



## Postoperative analgesic impact of femoral and pericapsular nerve block with and without lateral femoral cutaneous nerve block in orthopedic surgery

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### Abstract:

#### Objectives:

Pericapsular nerve block is an analgesic technique recently described with the aim of achieving the blockade of sensory branches of the anterior portion of the joint capsule. Our objective was to evaluate and compare the postoperative analgesic impact of pericapsular nerve block and femoral nerve block with and without lateral femoral cutaneous nerve block in patients with unilateral hip fracture, femoral neck, or intertrochanteric fracture. Methods: This was a prospective cohort study with data from patients collected in third-level complexity institutions: Hospital Universitario del Valle located in Cali, Colombia, and the Fundación Hospital San José Buga located in Buga, Colombia, for 12 months.

#### Results:

A total of 101 patients between men and women with a diagnosis of hip fracture were included. Analyses were performed in two groups pericapsular nerve block and femoral nerve block as well as by subgroups pericapsular nerve block +/- lateral femoral cutaneous nerve block, femoral nerve block +/- lateral femoral cutaneous nerve block. It was found that in the first 12 postoperative hours the score in the visual analog pain scale was significantly lower in the pericapsular nerve block group compared to the femoral nerve block group with and without the association of lateral femoral cutaneous nerve block ( $p=0.01$ ) although without difference in the subgroups. Conclusions: Pericapsular nerve block is a technique that with or without lateral femoral cutaneous nerve block association can achieve adequate analgesia in postoperative hours with a decrease in opioid administration as well

### KEYWORDS

Analgesia.  
Nerve block.  
Femoral Neck Fractures.  
Local anesthetics.  
Postoperative Period.

as its side effects. However, controlled, randomized clinical trials with a larger sample size are required to evaluate this superiority over conventional blocks.

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## PALABRAS CLAVE

Analgesia.  
Bloqueo nervioso.  
Fracturas del cuello femoral.  
Anestésicos locales.  
Periodo Posoperatorio.

### Impacto analgésico posoperatorio del bloqueo de los nervios femoral y pericapsular con y sin bloqueo del nervio cutáneo femoral lateral en cirugía ortopédica

#### Resumen:

#### Objetivos:

El bloqueo del nervio pericapsular es una técnica analgésica recientemente descrita con el objetivo de lograr el bloqueo de ramas sensitivas de la porción anterior de la cápsula articular. El objetivo de este estudio fue evaluar y comparar el impacto analgésico posoperatorio del bloqueo del nervio pericapsular y bloqueo del nervio femoral con y sin bloqueo del nervio cutáneo femoral lateral en pacientes con fractura unilateral de cadera, cuello femoral o fractura intertrocanterea. Material y Métodos: Este fue un estudio de cohorte prospectivo con datos de pacientes recolectados en instituciones de tercer nivel de complejidad Hospital Universitario del Valle ubicado en Cali, Colombia, y la Fundación Hospital San José Buga ubicado en Buga, Colombia, durante 12 meses. Resultados: Se incluyeron un total de 101 pacientes entre hombres y mujeres con diagnóstico de fractura de cadera. Los análisis se realizaron en dos grupos bloqueo del nervio pericapsular y bloqueo del nervio femoral, así como por subgrupos bloqueo del nervio pericapsular +/- bloqueo del nervio cutáneo femoral lateral, FNB +/- bloqueo del nervio cutáneo femoral lateral. Se encontró que en las primeras 12 horas postoperatorias la puntuación en la escala visual analógica de dolor fue significativamente menor en el grupo de bloqueo del nervio pericapsular respecto al grupo de bloqueo del nervio femoral con y sin asociación del bloqueo del nervio cutáneo femoral lateral ( $p=0,01$ ) aunque sin diferencia en los subgrupos.

#### Conclusiones:

El bloqueo del nervio pericapsular es una técnica que con o sin asociación al bloqueo del nervio cutáneo femoral lateral puede lograr una analgesia adecuada en el postoperatorio con una disminución de la administración de opioides así como de sus efectos secundarios. Sin embargo, se requieren ensayos clínicos controlados y aleatorizados con un tamaño de muestra mayor para evaluar esta superioridad sobre los bloques convencionales.

