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Ghaffari, Arash; Jørgensen, Marlene Kanstrup; Rømer, Helle; Sørensen, Maibrit Pape B.; Kold, Søren; Rahbek, Ole; Bisgaard, Jannie

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Arash Ghaffari*, Marlene Kanstrup Jørgensen, Helle Rømer, Maibrit Pape B. Sørensen, Søren Kold, Ole Rahbek and Jannie Bisgaard

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Abstract

Objectives: Continuous peripheral nerve blocks (cPNBs) have shown promising results in pain management after orthopaedic surgeries. However, they can be associated with some risks and limitations. The purpose of this study is to describe our experience with the cPNBs regarding efficacy and adverse events in patients undergoing orthopedic surgeries on the lower extremity in different subspecialties.
Methods: This is a prospective cohort study on collected data from perineural catheters for pain management after orthopedic surgeries in lower limbs. Catheters were placed by experienced anesthesiologists using sterile technique. After an initial bolus dose of 10–20 mL ropivacaine 0.5% (weight adjusted), the catheters were secured and connected to disposable mechanical infusion pumps with ropivacaine 0.2% (basal infusion rate = 6 mL/h; weight adjusted (0.2 mL/kg/h)). After catheterization, the patients were examined daily, by specially educated acute pain service nurses. Pro re nata (PRN) or fixed boluses (10 mL bupivacaine 0.25%; weight adjusted) with an upper limit of 4 times/day, were administered if indicated. Patients' demographic data, physiological status, and pre-op intake of opioids and other analgesics were registered. The severity of post-operative pain was assessed with 'Numeric Rating Scale' (NRS) and 'Face, legs, Activity, Cry, Consolability' (FLACC) scale for adults and children, respectively. The need for additional opioids and possible complications were registered.
Results: We included 547 catheters of 246 patients (Range 1–10 catheters per patient). Overall, 115 (21%) femoral, 162 (30%) saphenous, 66 (12%) sciatic, and 204 (37%) popliteal sciatic nerve catheter were used. 452 (83%) catheters were inserted by a primary procedure, 61(11%) catheters employed as a replacement, and 34 catheters (6.2%) used as a supplement. For guiding the catheterization, ultrasound was applied in 451 catheters (82%), nerve stimulator in 90 catheters (16%), and both methods in 6 catheters (1.1%). The median duration a catheter remained in place was 3 days (IQR = 2–5). The proportion of catheters with a duration of two days was 81, 79, 73, and 71% for femoral, sciatic, saphenous, and popliteal nerve, respectively. In different subspecialties, 91% of catheters in wound and amputations, 89% in pediatric surgery, 76% in trauma, 64% in foot and ankle surgery, and 59% in limb reconstructive surgery remained more than two days. During first 10 days after catheterization, the proportion of pain-free patients were 77–95% at rest and 63–88% during mobilization, 79–92% of the patients did not require increased opioid doses, and 50–67% did not require opioid PRN doses. In addition to 416 catheters (76%), which were removed as planned, the reason for catheter removal was leaving the hospital in 27 (4.9%), loss of efficacy in 69 (13%), dislodgement in 23 (4.2%), leakage in 8 (1.5%), and erythema in 4 catheters (0.73%). No major complication occurred.
Conclusions: After orthopaedic procedures, cPNBs can be considered as an efficient method for improving pain control and minimizing the use of additional opioids. However, the catheters sometimes might need to be replaced to achieve the desired efficacy.

***Corresponding author: Arash Ghaffari,** Interdisciplinary Orthopaedics, Aalborg University Hospital, Hobrovej 18-22 9100 Aalborg, Denmark, E-mail: a.ghaffari@rn.dk
Marlene Kanstrup Jørgensen, Helle Rømer, Maibrit Pape B. Sørensen and Jannie Bisgaard, Orthopedic Anaestesia Department, Aalborg University Hospital, Aalborg, Denmark
Søren Kold and Ole Rahbek, Interdisciplinary Orthopaedics, Aalborg University Hospital, Aalborg, Denmark

Keywords: continuous peripheral nerve block; lower extremity orthopaedic surgery; multimodal analgesia; postoperative pain; regional anesthesia.

Introduction

Poorly controlled pain after orthopedic procedures often leads to prolonged hospital stay and more complicated rehabilitation, and imposes a great burden to the healthcare system [1, 2]. In addition, uncontrolled acute post-operative pain has been shown to be a consistent risk factor for incidence of persistent or chronic postoperative pain, which can develop in as many as 10–50% of the patients [3].

