Factors affecting post-operative sleep in patients undergoing colorectal surgery – a systematic review

Nina Klemann[1], Melissa Voigt Hansen[2] & Ismail Gögenur[3]

ABSTRACT

INTRODUCTION: Understanding factors affecting post-operative recovery is of great importance to efforts at reducing morbidity and mortality after general surgery. Post-operatively, most patients suffer from objectively and subjectively measurable reduced sleep quality. We aimed to review the available literature on post-operative sleep in patients undergoing colorectal surgery.

METHODS: This systematic review was conducted according to the PRISMA guidelines, searching the electronic databases PubMed, Embase and the Cochrane Library. All articles were evaluated according to pre-defined inclusion criteria.

RESULTS: Five studies were included in the review. Sleep quality was affected by type of surgery (open or laparoscopic), the administration/mode of application of analgesics (epidural analgesia or continuous wound infusion) and the level of pain. Patients who listened to new age music and a "relaxing text" had better quality of post-operative sleep than controls. Overall, pain interfered with subjective, post-operative sleep quality and adequate treatment of pain improved subjective sleep quality.

CONCLUSION: Sleep quality is sensitive to various factors in the perioperative period, and impairment of sleep quality can be prevented by simple improvements in perioperative care.

Understanding factors affecting post-operative recovery is of great importance to efforts at reducing morbidity and mortality after general surgery. Post-operatively, patients suffer from reduced length of sleep, increased sleep-fragmentation and a changed sleep-architecture with reduced rapid eye movement (REM) sleep and slow-wave sleep, and increased light sleep (LS) [1, 2]. Post-operative subjective sleep quality has been investigated in patients undergoing different types of surgery (e.g. minor and major abdominal surgery, vascular and orthopaedic surgery) and has been found to be reduced in up to 55% of patients after surgery [1].

Many factors contribute to the development of post-operative sleep disturbances; such factors include pain [3], the surgical stress response [2], environmental factors (e.g. noise, light, nursing procedures, etc.) [3-5] and medication [2, 6, 7]. Post-operative pain at night has a detrimental effect on sleep [3, 5] and has many other undesirable consequences, e.g. lack of mobilisation and increased used of analgesics [3] during the post-operative period.

The degree and duration of REM sleep reduction is known to be related to the extent of the surgical procedure [8] with more profound disturbances after major surgery such as gastrostomy than after minor surgery such as herniorrhaphy or laparoscopic cholecystectomy [8, 9].

It has been shown that post-operative sleep disturbances may lead to the development of post-operative fatigue, episodic hypoxemia, haemodynamic instability, post-operative cardiac events and altered mental status [2, 10].

We wanted to conduct a focused analysis of the consequences of surgery on a homogenous group of patients with comparable risk of post-operative complications and comparable post-operative care. The aim of this review was to assess the available literature with regard to post-operative sleep disturbances in patients undergoing colorectal surgery.

METHODS

This systematic review was conducted according to the PRISMA guidelines [11]. Included were all randomised controlled trials (RCT) and cohort trials, involving adult colorectal surgery patients and investigation of sleep, evaluated subjectively or objectively, and starting no later than the second day after the operation. There was no restriction on the year of publication, and only articles in full-text and in English were evaluated.

Articles were found by the corresponding author (NK) and the second author (MVH) with the assistance of research librarians, searching the electronic databases of PubMed, Embase and the Cochrane Library on 11 March 2014.

We used the search strategy ((colorectal OR abdom*) AND surgery AND (sleep OR circadian rhythm)). Limits were "humans" and "age 19+". In Embase, the limits were "humans" and "adult 18 to 64" and "Aged 65+ years".

All articles were screened by title by the first author, excluding irrelevant articles and articles not available in English. The remaining articles were screened by abstracts, again excluding the irrelevant material and, fi-

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1) Department of Urology, Rigshospitalet
2) Department of Clinical Pharmacology, Bispebjerg Hospital
3) Department of Surgery, Koege Hospital, Denmark

