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Difference in postoperative opioid consumption after spinal versus general anaesthesia for ankle fracture surgery—A retrospective cohort study

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Abstract

Background: Surgical treatment of ankle fracture is associated with significant pain and high postoperative opioid consumption. The anaesthesia method may affect early postoperative pain. The main objective of the study was to compare postoperative opioid consumption after ankle-fracture surgery between patients treated with spinal anaesthesia and general anaesthesia.

Methods: We reviewed retrospectively the files of 586 adult patients with surgically treated ankle fracture in the years 2014 through 2016. The primary outcome was opioid consumption during the first 48 postoperative hours. Secondary outcomes were maximal pain scores, postoperative nausea and vomiting, the length of stay in the post-anaesthesia care unit, and opioid use in different time periods up to 48 h postoperatively. Propensity score matching was used to mitigate confounding variables.

Results: Total opioid consumption 48 h postoperatively was significantly lower after spinal anaesthesia (propensity score-matched population: effect size −13.7 milligrams; 95% CI −18.8 to −8.5; $P < .001$). The highest pain score on the numerical rating scale in the post-anaesthesia care unit was significantly higher after general anaesthesia (propensity score-matched population: effect size 3.7 points; 95% CI 3.2-4.2; $P < .001$). A total of 60 patients had postoperative nausea and vomiting in the post-anaesthesia care unit, 53 (88.3%) of whom had general anaesthesia ($P = .001$).

Conclusions: Patients with surgically treated ankle fracture whose operation was performed under general anaesthesia used significantly more opioids in the first 48 h postoperatively, predominantly in the post-anaesthesia care unit, compared with patients given spinal anaesthesia.

1 | INTRODUCTION

Surgical treatment of ankle fracture is associated with significant postoperative pain.[1,2] Inadequately treated pain and high opioid consumption after surgery can delay functional recovery, increase the risk of postoperative complications, prolong the hospital stay, and increase overall cost. High postoperative opioid consumption may be associated with an increased risk of long-term opioid use.[3,4] Persistent postsurgical pain is a common phenomenon after ankle fracture surgery.[5]

Most studies comparing the postoperative outcome, including opioid consumption,[6] between spinal anaesthesia (SA) and general anaesthesia (GA) after lower limb surgical procedures have been performed in patients with total hip and/or knee arthroplasty,[6-8] in which neuraxial anaesthesia is recommended over GA.[8] Only a few studies have compared differences between SA and GA in patients with surgically treated ankle fracture. A prospective cohort study compared postoperative pain and function after surgical ankle fracture fixation between patients given SA and GA. SA was associated with better functional outcome and less pain, but the evaluation took place 3 months after operation and opioid consumption was not reported.[9] A retrospective cohort study investigating primary surgical ankle fracture fixation compared opioid consumption between GA and SA alone and in combination with peripheral nerve blocks (PNB). The patients receiving SA used 22% less opioids compared with those given GA alone, but the opioid consumption was registered only during the first 24 h postoperatively.[10] None of the previous studies employed statistical matching techniques.

The main purpose of the present study was to compare total postoperative opioid consumption between SA and GA in patients with surgically treated ankle fracture in the first 48 h after the operation. This is the first study to report opioid consumption during the first 48 postoperative hours and to use propensity score matching (PSM) to mitigate the impact of confounding variables.

2 | METHODS

The present study is a retrospective cohort study. The study protocol was approved by the hospital administration. According to local policy, approval from the local ethics committee was not needed. The study was performed in Oulu University Hospital, Finland.

The data were collected from digital medical records and anaesthesia charts. All adult patients who had undergone a surgical ankle fracture procedure from 1 January 2014 through 31 December 2016 were reviewed. The patients were identified with the ankle fracture ICD-10 diagnosis codes S82.4-S82.8 and ankle fracture procedure classification code NHJ-10.[11,12] Exclusion criteria were fractures of both ankles, multiple fractures and/or major trauma, other surgical procedure done at the same time, reoperation of the ankle, and inadequate SA with subsequent conversion to GA during surgery.