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## GILTZA-HITZAK

Analgesia.  
Nerbio-blokeoa.  
Lepo femoralaren hausturak.  
Anestesiko lokalak.  
Iraupen ondoko aldia.

### Kirurgia ortopedikoan, ebakuntzaren osteko eragin analgesikoa: nerbio femoralaren eta perikapsularren blokeoa, alboko femoraleko larruzalaren blokearekin eta gabe.

#### Laburpena:

#### Helburuak:

Nerbio perikapsularren blokeoa arestian deskribatutako teknika analgesiko bat da, kapsula artikularraren aurreko zatiaren adar sensitiboak blokeatzea lortzeko helburuarekin. Azterlan horren helburua izan zen ebaluatzea eta alderatzea zer eragin analgesiko posoperatorioa duen nerbio perikapsularren blokeoak eta nerbio femoralaren blokeoak, albo bateko larruzaleko nerbio femoralaren blokeoarekin eta blokeatu gabe, aldaka, lepo femorala edo trokantreen arteko haustura duten pazienteetan. Materiala eta Metodoak: Kohorte prospektiboaren azterketa bat izan zen, Caliko (Kolonbia) Haraneko Unibertsitate Ospitalearen eta Bugako (Kolonbia) Hospital San José Buga Fundazioaren hirugarren mailako konplexutasun-erakundeetan 12 hilabetez bildutako pazienteen datuekin. Emaitzak: 101 paziente sartu ziren guztira aldaka-hausturaren diagnostikoa zuten gizon eta emakumeen artean. Analisisiak bi taldetan egin ziren: batetik, nerbio perikapsula-

rraren blokeoa eta nerbio femoralaren blokeoa, eta bestetik, nerbio perikapsularren blokeoa +/- alboko larruazaleko nerbio femoralaren blokeoa, FNB +/- alboko larruazaleko nerbio femoralaren blokeoa. Ebakuntza ondoko lehen 12 orduetan minaren ikusmen-eskala analogikoan puntuazioa nabarmen txikiagoa izan zen nerbio perikapsularren blokeo-taldean nerbio femoralaren blokeo-taldean baino, alboko larruazaleko nerbio femoralaren blokeoaren asoziazioarekin eta asoziaziorik gabe ( $p = 0,01$ ), baina alderik ez azpitaldeetan.

Ondorioak:

Nerbio perikapsularren blokeoa teknika bat da, alboko larruazaleko nerbio femoralaren blokeoari lotuta edo lotu gabe, ebakuntza ondoko aldi analgesia egokia lor dezakeena, opioideen ematea eta haren albo-ondorioak murriztuta. Hala ere, saiakuntza kliniko kontrolatuak eta ausazkoak behar dira, lagin-tamaina handiagoarekin, ohiko blokeen gaineko nagusitasun hori ebaluatzeko.

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## Introduction

Between 8000-10 000 hip fractures are diagnosed per year in Colombia, with a projection of an increase in the coming years<sup>1</sup>. Hip fractures are a frequent emergency in elderly patients, constituting a challenge for pain management<sup>2</sup>. The pericapsular nerve block (PENG)<sup>3,4</sup>, the femoral nerve block (FNB)<sup>5,6</sup>, and the lateral femoral cutaneous nerve (LFCN) blockade<sup>7</sup> have been effectively applied in patients with hip fracture<sup>8</sup>, reporting significantly reduced pain scores<sup>9-13</sup>. The present study aimed to evaluate the analgesic impact of FNB and PENG blocks with and without the LFCN blockade in patients with supra or intertrochanteric hip fractures.

## Materials and methods

### Study Design and Participants

This was an observational prospective cohort study in patients undergoing analgesic peripheral nerve blocks in orthopedic surgery to repair supra- or inter-trochanteric hip fractures in two different hospitals: Hospital Universitario del Valle and the Fundación Hospital San José Buga. This study was approved by the ethics committee of each institution.

Men and women over 18 years of age were included, with classification according to the American Society of Anesthesiology between I and III, and with intertrochanteric hip fracture or unilateral femoral neck fracture. We only included patients with the sufficient cognitive capacity (according to the patient's ability to answer three basic questions, mainly orientation: full name, age, and date) to assess and communicate the intensity of pain as well as to sign the informed consent to participate. For this study we used a convenience sampling method.

