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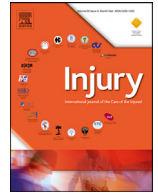
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# Complications with focus on delirium during hospital stay related to femoral nerve block compared to conventional pain management among patients with hip fracture – A randomised controlled trial.



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## ABSTRACT

**Introduction:** Patients with hip fracture often suffer complications leading to increased mortality and morbidity. Pain management are important, but opioids has many side effects. The aim of this study was to investigate whether Femoral Nerve Block (FNB) can reduce complications during hospital stay, with special focus on delirium compared to conventional pain management with opioids among patients with hip fracture, including those with dementia.

**Patients & Methods:** In a randomized controlled trial involving patients >70 years with hip fracture (trochanteric and cervical), including those with dementia. Preoperatively, patients (n=236) were consecutively assigned to receive FNB and opioids if required (intervention group, n = 116) or conventional pain management using opioids if required (control group, n = 120). Delirium was set according to different assessments and DSM-IV-TR criteria. Other complications were set by a specialist in geriatric medicine and a trained research nurse according to a predefined protocol.

**Results:** Most patients, 157 (66%), were women, mean age was 84 (±6.7) years and 109 (46%) patients had dementia disorders. Forty-four patients (38.9%) developed delirium preoperatively in the intervention group compared to 59 (49.2%) patients in the control group (p=0.116). Common postoperative complications were pre- and postoperative delirium, nutritional problems, anaemia, constipation and urinary tract infection with no significant difference between the groups. In the subgroup analysis among patients with dementia, a large proportion developed delirium postoperative (96.3%) and they had a long duration of delirium during hospital stay (5.9 ±1.8), however no difference between the groups.

**Conclusion:** Despite less preoperative pain and need of opioids, FNB did not reduce the incidence of complications. However, a preoperative FNB may result in less preoperative delirium, but this should be further investigated. As pain treatment, FNB is a good alternative with few documented adverse effects in order to reduce pain and opioids among patients with hip fracture.

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## Introduction

Patients with hip fracture have multiple comorbidities and often suffer complications, leading to increased morbidity and mortality [1-2]. Opioids are often used for pain management, but opioids increase the risk for adverse effects, particularly in the elderly, who are vulnerable to sedation and delirium [3-4].

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Delirium is a common complication among patients with hip fracture, about 54 % suffer postoperative delirium [5], depending on how it is assessed and defined [5,6]. Postoperative delirium is associated with longer hospital stay, increased medical complications, impaired short-term functional outcome and increased the risk of cognitive decline after the hospital stay [6-7]. There are many predisposing factors for postoperative delirium [5], some of them are cognitive impairment, preoperative delirium, opioid use and pain intensity [6,8,9].

There are several types of lower extremity peripheral nerve blocks (PNB) (for example: femoral nerve block, psoas compartment block and fascia iliaca block), which are all similar. Everyone aims to block parts of the hip to provide analgesia. In general, PNB is shown to reduce pain, opioid use and increase patient satisfaction [10,11] and reviews have shown similar result among patients with hip fracture [12-13]. In our study we used a femoral nerve block (FNB) which is a common and well evaluated among lower extremity blocks [10].

A Cochrane review by Guay (2018) show that lower extremity PNB can decrease the risk of pneumonia, reduce time to first mobilisation and cost of analgesics. However, there is an inconsistency whatever lower extremity PNB reduces delirium among patients with hip fracture. Further, studies investigated lower extremity PNB and delirium are small with various quality and excluded patients with cognitive impairment/dementia [12,15,16], which may be 50% of patients with hip fracture [17].

In one earlier study from the same population as the present study showed that patients with hip fracture, including those with dementia, who received femoral nerve block (FNB) assessed significant lower pain scores and required less opioids before surgery compared with those receiving conventional pain management [14]. However, in this study we want to investigate if a preoperative femoral nerve block has some impact on other outcomes, such as pre- and postoperative complications with special focus on delirium.

The aim of this study was to investigate whether FNB can reduce complications during hospital stay, with special focus on delirium compared to conventional pain management with opioids among patients with hip fracture, including those with dementia.

## Method

### Patients and methods

This randomized controlled trial (RCT) included patients aged  $\geq$  70 years with radiographically verified hip fracture who were admitted consecutively to an Orthopedic Ward in a Hospital of Northern Sweden between April 2009 and September 2011. Patients with cognitive impairment and/or dementia were included. Exclusion criteria were infection or previous vascular surgery in the inguinal area, which in this study was a contraindication to FNB.