Peripheral nerve block is a localized and region-specific analgesic option, and as a component of multimodal opioid sparing analgesia regimen, plays an important role in post-operative pain management [4–7]. Continuous infusion of local anesthetics by means of novel infusion pumps, provides a significantly longer duration of analgesia, which even facilitates the application in an ambulatory setting. The efficacy of continuous peripheral nerve blocks (cPNBs) in improving the pain control after orthopedic surgeries has been consistently shown in systematic reviews and meta-analyses [8–12]. Several studies indicated reduction in the use of opioids, and consequently, reduction in systemic opioid adverse effects [11, 13]. Other benefits included reduction in length of hospital stay [14] and faster recovery [15, 16].

However, peripheral nerve blocks can be associated with some risks and limitations [7, 17, 18]. The incidence of potential adverse events such as infection, catheter displacement and leakage of the anesthetics, depends on insertion technique and anatomic site of the catheters, and can easily influence the efficacy of peripheral nerve blocks and reduce the tendency to implement catheters as standard care. Furthermore, the variation of performance between different orthopaedic subspecialities is unknown. Although a large number of studies have been conducted to answer the aforementioned questions, the efficacy of peripheral nerve catheters has not yet been fully defined and there are still some ambiguities regarding the benefits and side effects.

The objective of this study is to describe our experience with continuous peripheral nerve block in patients undergoing surgeries on the lower extremity in different orthopedic sub-specialties. We compare the efficacy of peripheral nerve catheters regarding pain control and simultaneous opioid requirement, in addition to the rate of complications causing cessation of the catheterization.

Methods

Study design

This cohort study was performed on prospectively collected data from perineural catheters applied at Aalborg University Hospital (AAUH), Aalborg, Denmark, during the period from August 2019 to June 2020. The study was approved by the Danish Data Protection Agency 2008-58-0028, ID 2019-83. In Denmark, registry studies do not need ethical approval. The study follows the STROBE guidelines for reporting observational studies [19].

Participants

The indication for placement of pain catheters was post-operative pain, that expected to be severe and prolonged (more than 24 h). It was determined by the anesthesiologist in consultation with the surgeon in charge of the patient. Only patients with peripheral nerve catheters after orthopedic surgeries in lower limbs were included in the study. No restrictions were applied regarding the age of the participants. Catheters applied in an ambulatory setting, or indications other than perioperative pain were excluded from our study.

Catheters

All catheters were placed by anesthesiologists experienced in deployment of peripheral nerve catheters. Sterile technique was used, and catheterization were guided by ultrasound (High frequency linear probe (6–13 MHz)) for Echo-polyplex 90 (Temena) catheters, and/or nerve stimulator (current intensity = 0.3–0.6 mA, frequency = 2 Hz, pulse width = 0.1 msec) for Arrow StimuCath® (Teleflex Technologies) catheters. Most pain catheters were inserted under general anesthesia, whereas re-sitings and supplementary catheterizations were typically performed in awake patients. Catheters were inserted from 2 to 5 cm and a bolus dose of ropivacaine 0.5% 10–20 mL (adjusted to the weight of the patient) was administered through the catheter at the time of catheterization, to check the efficacy. Subsequently, the catheters were secured with medical glue and transparent occlusive dressing (Figure 1) and connected to disposable mechanical infusion pumps, CADD®-Solis VIP Ambulatory Infusion Pump (Smiths Medical), with a standard of ropivacaine 0.2% basal infusion rate 6 mL/h. For children boluses and infusions were adjusted by weight (0.2 mL/kg/h).

Follow-up

The infusion continued in the postoperative period. The patients were followed and assessed by two specially educated acute pain service nurses, who both have higher academic degrees in pain management, in addition to decades of experience in this field.[1] The pain nurses

1 Both pain nurses have academic diplomas in “Acute Pain”, and one has a master’s degree in “Pain Science and Multidisciplinary Pain Management”. One has 23 years and the other has 11 years of experience in pain management.

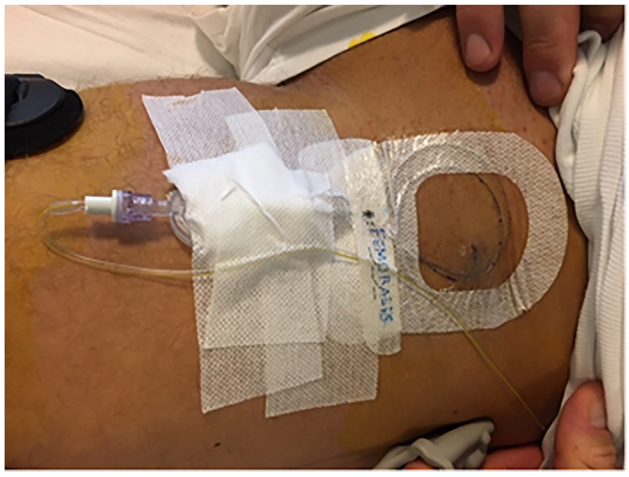

Figure 1: Photograph showing how the catheter is fixed in a patient.