Editorial Comment

The impact of spinal vs. general anesthesia for postoperative opioid consumption for ankle fractures was assessed retrospectively, with matching of cases between treatment groups. Findings showed less opioid consumption in the spinal anesthesia group over the hospitalization period, and predominantly in the post-anesthesia care unit. In the same (spinal anesthesia) group though, more opioid consumption was observed on the general ward, possibly a sign of rebound pain after regional anesthesia.

Pre- and intra-operative data were collected from the digital medical records and anaesthesia charts to characterize the study population (Table 1) and identify possible confounders for postoperative opioid consumption. The collected data also included the length of post-anaesthesia care unit (PACU) stays.

The information about the anaesthesia technique was collected from the digital anaesthesia charts. Due to the retrospective design of the study, the anaesthesia method was not preplanned. The anaesthesia was given according to the hospital's anaesthesia guideline for lower limb surgical procedures. The final decision between SA and GA and on postoperative analgesia was made by the attending anaesthesiologist based on possible contraindications and clinical assessment. When GA was selected, the induction was performed using an intravenous bolus of fentanyl and propofol, and maintenance of anaesthesia with sevoflurane. Fentanyl boluses were used for pain management during anaesthesia. A supraglottic airway device was used to secure the airway. If tracheal intubation was needed, rocuronium was used to facilitate the intubation in addition to fentanyl and propofol. Intrathecal or epidural analgesia were not used during GA. Intraoperative PNBs were not used. Bupivacaine was used for SA and intrathecal fentanyl was used to enhance the analgesic effect. Intrathecal morphine was not used in SA. The dosage of anaesthetics were adjusted individually by the attending anaesthesiologist.

In the PACU, pain was treated individually, mainly with oxycodone, acetaminophen, and ketoprofen. PNBs were used only if conservative pain management was insufficient. Acetaminophen was prescribed for almost every patient. NSAIDs (oral ibuprofen or intravenous ketoprofen) were not prescribed routinely but were administered for more intense pain. Opioids were given (intravenously and orally) whenever needed to reach the numeric rating scale (NRS) score ≤4. NRS was recorded when the patient arrived at the PACU, before and after the administration of analgesics and before the patient was discharged to the ward. An NRS score ≤4 was considered acceptable for discharge to the ward. According to our PACU guidelines, the anaesthetic effect (motor and sensory block) of SA must wear off before the patient can be discharged to the ward. In the ward, acetaminophen and NSAIDs were given routinely round the

TABLE 1 Patient characteristics

Parameters	All patients n = 586	Spinal anaesthesia n = 179 (30.5%)	General anaesthesia n = 407 (69.5%)
Gender male	49.3% (289)	45.8% (82)	50.9% (207)
Age	53 [36-64]	62 [49-73]	49 [32-60]
BMI	27.9 [24.9-31.2]	27.8 [24.8-31.5]	27.9 [24.9-30.9]
ASA	2 [1-2]	2 [2-3]	2 [1-2]
1-2	77.4% (452)	63.1% (113)	83.7% (339)
3-4	22.6% (132)	36.9% (66)	16.3% (66)
Smoking	36.3% (213)	34.6% (62)	37.3% (151)
Diabetes	12.8% (75)	19.7% (35)	9.9% (40)
Fracture type	% (n)		
Unimalleolar	29.5% (173)	29.6% (53)	29.5% (120)
Bimalleolar	27.8% (163)	27.4% (49)	28% (114)
Luxation and/or trimalleolar	42.7% (250)	43% (77)	42.5% (173)
Operation technique			
Unimalleolar fixation	46.2% (271)	49.2% (88)	45.0% (183)
Bimalleolar and/or trimalleolar fixation	43.9% (257)	39.1% (70)	45.9% (187)
Fibular rod only	4.4% (26)	6.7% (12)	3.4% (12)
Fibular rod + medial malleolar and/or posterior fixation	5.5% (32)	5.0% (9)	5.7% (23)
Surgical procedure time in minutes	56 [36-78]	53 [34-77]	58 [39-79]
Tourniquet time in minutes	58 [42-82] n = 493	55 [40-82] n = 144 (80.4%)	59 [42-82] n = 349 (85.7%)

Note: The values are shown as medians and interquartile range [25th - 75th percentiles], or percentiles (%) and number of patients (n).

