

Delirium after fast-track hip and knee arthroplasty

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Editor's key points

- Postoperative delirium (PD) in elderly patients can be problematic after major surgery.
- No cases of PD were found in elderly patients after fast-track joint replacement surgery.
- Multimodal analgesia and the fast-track regimen may contribute to the lack of PD.
- Further work is needed to establish causal factors for the absence of PD that was found.

Background. Postoperative delirium (PD) is a serious complication after major surgery in elderly patients. PD is well defined and characterized by reduced attention and disorientation. Multimodal optimization of perioperative care (the fast-track methodology) enhances recovery, and reduces hospital stay and medical morbidity. No data on PD are available in fast-track surgery. The aim of this study was to evaluate the incidence of PD after fast-track hip (THA) and knee arthroplasty (TKA) with anticipated length of stay (LOS) of <3 days.

Methods. In a prospective multicentre study to evaluate postoperative cognitive dysfunction, we included 225 non-demented patients with a mean age of 70 yr undergoing either THA or TKA in a fast-track set-up. Anaesthesia and postoperative pain management were standardized with limited opioid use. Nursing staff were trained to look for symptoms of PD which was assessed during interaction with healthcare professionals. Patients were invited for a clinical follow-up 1–2 weeks after surgery.

Results. Clinical follow-up was performed in 220 patients at a mean of 12.0 days after surgery while five patients were followed up by telephone. The mean LOS was 2.6 days (range 1–8 days). Twenty-two patients received general anaesthesia, and the rest had spinal anaesthesia. No patients developed PD (95% confidence interval 0.0–1.6%).

Conclusions. A fast-track set-up with multimodal opioid-sparing analgesia was associated with lack of PD after elective THA and TKA in elderly patients.

Keywords: anaesthesia recovery period; delirium; general surgery; postoperative complications

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Postoperative delirium (PD) is a heterogeneous condition characterized by an acute change in mental status with symptoms often fluctuating during the day.^{1–4} PD is associated with prolonged hospital stay and increased morbidity and mortality.^{5–6} The aetiology is multifactorial with several well-described risk factors such as increasing age and pre-operative cognitive impairment.^{4–5–7} Eliciting factors include polypharmacy, withdrawal states, electrolyte imbalances, and infection.^{4–5–7}

The incidence of PD after orthopaedic surgery is variable, probably in part due to the heterogeneity of surgical procedures.^{2–4–8} Elective and acute emergency surgery must be considered separately. A meta-analysis of PD after orthopaedic surgery showed an incidence of PD after elective surgery to be between 3.6% and 28.0%.⁸ Multimodal optimization of perioperative care (the fast-track methodology)

has been documented to enhance recovery and reduce hospital stay and medical morbidity,⁹ but no data on PD are available after major surgery. The aim of this study was therefore to evaluate the incidence of PD after fast-track hip (THA) or knee arthroplasty (TKA) with anticipated LOS <3 days.

Methods

The patients described here were included in a prospective multicentre study of postoperative cognitive dysfunction after fast-track THA and TKA. The study was approved by the regional Ethics Committee (Reg. No. H-3-2009-096) and patients gave written and oral informed consent before participation. The study was registered at ClinicalTrials.gov (ID No. NCT01103752).

Table 1 Pain regime according to hospital (A, B, C, and D)—all medication as oral administration

| Medication | A | B | C | D |
|-------------|----------------------------------|-----------------|------------------|----------------------------------|
| Routine | | | | |
| Paracetamol | 1 g every 6 h | 1 g every 6 h | 1 g every 6 h | 1 g every 6 h |
| Gabapentin | 300 mg morning 600 mg evening | — | — | 300 mg morning 600 mg evening |
| Tramadol | — | 50 mg every 6 h | — | — |
| Celecoxib | 200 mg every 12 h | — | — | — |
| Ibuprofen | — | — | 400 mg every 8 h | 400 mg every 8 h |
| On request | | | | |
| Oxycodone | 5 mg as needed | 5 mg as needed | 5 mg as needed | — |
| Tramadol | — | 50 mg as needed | — | 50 mg as needed |
| Morphine | 5 mg as needed | 5 mg as needed | 5 mg as needed | 5 mg as needed |

The inclusion period for this study began on February 15, 2010, and was concluded on August 16, 2011. Eligible patients were undergoing elective THA and TKA in a fast-track set-up at four hospitals (Holstebro, Århus, Hørsholm, and Gentofte). All participating departments had a routine fast-track set-up with anticipated length of stay (LOS) <3 days.¹⁰

The fast-track set-up started before surgery, when all patients received information about the surgical procedure, analgesia, anaesthesia, expected LOS <3 days, and the vigorous physiotherapy during hospitalization.¹⁰ All patients were instructed by physiotherapists in relevant exercise regimes meant for physical training before and after operation. Pre-operative information also included a thorough explanation of the practical issues all the patients face after operation. This thorough information is an important part in the optimized fast-track set-up and continued during hospitalization.