work based on a framework in collaboration with anesthesiologists, surgeons, nursing staff in the wards, physiotherapists, and other healthcare teams. For breakthrough pain, a bolus was administered by the acute pain service nurse if indicated. Further administrations, as pro re nata (PRN) or fixed boluses (10 mL bupivacaine 0.25%; weight adjusted) with an upper limit of 4 times/day, were planned. The insertion sites were inspected every day, except for weekends, for signs of inflammation and infection, and if needed, the dressings were improved. The catheters were replaced in cases that any adverse event happened, the catheters lost their efficacy, or the patients underwent new surgeries. This decision was made based on the judgement of the pain nurses in collaboration with the surgeon in charge of the patient, while the patients were also involved in this decision. In situations where the existing catheters were functional, but the pain relief was not adequate, adding an extra catheter was considered. Termination of catheterization was also determined by the pain nurses, in consultation with the surgeon in charge of the patient, based on the condition of the patient regarding pain, mobilization, type of surgery, and the postoperative need for opioids.

Data collection

In addition to demographic data, patients' physiological status assessed by American Society of Anesthesiologists (ASA) physical status classification system [20] was registered. The patients' status regarding pre-op intake of opioids and other analgesics was also recorded. For evaluating the severity of adults and older children's post-operative pain, we used an eleven-point Numeric Rating Scale (NRS 0–10) [21] 'at rest' and 'during mobilization'. For children under 5 years of age, Face, legs, Activity, Cry, Consolability scale (FLACC 0–10) [22] was used. Patients with NRS lower than 4 were assumed to have acceptable pain, while patients with NRS equal to or higher than 4 considered to suffer from pain. Pain assessment was performed during rest and mobilization. The definition of mobilization in our study was standing in up-right position, sitting in a chair, going to the toilet with or without support, and/or ambulation. The patients were mobilized as soon as there was no contra-indication for mobilization, based on surgeon's decision and the type of surgery. Moreover, whether the patient had adequate pain control, determined the time of mobilization. The need for additional analgesics was recorded as PRN opioid and increased opioid doses. Possible complications and adverse events that caused unplanned catheter removal were also registered.

Data were stored in a database, that had been created for this purpose, using REDCap electronic data capture tools hosted at Region Nordjylland, Denmark [23].

Study size

Sample size was based on availability of patients requiring perineural catheters for post-op pain management after lower limb orthopedic surgeries during the study period. No pre-study sample size calculations were performed for this descriptive study design.

Statistical methods

Descriptive statistics were applied to describe demographic data, duration of catheterization, efficacy, and adverse events. The duration of catheterization and the proportion of catheters with duration of more than two days, as an indicator of the length of pain management, were calculated. The efficacy was reported as proportions of the patients with acceptable pain level in each follow up visit, in addition to proportions of the patients, who did not require increased opioid doses or PRN opioids. The incidence of adverse events, which resulted in catheter removal, was reported as frequency and proportions. Descriptive statistical analysis and making plots were conducted in R (R Core Team, 2020) [24].

Results

Subjects

During the period of study, 271 patients received pain management with peripheral nerve catheters. After excluding 25 patients (8 patients with upper extremity catheters, 8 ambulatory patients, 3 patients with pain due to limb ischemia, and 6 patients in other departments), 246 consecutive patients were finally included in our study (table 1).

Overall, 547 catheters were applied in the study. The mean total number of catheters a patient received during the treatment course was 2.2 (Range 1–10), reflecting the number of simultaneous catheters, the rate of catheter replacements, and the number of operations the patient underwent. While 213 patient (=406 catheters) experienced cPNBs for only one operation, 28 patients (=111 catheters), 3 patients (=16 catheter), 1 patient (=9 catheters), and 1 patient (=5 catheters), received cPNBs for two, three, four, and five operations, respectively.

The catheters were applied in four different anatomic locations (Figure 2). In 452 instances (83%), application of

Table 1: The patients' characteristics admitted in different subspeciality sections.