Of 472 patients admitted to the Orthopedic Ward eligible for inclusion, 162 were excluded due to failed inclusion routines, 25 declined to participate, 5 interrupt their enrolment, 4 were randomized to FNB but did not receive the treatment, 1 received FNB postoperative and 1 received and 1 a postoperative epidural, 15 was not assessed postoperative, 5 went home before being assessed, 5 died before being assessed and 13 was missing due to medical reasons both pre and postoperative. Thus, 236 patients were included in the present study (Fig. 1). By routine, patients with cervical hip fracture was treated at the geriatric department postoperative. Patients with a trochanteric fracture was treated at the orthopedic ward postoperative. However, some of the patients with a trochanteric fracture, further need for rehabilitation were transferred after consultation to the geriatric ward. Excluded and included patients did not differ significantly in terms of age or sex.

### Study Procedure

When the patients arrive at the Orthopedic Ward, a nurse informed and invited patients with hip fracture to participate in the study, both orally and in writing. In cases of cognitive impairment, informed consent was obtained from patients and next of kin.

All participants received lots that were sequentially numbered, stratified according to type of fracture (cervical or trochanteric), and placed in opaque, sealed envelopes at the Orthopedic Ward. The nurse at the ward opened the envelopes.

Patients were assigned randomly to receive FNB and opioids if required (intervention group,  $n = 116$ ) or conventional pain management using opioids if required (control group,  $n = 120$ ).

The anesthesiologist administered each FNB as soon as possible after admission. FNB was performed by inserting an insulated plexus block needle (Pajunk ® GmbH UniPlex NanoLine 22G  $\times$  50 mm) in level with the inguinal-area, lateral to the femoral artery and at a depth of approximately 2–3 cm to provoke quadriceps contraction with a nerve stimulator (Braun Stimuplex® HNS 12). Forty milliliters of local anesthetic (levobupivacaine, 0.25%) were administered after an aspiration check. At least 34 different anesthesiologists with various training and FNB experience performed the FNBs. In cases of delayed surgery or if otherwise necessary, participants could receive one additional FNB.

Patients' wait times at the accident scene, in the ambulance, and at the Emergency Department (ED) varied: we defined baseline as the time of arrival at the Orthopedic Ward.

### Data Collection

#### Preoperative

Nurses at the Orthopedic Ward performed controls including blood pressure, saturation, pulse, respiratory rate and the amount of oxygen at baseline, 2, 6, 12 and 18 hours after inclusion. In the earlier study by Unneby et al. (2017) with the same sample, preoperative VAS at time points: baseline, 2, 6, 12 and 18 hours after inclusion and pre-operative opioid consumption was investigated. Delirium was assessed preoperatively using the Nursing Delirium Screening Scale (Nu-Desc) [18], as well as documentation in medical and nursing records. As for the assessments with Nu-Desc, nurse in charge of the patient performed the Nu-Desc three times a day preoperative.

#### Perioperative

Data registered from the perioperative period was time of surgery, amount of bleeding, baseline-, lowest-, highest- and the difference in systolic blood pressure. The difference of systolic blood pressure was calculated between highest and lowest.

#### Postoperative

Patients were assessed and interviewed day three-five postoperative by a trained research nurse. Patients were screened for cognitive status using Mini Mental State Examination (MMSE) [19], delirium using the Organic Brain Syndrome Scale (OBS) [20], depressive symptoms using the Geriatric Depression Scale (GDS-15) [21] and morale or subjected wellbeing using the Philadelphia Geriatric Center Morale Scale (PGCMS) [22]. Pre-fracture activities of daily living was set by using Barthel ADL Index [23,24] and pain by using visual analogue scale (VAS) [25]. Assessments as part of the delirium diagnosis contained the MMSE, OBS-scale, Nu-Desc and also documentation in medical and nursing records during hospital stay. Nu-Desc was performed by the nurse in charge of the patient three times a day, until seven days postoperative.

Before the study started, nurses on both orthopedic and geriatric wards was informed and trained using the assessment of Nu-Desc. During the study, nurses received ongoing information about