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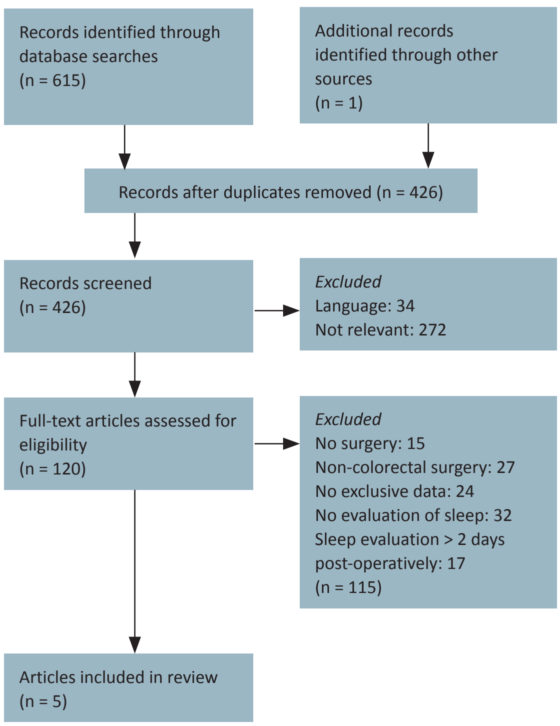
FIGURE 1

The selection process involved in identifying the eligible articles.



nally, the full texts of all remaining articles were read and evaluated for inclusion (see **Figure 1**).

To investigate colorectal surgery and post-operative sleep specifically, we excluded articles regarding non-colorectal surgery such as cholecystectomy and gastric bypass surgery. Some trials investigated the quality of sleep in larger groups of surgical patients, e.g. lung, prostate, orthopaedic surgery, etc. Articles were exluded if it was not possible to extract specific data on colorectal surgery patients.

Finally, articles investigating post-operative sleep starting more than two days post-operatively were also excluded as we wanted to focus on the effects of the surgical stress response on sleep disturbances. No restrictions were made regarding whether sleep disturbances were the primary or the secondary outcome of the study.

Title, authors, year of publication, in- and exclusion criteria, number of patients, study design, intervention, effect measure and primary and secondary outcome were registered for all included studies (**Table 1**).

Bias for each included study was evaluated using the Critical Appraisal Skills Programme (CASP) [12], a systematic programme designed to help identify population bias and randomisation bias.

RESULTS

A total of 268 articles were identified in the PubMed database, 282 articles in Embase and 65 in the Cochrane Library. One additional article was identified through a manual search of the reference lists. The selection process involved in identifying the eligible articles is presented in the flow chart in Figure 1. After evaluation of full-text articles, a total of five articles were eligible for inclusion.

All the included studies were RCTs, three of which were double-blinded. All included studies had subjective sleep quality as a secondary outcome, the primary endpoints being post-operative pain, parenteral morphine consumption and functional recovery. Four studies included patients undergoing open colorectal surgery [13-16] and one compared open colorectal surgery to laparoscopic surgery [17]. For details on the included articles, see Table 1.

Randomised controlled trials, double-blinded

One RCT [17] primarily investigated the difference between functional recovery, i.e. pain, fatigue, mobilisation and pulmonary function in patients undergoing open or laparoscopic colonic or sigmoid resection. The study included 60 patients, and the post-operative follow-up included an individual evaluation of sleep quality by the visual analogue scale (VAS) three nights prior to and seven nights after surgery. Sleep quality during the first post-operative night was found to be significantly poorer in patients operated laparoscopically than in patients operated by open procedure. From the second post-operative night, there was no difference in the subjectively registered quality of sleep or pain.

Another RCT [13] investigated the analgesic effect of continuous pre-peritoneal infusion of ropivacaine compared to infusion of a saline solution. The study included the subjective evaluation of post-operative sleep quality by VAS score each morning post-operatively. All 42 patients in the study were operated electively with a laparotomy due to colorectal cancer. The study found a significantly better quality of sleep on the first two post-operative nights in the group of patients randomised to receive ropivacaine infusion. In addition, pain was significantly reduced compared to those randomised to receive a saline infusion [13].

A randomised, double-blind study [14] investigated the subjectively evaluated quality of sleep in 50 elective colorectal surgery patients randomised to receive either epidural analgesia (EA) or continuous incisional (pre-peritoneal placement) infusion with an analgesic (ropivacaine 0.375%, 5 ml/h or 0.2%, 10 ml/h, respectively). Quality of night sleep was recorded using VAS each morning until discharge. A significantly better quality of sleep was seen on the second and third, but not on the first post-operative night in the group randomised for EA compared with those randomised for incisional infusion. For ethical reasons, the trial was terminated after interim analyses of the first 50 patients, showing lower pain scores at 24 h and shorter hospital stay in patients randomised to the EA group.