Patients' characteristics	Subspeciality					
	Trauma	Limb reconstruction	Foot and ankle	Pediatric surgery	Wound and amputation	Total
Median age (range) (years)	51 (12–91)	65 (32–92)	55 (18–80)	14 (3.8–38)	72 (4.9–93)	53 (3.8–93)
Sex						
Male, %	45 (54)	12 (40)	39 (65)	29 (60)	15 (60)	140 (57)
Female, %	38 (46)	18 (60)	21 (35)	19 (40)	10 (40)	106 (43)
Preoperative pain management						
No	55	16	45	48	11	175
Low-dose opioid[a]	18	6	9	0	10	43
High-dose opioid[b]	4	4	3	0	3	14
Other medication[c]	12	9	8	0	6	35
ASA[d]						
1	23	1	11	32	0	67
2	40	16	38	16	1	111
3	20	12	11	0	15	58
4	0	1	0	0	9	10
Total	83	30	60	48	25	246

[a]Patients with opioid consumption of less than 90 mg morphine equivalent per day at the time of admission. [b]Patients with opioid consumption of more than 90 mg morphine equivalent per day at the time of admission. [c]Patients with other pain treatments such as gabapentin, tricyclic antidepressants or pregabalin. [d]American Society of Anesthesiologists physical status classification system.

the catheters was performed by a primary procedure, whilst 61 catheters (11%) were employed as a replacement for malfunctioning catheters, and 34 catheters (6.2%) were employed as a supplement to the existing operational ones. Overall, six patients (2.4%) experienced more than two events of catheter replacement during the course of their treatment (Figure 3). Method for locating the nerves during the procedure of catheterization, was ultrasound in 451 catheters (82%), and nerve stimulator in 90 catheters (16%). In 6 catheters (1.1%), a combination of both methods was used.

Duration of catheterization

In all, the median duration a catheter remained in place was 3 days [2–5 days]. This duration varied in different anatomical areas and in different subspecialties (Figure 4). Overall, 409 of 547 catheters (75%) had a duration of more than two days. The proportion of catheters with a duration of more than two days, as an indicator of longer pain management period, differed significantly in four anatomic areas, and it was 81, 79, 73, and 71%, in femoral, sciatic, saphenous, and sciatic popliteal areas, respectively. This proportion varied also between different subspecialties, and 91% of the catheters in wound and amputations, 89% in pediatric surgery, 76% in trauma, 64% in foot and ankle surgery, and 59% in limb reconstructive surgery, remained in place for more than two days.

Efficacy

For the first 10 days after placing the catheters, the proportion of the patients, who reported to be pain free or feel pain, at rest and during mobilization, is depicted in Figure 5.

Regarding opioid administrations, the proportion of patients who required increased opioid doses, and PRN opioids during the first 10 days after catheterization is demonstrated in Figure 6.

Cessation of the treatment

In 416 of 547 catheters (76%), the cessation of the peripheral nerve block was as scheduled. In 27 cases (4.9%), the catheters were removed, since the patients were to leave the hospital (either were transferred to other hospitals or discharged from the hospital).

Overall, the reasons for unplanned discontinuation of the pain management with cPNBs were, loss of efficacy in 69 (13%), dislodgement in 23 (4.2%), leakage in 8 (1.5%), and erythema at the catheterization site in 4 catheters

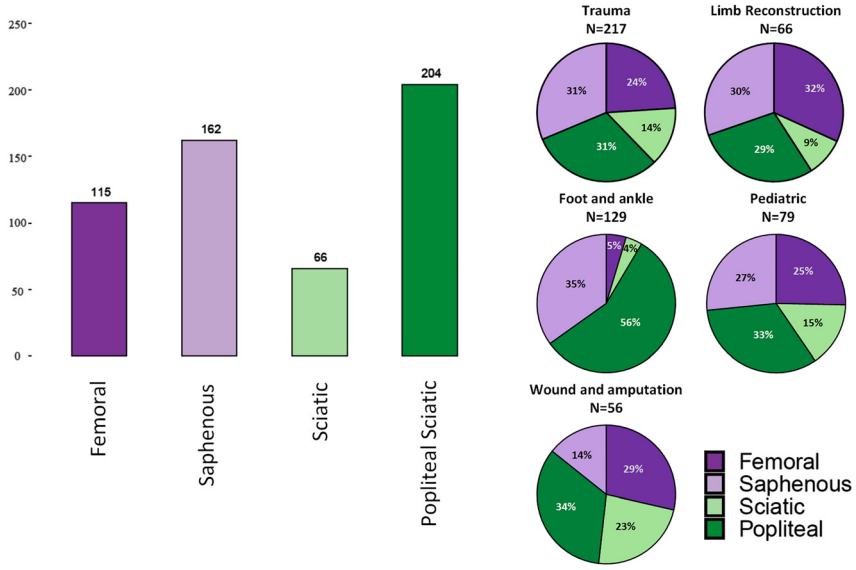

Figure 2: Bar-chart demonstrates the distribution of 547 catheters in different anatomic locations and pie-charts show the percentages of catheters implanted in these anatomic locations in different sub-specialities.