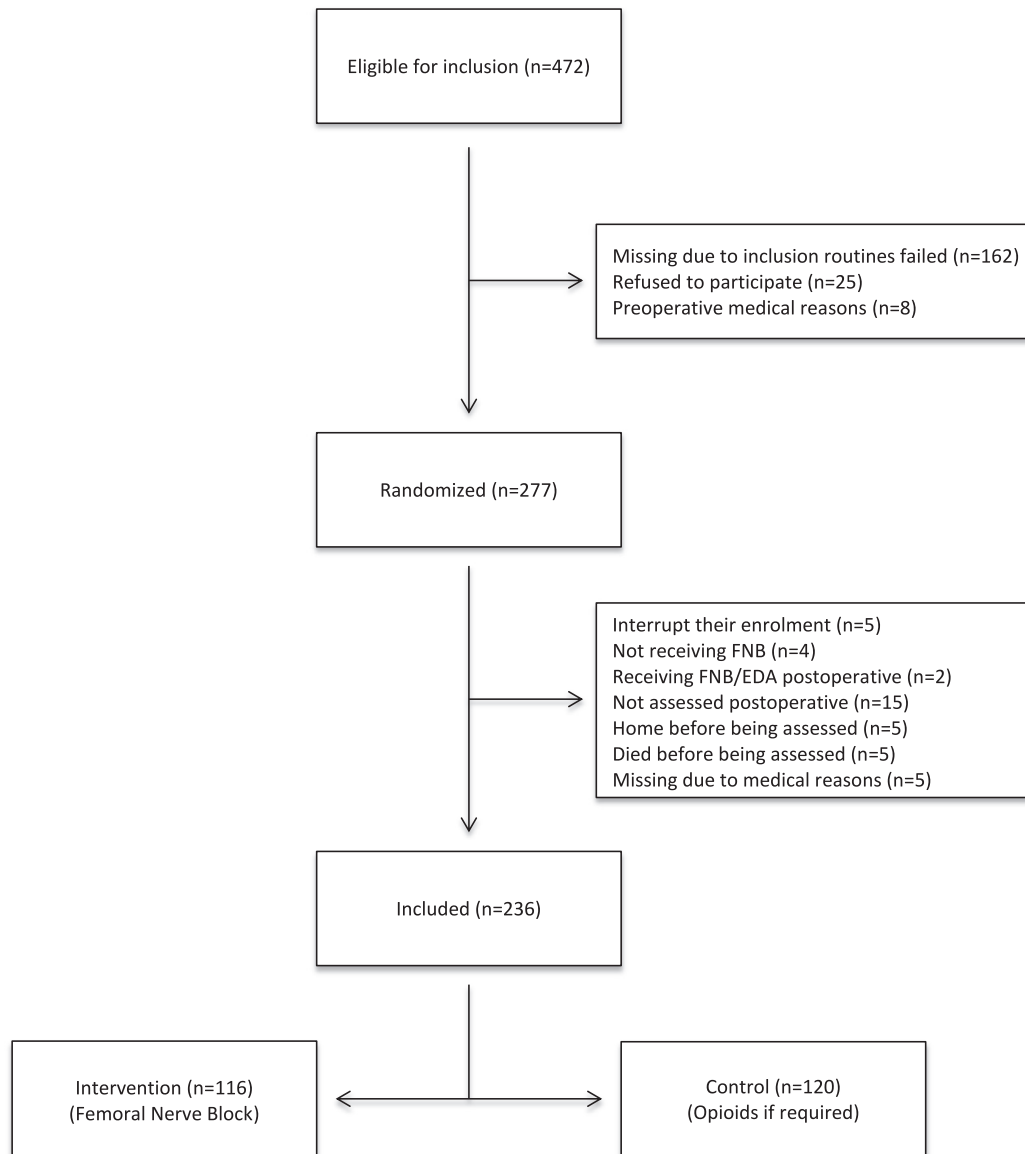


Fig. 1. Flow chart for the randomization. FNB= Femoral Nerve Block, EDA= Epidural.

the study in general and about the assessment Nu-Desc in particular from a research nurse. Further, in all nursing expeditions there was a brief written information how to assess and document Nu-Desc.

After the study was finished a specialist in geriatric medicine and a trained research nurse analyzed patients medical and nursing records from hospital stay according to a pre-set protocol. This protocol was defined before the study started and included specific criteria for each complication. A broad definition was chosen to describe the wide spectrum of complications.

The complications were classified dichotomously (present/absent). However, complications, except for delirium, were not defined as pre- and postoperative. A specialist in geriatric medicine analyzed the assessments (Nu-Desc, MMSE, OBS, GDS, PGCMS and Barthel ADL Index) and documentations (including participants medical and nursing records during hospitalization) to ascertain whether the participants met the DSM-IV TR criteria for delirium, dementia and depression [27].

Other data collected afterwards were type of fracture, number of medications at admission, time to surgery, length of hos-

pital stay, time to FNB, American Society of Anesthesiologists physical status classification (ASA) [26], preoperative blood values (hemoglobin, creatinine, Sodium, Potassium, C-reactive protein) and postoperative opioid consumption. Patients with preoperative ongoing opioids were excluded in the analysis regarding postoperative opioid consumption. Morphine equivalents were calculated to intravenous morphine using eOpioid™, from developer ©SentientWare™, LLC, 2009.

#### Analysis

All analyses were based on the intention-to-treat principle, i.e. all available data were used according to initial allocation and irrespective of the level of attendance. All tests were two tailed, and analyses were performed using IBM SPSS Software (version 25.0). Data are presented as means  $\pm$  standard deviations as well as frequencies and percentage.

Student's *t* test, the chi-squared test and when appropriate Fisher's exact test was used to analyze differences in baseline characteristics, complications and opioid consumption between the in-

**Table 1**

Baseline characteristics of the 236 patients with hip fracture randomized to intervention (femoral nerve block) or to control group (opioids if required).

