Sleep disturbances after fast-track hip and knee arthroplasty

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Background. Major surgery is followed by pronounced sleep disturbances after traditional perioperative care potentially leading to prolonged recovery. The aim was to evaluate the rapid eye movement (REM) sleep duration and sleep architecture before and after fast-track hip and knee replacement with length of stay (LOS) < 3 days. The primary endpoint was REM sleep duration on the first postoperative night compared with before operation.

Methods. Ten subjects (≥ 60 yr) receiving spinal anaesthesia and multimodal opioid-sparing postoperative analgesia for total hip or knee arthroplasty were included. Ambulatory polysomnography was performed one night before operation at home, continuously during hospitalization, and on the fourth postoperative night at home. Sleep staging was performed according to the American Academy of Sleep Medicine manual. Opioid use, pain, and inflammatory response (C-reactive protein) were also evaluated.

Results. The mean LOS was 1.5 (1–2) days. The mean REM sleep time decreased from a mean of 18.2 (9.5–23.5)% of total sleep time to 1.2 (0–5.8)% on the first postoperative night (P = 0.002); awake time increased from 19.1 (3.7–44.4)% to 44.3 (12.2–70.6)% (P = 0.009); and sleep architecture on the first postoperative night was more disturbed than before operation. Sleep architecture normalized on the fourth postoperative night. There was no association between opioid use, pain scores, and inflammatory response with a disturbed sleep pattern.

Conclusions. Despite ultra-short LOS and provision of spinal anaesthesia with multimodal opioid-sparing analgesia, REM sleep was almost eliminated on the first postoperative night after fast-track orthopaedic surgery but returned to pre-admission levels when at home on the fourth postoperative night.

Keywords: recovery, postoperative; REM sleep; sleep

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A normal sleep pattern and cycle is important to achieve normal function of physiological and mental processes. Stage N1 (non-rapid eye movement sleep, stage 1) is light sleep (drowsiness) and progresses to deeper sleep in stages N2 and N3. The deepest sleep stages are also called slow wave sleep (SWS). Rapid eye movement (REM) sleep is the sleep stage where dreaming occurs. Normal sleep patterns show a marked rhythmicity with each cycle made up of stages N1, N2 and N3 and REM lasting for ~90 min. Physiologically, sleep is thought to have a restorative function during REM and SWS phases, whereas lighter sleep stages promote hormone secretion facilitating protein synthesis and anabolic processes. Even though the specific role of sleep is yet to be thoroughly elucidated, there is little doubt that proper sleep is an important factor in rehabilitation after surgery.

After major abdominal surgery, patients experience severe sleep disturbances with loss of REM sleep immediately after surgery and a tendency for a rebound phenomenon within the first week after surgery. Sleep deprivation can lead to hyperalgesia and cognitive problems, and the rebound of REM sleep with increased duration and intensity can increase the risk of respiratory and cardiac complications. Many pathophysiological mechanisms for sleep disturbances have been suggested, but the main contributing factors remain unknown. Postoperative pain is a major factor, but the administration of opioids to relieve pain also disturbs sleep. There is evidence to suggest that the severity of the surgical trauma is an important factor for postoperative sleep since minor surgical insults like laparoscopic cholecystectomy or hernia repair cause less sleep disturbance than major abdominal surgery.
To our knowledge, objective measures of sleep after major orthopaedic surgery with a fast-track setup (regional anaesthesia, opioid-sparing multimodal analgesia, mobilization on the day of surgery and planned length of stay (LOS) of 1–3 days) have not been published. Since postoperative sleep disturbances can delay recovery, the aim of this study was to evaluate whether severe sleep disturbances were also present after fast-track hip or knee arthroplasty. The primary endpoint was REM sleep duration before operation compared with the first night after operation.