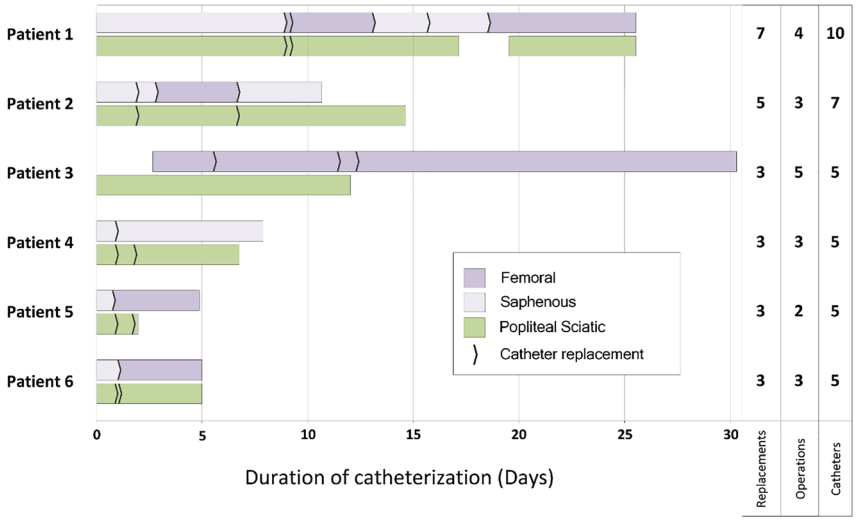

Figure 3: Patients (n=6) who had more than two events of catheter replacement during the course of pain management with cPNBs. The table at the right shows the number of catheter replacements, number of operations and the total number of catheters in these patients.

(0.73%). The proportion of reasons for cessation of catheterization in different anatomic locations are demonstrated in Figure 7.

No major complication has been observed during the study period.

Discussion

Numerous benefits of peripheral neural catheters in the management of post-operative pain have been evidenced by several experimental studies, systematic reviews, and meta-analyses. We investigated the use of lower limb cPNBs in a broad range of patients undergoing various orthopedic surgeries, and our findings support that cPNBs can be employed to relieve pain and reduce the use of opioids. We find it a reliable and effective method, for several days after surgery, with low incidence of adverse events.

In literature, cPNBs as a component of postoperative opioid sparing multimodal analgesia has been strongly recommended due to its many advantages, and their use has become very common in recent decades [5]. However, variable success rates have been reported in literature depending multiple factors, including patients' characteristics, the method of application of analgesia, and the approach for outcome evaluation. Pain is indeed a multifactorial entity and hard to evaluate since it may even be affected by psychological factors such as anxiety and personality. In our study, a substantial and relatively constant proportion of the post-operative patients were pain-free 'at rest' and 'during activities' for the several

