Intravenous dexamethasone in pain treatment after video-assisted thoracoscopic surgery

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Original Article

Neuropathic pain after orthopaedic surgery with continuous peripheral nerve block

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ABSTRACT

INTRODUCTION. Continuous peripheral nerve blocks (cPNBs) have shown favourable post-operative pain control results but may be associated with a risk for long-term neurological complications. This study sought to examine factors associated with persistent post-operative pain and potential neuropathy after orthopaedic lower-limb surgery with the use of post-operative cPNB.

METHODS. Patients who underwent lower limb orthopaedic procedures with cPNBs between November 2021 to May 2022 were included. Patient demographics and perioperative data were noted. At discharge, patients completed the PainDetect (PD) questionnaire and were followed up six months after discharge.

RESULTS. Seventy-seven patients with a total of 171 catheters completed the follow up. The median time to follow-up was 214 days after catheter removal, and 18 patients (23%) had a PD score ≥ 13. Univariate analysis showed that multiple variables were associated with a PD score ≥ 13 at the six-month follow-up. Multiple logistic regression showed that a high PD score at discharge, high BMI and longer duration of cPNBs were associated with higher risk of having a PD score ≥ 13 at the six-month follow-up.

CONCLUSION. Several factors were associated with a higher risk of having possible neuropathy after six months. BMI, duration of catheter and PD score at discharge were correlated with risk of possible neuropathic pain.

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TRIAL REGISTRATION. The study was a quality control project and therefore did not require registration under Danish law.

Regional anaesthesia using peripheral nerve blocks (PNBs) has been shown to effectively control post-operative pain in lower-extremity procedures, yielding reduced opioid consumption, shorter hospital stays and high patient satisfaction [1]. Continuous PNBs (cPNBs) can provide long-lasting analgesia by placing the catheters near the peripheral nerve or plexus and conducting continuous infusion of anaesthetics [1]. However, studies comparing the efficacy of cPNBs to single-injection PNBs have produced inconsistent findings, with some showing a preference for cPNBs owing to their longer duration of action and lower opioid consumption [1-3], whereas others have raised concerns about potential long-term neurological complications associated with cPNBs [4].

Although cPNBs have proven useful in orthopaedic lower-limb surgery, knowledge is limited of their potential

long-term complications. Reported rates of neurological complications have been low to moderate, with short-term and long-term complication rates falling in the 0-11% and 0-4% range, respectively [5]. Recently, increased attention has been devoted to catheter-related long-term neurological complications that may occur after cPNBs [4, 6, 7]. However, these studies have not included systematic follow-up but relied on patients seeking medical attention and may therefore have underreported the occurrence of catheter-related nerve injuries.

Various variables have been identified as potential risk factors for nerve injury, e.g., sex, age, BMI, smoking and many more [2, 7-11]. Even so, risk factors for persistent neuropathy of cPNBs have not been adequately described [7, 9, 12].

The aim of the study was to investigate the point prevalence of possible neuropathy six months after application of cPNBs in orthopaedic patients who underwent lower-limb procedures. The study also aimed to identify any risk factors associated with possible neuropathy.

METHODS

This cohort study was conducted at a university hospital in Denmark. Patients were included from November 2021 to May 2022 and data were collected prospectively. The study was approved by the Danish Data Protection Agency (ID 2021-227). The study follows the STROBE guidelines for reporting of observational studies.

Participants

The study included orthopaedic patients of any age who underwent scheduled or acute lower-limb procedures with post-operative cPNBs. Patients were included by the pain management nurses of the department who have special training in acute pain treatment. Patients suffering from cerebral paresis, cognitive impairment (e.g., dementia, memory difficulties or mental retardation), lethargy or severe concussion after head trauma were excluded as were patients who were unable to speak Danish or English, and patients who were transferred to another hospital or had their catheters removed before evaluation by the department's pain nurses.

Catheterisation

Indication for catheterisation was anticipated severe post-operative pain lasting more than 24 hours. Catheterisations were performed by experienced anaesthesiologists using ultrasound as guidance. Catheter efficacy was verified by administration of a 10-20 ml bolus of 5 mg/ml ropivacaine. Thereafter, catheters were attached to infusion pumps with continuous infusions of ropivacaine 2 mg/ml at rates of 5-6 ml/h for adults and 0.04 mg/kg/h for children.