Methods

The study was approved by the regional Ethics Committee (reg. no. H-2-2010-011) and the subjects gave written and oral informed consent before participating. The study was registered on ClinicalTrials.gov (ID NCT01144130). Enrolment for this study began on April 20, 2010 and concluded on September 15, 2010. We studied 10 subjects, ≥ 60 yr, undergoing either total hip arthroplasty (THA) or total knee arthroplasty (TKA) in a standardized fast-track setup with well-defined discharge criteria and estimated LOS < 3 days. Exclusion criteria were neurological disease, use of sedatives or hypnotics, alcohol abuse (more than 35 units per week) or dementia (defined as a Mini Mental State Examination (MMSE) score of < 24).

All subjects received spinal anaesthesia with local anaesthetic with no opioid added [TKA received 7.5 mg of hyperbaric bupivacaine (0.5%) and THA 12.5 mg of isobaric bupivacaine (0.5%)]. On request, supplemental propofol was administered during surgery but all subjects maintained secure airways unassisted during the procedure. All TKA subjects received local infiltration analgesia by the surgeon before wound closure with 150 ml of ropivacaine 0.2%. All subjects received standardized opioid-sparing postoperative pain management with oral celecoxib 200 mg and slow-releasing acetaminophen 2 g twice daily and gabapentin 300 mg in the morning and 600 mg in the evening. This regime started on the morning of surgery; no opioid or benzodiazepines were administered on the morning of surgery. The standard regime was combined with morphine 5 mg orally as supplemental analgesia on request up to six times daily. All medication administered during hospitalization was registered. Subjects were discharged to their own home when they fulfilled standardized discharge criteria.

Pain medication upon discharge was adjusted according to individual need during hospitalization and consisted of acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs), and weak or strong opioids only on request.

Subjects were studied for two nights in their own home, once before operation at least 3 days before surgery and once on the fourth postoperative night. The primary investigator (L.K.) performed electrode placement and tested the equipment in the home, whereupon the subject slept in their usual environment without the investigator present. Sleep monitoring was also performed continuously during hospital stay to ensure that daytime napping was also recorded. Due to the complexity of the study (evaluating sleep with multiple electrodes during a surgical period), it was decided to limit the number of nights of recording to a minimum to gain knowledge of the primary endpoint: REM sleep change from preoperative to first postoperative night.

Sleep monitoring was performed using Trackit™ Ambulatory EEG (Lifelines Ltd, 7 Clarendon Court, Over Wallop, Nr. Stockbridge, Hants, UK) continuously recording EEG (F3, F4 and A1, A2 from the frontal and mastoid regions, respectively), submental EMG, electrooculography (recorded from the left upper eyelid and just below the right oculomotorius muscle) and three-lead ECG. During the study nights, subjects were asked to wear a pulse oximeter (Nonin Medical Inc., Plymouth, MN, USA). All data were stored on the Trackit™ memory card and later transferred to a personal computer for analysis. On the first preoperative night, subjects also wore truncal and abdominal respiratory sensors (SleepSensor, S.L.P. Inc., St Charles, IL, USA) and nasal air flow meter (PRO-Tech, Pro-Flow Nasal Cannula P/N 1257, Pro-Tech Services, Inc., Mukilteo, WA, USA). Periodic lower limb (PLM) movements were recorded from anterior tibialis bilaterally on the first night of monitoring. PLM measurements were not possible after surgery due to interference with bandages and physical therapy.

Sleep stage analysis was performed manually by 30 s epochs as described in the American Academy of Sleep Medicine Manual for the Scoring of Sleep and Associated Events (AASM). Total sleep time (TST) was defined as minutes spent asleep during the night, sleep period time (SPT) was defined as minutes from initial sleep onset until final morning awakening, and awake time (AT) was defined as time awake during the night after initial sleep onset. Daytime sleep staging was evaluated separately. Evaluation was performed by the primary investigator (L.K.) and an experienced polysomnographic technician (trained neurophysiologist). There were no discrepancies in the interpretation between the two evaluations.