Randomised controlled trials, unblinded

One non-inferiority study [15] compared the analgesic effect of epidural versus pre-peritoneal infusion of ropivacaine in 106 patients operated for colorectal cancer. The study included a subjective evaluation of sleep quality measured by the visual numerical rating scale (VNS) for the first three nights post-operatively.

Preperitoneal infusion of ropivacaine was found not to be inferior to epidural administration in post-operative management of pain. The subjective quality of sleep was significantly better only on the third day (72 h) of evaluation ($p = 0.009$) in the patients randomised to pre-peritoneal infusion of ropivacaine.

Another RCT [16] investigated the effect of guided imaging (GUI) on post-operative pain and quality of sleep, both evaluated subjectively (VAS). The GUI regimen consisted of listening to a tape recording of new age music and the reading of a relaxing text before, during and after the operation (performed in spinal analgesia). A total of 86 patients scheduled for anorectal surgery for benign causes were randomised to either GUI or a standard regimen. Most patients spent the first 24 h in the hospital and had their sleep evaluated.

The study showed no significant difference in post-operative pain between the two groups, but sleep was found to be significantly better among patients in the intervention group.

DISCUSSION

We included five RCTs; three double-blinded and two unblinded. All included studies evaluated subjective post-operative sleep, and all found significant changes in subjective sleep quality post-operatively. None of the studies measured post-operative sleep by objective measures. Four studies [13-16] had primary outcomes related to analgesia, and all found significant differences between the groups in terms of post-operative, subjective sleep quality. Three studies found significantly lower pain scores in groups with better sleep quality. One study [15] found a significantly lower percentage of patients suffering from post-operative nausea and vomiting in the group with better sleep quality.

In the RCT investigating functional recovery between groups operated with open surgery or laparoscopically [17], sleep was found to be significantly poorer on the first post-operative night in the laparoscopically operated patients. This runs contrary to expectations because of the well-documented lower stress response that is seen in minimally invasive surgery. An explanation of this unexpected finding could be that pain was found to be significantly more severe in the laparoscopic group on the first post-operative night and that they also underwent surgery for a longer time [3, 5].

In one study [14], dynamic pain scores during mobilisation decreased steadily in the continuous wound infusion (CWI) group, but remained fairly constant (and lower) in the EA group. The decrease in pain is in agreement with the results from the study comparing CWI to continuous epidural infusion (CEI) [15] where the analgesic effect of CWI was found to be most effective at 72 h, possibly owing to an accumulation of the analgesic and anti-inflammatory effect [13].

A possible source of bias is the fact that patients allocated to the EA group received analgesics both pre- and intraoperatively, whereas patients in the CWI group commenced treatment with analgesics when the multi-holed catheter was placed at the end of the surgery. Considering the possible benefit of accumulation of analgesics in the CWI group, it might have been relevant to compare the two treatment modalities for at least 3-4 days and not, as was the case, remove all catheters after 48 h. Also, it should be noted that patients in this study [14] differed significantly in terms of the intraoperative consumption of sufentanil (21 ± 14 microgram in the EA group versus 53 ± 23 microgram in the CWI group, $p < 0.001$).

Population bias

Four of the included studies offer statistical analysis of baseline characteristics which shows that the groups did not differ significantly with regard to age, height, weight, sex and surgical procedures [13, 15], demographic data [14, 17], American Society of Anaesthesiologists (ASA) score [13, 15, 17], concomitant disease and preoperative morbidity [17].

! KEY POINTS

Following surgery, patients suffer from reduced length of sleep, increased sleep fragmentation and a changed sleep architecture with increased light sleep and reduced rapid eye movement sleep and slow-wave sleep.

Post-operative pain at night has a detrimental effect on sleep and has many other undesirable consequences, e.g. lack of mobilisation and increased used of analgesics.

Post-operative sleep disturbances may lead to the development of post-operative fatigue, episodic hypoxaemia, haemodynamic instability, post-operative cardiac events and altered mental status.

In this review we found sleep quality to be affected by type of surgery (open or laparoscopic), the administration/mode of application of an analgesic (epidural analgesia or continuous wound infusion) and level of pain. We also found better quality of post-operative sleep among patients who listened to new age music and the reading of a relaxing text compared to controls.