Inclusion criteria were age ≥60 yr and ASA physical health class I–IV. Patients were excluded if they had been anaesthetized within the past 30 days, had dementia [defined by Mini-Mental State Examination (MMSE) ≤23],¹¹ or Parkinson's or other neurological disease causing functional impairment. Patients with a history of alcohol abuse (≥35 units per week) or daily use of hypnotics or anxiolytics were also excluded, and also those with severe hearing or visual impairment. All patients had to be fluent in written and spoken Danish.

All patients received standardized anaesthesia and post-operative analgesia according to the centre they were affiliated to (Table 1). All patients fasted for 6 h without solids and 2 h without clear liquids. No patients were given sedative premedication.

Spinal anaesthesia was the standard anaesthetic method. Propofol infusion was given if sedation was needed during surgery. Level of sedation was adjusted, so patients were relaxed and drowsy but able to secure their airways. General anaesthesia was used only if spinal anaesthesia was unsuccessful or contraindicated. Surgery was performed by experienced arthroplasty surgeons at consultant level.

All patients received standardized postoperative care with well-defined discharge criteria.¹⁰ The postoperative

Table 2 List of the main DSM-IV criteria used in this study. The nurses' evaluation focused mainly on 1 and 2 to arise suspicion of PD

DSM-IV main criteria¹²

1. Disturbance of consciousness, with reduced ability to focus and sustain attention
2. Change in cognition (e.g. disorientation, memory deficits) not previously accounted for or explained by evolving dementia
3. Development during hours or days and often fluctuation during the day
4. There is evidence from the history, laboratory findings, or physical examination that the disturbance is caused directly by a general medical condition

mobilization was started on the day of surgery with support from nursing staff and intensive physiotherapy was started the next day. Patients performed exercises on their own between ambulatory training with healthcare professionals. Instruction in these exercises and the use of crutches was given before surgery. The amount of exercise and training was not restricted.

The primary aim was to assess the incidence of PD defined according to the DSM-IV criteria (Table 2).¹² Nursing staff were trained to focus on symptoms of delirium after operation and report in nurses' charts and to the surgeon in charge of post-operative care if symptoms indicating delirium arose.¹³ All patients were evaluated several times a day by a physiotherapist, during ambulatory training, and nursing staff during peri-operative care. The registered nurses in the ward performed the evaluation for PD while undertaking their regular post-operative care. As such, the patient was evaluated at least once during every 8 h nursing shift, but often there were more than one interaction and evaluation during the daytime. If the patient for some reason was not able to follow the mobilization regime, it was described in the nurses' charts if this was related to symptoms indicating inattention, confusion, disorientation, or changes in level of consciousness. All nursing and

hospital records were reviewed for the presence of these symptoms and signs. All use of opioids and sedatives was recorded. The primary investigator (L.K.) undertook regular visits to all centres to ensure that all centres followed the protocol and recorded all the data relevant for the study.

Other postoperative complications, including pneumonia, pulmonary embolism, deep venous thrombosis, myocardial infarction, stroke, infection, and admission to the intensive care unit, were recorded during the follow-up period. A pre-planned clinical follow-up was scheduled between 1 and 2 weeks after surgery and was performed by an assigned research nurse. Patients without clinical follow-up were contacted by telephone by the research nurse.

Statistics

Continuous data are reported as mean or median with range or inter-quartile range (IQR), and the incidence of PD is reported with 95% confidence interval.

Table 3 Patient characteristics [mean (range)], co-morbidity [total number (per cent of total)]. Heart disease—atrial fibrillation, cardiomyopathy, ejection fraction < 40%, severe heart valve defect, angina, heart failure. Lung disease—COPD, restrictive lung diseases, lung cancer

| Patient characteristics | |
|---------------------------|--------------|
| Sex (male/female) | 111/114 |
| Age (yr) | 69.4 (60–86) |
| MMSE | 28.6 (24–30) |
| ASA I/II/III/IV | 69/143/13/0 |
| BMI (kg m ⁻²) | 27.3 (17–40) |
| Smoking daily | 22 (9.7%) |
| Alcohol >2 units per day | 24 (10.6%) |
| Hypertension | 126 (56.0%) |
| Lung disease | 15 (6.7%) |
| Heart disease | 28 (12.4%) |
| Diabetes (type I/II) | 1/17 |
| Depression | 17 (7.5%) |
| Length of stay (days) | 2.6 (1–8) |

Results

We enrolled 225 patients in the study. Eighty-four patients declined to participate and stated the inconvenience of extra hospital visits as the reason. Two patients were excluded due to an MMSE score of <24. Patient characteristics and co-morbidities are listed in Table 3. Eighty-one patients had TKA and 144 THA. None had bilateral surgery. No patients were lost to follow-up during hospitalization, but five patients, who declined to participate in the post-operative follow-up due to the inconvenience of another hospital visit, were contacted by telephone after discharge.

