 (−0.3–4.1)	0.06
CAI; events.h^{-1}	2.1 (−0.2–4.4)	1.7 (0.6–2.8)	0.56
MAI; events.h^{-1}	5.4 (1.7–9.0)	2.9 (−0.8–6.7)	0.37
HI; events.h^{-1}	13.4 (8.7–18.1)	14.7 (10.2–19.1)	0.67
ODI; events.h^{-1}	29.0 (19.8–381)	28.0 (20.3–35.7)	0.89
Mean S_pO_2; %	91.5 (90.4–92.7)	91.1 (89.6–92.5)	0.60
Time with S_pO_2 < 90%; %	24.6 (11.6–37.5)	25.3 (10.1–40.5)	0.93
Supine time; %	93.7 (88.0–99.3)	98.4 (95.2–101.7)	0.16
Postoperative night 3	(n = 12)	(n = 10)	
AHI; events.h^{-1}	37.2 (17.8–56.6)	28.1 (15.8–40.3)	0.41
OAI; events.h^{-1}	15.2 (−0.1–30.5)	7.9 (0.3–15.6)	0.16
CAI; events.h^{-1}	4.5 (0.7–8.4)	2.7 (0.2–5.2)	0.22
MAI; events.h^{-1}	28.3 (4.5–52.2)	7.8 (−1.3–16.9)	0.05
HI; events.h^{-1}	13.6 (6.0–21.2)	16.2 (8.5–23.9)	0.58
ODI; events.h^{-1}	41.3 (20.0–62.6)	34.5 (20.9–48.1)	0.59
Mean S_pO_2; %	91.5 (89.7–93.3)	93.1 (91.3–95.0)	0.14
Time with S_pO_2 < 90%; %	19.7 (2.1–37.3)	14.1 (−3.4–31.5)	0.51
Supine time; %	97.7 (94.8–100.6)	100.0 (100.0–100.0)	0.10

AHI, apnoea-hypopnoea index; CAI, central apnoea index; HI, hypopnoea index; MAI, mixed apnoea index; OAI, obstructive apnoea index; ODI, oxygen desaturation index.

anaesthetic agents on OSA severity during the first postoperative night in our study. Firstly, although desflurane has lower blood: gas and oil: gas partition coefficients than sevoflurane, reducing absorption from the fat compartment and resulting in quicker induction and emergence times, the improved recovery profile does not appear to extend beyond a period of 15–30 min [18]. Therefore, differences in pharmacodynamics between these agents may be too small to have an impact on postoperative OSA severity. Secondly, administration of intravenous morphine postoperatively could have neutralised any potential beneficial effects of the short-acting agents. Indeed, patients in the short-acting group actually received more morphine in the recovery area (mean difference of 6 mg). This phenomenon, known as secondary hyperalgesia, is well known after remifentanil administration and primarily occurs during the first two postoperative hours [29, 31]. However, intravenous administration of long-acting opioids after a painful surgical procedure is consistent with standard postoperative pain management [32, 33] and mirrors the daily practice of the recovery area.

The decrease in supine AHI on the first postoperative night compared with the pre-operative baseline seen in our study might be due to greater time awake (which artificially decreases the AHI on polygraphy recordings) or a

Table 3 Data from the generalised estimating equations model for secondary sleep-related outcomes. Values are mean (95% CI).

	Pre-operative night n = 49	Postoperative night 1 n = 49	Postoperative night 3 n = 22	p value
Supine AHI; events.h^{-1}	26.7 (21.5–33.1)	20.1 (16.2–25.0)‡	32.6 (24.6–43.4)¶	< 0.01
AHI; events.h^{-1}	18.5 (14.4–23.8)	19.7 (15.8–24.7)	32.3 (24.3–43.0)‡¶	< 0.01
OAI; events.h^{-1}	4.4 (2.5–7.7)	2.9 (1.3–6.4)	11.0 (6.1–19.7)¶	< 0.01
CAI; events.h^{-1}	2.0 (1.2–3.2)	1.9 (1.1–3.4)	3.5 (2.1–5.9)	< 0.01
MAI; events.h^{-1}	1.4 (0.4–0.8)	0.7 (0.3–1.4)	2.2 (1.2–4.1)¶	< 0.01
HI; events.h^{-1}	10.6 (8.6–13.2)	14.0 (11.3–17.4)	14.9 (10.9–20.2)	0.09
ODI; events.h^{-1}	21.9 (17.6–27.2)	28.5 (23.5–34.6)‡	37.7 (28.7–49.6)‡	< 0.01
Mean S$_p$O$_2$; %	92.5 (91.8–93.1)	91.3 (90.4–92.1)‡	92.3 (91.3–93.4)	0.01
Time with S$_p$O$_2$ < 90%; %	11.8 (7.3–19.2)	24.9 (17.2–36.2)‡	16.7 (8.8–31.5)	< 0.01
Supine time; %	53.1 (96.0–93.0)	96.0 (93.0–99.1)‡	98.8 (97.6–100.1)‡	< 0.01

AHI, apnoea-hypopnoea index; CAI, central apnoea index; HI, hypopnoea index; MAI, mixed apnoea index; OAI, obstructive apnoea index; ODI, oxygen desaturation index.
*Indicating a time effect.
‡p < 0.05 compared to pre-operative night.
¶p < 0.05 compared to postoperative night 1.