Patients who did not meet the inclusion criteria, contraindication for these techniques, allergy to local anesthetics, infection of the puncture site, non-suspended management of anticoagulant or antiaggregant

therapy, patients with fractures involving the acetabulum, or fracture of the acetabulum, finally, patients with hip fracture considered pathological and patients with chronic use of opioids were excluded.

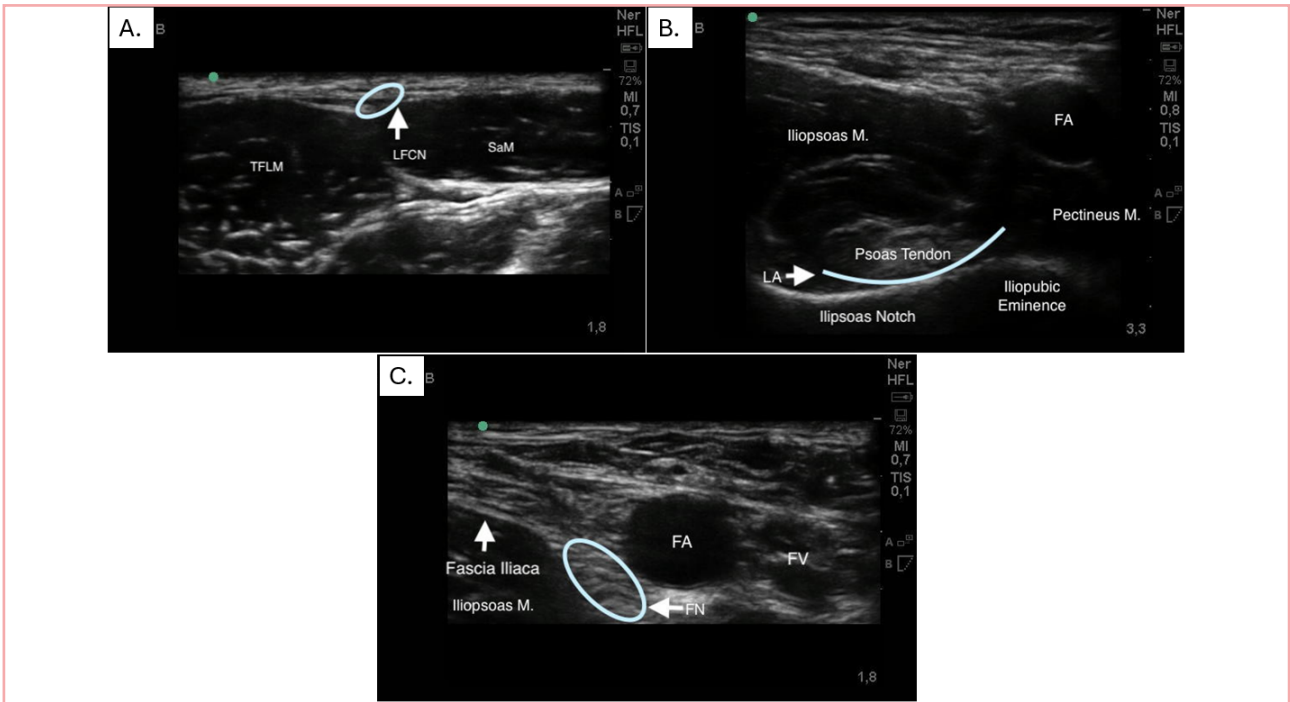
### Procedure

Once the patient was scheduled to enter the operating room, we proceeded to the preparation, processing of informed consent, and resolution of doubts, surgery time was not affected; both the information and the procedure were carried out in the shortest possible time. To carry through the procedure in all groups, the patient was placed in a supine position, with basic monitoring including non-invasive blood pressure measurement, pulse oximetry, and electrocardiogram.