Eighteen patients received opioids before operation (tramadol 50 mg three to four times per day).

Spinal anaesthesia was used in 203 (90.2%) patients, and 101 (49.7%) of these received propofol sedation, the total mean dose being 2.17 mg kg⁻¹ (range 0.24–6.98 mg kg⁻¹, IQR 1.45–2.71 mg kg⁻¹). Twenty-two patients (9.8%) received general anaesthesia; nine of these received total i.v. anaesthesia with propofol (mean 12.5 mg kg⁻¹) and remifentanyl (mean 0.062 mg kg⁻¹) and 13 patients received volatile anaesthesia.

A total of 18.6% (n=42) patients were managed without rescue opioids. The remaining patients received small doses of a supplemental oral opioid either with oxycodone, morphine, or ketobemidone (Table 4). Twenty-nine patients needed both oxycodone and morphine to manage their pain after operation. Ten patients received sleep medication (Zolpidem® or Zipoclon®) while in hospital. No other sedatives were administered.

No patients developed delirium (95% CI 0.0–1.6%) during their hospital stay nor when assessed at the follow-up visit (n=220) or by telephone (n=5).

Seven patients had postoperative complications within the first postoperative week. One patient was reoperated on due to wound complications on day 4, and LOS was 8 days. Two patients were reoperated on day 2 with debridement, and LOS was 4 days in both patients. Three patients developed superficial wound infection, one patient needed i.v. antibiotics and two patients were managed on oral antibiotics. Two patients developed gastric ulcer on the third postoperative day and were transferred to another ward and treated there. Six patients needed blood transfusions

Table 4 Opioid administered as supplement to standard analgesic regime according to hospital (A, B, C, and D), in the PACU and during hospitalization where median and range are reported

| | A | B | C | D | Total |
|---|------------------|------------------|------------------|------------------|-------|
| No. of patients | 77 | 102 | 21 | 25 | 225 |
| No. of patients receiving opioid in PACU | 36 | 62 | 7 | 12 | 117 |
| No. of patients receiving oxycodone in hospital | 70 | 57 | 8 | 0 | 135 |
| Oxycodone dose (mg kg ⁻¹ day ⁻¹) | 0.14 (0.01–0.64) | 0.14 (0.04–0.53) | 0.16 (0.11–0.34) | NA | |
| No. of patients receiving morphine in hospital | 0 | 56 | 8 | 13 | 77 |
| Morphine dose (mg kg ⁻¹ day ⁻¹) | NA | 0.14 (0.01–0.83) | 0.10 (0.02–0.79) | 0.13 (0.01–0.41) | |
| No. of patients receiving other opioid (ketobemidone) | 0 | 4 | 0 | 1 | 5 |
| Ketobemidone in equipotent morphine dose (mg kg ⁻¹ day ⁻¹) | NA | 0.27 (0.11–0.65) | NA | 0.18 (NA) | |

in the postoperative period, but this did not prolong stay. All patients were discharged to their own home. No other complications or readmissions were reported during the follow-up (median 12.0 days, range 5–36 days).

Discussion

This study reports no cases of PD in an elderly patient population after fast-track elective THA and TKA during hospitalization and 1–2 weeks follow-up. The fast-track set-up has reduced LOS from 7 to 10 days to a median of 3 days in a decade after hip or knee arthroplasty.¹⁴

However, there are some limitations to our study. We studied only the subset of arthroplasty patients with MMSE >23 in a fast-track set-up. We believe that our results have important clinical implications, since orthopaedic patients traditionally have had a high risk of PD,^{8 13 15} and many of the postoperative measures from the fast-track regime can be implemented in a wide array of surgical procedures. Furthermore, the elderly patient undergoing joint replacement surgery accounts for an increasing percentage of the surgical population and it is important to clarify the risk of PD due to the increased risk of complications and prolonged hospital stay.

Our patient population consisted of relatively healthy and cognitively intact elderly patients according to the exclusion criteria. Prior studies have clearly shown that preoperative cognitive impairment predisposes to development of PD.^{2 4 16 17} However, it is worth noting that only two patients were excluded due to an MMSE score of <24.