Apart from the objective sleep data, subjects were also asked to fill out the Pittsburg Sleep Quality Index (PSQI) questionnaire to illustrate subjective sleep parameters (sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, daytime dysfunction, and use of sleeping medications) before and after operation. PSQI has seven components which range 0–3 and these are combined to yield a global PSQI score ranging from 0 to 21, where 0 indicates no difficulty and 21 is severe difficulty in all areas. The PSQI is designed to screen for long-term changes in subjective sleep parameters. However, to give an idea of the subjective changes after operation compared with before operation, we chose to administer this questionnaire at the preoperative and the last postoperative sleep measurement (at least 1 week apart), despite PSQI not having been designed as a screening tool for repeated measures.

All medication was registered before operation and during hospitalization and pain medication used from discharge until last postoperative monitoring. Throughout the monitoring period, subjects were not allowed to receive any
sedatives or hypnotics except propofol during the surgical procedure. This was in accordance with the standard setup in the fast-track regime. Furthermore, subjects were asked to score their pain at rest using the visual analogue scale (VAS) every morning and night on the days of sleep monitoring. Blood samples to evaluate inflammatory response [C-reactive protein (CRP)] were drawn after sleep monitoring and were analysed using standard methods in the hospital.

No subjects received medication known to modulate sleep before operation, and preoperative baseline measurements were performed well in advance of surgery to exclude anxiety immediately before scheduled surgery.

Statistics

Estimated sample size for the primary endpoint was calculated based on normative material of sleep stages and SPT. We estimated that REM sleep constitutes 25% of SPT in normal subjects with an average SPT of 8 h per night. A reduction in REM sleep by 20% from preoperative to postoperative levels (on the first night) was considered to be clinically relevant. With a power of 0.80 and a two-sided significance level of 5%, we estimated that 10 subjects needed to be evaluated.

For statistical analysis of sleep measures, Wilcoxon’s signed-rank test was used. Analysis of paired observations on sleep measures was performed as paired analysis between post- and preoperative measures. Evaluation of a correlation between the primary endpoint (change in REM sleep time from preoperative levels to levels on the first postoperative night as a per cent of SPT) was performed using the Spearman correlation and plots of the three possible variables, CRP response on the morning after surgery, VAS score as a mean between the score on the first postoperative night and the following morning, and total opioid use from the end of the procedure until the following morning.

Results

Fifteen patients were approached to participate in the study but five declined and a total of 10 subjects were enrolled in the study. Subject characteristics are listed in Table 1. Six had THA and four had TKA. None of the patients received a sedative before surgery. The only preoperative medication given on the morning of surgery was acetaminophen (1 g) and gabapentin (600 mg). Three subjects received intra-operative sedation with propofol infusion [mean 109.6 mg (88–121 mg)]. The level of sedation was adjusted, so subjects were relaxed and drowsy but able to maintain their airways. None had blood transfusion or postoperative complications within the study period.

Sleep monitoring was performed at a mean of 7.5 days (range 5–14) before surgery. All subjects underwent monitoring continuously during their hospitalization. Only one subject was monitored on the second postoperative night since all other patients were discharged before 36 h after operation. One patient experienced problems with the equipment on the last monitoring night at home and the data were insufficient for analysis. Oximetry probes were used during all sleep monitoring periods. However, technical difficulties with the probes rendered four subjects without measurable data. Saturation data from the remaining six subjects showed no prolonged desaturation. No subjects received oxygen treatment in the ward after the first mobilization which took place within the first 3 h after the subjects returned to the ward (standard regime).

SPT showed only non-significant changes from the baseline (Table 2), but when evaluating individual hypnograms, substantial disturbances in sleep architecture were clear. These included periods of AT during the first postoperative night compared with the baseline (Fig. 1). All subjects had severe disturbances in the normal rhythmicity of sleep on the first postoperative night with many movement arousals and long periods of wakefulness.