In-hospital evaluation

Patient characteristics were gathered from the electronic patient record. After surgery, patients were evaluated daily by the pain management nurses who assessed mobilisation, pain (on a numeric rating scale (NRS)) at rest and activity, and requirement for supplementary opioids. The decision to remove or replace catheters was based on several factors, including catheter efficacy, potential side effects of the catheter and/or a requirement for additional surgery and the patient's need for mobilisation along with pain and opioid consumption.

At discharge, post-operative pain was evaluated using NRS and PainDETECT (PD). Furthermore, opioid consumption, duration of catheter placement and reason for discontinuation of the catheter were noted.

Six-month follow-up

Six months after surgery, a follow-up evaluation was conducted via telephone calls by either the pain nurses or a medical student. Patients were interviewed regarding satisfaction with their pain treatment six months after

surgery, current NRS, pain treatment and return to work/school. Furthermore, they were asked to complete the PD questionnaire. To detect as many patients as possible with possible neuropathic pain, a PD score < 13 was defined as low possibility of neuropathy and PD score ≥ 13 was defined as possible neuropathy, grouping together medium (PD score 13-181) and high (PD score ≥ 19) risk scores [13, 14]. The PD questionnaire was originally developed and intended for lower-back pain but has subsequently been tested and validated in a wide range of settings and populations, including musculoskeletal pain and post-surgical pain after orthopaedic surgery [13].

Statistics

Descriptive data analysis was performed on all baseline data. Many patients had multiple catheters and hence data are reported both per patient and per catheter. Data are presented using median with interquartile range (IQR) or absolute number with percentages. Fisher's tests and Mann-Whitney U tests were used to investigate differences between the groups. Analysis of variables with three or more predefined groups were done using χ^2 tests. Logistic regression was used to examine independent risk factors for possible neuropathy. We conducted a multivariate logistic regression analysis to calculate the odds ratio for risk factors associated with possible neuropathy as the dependent variable. We included relevant independent variables such as age, sex and pain at discharge demonstrated by PD, to construct the full logistic regression model. To identify the most significant predictors of the outcome (PD score ≥ 13), we applied the stepwise selection method [15]. We estimated odds ratios and their corresponding 95% confidence intervals (CI) to quantify the strength of the association between each independent variable and PD score ≥ 13. The statistical significance level was set at $p < 0.05$. Descriptive statistics were performed using R Statistical Software (v4.1.2: R Core Team 2021).

Sample size estimation

The study size was determined by convenience sampling. The study was conducted as a follow-up to a quality control study, and hence no more patients were available than those included in the prespecified timeframe.