	Total:	Intervention (n = 116)	Control (n = 120)	p-value
Age, mean ( $\pm$ SD)	84.1(6.7)	83.7(7.1)	84.4(6.4)	0.430
Female, n (%)	156(66.1)	79(68.1)	77(64.2)	0.523
Residential care facility, n (%)	103(43.6)	50(43.1)	53(44.2)	0.869
Hear with/without hearing aids, n (%) (n=108/113)	212(96.4)	104(96.3)	108(96.4)	0.958
Can read with/without glasses, n (%) (n=108/113)	159(74.5)	81(78.6)	77(70.6)	0.182
Barthel, mean ( $\pm$ SD) (n=112/116)	15.7 (4.6)	15.4(4.8)	15.9(4.4)	0.312
Fracture				
Trochanteric, n (%)	111(47)	52(44.8)	59(49.2)	
Cervical, n (%)	126(53.2)	64(55.2)	61(50.8)	0.504
<b>Diagnoses and Medical conditions</b>				
Depression, n (%)	67(28.3)	35(30.2)	32(26.4)	0.524
Dementia, n (%)	109(46.2)	52(44.8)	57(47.5)	0.681
Stroke, n (%)	41(17.4)	16(13.8)	25(20.8)	0.154
Heart Failure, n (%)	47(19.9)	27(23.3)	20(16.7)	0.204
Diabetes, n (%)	45(19.1)	21(18.1)	24(20)	0.711
Hypertension, n (%)	128(54.2)	59(50.9)	69(57.5)	0.306
Atrial fibrillation, n (%)	38(16.1)	17(14.7)	21(17.5)	0.552
Myocardial Infarction, n (%)	42(17.8)	22(19)	20(16.7)	0.644
Angina, n (%)	50(21.2)	21(18.1)	29(24.2)	0.254
<b>Medications at admission</b>				
Number of drugs, mean ( $\pm$ SD) (n=116/119)	6.5(3.8)	6.4(4.1)	6.5(3.4)	0.754
Strong Opioids, n (%)	15(6.4)	7(6)	8(6.7)	0.942
Weak Opioids, n (%)	4(1.7)	3(2.6)	1(0.8)	0.297
Neuroleptics, n (%)	12(5.1)	7(6)	5(4.2)	0.523
Antiepileptic, n (%)	17(7.2)	8(6.9)	9(7.5)	0.858
Antidepressant, n (%)	83(35.2)	34(29.3)	49(40.8)	0.064
Benzodiazepines, n (%)	31(13.1)	13(11.2)	18(15)	0.388
Sleeping pills, n (%)	84(35.6)	40(34.5)	44(36.7)	0.726
Preoperative blood-values				
Haemoglobin, mean ( $\pm$ SD) (n=115/120)	122.9 (15.1)	124.8(13.6)	121.2(16.3)	0.066
Creatinine, mean ( $\pm$ SD) (n=115/120)	80.3 (25.9)	81.9(28.2)	78.9(23.5)	0.38
Sodium, mean ( $\pm$ SD) (n=116/120)	137.4 (3.5)	137.3(3.7)	137.4(3.3)	0.866
Potassium, mean ( $\pm$ SD) (n=115/120)	4.3 (0.5)	4.3(0.5)	4.3(0.5)	0.99
C-reactive protein (CRP), mean ( $\pm$ SD) (n=111/113)	19 (33.3)	18.3(28.9)	19.7(37.2)	0.761
<b>Characteristics according to surgery and treatment</b>				
Time to surgery (hours), mean ( $\pm$ SD)	16.2 (10.4)	15.9(10.7)	16.5(10.1)	0.636
Time to FNB (minutes), mean ( $\pm$ SD)		81.8 (95.8)		
ASA				
ASA 1–2, n (%)	90(38.3)	44(37.9)	46(38.7)	
ASA 3–4, n (%)	145(61.7)	72(62.1)	73(61.3)	0.909

intervention and control groups. The significance level was set to  $p < 0.05$ . Subgroup analyses were performed with data from patients diagnosed with dementia. It was 24 different complications included in the analyses in terms of number of complications (Table 3 & 4).

#### Study Sample

A power analysis was performed on postoperative delirium to determine required number of patients. The calculation was carried out from a previous study including 40 patients [28]. In that study 12 patients (30%) developed postoperative delirium in the group that received opioids compared with 6 patients (15%) in the group that received FNB. According to this, 120 patients were required in each group to receive a power of 80% with a significance of 0.05.

#### Results

Of the 236 included participants, 157 (66%) were women. The mean age was 84 ( $\pm$ 6.7) years, 103 (43.5%) participants lived in residential care facilities, and 109 (46%) participants had dementia diagnoses. Baseline, pre-, peri- and postoperative characteristics did not differ significantly between the two groups (Table 1 & 2). No adverse events were found related to the FNB.