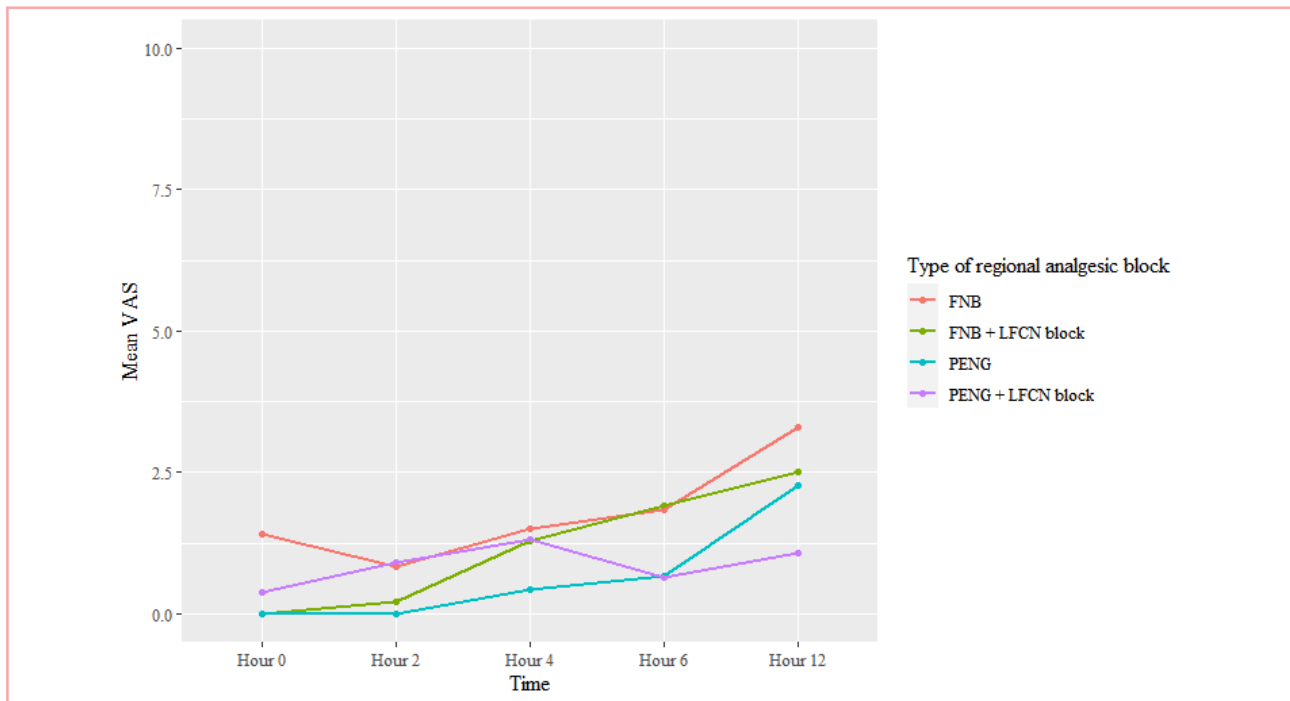
Under asepsis and antisepsis techniques with the use of US (Sonosite Turbo M Ultrasound) and two ultrasound probes, low-frequency convex (2-5 mHZ) to perform PENG, and high-frequency linear probes (5-10 mHZ) for performing FNB, LFCN or even some PENG approaches if adequate window visualization was achieved. The use of ultrasound (US) has been increasingly used in anesthetic practice, improving the success rate of nerve blocks and reducing complications<sup>14-17</sup>, helping to identify anatomical structures in real-time and observing the precise arrangement and distribution of the local anesthetic around the nervous structure<sup>18</sup>.

In the group of patients who underwent LFCN, this was done initially by looking for the lateral border of the sartorius muscle and the nerve was located between the tendon of the fascia lata and the sartorius muscle, 10 ml of simple bupivacaine 0.2% was administered. (Figure 1A).

In patients undergoing PENG (Figure 2), the transducer was located in the transverse plane of the anterior-inferior iliac spine, then rotated 45 degrees to align it with the iliopectineal eminence and visualize the structures described in the literature these are<sup>19</sup>: Antero iliac



**Figure 1.** A. LFCN block. TFLM (Tensor Fascia lata muscle), LFCN (Lateral femoral cutaneous Nerve), SaM (Sartorial Muscle). B. PENG block. FA (Femoral Artery), LA. Local anesthetic, ideal site. C. Femoral Block. FA (Femoral artery), FV (Femoral vein), FN (Femoral Nerve).