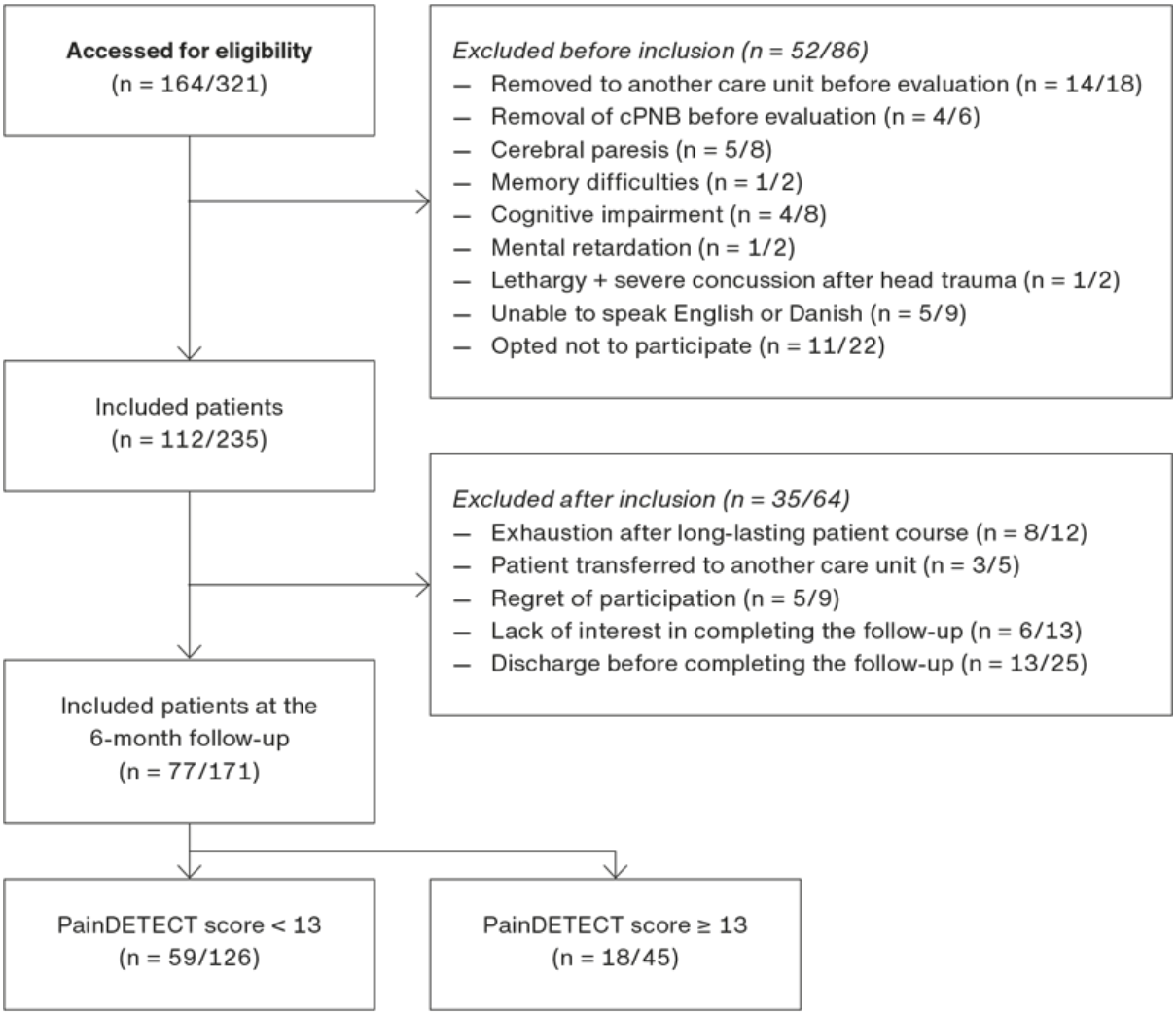
Trial registration: The study was a quality control project which does not require registration under Danish law.

RESULTS

Participants

We screened 164 patients with a total of 321 cPNB catheterisations, and 77 patients with 171 catheters were analysed. See **Figure 1** for a flow diagram. The median number of catheters per patient was two (IQR: 1-7) with 53 patients (69%) having two catheterisations.

FIGURE 1 Flow chart of patient inclusion and exclusion. Numbers are represented as patients/catheters.



cPNB = continuous perineural block.

Patient characteristics

Table 1 presents the characteristics of patients grouped into PD score < 13 and PD score ≥ 13. Overall, no significant differences were observed in patient characteristics between the two groups, except for previous smoking status and PD at discharge.

TABLE 1 Characteristics of all included patients and patients with a PainDETECT score ≥ 13 or < 13.