The intervention group had 20% lower incidence of preoperative delirium compared with control group. However, there was no sig-

nificance difference between the groups regarding the number of patients suffered pre- and postoperative delirium, or the duration of delirium (Table 3.)

Overall, the number of complications among patients with hip fracture was 5.7 ( $\pm$ 2.5) with no significant difference between intervention and control group (Table 3). In total, the most common complications were postoperative delirium (73.4%), nutritional problems (70%), anaemia (66%), constipation (64%), urinary tract infection (45%) and preoperative delirium (44%). None of these complications showed a significant difference between the groups (Table 3).

The intervention group had significant higher documented adverse drug effects than control group (8 (7.1%) vs 0 (0%),  $p=0.003$ ; Table 3). After analysing medical records among patients with documented drug adverse effects, it was found that all of these eight adverse effects were in the postoperative phase. There was no significant difference according to postoperative amount of milligram opioids from postoperative day 1–5 (data not shown).

In the subgroup analysis among patients with dementia, a large proportion developed delirium postoperative (96.3%) and they had a long duration of delirium during hospital stay ( $5.9 \pm 1.8$ ). Fewer patients in the intervention group had diarrhea compared with patients in the control group (6 vs 18,  $p=0.010$ ), but no other significant difference was found between the groups among patients with dementia (Table 4). In a subgroup analysis among patients without dementia, no significant difference was found according

**Table 2**  
Peri- and postoperative characteristics of the 236 patients with hip fracture randomized to intervention (femoral nerve block) or to control group (opioids if required) and postoperative characteristics of the subgroup sample among 109 patients with hip fracture randomized to intervention (femoral nerve block) or to control group (opioids if required).

	Total:	Intervention (n = 116)	Control (n = 120)	p-value
<b>Perioperative characteristics</b>				
Time of surgery (minutes), mean (±SD) (n=112/115)	73.2 (40)	70.3(38)	76.1(41.8)	0.270
Saturation, mean (±SD) (n=104/109)	97.2 (2.8)	96.9(3.5)	97.4(1.9)	0.275
Bleeding (ml), mean (±SD) (n=82/80)	278.7 (298.9)	282.3(332.3)	275(262.4)	0.878
Blood pressure (baseline), mean (±SD) (n=103/109)	149.7 (27.1)	153.9(28.3)	145.7(25.5)	<b>0.028</b>
Blood pressure (lowest), mean (±SD) (n=105/109)	97.6 (16.9)	98.5(17.7)	96.7(16)	0.418
Blood pressure (highest), mean (±SD) (n=105/109)	157.2 (25.3)	160.3(25.9)	154.2(24.5)	0.077
Blood pressure (difference)*, mean (±SD) (n=105/109)	59.6 (25.2)	61.8(26.9)	57.6(23.3)	0.219
<b>Postoperative characteristics</b>				
MMSE, mean (±SD) (n=111/116)	14.9 (9)	15.7(8.9)	14.1(8.9)	0.204
GDS, mean (±SD) (n=93/93)	4.4 (2.9)	4.5(3.1)	4.2(2.7)	0.382
PGCMS, mean (±SD) (n=91/92)	10.3 (3.8)	10.3(3.6)	10.4(3.9)	0.85
VAS mm 3-5 days postoperative, mean (±SD) (n=82/86)	31.4 (26.5)	33.6(29.4)	29.2(23.4)	0.289
Length of hospital stay, days, mean (±SD) (n=114/117)**	25.1(16.8)	25.9 (19.8)	24.3 (13.4)	0.454
<b>Postoperative characteristics of the 109 patients with hip fracture and dementia randomized to intervention (femoral nerve block) or to control group (opioids if required).</b>				
	<b>Total</b>	<b>Intervention (n = 52)</b>	<b>Control (n = 54)</b>	<b>p-value</b>
MMSE, mean (±SD) (n=50/54)	8.7 (7.1)	9.4 (7.3)	8(6.8)	0.328
GDS, mean (±SD) (n=33/33)	4.8 (3.3)	4.9 (3.5)	4.7 (3.1)	0.824
PGCMS, mean (±SD) (n=31/32)	9.6 (3.7)	8.9 (3.6)	10.2(3.8)	0.208
VAS mm 3-5 days postoperative, mean (±SD) (n=33/29)	25.7 (25.7)	28.6(27.4)	22.6(23.6)	0.363
Length of hospital stay (days), mean (±SD) (n=52/56)**	25.5(22)	25.6(16.2)	25.5(19.1)	0.981

\*The difference in blood-pressure is calculated between the highest and lowest value.

\*\*Length of hospital stay includes rehabilitation at the geriatric ward.

to complications between intervention and control group (data not shown).