Abbreviations: ASA, American Society of Anaesthesiologists -classification score; BMI, body mass index.

clock if there were no contraindications. Long-acting oxycodone was added to the medication if the pain was moderate to severe and/or persistent. The patient were given short-acting oxycodone perorally when needed.

2.1 | Primary outcome

The primary outcome was the total opioid consumption during the first 48 postoperative hours. Postoperatively administered opioids were converted into the intravenous equianalgesic dose of oxycodone in milligrams. Based on the recommendations in the product characteristics of intravenous oxycodone[13] and considering the variance in oral bioavailability found in different studies,[14-17] we applied a conversion ratio of 1:2 between intravenous and oral oxycodone. The amount of oral codeine was converted into intravenous equianalgesic oxycodone in a relation of 20:1.[18] Intravenous fentanyl was converted into intravenous equianalgesic oxycodone in a relation of 1:75.[17,18] Opioid consumption during the surgical procedure, including intrathecal administration of fentanyl, was recorded but was not included in the analysis of postoperative opioid consumption.

2.2 | Secondary outcomes

Postoperative opioid consumption during the first 48 h was subdivided for secondary analysis to the PACU stay and time periods in the ward after surgery (the first 12 h, 12-24 h, 24-48 h). The subdivision was made to investigate the course of opioid consumption between GA and SA as the immediate postoperative hours are clinically interesting time periods.[6] The highest pain score reported by the patient during the PACU stay was used in the analysis. Clinically significant pain was reported and defined as NRS >5 because it has been noticed to be the cut-off point for preferred additional analgesic dose,[19] and we wanted to clearly differentiate patients with significant pain. Information on postoperative nausea and vomiting

(PONV) during the stay in the PACU was also recorded. The patient was considered to have PONV if an antiemetic was needed or if PONV was clearly documented in the digital anaesthesia records. NRS scores and PONV were not documented routinely in the ward and therefore are not reported.

2.3 | Statistical analysis

Statistical analysis was performed using SPSS (IBM SPSS Statistics for Windows, version 25.0; IBM Corp, Armonk, New York). Categorical data are expressed as numbers (*n*) and percentages (%). Continuous variables are presented as medians and 25th and 75th percentiles. Categorical data were tested using Pearson's χ^2 and continuous variables using the non-parametric Mann–Whitney *U*-test. Propensity score matching (PSM) was performed using the PSM tool in SPSS to compare SA and GA by pairing patients with similar characteristics and demographics. The variables used in the analysis were sex, age, body mass index (BMI), ASA class, smoking, and diabetes, as these variables are related to the study outcome[20] and are shown to have an effect on postoperative opioid consumption.[21-23] There were no missing variables, but the PSM sample size was limited by the number of patients with SA. The effect sizes and 95% confidence intervals (CI) were calculated by using either an independent samples *t*-test or Welch test, the latter if Levene's test showed a significant *P*-value ($P < .05$). A parametric test was used to calculate effect sizes because it gives descriptive results with clinical values and could be used, as parametric statistics do not require an assumption of normal distribution if the data set is sufficiently large.[24] A two-sided *P*-value <0.05 was considered statistically significant.

3 | RESULTS

The patient characteristics are shown in Table 1. A total of 662 patients were identified and 586 patients were included in the analysis, of whom 179 received SA and 407 had GA. Patients who received SA were older, had a higher ASA classification, and more commonly had diabetes than patients in the GA group. For the PSM population, 354 patients were paired, with 177 patients each in the SA and GA groups.