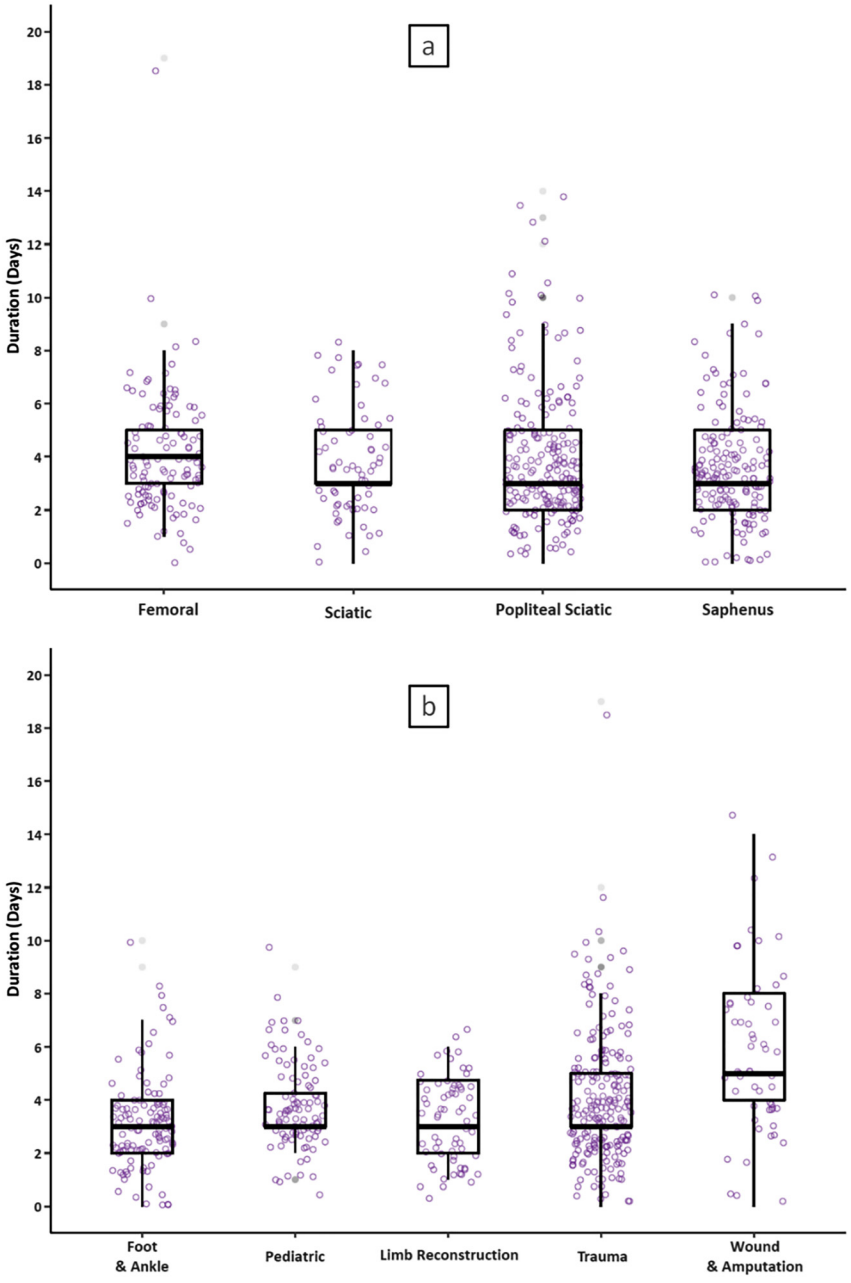

Figure 4: Scatterplots show the catheters' duration and box-and-whisker depicts the median and interquartile range for the number of the days a catheter remained in place based on: (a) catheters' anatomic place, (b) different subspecialities.

days following catheterization. However, the proportion of pain-free patients 'during activities' were moderately lower. This relatively lower success rate in pain relief during activities was also in agreement with other studies [7, 8, 12]. Xu et al. in a Cochrane systematic review found that peripheral nerve blocks as adjunctive techniques to systemic analgesia, resulted in a lower pain intensity score 'at rest', during the first 72 h after major knee surgeries. The results regarding pain 'on movement' during the first 48–72 h, however, were not as favorable, and demonstrated no difference compared to systemic analgesia alone [12].

Several studies have found between 10 to 40% failure rate of cPNBs, depending on catheters' anatomical location and insertion method [4, 25–27]. The rate of treatment failure in our study was relatively low, given that we had to remove 13% of the catheters due to inefficacy. The percentage of the catheters, that were applied as a replacement for inefficient catheters, or a supplement for an existing catheter were 11 and 6%, respectively. Furthermore, only six patients (2.4%) had catheter replacements more than twice, and most of the replacements took place in case of new operations. In patients with multiple catheter replacements, it was decided to continue the pain

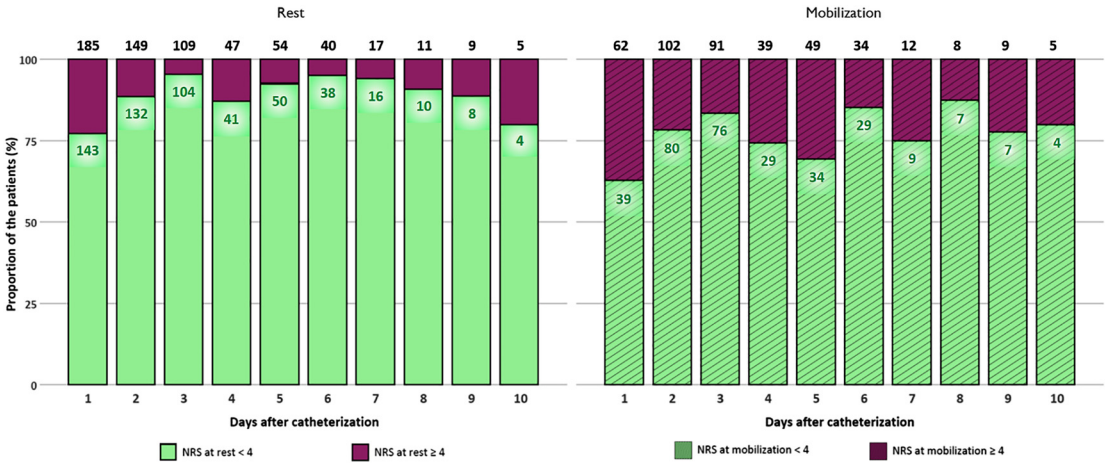

Figure 5: 100% Stacked-bar-charts show the proportion of patients with and without pain, in each day following catheterization. (The left chart demonstrates the proportions at rest, while right chart shows the values during movement. The green numbers inside the bars demonstrate the number of patients without pain in each day, while the black numbers above the bars show the sum of patients visited in each day).