## Discussion

In this study, patients receiving a preoperative FNB had 20 % lower preoperative incidence of delirium without significance difference. Further, there were no differences between receiving a preoperative FNB or conventional pain management among postoperative delirium or other common complications. A large proportion of patients with dementia developed delirium postoperative and they had also a long duration of delirium during hospital stay.

As we could find, we are the first who investigated delirium in the preoperative phase comparing FNB vs opioid use. From the present study, patients with FNB resulted in 20% less incidence of preoperative delirium compared with control group but with no significant difference between groups. This could be due to lack of power. Even though interventions focus on reducing analgesia have shown to be effective and recommended [29,30]. Unfortunately, a preoperative FNB did not make a difference according to delirium despite less preoperative pain and opioid use. Since this was a clinical study with both many different anesthesiologists and with various training of performing FNBs it is reasonable to believe that the analgesic effect varied between patients and that could have affected the need for preoperative opioids and therefore affected the outcome according to delirium. Further, it is also reasonable to believe that a preoperative FNB is a too small part of the care for patients with hip fracture to make a difference according to pre- and postoperative delirium, including other common complications significant with opioids. Hospitalization itself can be a risk to develop delirium and a multifactorial approach is recommended to reduce the risk of the syndrome [29].

Delirium is a common complication among patients with hip fracture, with a duration of about 3–10 days [30–32] which is line with our result, but with no difference between the groups. It is also well known that the development of delirium is associated with worse outcomes [29, 33]. Delirium is common already in the preoperative phase and the majority of patients continue to suffer from delirium postoperative [34]. There is an evidence that lower extremity PNB can reduce pain and opioid use [14,15,35] and reasons for developing delirium can be pain intensity and/or opioid use [34,35]. However, the evidence whether lower extremity PNB can reduce the incidence of delirium among patients with hip fracture is not clear. Some studies suggest that lower extremity PNB can reduce postoperative delirium [12,35]. However, in a Cochrane review by Guay (2017) it was stated that there was not enough evidence to conclude that lower extremity PNB reduce delirium among patients with hip fracture. In the present study, a preoperative FNB did not reduce the incidence of postoperative delirium. One may reflect on why studies mostly focusing on the postoperative delirium since the FNB often is administered preoperative and the effect of a FNB is shown to be over after 12 hours [14].

Besides delirium, patients with hip fracture suffer numerous of complications [44]. Overall, there is a high risk among patients with hip fracture to accumulate opioids, suffer sedation and respiratory depression. That makes it important to be careful with the use of opioids [35]. As we found in our study, complications as urinary tract infections, anemia, constipation and pneumonia are present in several other studies [1,36–38]. A review by Guay (2017) has reported that PNB can reduce the risk of pneumonia if the nerve block was administered in the postoperative phase and the review by Riddell (2016) reported that patients with FNB suffered fewer postoperative respiratory complications. However, Abou-Setta et al (2011) did not show less respiratory infection. In our study with the nerve block administered preoperative, patients

**Table 3**

Pre- and postoperative complications in the intervention (femoral nerve block) and control group (opioids if required) during hospital stay.

	Total:	Intervention (n=116)	Control (n=120)	p-value
Number of complications, mean ( $\pm$ SD) (n=109/114)	5.7 (2.5)	5.6 (2.7)	5.7(2.3)	0.841
Delirium preoperative, n (%) (n=113/120)	103(44.2)	44(38.9)	59(49.2)	0.116
Delirium postoperative, n (%)	173(73.43)	88(75.9)	85(70.8)	0.383
Delirium, number of days, mean ( $\pm$ SD) (n=114/120)	3.9 (2.9)	3.8(2.8)	4.1(3)	0.499
Pneumonia, n (%)	28(11.9)	13(11.2)	15(12.5)	0.759
Urinary Tract Infection, n (%)	107(45.3)	52(45.5)	55(45.8)	0.877
Wound Infection, n (%)	31(13.1)	16(13.8)	15(12.5)	0.769
DVT, n (%)	2(0.8)	1(0.9)	1(0.8)	0.981
Pulmonary Embolism, n (%)	1(0.4)	1(0.9)	0(0)	0.308
Constipation, n (%) (n=116/119)	151(63.8)	75(64.7)	75(63)	0.795
Diarrhea, n (%) (n=116/119)	59(25.1)	24(20.7)	35(29.4)	0.123
Urinary Retention, n (%)	58(24.6)	24(20.7)	34(28.3)	0.173
Heart Failure, n (%)	40(16.9)	19(16.4)	21(17.5)	0.819
Myocardial Infarction, n (%)	9(3.8)	3(2.6)	6(5)	0.333
Stroke, n (%)	6(2.5)	2(1.7)	4(3.3)	0.432
TIA, n (%)	2(0.8)	1(0.9)	1(0.8)	0.981
Anaemia, n (%)	156(66.1)	76(65.5)	80(66.7)	0.852
Decubitus, n (%)	96(40.7)	47(40.5)	49(40.8)	0.961
Sleep Disturbance, n (%)	58(24.6)	33(28.4)	25(20.8)	0.174
Nutritional Problems, n (%)	167(70.8)	82(70.7)	85(70.8)	0.981
Gastritis, n (%) (n=116/118)	14(6)	7(6)	7(5.9)	0.974
Ulcer, n (%)	5(2.1)	3(2.6)	2(1.7)	0.624
Luxation, n (%)	2(0.8)	1(0.9)	1(0.8)	0.981
Fracture during hospital stay, n (%) (n=114/118)	1(0.4)	1(0.9)	0(0)	0.308
Falls during hospital stay, n (%) (n=114/118)	48(20.7)	24(21.1)	24(20.3)	0.893
Documented drugs adverse effects, n (%) (n=112/116)	8(3.5)	8(7.1)	0(0)	<b>0.003</b>