	PD score ≥ 13 (n = 18)	PD score < 13 (n = 59)	Total (N = 77)	p value
Sex, n (%)				1
Female	8 (44)	28 (47)	36 (47)	
Male	10 (56)	31 (53)	41 (53)	
Age, median (IQR), yrs	52 (35-62)	54 (24-63)	54 (26-63)	0.6
BMI, median (IQR), kg/m²	26.7 (25.1-29.9)	23.9 (22.0-29.4)	25.3 (22.7-29.4)	0.08
ASA Physical Classification, n (%)				0.4
I	5 (28)	20 (34)	25 (32)	
II	11 (61)	33 (56)	44 (57)	
III	1 (6)	6 (10)	7 (9)	
IV	1 (6)	0	1 (1)	
Smoking, n (%)				0.002
No	7 (39)	41 (69)	48 (62)	
Yes	4 (22)	15 (25)	19 (25)	
Previous smoker	7 (39)	3 (5)	10 (13)	
Comorbidity, n (%)				0.06
No	16 (89)	57 (100)	73 (97)	
Renal insufficiency	0	0	0	
Previous opioid abuser	2 (11)	0	2 (3)	
Current opioid abuser	0	0	0	
Catheter count in each patient, n (%)				0.3
1	3 (17)	7 (12)	10 (13)	
2	11 (61)	42 (71)	53 (69)	
3	1 (6)	6 (10)	7 (9)	
4	1 (6)	3 (5)	4 (5)	
5	0	1 (2)	1 (1)	
6	1 (6)	0	1 (1)	
7	1 (6)	0	1 (1)	
Catheters/patient, median (range), n	2 (1-7)	2 (1-5)	2 (1-7)	0.8
Catheterisation days, total, median (range), n	8 (6-13)	8 (6-10)	8 (6-10)	0.2
Opioid at discharge, n (%)				1
No	1 (6)	3 (5)	4 (5)	
Yes	17 (4)	55 (95)	72 (95)	
PD score at discharge, n (%)				0.005
0-12	5 (28)	38 (69)	43 (59)	
13-18	8 (44)	12 (22)	20 (27)	
19-36	5 (28)	5 (9)	10 (14)	

ASA = American Society of Anesthesiologists; IQR = interquartile range; PD = PainDETECT.

Catheter characteristics

Table 2 presents the characteristics of catheters grouped by PD score < 13 and PD score ≥ 13. Preoperative pain treatment (opioid and non-opioid) was used in 117 catheters (66%). The most common preoperative pain medication was opioids (44 patients, 25%). A significantly higher proportion of patients in the PD score ≥ 13 group received preoperative analgesics.

TABLE 2 Characteristics of catheters from all included patients and from patients with a PainDETECT score ≥ 13 or < 13.

	PD score ≥ 13 (n = 45)	PD score < 13 (n = 126)	Total (N = 171)	p value
Preoperative analgesics, n (%)[a]				0.002
No	24 (51)	101 (79)	125 (71)	
Low-dose opioid	16 (34)	16 (13)	32 (18)	
High-dose opioid	0	2 (2)	2 (1)	
Gabapentin	5 (11)	7 (5)	12 (7)	
Other	2 (4)	2 (2)	4 (2)	
Preoperative ketamine infusion, n (%)				0.2
No	40 (89)	120 (96)	160 (94)	
Yes	1 (2)	1 (1)	2 (1)	
Not relevant	4 (9)	4 (3)	8 (5)	
Catheterization setting, n (%)				0.02
Outpatient clinic	1 (2)	0	1 (1)	
Post-operative	20 (44)	72 (57)	92 (54)	
Post-anaesthesia case unit	2 (4)	2 (2)	4 (2)	
Pre-operative	7 (16)	30 (24)	37 (22)	
Ward:				
Primary	9 (20)	8 (6)	17 (10)	
Re-insertion	5 (11)	14 (11)	19 (11)	
Supplementary	1 (2)	0	1 (1)	
Single shot, n (%)				0.2
No	25 (61)	90 (74)	115 (71)	
Yes	16 (39)	32 (26)	48 (29)	
Section, n (%)[a]				0.008
Arthroplasty	8 (16)	6 (4)	14 (7)	
Foot & wound	8 (16)	34 (21)	42 (20)	
Paediatrics	0	15 (9)	15 (7)	
Limb reconstruction	9 (18)	28 (18)	37 (18)	
Sport & trauma	25 (50)	77 (48)	102 (49)	
Indication, n (%)				0.02
Pre-operative pain	41 (91)	123 (98)	164 (96)	
Wound	0	2 (2)	2 (1)	
Ischaemia	0	0	0	
Outpatient	4 (9)	1 (1)	5 (3)	
Anatomical location, n (%)				0.049
Femoral	8 (18)	8 (6)	16 (9)	
Saphenous	17 (38)	56 (44)	73 (43)	
Sciatic	2 (4)	1 (1)	3 (2)	
Popliteal	18 (40)	61 (48)	79 (46)	
Method, n (%)				0.2
US	43 (96)	125 (99)	168 (98)	
US + NS	2 (4)	1 (1)	3 (2)	
Duration, median (IQR), days	4 (3-6)	3 (3-5]	3 (3-5)	0.1
Cause of removal, n (%)				0.2
Planned	38 (84)	104 (84)	142 (84)	
Leakage	3 (7)	1 (1)	4 (2)	
Erythema	0	1 (1)	1 (1)	
Dislodgement	0	2 (2)	2 (1)	
Effect loss	4 (9)	16 (13)	20 (12)	