The primary outcomes are shown in Table 2 for the whole study population and the PSM population. The total opioid consumption was significantly lower in the SA group during the first 48 postoperative hours. These results were comparable between the whole study population and the PSM population. When opioids administered in the PACU were excluded from the analysis, the difference in opioid consumption remained statistically significant during the first 48 postoperative hours in the whole study population but not in the PSM population. We conducted a sensitivity analysis of the primary outcome by including all patients to the analysis but assuming zero opioid consumption for the patients discharged 24 h postoperatively. The difference between the study groups in opioid consumption during the first 48 h was still significant (whole study population: effect size −13.2 mg; 95% CI −16.3 to −10.0, $P < .001$ vs. PSM population: effect size −10.3 mg; 95% CI −14.2 to −6.3, $P < .001$).

The comparison of opioid consumption in different time periods between the SA and GA groups in the PSM population is shown in Figure 1. The SA group required significantly less opioids than the GA group during the stay in the PACU (effect size −10.3 mg; 95% CI −12.1 to −8.5; n = 354; $P < .001$). The SA group needed more opioids than the GA group after discharge from the PACU until 12 h post operation in the ward, and this result was statistically significant in the PSM population (effect size 1.9 mg; 95% CI 0.6 to 3.2, $P = .003$) (Figure 1). Opioid consumption levelled again between the SA and the GA groups in the first 24 h postoperatively. The opioid consumption in different time periods was practically similar in the whole study population.

The secondary outcomes during the PACU stay are shown in Table 3. The NRS scores for pain were recorded from 552 patients out of 586 during the PACU stay. NRS scores were significantly lower in the SA group. In the whole study population, NRS ≥5 was

TABLE 2 Primary outcome. Opioid consumption in milligrams compared between spinal and general anaesthesia patients during the first 48 h post operation

	Spinal anaesthesia	General anaesthesia	*P*-value	Effect size	95% CI
Whole study population					
Opioids 48 h post operation, mg	23 [12.5-35] n = 122	38.5 [24-56] n = 260	<0.001	-16.6	-20.6 to −12.5 n = 382
Opioids 48 h post operation, PACU opioids excluded, mg	15 [9-26] n = 122	20 [10-34] n = 260	0.013	-5.1	-8.3 to −2.0 n = 382
Propensity score-matched population					
Opioids 48 h post operation, mg	23 [13-35] n = 120	35 [23-53] n = 116	<0.001	-13.7	-18.8 to −8.5 n = 236
Opioids 48 h post operation, PACU opioids excluded, mg	15 [9.5-27] n = 120	17.5 [10-30] n = 116	0.25	-3.5	-7.6 to 0.5 n = 236

Note: Values are shown as medians and interquartile range [25th-75th percentiles] with the number of patients (n) and the effect size and 95% confidence intervals (CI). Opioids are shown as the intravenous equianalgesic dose of oxycodone in milligrams.

Abbreviations: Effect size, difference in mean values of opioid consumption in milligrams; PACU, post anaesthesia care unit.

reported by 221 (40%) patients of whom 209 (95%) had GA. The results were comparable in the PSM population. A total of 60 patients had PONV during the PACU stay, and of those, 53 (88.3%) were treated with GA.

NSAIDs and acetaminophen were administered significantly more often for immediate postoperative pain after GA, and the percentages were comparable between the whole study population and PSM population (whole study population: ketoprofen 100 mg: SA 15.1% (27) vs. GA 47.7% (194); P <.001; and acetaminophen 1 g: SA 62% (111) vs. GA 74.4% (302); P =.004). Postoperative PNBs were used seldom, in only 17 patients. There were no differences between the study groups in the use of PNBs. The length of PACU stay was significantly longer in the SA group (whole study population: effect size 21 min; 95% CI 8 to 33; P <.001).

In the whole study population, the median dose of bupivacaine used for SA was 10 mg (10-12) and the median dose of intrathecal fentanyl was 20 μg (14-25). Intrathecal fentanyl was administered to 129 patients out of 179 who were operated under SA. The median dose of intravenous fentanyl administered during GA was 225 μg (150-300).