Table 4 Acute pain-related outcomes. Data are mean (95%CI) or number (proportion).

	Standard agents	Short-acting agents	p value
Recovery area			
i.v. morphine equivalent consumption; mg	7 (4–10)	13 (10–16)	0.02
Postoperative day 1			
i.v. morphine equivalent consumption; mg	6 (0–11)	4 (2–6)	0.51
PONV	2/23 (9%)	1/23 (4%)	1.00
Pruritus	0/23	0/23	–
Postoperative day 2			
i.v. morphine equivalent consumption; mg	12 (2–23)	8 (4–12)	0.30
PONV	4/24 (17%)	2/25 (8%)	0.42
Pruritus	1/24 (4%)	0/25	0.49
Postoperative day 3			
i.v. morphine equivalent consumption; mg	10 (3–18)	6 (3–9)	0.19
PONV	6/24 (25%)	2/23 (9%)	0.25
Pruritus	0/24	2/23 (9%)	0.23
VAS satisfaction score	9.0 (8.6–9.4)	9.4 (9.0–9.7)	0.82

i.v., intravenous; PONV, postoperative nausea and vomiting; VAS, visual analogue scale score (from 0–10).

decreased proportion of rapid eye movement sleep [34] (because respiratory events occur predominantly during this phase). Subsequently, apnoeic and hypopnoeic events, and the oxygen desaturation index all increased on the third postoperative night compared with previous recordings, potentially due to a rebound in the amount of rapid eye movement sleep, as reported previously [35]. Unfortunately, we cannot confirm this because sleep stage data are not available from polygraphy. However, polygraphy data from 38 sleep apnoea patients showed that time in rapid eye movement sleep was lowest on the first postoperative night and increased up to the fifth postoperative night [34]. Therefore, it is possible that the negative impact of general anaesthesia on OSA severity could increase further after the third postoperative night.

The pre-operative AHI values of 17.6 and 19.4 events.h^{-1} in the two groups in our study might seem high for unselected patients, but are in line with the results of a recent meta-analysis showing that the mean (95%CI) AHI was 15.5 (12.9–18.2) events.h^{-1} in a general population

aged 65–79 years [36]. Moreover, rates of sleep apnoea in our study (85% with an AHI of 5 events.h^{-1} or more) and those reported previously [12, 13] suggest that OSA is highly prevalent in pre-operative populations. Therefore, implementation of protocols to manage OSA patients undergoing surgery would place a significant burden on anaesthetic departments. Thus, recommendations based on evidence rather than expert opinion are essential. Furthermore, current inclusive respiratory event definitions and highly sensitive nasal pressure sensors may artificially elevate the AHI, as previously suggested by our group [37]. On that basis and given that some older studies were performed between 2006 and 2010 [12], we also wonder whether the current AHI threshold should be revised, as previously suggested [38].

Further research is needed to determine which patients are at increased postoperative risk based on different definitions of OSA. For example, data from a recent prospective study showed that only severe OSA (AHI > 30 events.h^{-1}) was significantly associated with a composite cardiovascular event outcome [13]. Therefore, we believe that not only the recommendations for OSA management during anaesthesia, but also the AHI threshold above which they are implemented should be revised.

Although rigorously designed to minimise bias, our study has some limitations. Polygraphy does not record total sleep time, meaning that differences in sleep quality between recording nights may have contributed to the AHI variations observed. We were aware of this limitation but elected not to perform standard polysomnography with an electroencephalogram because this would create more distress for patients already under stress in a peri-operative setting. Nevertheless, the polygraphy system we used has been validated against polysomnography with a high sensitivity and specificity [23], and therefore we do not believe this represents a major limitation. In addition, early discharge or withdrawal of consent reduced the number of patients participating in the final assessment, although total numbers were still sufficient based on sample size calculation. Nevertheless, secondary sleep outcomes should be considered as exploratory, requiring further investigation. Finally, registration of the study was performed after the inclusion of the first two patients, but we do not believe that this short delay impacted the validity of our results.

In conclusion, short-acting agents do not appear to reduce the impact of general anaesthesia on OSA severity compared with standard agents, suggesting that current recommendations for use of these agents in patients with OSA should be revised.

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Supporting Information

Additional supporting information may be found online via the journal website.

Figure S1. Change in pain score over time (values are shown as mean with 95%CI). The generalised estimating equations model showed that there was no significant interaction (p = 0.15), group effect (p = 0.43) or time effect (p = 0.37). RA, Recovery are; POD, postoperative day.

Table S1. Baseline and clinical characteristics for patients who completed the study vs. those who did not have the final polygraphy. Data are mean (SD), median (IQR [range]) or number (proportion) as appropriate.

Table S2. Differences in sleep study data for postoperative night one vs. baseline in patients who completed the study vs. those who did not have the final polygraphy. Data are mean (95%CI).