**Figure 2.** Blockade type and mean score of VAS in the first 12 postoperative hours. Source: Original.

spine inferior, iliopectineal eminence, iliopsoas muscle and tendon, femoral artery, nerve and vein, plane approach with a 22 G x 80 or 100 mm echogenic needle seeking to position it below the psoas tendon, once in this position and previous negative aspiration, the injection of the local anesthetic Bupivacaine 0.2% (obtained from a mixture of bupivacaine 0.5% 4 ml + 6 ml of SSN 0.9%) was performed, observing the distribution of the anesthetic around the tendon for a volume of 15-20 ml.

In patients with an indication for FNB (Figure 1C), an ultrasound scan was also performed with localization in the inguinal region with a high-frequency transducer of a plane of artery, vein, and femoral nerve, at a proximal level, even without observing its bifurcation, this also with or without the association of the LFCN 15 ml of 0.2% bupivacaine was administered.

An analgesic scheme was maintained this consisted of the administration of diclofenac 0.8-1 mg/kg IV (maximum dose 75 mg) IV every 12 hours for 24 hours, if there was no contraindication or dipyron 1 g every eight hours IV, acetaminophen 1 g orally every 6 hours, or if there was no tolerance to the oral route acetaminophen 15 mg/kg IV (maximum dose 1 g.) every six hours. On the other hand, rescue analgesia will consist of 3 mg IV morphine or its equivalent in hydromorphone: 0.6 mg IV single dose or every three hours if a repeat dose is required only if a Visual Analog Scale (VAS) score is greater than five points.

As a surgical anesthetic technique, spinal anesthesia was performed with 0.5% heavy bupivacaine to achieve a minimum level of T10, without opioid administration.

#### Registration and collection of information

- According to the above, the patients were divided into 4 groups:
- PENG block plus LFCN block.
- FNB plus LFCN block.
- PENG block only.
- FNB only.

Pain intensity was assessed regularly (2, 4, 6, 12, and 24 hours after anesthesia) with VAS. During rest time with values in a range of 11 points from 0 to 10. Patient satisfaction data was also recorded at the 12 hours: Very satisfied, satisfied, not very satisfied, not satisfied; as well as consumption of opioids in the POP. Information about complications attributable to the block such as hematoma, infection, and loco-regional pain was collected. The data was gathered by the anesthesiology resident in the operating room who registered the type of block, in addition to auxiliary nursing staff who knew about the study and carried out the questionnaire about the evolution of the pain in the POP period, as well as the review of the clinical history about the analgesic regimen and the opioid rescue doses if administered. The data was handled in an Excel database (Microsoft Office).

#### Statistical analysis

A descriptive analysis of the sociodemographic and exposure variables was carried out regarding each type of block, the qualitative variables were in tables of frequencies and proportions, and the quantitative variables with median and IQR or Mean and standard deviation (SD). To assess the association, chi-square or Fisher's exact tests were used for the qualitative variables and t-student or Mann Whitney U test for the quantitative ones; p-values less than 0.05 were considered statistically significant.

To demonstrate the changes or effects over time regarding pain, a longitudinal model was adjusted with a pain scale as a variable in each of the patients, for different hours (Hours 0, 2, 4, 6, and 12). The four blocks were considered as factors in order to evaluate statistically significant differences between the methods.

#### Results

The study included a total of 101 patients who had the following characteristics: mean age  $81.53 \pm 6.85$  years, 63% women and the rest men, with frequent comorbidities 70% with AHT, 25% with DM2; all belonging to an ASA II and III classification (46 vs 53% p: 0.6) (Table 1). No important demographic differences were found in these groups.

Five of these patients were lost to follow-up in the POP period for external reasons, not associated with complications from the block. Finally, the results of 96 patients were analyzed. Of these 96 patients, 24 were from the FNB group, 24 were from the FNB + LFCN group, 25 were from the PENG group, and 23 were from the PENG+ LFCN group.

Surgery time, defined from the incision to the skin closure, was 57 minutes on average. Pain intensity was measured using an analog pain scale in a range from 0 to 10, the measurement was performed at rest time.