Overall, the studies show that pain interferes with subjective post-operative sleep quality and that an adequate treatment of pain improves subjective sleep quality.

TABLE 1

An overview of the included studies.

Reference	n/sex	Age, yrs, mean ± SD (range)	Operation/diagnosis	Benign/malignant
Jouve et al, 2013 [14]	EA:13 M, 11 F CWI: 13 M, 13 F	EA: 63 ± 12 CWI: 68 ± 9	Open, colorectal resection Midline incision No stoma	Not stated
Beaussier et al, 2007 [13]	Ropivacaine: 14 M, 7 F Control 11 M, 10 F	Ropivacaine: 58 ± 10 Control: 62 ± 9	Resection of malignant colorectal tumours	Malignant
Bertoglio et al, 2012 [15]	CEI: 27 M, 26 F CWI: 28 M, 2 5F	CEI: 64, 51 ± 6.66 CWI: 65.7 ± 7.82	Open, non-emergency colorectal cancer surgery	Malignant
Renzi et al, 2000 [16]	GUI: 21 M, 22 F Control: 28 M, 15 F	GUI: 48 (25-72) Control: 44 (18-70)	Benign, ano-rectal disease	Benign
Basse et al, 2005 [17]	Open: 14 M,16 F Laparoscopic: 14 M, 16 F	Open: 75[a] (57-90) Laparoscopic: 75.5[a] (58-85)	Right hemi-colectomy or sigmoid resection, Open or laparoscopic surgery	14 benign 46 malignant

CEI = continuous epidural infusion; CRP = C-reactive protein; CWI = continuous wound infusion; EA = epidural analgesia; F = female; GUI = guided imaging; M = male; P = plasma concentration; RCT = randomised controlled trial; S = serum concentration; SD = standard deviation; VAS = visual analogue scale; VNS = verbal numerical rating scale.
a) Median.
b) Pain experienced during mobilisation from supine to sitting position, recorded in 100 mm VNS.

Two studies [13, 15] only included patients with ASA scores I-II, which reduces the generalisability of the results to the general group of colorectal cancer patients, which also includes many patients with ASA score III [18].

Study design bias

When evaluating sleep, the gold standard for sleep monitoring is polysomnography (PSG); a combination of electroencephalography using scalp electrodes, electromyography where electrodes are placed over specific muscle groups, and electrooculography where electrodes measure the movement of the eyes [19].

A less resource-intensive, but valid method is an actigraph, which is a wrist-borne activity registration device [20]. An actigraph measures the activity level of the patient and can be used to distinguish between awake and asleep activity patterns.

Finally, evaluation forms can be used as a self-reporting, subjective measure for the quality of sleep (QOS), e.g. the VAS and the VNS. VAS is a 100 mm scale ranging from 0 (very poor QOS) to 10 (excellent QOS) [13]. VNS is an 11-point scale, zero being “poor quality” and ten “excellent quality”.

None of the included studies involved PSG, and only one study [17] used actigraphy, but as a measure of physical activity during daytime; it did not provide night-time results or other specific sleep data. Instead, all studies used VAS or VNS that are subjective and hence less precise measuring tools.

It has been shown that a change in VAS of 10 mm or more correlates with a clinically significant change in the patient’s subjective perception of the QOS [21].

Of the included studies, three [13, 16, 17] used VAS and two VNS [14, 15] to measure QOS. Of the three studies using VAS, only one study [17] included preoperative values of QOS.

The same study found clinically significant changes (a change of 10 mm or more) in QOS between evaluated