**Table 4**

Pre- and postoperative complications among patients with dementia in the intervention (femoral nerve block) and control group (opioids if required) during hospital stay.

	Total	Intervention (n=52)	Control (n=57)	p-value
Number of complications, mean ( $\pm$ SD) (n=48/54)	6.5 (1.8)	6.1 (1.9)	6.8 (1.6)	<b>0.036</b>
Delirium preoperative, n (%) (n=51/57)	75(69.4)	33(64.7)	42(73.7)	0.312
Delirium postoperative, n (%)	105(96.3)	50(96.2)	55(96.5)	1.000
Delirium, number of days, mean( $\pm$ SD)	5.9 (1.8)	5.8(1.7)	6(1.9)	0.509
Pneumonia, n (%)	13(11.9)	3(5.8)	10(17.5)	0.058
Urinary Tract Infection, n (%)	51(46.8)	23(44.2)	28(49.1)	0.609
Wound Infection, n (%)	16(14.8)	5(9.6)	11(19.3)	0.154
DVT, n (%)	0(0)	0(0)	0(0)	-
Pulmonary Embolism, n (%)	0(0)	0(0)	0(0)	-
Constipation (n=52/56), n (%)	75(69.4)	38(73.1)	37(66.1)	0.430
Diarrhea (n=52/56), n (%)	24(22.2)	6(11.5)	18(32.1)	<b>0.010</b>
Urinary Retention, n (%)	31(28.4)	11(21.2)	20(35.1)	0.107
Heart Failure, n (%)	20(18.3)	9(17.3)	11(19.3)	0.789
Myocardial Infarction, n (%)	4(3.7)	0(0)	4(7)	0.120
Stroke, n (%)	2(1.8)	1(1.9)	1(1.8)	1.000
TIA, n (%)	1(0.9)	1(1.9)	0(0)	0.477
Anaemia, n (%)	81(74.3)	37(71.2)	44(77.2)	0.471
Decubitus, n (%)	47(43.1)	21(40.4)	26(45.6)	0.582
Sleep Disturbance, n (%)	26(23.9)	14(26.9)	12(21.1)	0.473
Nutritional Problems, n (%)	87(79.8)	39(75)	48(84.2)	0.231
Gastritis (n=52/56), n (%)	2(1.9)	0(0)	2(3.6)	0.496
Ulcer, n (%)	4(3.7)	2(3.8)	2(3.5)	1.000
Luxation, n (%)	2(1.8)	1(1.9)	1(1.8)	1.000
Fracture during hospital stay, n (%) (n=51/57)	0(0)	0(0)	0(0)	-
Falls during hospital stay, n (%) (n=51/57)	31(28.7)	16(31.4)	15(26.3)	0.562
Documented drugs adverse effects, n (%) (n=49/56)	3(2.9)	3(6.1)	0(0)	0.098

in the intervention group did not suffer less pneumonia compared to the control group. Another complication investigated according to PNB is myocardial ischemia, the review by Guay (2017) could not draw any conclusion that PNB reduce the incidence of myocardial ischemia. Which are in line with the findings in our study. However, among cardiovascular events, a review by Ridell (2016) reported that a FNB resulted in lower serum troponin levels. In the review by Abou-Setta et al. 2011, incidence of complications as DVT, nausea or vomiting, surgical wound infection, urinary retention and urinary tract infection was not less by patients receiving lower extremity PNB. In the present study, patients suffer compli-

cations in a greater extent compared to other studies [2,37]. It may be due to the long hospital stay with a mean of 25.1 days. It can be compared with Nordström et al. (2016) which reported 14.9 days for patients cared by a geriatric ward [40].