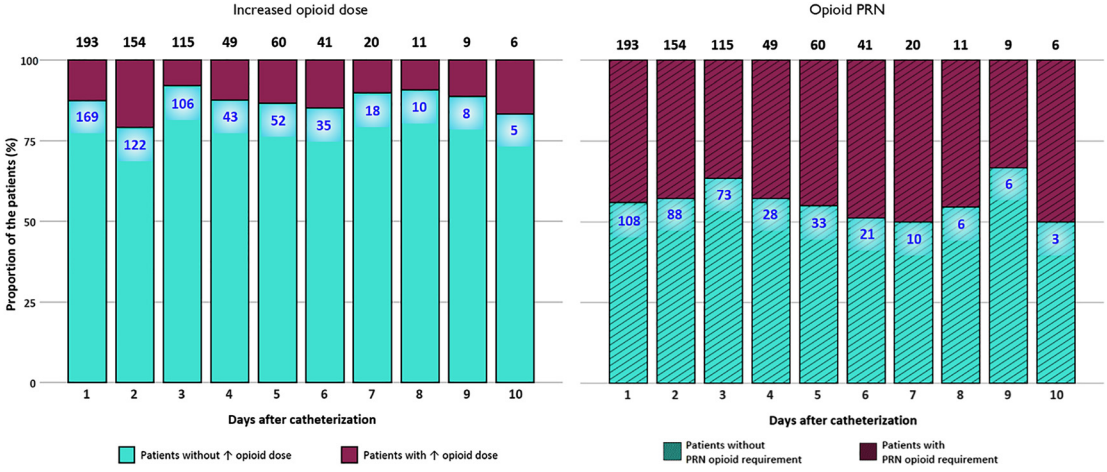

Figure 6: 100% Stacked-bar-charts show the proportion of patients without increased opioid doses and PRN opioid doses, in each day following catheterization. (The red numbers inside the bars show the number of patients requiring increased opioid doses and PRN opioid doses and the blue numbers above the bars show the total number of patients with and without need for increased opioid doses and opioid PRN doses).

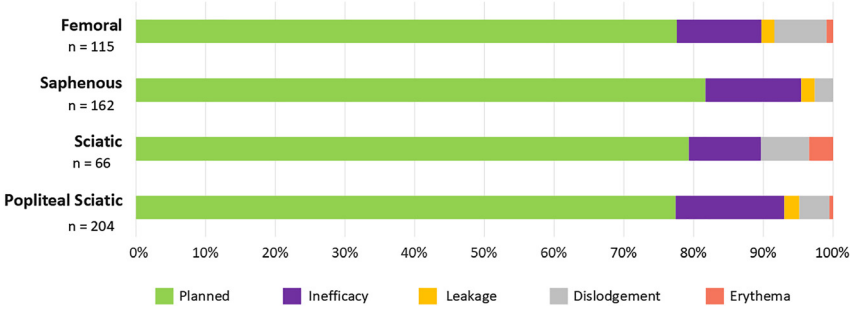

Figure 7: The proportion of the reasons for removing catheters in different anatomic locations.

management with nerve catheters, although there were alternative analgesic methods. Since the patients had favorable experience with previous catheters regarding pain control, and also because of the patients' age and comorbidities, considering risks and complications associated with the use of opioids. The patients had a central role in this decision.

Misplacement of catheters in relation to the target nerve can lead to primary failure of the catheters, while catheter migration, dislodgment and obstruction after a proper primary position can result in a secondary failure of treatment. In our study, placement of most of the catheters were guided by ultrasound, which theoretically improves the block success rate and reduces the amount of anesthetic needed by enabling injection of anesthetics in the right place after visualization of the nerve [28, 29], however, we could not strongly conclude on this, due to disproportionate number of catheters in our study, sited by these two methods in different anatomic locations. The catheters were fixed cautiously after insertion and the dressings were observed every day during follow up visits, since optimized securement of the catheters can have a significant role in durability of catheters [31–33]. We did not investigate whether inserting catheters under general anesthesia would have any influence on the efficacy and failure of the catheters. It might be preferred to use the catheters in an awake patient, however sometimes it is not possible due to affecting the operation field or the pain and discomfort associated with positioning some patients, in which case satisfactory pain control, reduction in opioid use, and no sign of nerve damage, to some extent, would indicate an acceptable catheterization.