Study design	Intervention	Outcome primary	secondary	tertiary	Post-operative sleep quality
RCT Double-blinded	CEI vs CWI of analgesia (ropivacaine 0.375%, 5 ml/h vs ropivacaine 0.2%, 10 ml/h)	Dynamic pain score[b]	Time to return of gut function Time to full oral diet Quality of sleep (VAS) Length of hospital stay Analgesic technique related side-effects (e.g. urine retention)	Post-operative morbidity and readmission Residual peri-incisional 3 months post-surgery	Epidural vs CWI ↑ ($p < 0.001$, measured daily until discharge)
RCT Double-blinded	CWI (ropivacaine 0.2%, 10 ml/h) vs saline	Parenteral morphine consumption (mg)	Pain at rest and mobilisation Time to first bowel movement Time to first flatus Mental function, quality of sleep (VAS) Duration of admission Post-operative nausea and vomiting	None stated	Ropivacaine vs saline ↑ ($p < 0.001$ on 1st and 2nd post-operative night)
RCT Not blinded	CEI vs CWI of analgesic (ropivacaine 0.2%, 10 ml/h)	Post-operative pain at rest and coughing (VAS)	Quality of sleep (VNS) Morphine consumption Rescue analgesia Time to first flatus and stool Post-operative nausea and vomiting	None stated	Incisional vs epidural ↑ (on post-operative days 1-3, $p = 0.009$)
RCT Not blinded	GUI vs standard care	Post-operative pain (VAS)	Quality of sleep (VAS)	Nature of first micturition (normal or difficult, e.g. need for catheterisation)	GUI vs standard care ↑ ($p = 0.01$)
RCT Double-blinded	Open vs laparoscopic surgery	Functional recovery: Pain at rest and activity, fatigue, Pulmonary function, oxygen saturation, heart rate Mental function, quality of sleep (VAS) Mobilisation, physical motor activity Nausea and vomiting, time to 1st defaecation S-albumin and P-CRP pre- and post-operatively	None stated	None stated	Laparoscopic vs open ($p < 0.05$ on first post-operative night, hereafter $p > 0.05$)

nights in both open surgery and laparoscopically operated patients.

The study comparing wound infusion of ropivacaine with saline [13] found a clinically significant difference in QOS between the two post-operative nights in the group randomised to receive the saline infusion. The last of the three studies using VAS pooled all data from the post-operative course, and comparable data from each night were therefore not available.

All the included studies had sleep quality as a secondary and not as a primary outcome. Thus, a limitation of this review is the fact that sample size calculations are based on other parameters than sleep.

All studies include patients undergoing colorectal surgery; however, the studies differ as one only included benign [16], others only malignant [13, 15] and yet others both malignant and benign [17] cases. One study did not state whether patients were operated due to malignant or benign diagnoses [14]. This is, however, relevant since a previous study on sleep in cancer patients found insomnia in up to 30% of the patients stating thoughts, pain or discomfort, and concerns as the main contributors to their insomnia [22].

Also, many colorectal cancer patients are operated laparoscopically [18] and the results of the studies involving patients operated with open surgery [14, 15] may not be directly comparable to the results obtained in these patients, since total sleep time, diurnal sleep distribution and need for sleep 30 days post-operatively has previously been shown to differ between groups of patients undergoing laparoscopic versus open surgery [9, 23].

Two studies [15, 17] mention the performance of additional perioperative resections (e.g. uterine), but only one study lists this as an exclusion criterion [15]. One study [17] specifically mentions the performance of additional resections of e.g. small bowel or uterus, and mentions that this does not lead to exclusion.

Post-operative pain has a detrimental effect on sleep.

Factors affecting post-operative sleep in colorectal surgery patients

All of the included studies found significant differences in subjective sleep quality between the evaluated groups, which illustrates that sleep quality is sensitive to many different physiological and psychological factors in the perioperative period.

In this review we found that sleep quality was affected by type of surgery (open or laparoscopic), the administration/mode of application of an analgesic (EA or CWI) and the level of pain. We also found that patients who listened to new age music and the reading of a relaxing text had better quality of post-operative sleep than controls.

Overall, the studies show that pain interferes with subjective post-operative sleep quality and that an adequate treatment of pain improves subjective sleep quality.

CONCLUSION

More studies evaluating sleep as the primary outcome in colorectal surgery patients are needed. In order to determine the direct effects of colorectal surgery on post-operative sleep pattern, these studies should involve an objective evaluation of sleep by means of PSG and, ideally, also a subjective evaluation of sleep quality in order to correlate the objective and subjective findings and hence allow us to better understand the consequences of surgery on post-operative sleep. It remains undetermined if sleep disturbances may cause increased morbidity after surgery.

CORRESPONDENCE: *Nina Klemann,* Urologisk Klinik, Rigshospitalet, Blegdamsvej 9, 2100 København Ø, Denmark. E-mail: ninakhp@gmail.com

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CONFLICTS OF INTEREST: Disclosure forms provided by the authors are available with the full text of this article at www.danmedj.dk

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