Patients receiving FNB had a higher number documented adverse drug effects. Of the eight adverse drug effects it was found that six of them to be side effects from opioids in the postoperative phase during hospital stay. When interpreting these results, the drug adverse effects was not set by any standard protocol. Among the elderly, the adverse drug effects can be less apparent and diffuse than among younger people [41]. It can be a under estimation

from the health care professional how well it was assessed and evaluated.

Overall, when comparing complications according to lower extremity PNB, there is an inconsistency in the literature. Since studies include different types of lower extremity PNBs with single dose or continuous with a catheter both pre and postoperative [12,15,35,39], which make it difficult to draw clear conclusions among the relationship with other studies investigating complications.

In our study, patients with dementia had a high incidence of developing both pre- and postoperative delirium. This has also been found in other studies investigating patients suffering hip fracture [31,32]. It makes it difficult to draw a conclusion whether lower extremity PNBs decreases the prevalence of delirium among the representative sample of patients with hip fracture, since previous studies investigating lower extremity PNB and delirium excluded patients with cognitive impairment/dementia [12,15]. In our study, there was no difference incidence of pre- and postoperative delirium among patients with dementia. However, we have shown from a previously study that patients with dementia received less amount of milligram opioids without assessing more pain and since opioids have negative side effects, alternative is highly preferred [11,14].

Patients with dementia receiving conventional pain management had significant more diarrhea than patients receiving FNB. Usually, patients with hip fracture and opioid use are known to suffer constipation as a common side effect [4,42]. The results from our study might be diarrhea because of constipation or due to excessive laxatives since the diarrhea were assessed during hospital stay.

As we found, we are the first study to investigate the number of complications among patients with hip fracture receiving FNB compared to conventional pain management. Patients receiving FNB suffered less number of complications compared to conventional pain management. The present study resulted in almost one less complication among patients with dementia receiving FNB. Patients who have a dementia diagnosis and suffer a hip fracture need special attention during hospitalization, especially since patients who suffer complications are also associated with longer hospital stay and higher mortality rate [2].

Since opioids is well known to have many side effects, alternatives are highly desired [11]. After this study was finished, FNB was implemented in the clinical practice for all patients with hip fracture and it can be performed both at the ED and in Orthopedic ward. In the present study, FNB was administered with a nerve stimulator. Since a few years the anesthesiologist was trained to perform FNB with ultrasound guidance and this is now the routine in our hospital. Ultrasound guidance is reported to be superior compared to other techniques, however, the results can be depending on how well the specialists perform the chosen technique [43]. There is not any conclusion drawn which technique that should be considered as “golden standard”. One study recommend that anesthesiologists should have knowledge to perform peripheral nerve blocks with neurostimulation as well as ultrasound guidance and choose technique depending on the clinical environment [44]. Complication rate are similar using neurostimulation compared to ultrasound guidance [45].

### Strengths and Limitation

Since we included patients with dementia in this study, our results were obtained from a representative sample of patients with hip fracture 70 years or older. It is known that approximately 50% of this population have dementia [17]. Another strength is that the protocol with complications was systematically analysed and was set before the reviews of medical and nursing records started. The

delirium diagnosis was thorough reviewed with different assessments and performed throughout day and night. In addition, with a specialist in geriatric medicine analysing the assessments, nursing and medical records makes the diagnosis of delirium be confident. A limitation is our power calculation, it was performed on postoperative delirium since there are, as we know no research on preoperative delirium among patients with hip fracture receiving a preoperative single dose FNB compared with opioids. This makes it unclear however the power calculation is satisfying in terms of preoperative delirium.

A limitation was that other complications, except for delirium, was not divided as pre- and postoperative which makes it hard to draw clear conclusions about the preoperative effect of the nerve block. Regarding the analyses according to complications, many comparisons has been analysed which increases the risk of some random significance, which means that we cannot draw too much conclusions about the significant results.

Another limitation was the documentation of complications regarding the adverse drug effects. The staff did not observe, assess or document adverse drug effects in an standardized way, it could vary from patient to patient, which make the result slightly uncertain.

### Conclusion

Despite less preoperative pain and need of opioids, FNB did not reduce the incidence of complications. However, a preoperative FNB may result in less preoperative delirium, but this should be further investigated. As pain treatment, FNB is a feasible alternative with few documented adverse effects in order to reduce pain and opioid use among patients with hip fracture. The next step might be to explore how the patients experience pain management in general and FNB in particular.

#### Registration

RCT, registered ISRCTN46653818

### Ethical Considerations

This study was approved by a regional ethical review board, Sweden, (DNR 08-121M).

In the present study a large proportion of patients with hip fracture had dementia. Since patients with dementia overall are frail and even more sensitive to opioids it is important to investigate other options of pain management and therefore it seemed unethical not to include these patients.

### Declaration of Competing Interest

All of the authors declare that they have no conflict of interest with regard to the content of this study.

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