By more widespread use of cPNBs, greater knowledge has been achieved regarding their complications and potential adverse events. Minor complication such as intraneural injection, vascular puncture, or local inflammation can occur frequently with cPNBs, however, they are usually transient and self-limited. Meanwhile, the risk of serious complications, such as significant nerve injury, bleeding, and anesthetic toxicity are comparatively low [17, 25–27]. We did not observe any major complication during this study. This might be attributable to application of standard and up-to-date techniques in deployment and maintenance of the catheters by a team of anesthesiologists and acute pain service nurses, specially educated and experienced in nerve blocks. Theoretically, the risk of infection after cPNBs would rise due to existence of the foreign body and large proportions of catheters in other studies have showed positive culture for microbial growth (6–57%), yet the incidence of systemic or local infection was quite low (0–3%) [28]. Previous studies considered the duration of catheterization more than 48 h to be an important risk factors for infection [28]. However, even though most of the catheters in our study remained in place for more than two days, we did not find any case of catheter infection. In addition to application of sterile techniques for catheterization, we consider daily routine visits to be an important contributing factor, which facilitates detection and prevention of the infection in early pre-clinical stages. There is a strong suggestion in literature that catheter insertion sites should be inspected every day to avoid progression of infection, since the time interval between the onset of symptoms and infection progression is usually less than 48 h [29]. In our study, we did unplanned removal of 4 out of 547 catheters due to erythema which might have avoided progression to clinical infection.

As an alternative to cPNBs, single-injection nerve blocks (sPNBs) can also provide excellent analgesia for up to 24 h, but for this period a dense motor and sensory block must be anticipated, which increases the risk of falls and positioning injuries [30]. On the other hand, cPNBs offer more flexibility in both duration and density of local anesthesia, in which by reducing the concentration of the local anesthetic and thereby reduction of dense motor and sensory blocks, the risk of systemic toxicity, falls and positioning injury would decrease [31]. Bingham et al. [32] in a systematic review and meta-analysis showed that cPNBs provide superior pain control, less opioid consumption, and greater patient satisfaction than sPNBs. In addition, the risk of rebound pain phenomenon, as a severe pain that can occur once regional anesthesia wears off, is reduced with cPNBs compared to sPNBs [33, 34]. Another challenge that we faced in this study was a significant proportion of patients that required a combination of catheters in different anatomic places. This is because surgical sites in the lower extremity are typically innervated by multiple nerves and thus, one perineural infusion usually is not able to provide optimal analgesia. In these circumstances, a combination of cPNBs and sPNBs can be applied to achieve the most effective analgesia [30]. Liposomal bupivacaine as an innovative therapy might have the potential to address the limitation in duration of action of peripheral nerve blocks after a single injection. The gradual process of lipid degradation and clearance of liposomal bupivacaine can be used to extend its duration of action [35], nevertheless, several systematic reviews and meta-analyses have failed to demonstrate the superiority of liposomal over the non-liposomal form of the anesthetic

[36–39], and it has currently been only approved for few indications by the US Food and Drug Administration (FDA) and European Medicines Agency (EMA) [40, 41].

Our study has several limitations. A major limitation of our study is the technique of giving an initial bolus of ropivacaine followed by placement of the catheter, which may lead to a significant overestimation of the potential benefits of the cPNBs, in case a successful initial block ends to improper catheter position. Besides, most of catheterizations in our study were done under general anesthesia and accordingly, the efficacy of the catheters could not be accurately assessed until the patients were fully awake. Another possible weakness of our study is that the patients were investigated until removal of the catheters, and therefore the effect of nerve blocks on patients' rehabilitation, and possible complications such as rebound pain, late infection, and nerve injury, remain unstudied. Accordingly, an additional study is required to observe and determine late outcomes and complications, that might emerge after removing catheters. Finally, we could not perform any comparison regarding the outcome of cPNBs between different types of surgeries, since the number of patients in each category was not sufficient and could result in underpowering of our statistical comparisons.

In conclusion, cPNBs can be considered as an efficient method for improving pain control after various orthopaedic surgeries and minimizing the use of additional opioids, however, the catheters sometimes might need to be replaced or relocated in order to achieve the desired efficacy. Accordingly, further investigation is needed to explore the efficacy of cPNBs employing different analgesic regimens, in different anatomic locations and after various types of surgeries.

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Author contributions: MJ, HR and MS conceived the original idea, MJ, JB, OR and SK developed the study design, HR and MS examined the patients and collected the data, HR and MS registered the data in the database, JB and AG analysed the data, AG designed the figures, and all authors discussed the results and contributed to writing the final manuscript.

Competing interests: The authors declare that they have no known competing financial or personal interests that could have appeared to influence the work in this paper.

Informed consent: Not required for this work.

Ethical approval: It was a registry study and did not need ethical approval. The study was approved by the Danish Data Protection Agency 2008-58-0028, ID 2019-83.

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