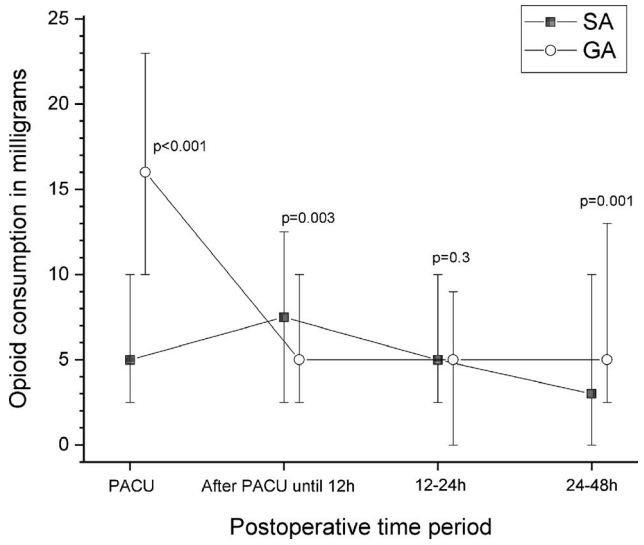

FIGURE 1 The opioid consumption in different time periods between spinal and general anaesthesia in the propensity score-matched population. Values are shown as medians and 25th - 75th percentiles. Opioid consumption is shown as the intravenous equianalgesic dose of oxycodone in milligrams. PACU, post anaesthesia care unit; SA, spinal anaesthesia; GA, general anaesthesia

4 | DISCUSSION

In the present study in patients undergoing ankle fracture fixation, the total opioid consumption was significantly higher in the GA group than in the SA group during the first 48 postoperative hours. However, the difference resulted from the PACU period where the difference in opioid consumption was most pronounced. The need for opioids became evident in GA patients soon after the arrival to the PACU. The patients in the SA group needed less opioids in the PACU due to ongoing anaesthetic and analgesic effect of SA. The difference in the total opioid consumption between the study groups during the first 48 h postoperatively was not clinically relevant after the opioids used in the PACU were excluded from the analysis.

The difference in opioid consumption during the immediate postoperative period have been reported in patients with lumbar spinal surgery and total knee arthroplasty, but without benefit on total opioid consumption in the SA group during the 24 h follow-up.[6,25] A retrospective study in patients with surgically treated ankle fracture and 24 h postoperative follow-up noticed significantly higher total opioid consumption in patients with GA compared with SA but did not report opioid consumption during different time periods.[10] To our knowledge, this is the first study comparing opioid consumption 48 h postoperatively and NRS values during the PACU stay between SA and GA after surgically treated ankle fracture.

In the present study, the patients given SA required more opioids than patients given GA after the discharge from the PACU to the ward during the first 12 h postoperatively. It can be speculated that as the patients in the GA group had significantly higher NRS values during the PACU stay and were administered significantly more opioids, and were also given NSAIDs and acetaminophen more often, the need for pain medication might have been more stable in the ward after the most intense pain was already treated in the PACU. Moreover, the patients in the SA group were discharged to the ward after the anaesthetic effect of SA had worn off. However, some of the analgesic effect of intrathecal fentanyl might have lasted to the ward. Consequently, the need for opioids became more evident after the analgesic effect of fentanyl wore off. The median

TABLE 3 Secondary outcomes during the PACU stay compared between the whole study population and propensity-matched population

	Whole study population (n = 586)			Propensity score-matched patients (n = 354)		
	SA (n = 179)	GA (n = 407)	*P*-value	SA (n = 177)	GA (n = 177)	*P*-value
NRS in PACU	1.5 [0-4]	6 [4-8]	<0.001	2 [0-4]	6 [4-7]	<0.001
NRS ≥5 in the PACU	7.1% (12)	54.5% (n = 209)	<0.001	12.4% (22)	58.8% (n = 104)	<0.001
Length of PACU stay in minutes	157 [120-214]	140 [109-185]	0.001	158 [120-215]	146 [110-188]	0.016
PONV in the PACU	3.9% (7)	13% (53)	0.001	4.0% (7)	15.3% (27)	<0.001