IQR = interquartile range; NS = nerve stimulator; PD = PainDETECT; US = ultrasound.
a) Multiple categories may apply; hence, the total may exceed 100%.

In 30% of cases, a single-shot blockade was used before cPNB, with no difference between the groups.

Follow-up

Among the 77 patients in the study, 18 patients with a total of 45 catheters had a PD score ≥ 13, indicating a 23% point prevalence of possible neuropathy at six months after cPNB application. Of these, 12 had a PD score > 18. Data from the six-month follow-up are presented in **Table 3.**

TABLE 3 Summary of six-month follow-up for all included patients and patients with a PainDETECT score ≥ 13 or < 13.

	PD score ≥ 13 (n = 18)	PD score < 13 (n = 59)	Total (N = 77)	p value
Time since last catheter removal, median (IQR), days	213 (177-223)	214 (179-224)	214 (179-224)	0.7
Back to work/school, n (%)				0.0009
No	10 (56)	8 (14)	18 (23)	
Yes	4 (22)	36 (61)	40 (52)	
Not relevant[a]	4 (22)	15(25)	19 (25)	
Pain, median (IQR), NRS				
Rest[b]	4 (1.3-6)	0 (0-1.5)	0 (0-3)	< 0.0001
Activity[c]	6.5 (4-8)	2 (0-5)	4 (1-7)	0.0002
Analgesics at follow-up, n (%)[d]				< 0.0001
No	5 (23)	50 (82)	55 (66)	
Opioid	2 (9)	5 (8)	7 (8)	
Opioid PRN	4 (18)	5 (8)	9 (11)	
Gabapentin	5 (23)	0	5 (6)	
Pregabalin	4 (18)	1 (2)	5 (6)	
TCA	1 (5)	0	1 (1)	
SNRI	1 (5)	0	1 (1)	
Would consider cPNB again, n (%)				0.6
No	1 (6)	2 (3)	3 (4)	
Yes	17 (94)	56 (97)	73 (96)	
Satisfaction with the pain service, median (IQR), NRS	9.5 (8-10)	10 (8-10)	10 (8-10)	0.6
PD score at follow-up, n (%)				-
0-12	0	59 (100)	59 (77)	
13-18	6 (33)	0	6 (8)	
19-36	12 (67)	0	12 (16)	

cPNB = continuous perineural block; IQR = interquartile range; NRS = numerical rating scale; PD = PainDETECT; PRN = pro re nata; SNRI = serotonin and norepinephrine reuptake inhibitors; TCA = tricyclic antidepressant.
a) Patients who were retired from work.
b) At the operated site at rest.
c) At the operated site at the activity.
d) Some patients received multiple analgesics, hence total is > 100%.

Significantly more patients in the PD score ≥ 13 group received analgesics at follow-up compared with the PD score < 13 group (73% and 18%, respectively). However, despite receiving more analgesics, the PD score ≥ 13 group still had significantly higher pain scores than the PD score < 13 group at rest (NRS 4 versus 0, $p < 0.001$) and at activity (NRS 6.5 versus 2, $p < 0.001$).

Generally, patients reported a high satisfaction with their pain treatment, and most of the patients would consider catheterisation with cPNBs if they were to undergo surgery again.

Odds of possible neuropathic pain

Compared with the patient who had a PD score PD score < 13 at discharge, the odds of having PD score ≥ 13 at the six-month follow-up were 5.1 (95% CI: 1.2-21.5, p = 0.02) and 6.6 (95% CI: 1.1-38.8, p = 0.04) times greater for patients who had PD score of 13-18 and 19-38, respectively.