There were no significant differences between the pain scores in the analysis by subgroups, however when comparing the FNB groups with the PENG block, significant differences were found in the first 12 hours in favor of the PENG block with or without the association of LFCN (Figure 2), however, it is necessary to highlight that in both groups the general VAS average was less than two points in the first 12 hours (Table 2).

No use of high-potency opioids such as morphine was recorded in the first 12 POP hours in any of the patient groups. No rescue locks were needed. No statistically significant differences were found in the consumption of weak opioids such as Tramadol (six patients), or in the limitation of positioning during the placement of neuraxial anesthesia due to severe pain (seven patients p= 0.62). The position chosen for the placement of anesthesia was chosen by the treating anesthesiologist, 44.6% in lateral decubitus and 52% in a sitting position. The satisfaction of the patients with the procedure was also measured, it was observed that in the four groups, there is a tendency for patients to be satisfied and very satisfied with the analgesia provided (Figure 3). The

**Table I**  
Postoperative pain analog scale score measured with VAS (from 0 to 10)

Variables	FNB + LFCN	FNB	PENG + LFCN	PENG	Total	P-value
Sociodemographic						
Sex	n = 25	n = 25	n = 25	n = 26	n = 101	0.11
Female	12(48)	14(56)	20(80)	17(65.38)	63(62.38)	
Male	13(52)	11(44)	5(20)	9(34.62)	38.53(6.85)	
Age	n = 25	n = 25	n = 25	n = 26		0.76
Median	81.88(6.2)	82(7.33)	82.04(6.19)	80.27(7.76)	81.53(6.85)	
Comorbidity	n = 25	n = 25	n = 25	n = 26	n = 101	
AH	20(80)	17(68)	16(64)	18(69.23)	71(70.3)	0.64
DM2	5(20)	7(28)	6(24)	8(30.77)	26(25.74)	0.83
CRD	3(12)	2(8)	1(4)	3(11.54)	9(8.91)	0.73
Osteoporosis	2(8)	1(4)	3(12)	1(3.85)	7(6.93)	0.62
OSA	1(4)	1(4)	1(4)	0(0)	3(2.97)	0.78
COPD	1(4)	2(8)	1(4)	1(3.85)	5(4.95)	0.88
Heart failure	1(4)	1(4)	1(4)	1(3.85)	4(3.96)	1
Disease cardiac valve	0(0)	0(0)	1(4)	1(3.85)	2(1.98)	0.57
Ischemic cardiomyopathy	0(0)	1(4)	1(4)	2(7.69)	4(3.96)	0.58
Other	n = 6	n = 6	n = 5	n = 2	n = 19	
Ischemic stroke	0(0)	2(33.33)	2(40)	0(0)	4(21.05)	
History of Pulmonary Thromboembolism	1(16.67)	0(0)	0(0)	0(0)	1(5.26)	0.33
Colon cancer	0(0)	1(16.67)	0(0)	0(0)	1(5.26)	
Dementia, Alzheimer	1(16.67)	0(0)	0(0)	0(0)	1(5.26)	
Senile dementia	0(0)	1(16.67)	0(0)	0(0)	1(5.26)	
Auricular flutter	0(0)	1(16.67)	0(0)	0(0)	1(5.26)	
Chronic Venous Insufficiency	0(0)	0(0)	0(0)	1(50)	1(5.26)	
Osteoarthritis	0(0)	0(0)	1(20)	0(0)	1(5.26)	
Parkinson	4(56.67)	1(16.67)	1(20)	1(50)	6(36.84)	
Anxiety Disorder	0(0)	0(0)	1(20)	0(0)	1(5.26)	
ASA classification	n = 25	n = 25	n = 25	n = 26	n = 101	0.6

II	10(40)	10(40)	14(56)	13(50)	47(46.53)
III	15(60)	15(60)	11(44)	13(50)	54(53.47)

Source: Original. FNB: Femoral nerve block; LFCN: Lateral femoral cutaneous nerve; PENG: Pericapsular nerve block; AH Arterial hypertension; DM2: Diabetes mellitus 2; CRD: Chronic renal disease; OSA: Obstructive sleep apnea; COPD: Chronic Obstructive Pulmonary Disease; ASA: American Society of Anesthesiology.