During the first postoperative night, we found a major decrease in amount of REM sleep time (P=0.002) and an increase in AT (P=0.009) as a percentage of SPT; this was also apparent in the hypnograms (Fig. 1). There were no significant changes in the number of arousals and time spent in stage N1, N2 or N3 on the first postoperative night compared with the preoperative night (Table 2). Six subjects experienced a total loss of REM sleep on the first postoperative night, and four experienced some REM sleep (range 1–6% of TST) but far below preoperative levels (Fig. 2). There was no daytime REM sleep during hospitalization. Results from the fourth postoperative night showed a return to preoperative levels of all sleep stages and number of arousals.

Results from the PSQI questionnaire revealed no major differences in global PSQI scores between pre- and postoperative assessment. The global PSQI score changed less than three points from preoperative assessment (mean score 8, range 1–16) to the fourth postoperative night (mean score 7, range 2–14). The main subjective complaint during the night was inability to lie in a comfortable position without pain. Disturbances from other patients were among the disruptions noted. Disturbances from staff were not recorded to be an issue.

The VAS scores at rest in the morning and evening of the preoperative night of sleep monitoring were 44 (10–67) and 47 (10–71) mm, respectively, compared with 23 (0–61) and

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**Table 1** Baseline and perioperative characteristics [mean (range)]. Values are given as frequencies or median (range). BMI, body mass index; POD1, postoperative day 1; LOS, length of stay

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<th>Subject characteristics</th>
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<td>Sex (male/female)</td>
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<td>ASA (I/II/III)</td>
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<td>Duration of surgery (min)</td>
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32 (5–67) mm on the first morning and night after operation. CRP results for all subjects were below 10 mmol litre\(^{-1}\) before operation, 87 mmol litre\(^{-1}\) (57–159) after the first postoperative night and 140 mmol litre\(^{-1}\) (73–279) after the last postoperative sleep monitoring. All subjects received opioid in the immediate postoperative period. The mean opioid use (equipotent morphine dosage) in the first 24 h after surgery amounted to 23.5 mg (median 20 mg, range 10–42.5 mg). All subjects were discharged with acetaminophen 1 g 6 h, three patients were discharged with NSAIDs, two with weak opioid and one with strong opioid by request. No subjects received sleep medications. There was no association between sleep disturbance and level of pain \((\rho=-0.19)\), amount of opioid use \((\rho=-0.31)\), or inflammatory response \((\rho=-0.57)\), all \(P>0.1\).

### Discussion

This study aimed to evaluate whether the previous reports of postoperative sleep disturbance after major surgery with traditional care\(^4\)–\(^6\) \(^15\) \(^22\) are also present after fast-track...
THA and TKA with very short LOS (1–2 days), early mobilization, and multimodal analgesia. We hypothesized that the reduced impact of surgery in the fast-track setup would reduce postoperative sleep disturbances.

Our results show that REM sleep was severely reduced (92%), awake-time increased (149%), and sleep architecture severely fragmented on the first postoperative night compared with preoperative levels. Other sleep stages were not significantly changed. Interestingly, and in contrast to prior studies, we found sleep architecture returned to preoperative levels on the fourth postoperative night when subjects had been discharged and slept at home for one to two nights. Whether this is due to the short LOS or the differences between surgical procedures is unknown, but our results illustrate that the severe sleep disturbances seen immediately after other types of major non-cardiac surgery are also present in a fast-track arthroplasty setup with standardized postoperative care and a multimodal opioid-sparing analgesic regime with relatively limited postoperative pain.

There are some limitations to this study. The group was small but the study design with paired observations and each subject and patients serving as their control (preoperative vs postoperative data) strengthened our findings. Due to technical problems, complete oxygen saturation data were not available, but in the six subjects with saturation data, sustained hypoxic periods were not observed.