Furthermore, a BMI > 25 kg/m^2 was associated with an odds ratio for having a PD score ≥ 13 at follow-up of 6.9 (95% CI: 1.4-33.7, p = 0.02), and the duration of the catheter increased the odds ratio by 1.2 (95% CI: 1.03-1.3, p = 0.02) for each day the catheter was in use.

DISCUSSION

This study evaluated the prevalence and risk factors of potential neuropathy six months after cPNBs in orthopaedic patients with lower-limb surgery and assessed patient satisfaction with the pain service. Our findings indicate that 23% of patients experienced persistent possible neuropathic pain – as determined by a PD score ≥ 13 six months after cPNB application. Both groups reported high levels of satisfaction even though patients with a PD score ≥ 13 had higher pain scores and used more analgesics.

Multiple variables were associated with a PD score ≥ 13 in the univariate analysis; previous smoking, PD at discharge, preoperative analgesics, catheterisation setting, section, indication and anatomical location. However, only a few variables were significantly correlated in the multivariable analysis.

The study found an increased risk of possible neuropathic pain after six months in patients with a BMI > 25 kg/m^2 with an odds ratio of 6.9 compared with patients with a BMI ≤ 25 kg/m^2. Multiple studies have examined BMI as a risk factor for neurological complications associated with cPNBs, but results have been mixed. Multiple studies found a higher incidence with increasing BMI [9, 11], but some found the inverse relation [7]. One might expect the catheters to be more difficult to place and that the risk of secondary displacement would be higher in patients with a higher BMI. The high correlation between PD at discharge and at follow-up may possibly confirm the association between uncontrolled acute pain and the risk of developing persistent post-operative pain, or be due simply to pre-existing neuropathy, either before surgery or right after, due to direct injury of the nerve because of the trauma, the surgery or the catheter. In future research, patients with a previous history of neuropathic pain should be identified and analysed as a subgroup.

The odds of having a PD score ≥ 13 increased every day the catheter remained in situ. Previous studies have primarily focused on the increased risk of infection caused by longer catheter duration, not on neurological complications [10, 12, 16]. The duration may potentially have been confounded by the indication because the catheters may have been kept in place for patients with high pain levels. The longer catheter duration may be a proxy measure for pain level. Hence, acute pain may be a risk factor for persistent pain without catheter duration being an independent risk factor for persistent pain.

The significant number of patients with possible neuropathic pain who were treated with opioids and non-opioid pain treatment preoperatively agrees with previous studies. Previous studies showed that a daily dose of 30 mg equivalent dose morphine or higher for 90 days or more was an independent risk factor for both nociceptive and neurological pain related to cPNBs [11, 17].

This study represents a centre with a medium-to-high volume of cPNB applications, with catheters being applied every day. Centres with fewer patients might be less trained in the application of cPNBs and therefore have a higher complication rate.

Limitations

A major limitation of our study is the small sample size. A definite diagnosis of neuropathy is based upon a neurologic exam, but this study relied on PD scores instead of the gold standard test. This was chosen because previous studies have found PD to be a good screening tool with a fairly high sensitivity [13]. To describe actual neuropathic pain (defined by the International Association for the Study of Pain (IASP) as "Pain caused by a lesion or disease of the somatosensory nervous system") requires not only symptoms correlated with neuropathy but also a demonstrable lesion [18].

Another limitation was potential selection bias. Patients with complications may be more likely to have their catheters removed early and hence not be included. Likewise, patients with complications may be less likely to participate in the follow-up.

Because a large proportion of the patients received cPNBs due to either trauma or joint replacement surgery, their preoperative PD score was not assessed. Assessing PD in an otherwise painful situation was not deemed meaningful. Therefore, this study was unable to investigate whether the possible neuropathic pain was present prior to catheterisation or was caused by the catheters, the surgery or the trauma.

CONCLUSION

Persistent post-operative pain with possible neuropathy six months after lower-limb orthopaedic surgery using cPNB was associated with a high PD score at discharge, preoperative analgesic intake (opioid and non-opioid), longer duration of cPNBs, higher BMI and previous smoking. Possible neuropathic pain after six months warrants further investigations (e.g., electrodiagnostic testing) and, if needed, initiation of relevant pharmacologic and/or non-pharmacologic interventions for chronic neuropathic pain.

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