One problem was that there were variations in the postoperative regime between the hospitals, including the postoperative analgesic regime, but this did not seem to have had a significant impact on PD, since none was found. Another problem was that inclusion was not consecutive because the research staff was only capable of evaluating four patients per week, and when this number was reached, no more patients were asked to participate that week. Patients not included could have suffered from PD, but we do not believe that there was a significant selection bias with this mode of inclusion. A few patients declined clinical follow-up and this was related to the inconvenience of an additional hospital visit during the study period. Some patients may have declined to participate in the study due to concern for their cognitive abilities and they could have been more prone to PD. However, even if all patients who declined the follow-up visit ($n=5$) did develop PD, the incidence in this population would remain very low.

In the literature, the incidence of PD varies greatly from about 4% to about 70% in various circumstances.^{5 8 18} After elective orthopaedic surgery, a recent review shows a range from 3.6% to 28.0%, but the results are based on heterogeneous samples from a selection of original studies.^{6 8 13 19} Our result is in contrast with these previous findings and even the studies with the lowest reported incidence is higher than our finding.^{8 13} It is a major problem for comparison that studies have focused on heterogenic surgical populations

and lack differentiation between acute and elective surgery. In some studies, LOS is even omitted.^{13 18 20} Acute surgery, night-time surgery, and long duration of anaesthesia have all been shown to increase the risk of PD,^{8 13 19} and it is clear that there needs to be a distinction between elective and acute surgery. Our population was homogenous and all patients were cognitively intact before operation; all had well-planned admissions and short duration of anaesthesia and all surgical procedures were performed during daytime on the same day as admission. Furthermore, the mean LOS was 2.6 days, all patients returned home upon discharge, and there was a low level of postoperative complications. All these factors could account for the lack of PD.

A single patient had a LOS of 8 days: this was due to reoperation 4 days after primary surgery, but overall median LOS was 2 days. Two patients developed a stomach ulcer and were transferred to another department which prolonged hospital stay. Previous studies from various fields report a much longer LOS,^{5 6 20} some even a LOS of up to 3 weeks and a number of patients being discharged to rehabilitation institutions.^{5 18} Comparison with our fast-track regime is therefore difficult. A short LOS could be an important factor in preventing PD due to the quick return to normal routines combined with intensive training and several activities during hospitalization to mimic daily routines as well as multimodal opioid-sparing analgesic strategy.

Within the fast-track set-up, it is a key factor to engage individual patients in their own rehabilitation. This is achieved by early mobilization and ambulatory training with a physiotherapist or healthcare professional several times daily. Patients were encouraged to have all meals in a designated area away from their bed. All these measures help the patients return to a more normalized routine similar to their home environment, and they are also helpful in maintaining a daily rhythm, with regular mealtimes and activities. Previous studies have found that an effective intervention for patients at risk of developing PD is reorientation and a steady schedule,^{3 4 17} which is intrinsic in the fast-track set-up.

Many of the previous studies evaluating PD have used the confusion assessment method (CAM) criteria as their main focus.^{3 21 22} This approach is validated and the CAM shows a high inter-observer reliability.^{3 21 22} The limitation with the CAM screening procedure is often the frequency of screening, and with the fluctuation in symptoms being a key factor in PD, a high frequency of evaluations is important. We believe that an assessment performed by a trained nurse with a direct focus on cognition during their 24 h patient care would offer a more reliable estimation of the incidence of PD than one or two daily evaluations of 5–10 min. We used DSM-IV criteria based on careful observation during the several one-on-one activities during the day between the patient and a healthcare professional trained to look for cardinal symptoms of delirium. All discrepancies in the activities were recorded in either nurses' records or patients' records and it is not likely that any cases of PD were missed. In contrast to many previous studies^{2 5 18 23} where screening for PD is only done once or sometimes twice daily, our method with

the high frequency of one-on-one evaluations by trained staff makes it unlikely that PD was missed and we find our method of evaluation to be valid. It could be speculated that some cases would be missed simply due to the fact that patients were discharged very early (median LOS 2 days) and PD could theoretically develop after discharge. However, all patients were followed up at median 12 days after operation and no patients reported any symptoms that could indicate PD.

In conclusion, a fast-track set-up with multimodal opioid-sparing analgesia was associated with a lack of delirium after elective hip and knee arthroplasty in elderly patients. We believe that the lack of PD after fast-track surgery is partly explained by the fact that the patient population consisted of relatively healthy and cognitively intact elderly patients who underwent a well-planned elective surgical procedure. They were all thoroughly informed about what to expect regarding level of pain and functional limitations after operation and they were actively involved in their own rehabilitation.

Declaration of interest

None declared.

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