**Table II**  
Postoperative pain analog scale score measured with VAS (from 0 to 10)

	FNB + LFCN	FNB	P-value	PENG + LFCN	PENG	P-value	Total	P-value Total
Hour 0	n = 24	n = 24		n = 23	n = 25		n = 96	
Median (IQR)	0(0- 0)	0(0.075)	0.01	0(0- 0)	0(0- 0)	0.03	0(0- 0)	0.01
Hour 2	n = 24	n = 24		n = 23	n = 25		n = 96	
Median (IQR)	0(0- 0)	0(0.05)	0.12	0(0- 0)	0(0- 0)	0.02	0(0- 0)	0.04
Hour 4	n = 24	n = 24		n = 23	n = 25		n = 96	
Median (IQR)	0(0- 3)	0(0.2.25)	1	0(0 -0.5)	0(0- 0)	0.30	0(0- 2)	0.33
Hour 6	n = 24	n = 24		n = 23	n = 25		n = 96	
Median (IQR)	0(0- 3.25)		0.58	0(0 -1)	0(0- 0)	0.05	0(0- 2)	0.04
Hour 12	n = 24	n = 24		n = 23	n = 25		n = 96	
Median (IQR)	2(0- 3.25)	2.5(1.75- 5)	0.21	0(0- 1.5)	2(0 -3)	0.10	2(0 -4)	0.01

Source: Original. FNB: Femoral nerve block; LFCN: Lateral femoral cutaneous nerve; PENG: Pericapsular nerve block; IQR: Interquartile range.

supplementary material shows all variables registered in our study.