A limitation in our design with only one preoperative night of monitoring is the risk of first night effect (FNE). The FNE is defined by changes in the polysomnography (PSG) on the first night of recording given the unusual situation for the patient. However, the pattern of FNE is complex and several studies have yielded conflicting results. Studies have shown that the FNE affects a number of individuals anxiety and unknown environment shown to be a factor. There are few studies on the elderly and it seems that normal sleepers tend to experience less of an FNE than insomniacs or patients with other sleep disorders. Currently, there are no data on FNE in an elderly surgical population. The normal changes seen on the first night of PSG are a reduction in R and N3 sleep, and a secondary increase on the following nights. Our results from the first night do not indicate a reduction in these stages on the preoperative night. Thus, we believe that the FNE in this study, with ambulatory monitoring at home in normal sleepers, is minimal compared with potential FNE in sleep laboratories.

Impaired sleep might in part be due to inflammatory surgical stress response in conjunction with postoperative pain and discomfort. A single preoperative high-dose injection of methylprednisolone reduced inflammatory response (CRP) and postoperative pain after TKA, but it is unknown whether the positive effect on postoperative pain and inflammation from steroids modifies the postoperative sleep architecture. Interestingly, subjects reported less fatigue within the first 48 postoperative hours but simultaneously reported poor sleep quality after a single dose of methylprednisolone. Most of our subjects reported having had a decent night’s sleep during the first postoperative night. However, PSG monitoring clearly showed that this was not the case in any of our subjects (Fig. 1). This serves to substantiate the fact that subjective measures are of limited value when studying postoperative sleep architecture. Our study was not powered to evaluate the complex effect and individual consequences of the inflammatory response.

Postoperative analgesic regime can have an impact on sleep. All subjects received gabapentin 900 mg day⁻¹ as part of the postoperative analgesic regime, and both gabapentin and pregabalin have been found to have a positive effect on sleep fragmentation with a decrease in arousals and increase in N3. However, the dosage in these studies was substantially higher than in our study, which could account for the lack of impact on N3. Opioids are also known to affect sleep with a reduction in REM sleep and N3 and an increase in stage N1 and N2 sleep. Opioids also increase the risk of central apnoeas during sleep potentially worsening postoperative sleep disturbances. Our study cannot exclude that even a small dose of opioid plays a role in disturbed sleep on the first postoperative night.

Anaesthesia per se can also affect the sleep pattern. However, the only study performed where anaesthesia (isoflurane) alone was evaluated without surgery showed only transient negligible effects on the nocturnal sleep pattern. Since our subjects received regional anaesthesia, we do not believe this to be a major factor in explaining the pronounced sleep disruption on the first postoperative night.

Noise and frequent observations by nursing staff combined with postoperative pain affect sleep. In the fast-track setup, noise and disturbances during the night were limited because LOS was only 1–2 days and there were no standard routines from nursing staff during the night. However, our subjects did sleep in multi-bed rooms on the regular ward and this could be conceived to be a weakness in our design. Nevertheless, we believed it important to illustrate sleep disturbances in a setup used in most hospitals, despite the limited ability to control environmental factors in the sleep disturbances. The body position can also affect sleep, and even though our subjects were not hindered by drains and catheters, they might still have felt encumbered by the operated limb to affect their sleep pattern negatively with more arousals. However, the setup reflects the clinical conditions and reality for such patients and does not limit the relevance of the results.

Rebound of longer and more intense periods of REM sleep and SWS after nights of sleep deprivation has been described. Previous studies have found REM rebound to occur during the second to fourth postoperative night and to return to preoperative levels after ~1 week. In contrast, we found the sleep cycle to return to preoperative levels on the fourth night. It has been speculated that the pronounced rebound of REM sleep, with altered autonomic regulatory mechanisms leading to reduced sensitivity to hypoxia and hypercapnia, could lead to cardiac and respiratory complications. Our study focused on sleep architecture and was not powered to evaluate cardiac outcomes.
In conclusion, there was a pronounced decrease (93%) in REM sleep time on the first postoperative night with severe disturbances in sleep architecture, but a return to preoperative levels on the fourth night after fast-track THA and TKA (LOS 1.5 days). Future studies should focus on the relative role of pain, opioid, and inflammatory response in order to reduce sleep disturbances and fragmentation after major surgery.

Declaration of interest
None declared.

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