Note: The values are shown as medians and interquartile range [25th - 75th percentiles], or percentiles (%) and number of patients (n).
Abbreviations: GA, general anaesthesia; PACU, post-anaesthesia care unit; PONV, post-operative nausea and vomiting;SA, spinal anaesthesia.

dose of intrathecal fentanyl used in our study population was 20 micrograms and its effect can be expected to last up to 4 h.[26] In the present study, an average time from the administration of SA to the discharge to the ward was 3.5 h. In a previous study in patients with total knee arthroplasty, a significant increase in pain sensation and opioid consumption was noticed in patients given SA compared with patients given GA after 6 h postoperatively.[6] Additionally, an increase in pain sensation and opioid consumption, a phenomenon called rebound pain, has been reported in patients after a PNB has worn off.[27-29] As far as we know, rebound pain has not been clearly documented after SA.

After the PACU period, the opioid consumption in the GA group was more stable and slowly decreased during the follow-up period. In the SA group, decrease in the opioid consumption was more evident after 12 postoperative hours. However, opioid consumption converged between the SA and GA groups during the follow-up period and a longer lasting opioid sparing effect of SA was not noticed in our study.

In this study, over 50% of the patients in the GA group reported NRS ≥5. This finding is supported by a previous study comparing the worst reported NRS scores after various surgical procedures.[1] The optimal cut-off value between mild and moderate postoperative pain is suggested to be at NRS ≥4.[19] NRS has been suggested to be misleading when used alone to evaluate pain and may lead to increased opioid consumption and adverse effects.[30] Patients in our PACU are asked about the need for pain medication, regardless of NRS score.

The present study has strengths and limitations. The large study population gave us an opportunity to use PSM analysis to evaluate our results more critically by mitigating confounding factors related to the retrospective study design. However, PSM analysis cannot control unknown or unmeasured factors which may cause bias on the outcome. Also, less variables used in the PSM reduces effective adjustment for confounders. Multiple statistical tests increase the risk of a false positive finding, where the *P*-value falls below the significance threshold because of random chance. Therefore, the evaluation of the results should focus on effect size and clinical relevance and less on statistical significance.

Approximately one-third of the patients were discharged after the first 24 h. Thus, a smaller sample size reduced the power of the results at 48 postoperative hours. Early discharge could cause significant bias by falsely inflating the opioid consumption if the discharged patients used significantly less opioids leaving patients with pain to the analysis of the primary outcome. This bias was evaluated with the sensitivity analysis, and the results did not differ markedly from the original primary outcome. The main determiner for hospital stay of 48 h, or longer, was the severity of trauma. Factors such as age and comorbidities had some effect on the length of hospital stay.

Due to the retrospective study design, the exposure (SA or GA) was not allocated randomly and distribution between the study groups was uneven. The PSM analysis most likely mitigated some of the selection bias between SA and GA. However, the choice of anaesthesia modality was confounded by unmeasured factors (patient preference, pain catastrophizing, anxiety, etc), which can have influence on the opioid consumption.

Moreover, postoperative pain medication and practices were heterogeneous. Opioids were not administered only if needed, which could have had some effect on total opioid consumption. However, this heterogeneity most likely influenced both study groups somewhat randomly due to the relatively large cohort. Habitual opioid users or patients with chronic pain were included in the analysis since they were few. This could have been a source of significant bias had there been a large number of habitual opioid users. Pain scores and PONV were not routinely documented in the ward. This information would have been valuable when evaluating opioid side effects.

5 | CONCLUSION

Our results suggest that GA, compared with SA, is associated with an increase in total opioid consumption in the first 48 h after surgical ankle fracture fixation, mainly due to a higher opioid consumption in the PACU. Randomized controlled studies are needed to evaluate the effects of different anaesthesia and analgesia modalities on pain sensation and opioid consumption more comprehensively after ankle fracture surgery.

CONFLICT OF INTERESTS

The authors have no conflict of interest.

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