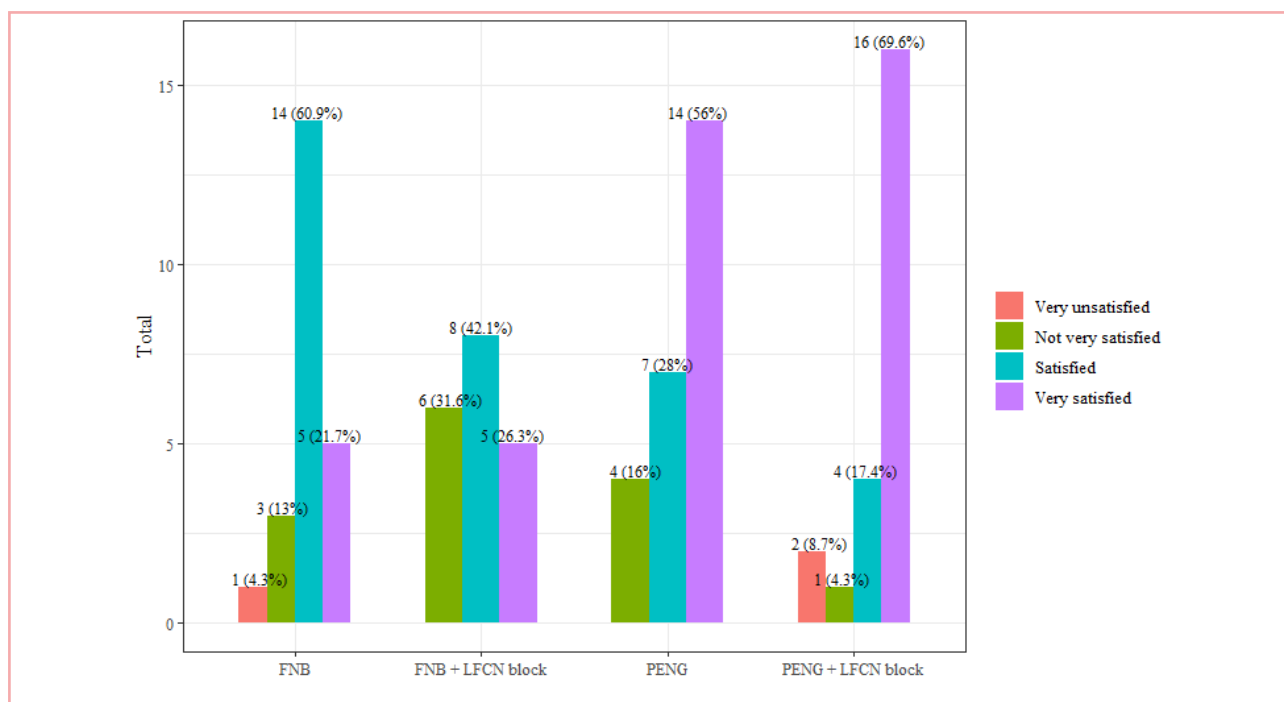
### Discussion

In this study we hypothesized that with a PENG block with or without the association of LFCN it is possible to achieve optimal analgesia without compromising motor function, with an earlier start of physical therapy, shorter hospital stay, greater patient satisfaction, and less opioid requirement and in turn lower incidence of side effects, being a very useful tool in the context of multimodal analgesia. Pain management is a key component in the perioperative period of the patient diagnosed with hip fracture. It has been associated with postoperative complications such as prolonged bed stay, increased risk of delirium, delayed ambulation, and develop-

ment of physical therapy<sup>20,21</sup>. It is for that reason that adequate pain management improves the quality of life and facilitates rehabilitation after these incidents.

The use of intravenous analgesia has been classically described, using opioid and non-steroidal anti-inflammatory drugs, which manage to provide adequate levels of analgesia, although with important secondary and adverse effects such as nausea, vomiting, kidney damage, and delirium. The use of regional analgesia techniques and peripheral nerve blocks favors better pain control<sup>4,20</sup>. Compared with systemic analgesia, the authors have reported VAS scores during movement of 3.4 on a numerical scale from 10 to 30 minutes after the block<sup>22</sup>.

The sensory innervation of the hip is complex, different nerve fibers are involved. From histological fin-



**Figure 3.** Patient satisfaction. Source: Original.

dings, it is known that the anterior joint capsule is made up of sensory fibers from the femoral, obturator, and accessory obturator nerves, while the posterior portion of the capsule mainly comprises mechanoreceptors and is innervated by branches of the sciatic nerve<sup>4,23</sup>. The femoral nerve is the longest branch of the lumbar plexus with articular sensory branches ending in the anterior capsule, which supplies the lateral and superomedial area of the hip capsule, the obturator nerve supplies the inferior medial capsule, and finally, the accessory obturator nerve, present in up to 30% of cases, contributes to the medial innervation of the capsule<sup>19</sup>.

The PENG block seeks to cover these sensitive branches in the anterior portion of the capsule, which means better analgesia compared to FNB, Fascia iliaca compartment block (FN, LFCN + ON), 3-in-1 block (FN, LFCN, ON); It is further associated that these last blocks not only cause sensory block but also motor block, by blocking mixed nerves<sup>15</sup>. To date, there is no record in the literature of major complications such as bruising or organ damage associated with this type of blockade<sup>19</sup>. Thanks to the upswing of PENG since 2018, different studies have been carried out in the last 3 years, mainly reviews and case series, some randomized clinical trials where it has been compared its effectiveness for pain control as well as with classical analgesic techniques<sup>23,24</sup>.

There are currently records of the PENG block as analgesia in hip procedures, as well as reports of its use as an anesthetic technique for hip arthroplasty or arthroscopy in combination with local anesthetics, IV

analgesics, and other blocks (Sciatica, LFCN)<sup>19</sup>, which has extended the potential of this technique even further.

This observational study, carried out in two hospital centers in patients with proximal hip fractures, observed significant differences in the first 12 hours in terms of pain control when comparing the PENG vs FNB block with or without the association of LFCN. Additionally, we can say that the PENG block, despite being a recently described technique, is a fairly effective and safe technique, which manages to provide an adequate degree of analgesia as well as significantly reduce the consumption of opioids in the first POP hours.

Both FNB and PENG achieve adequate pain modulation, reduce opioid consumption in POP, avoid their secondary or adverse effects, and also improve patient satisfaction.<sup>[25]</sup> With a median duration of analgesia reported in previous clinical trials of 15 hours 35 minutes for FNB and up to 22 hours 50 minutes for PENG<sup>25</sup>.

Peripheral nerve blocks are currently a fundamental pillar in pain control both intraoperatively and in the POP period and should be used whenever possible.

### Limitations

No differences were found in the analysis by subgroups, which could be related to an insufficient sample size. This was an observational study with no randomization made for the selection of patients, possibly causing a potential selection bias. Another limitation is that although the type of procedure performed on each patient was recorded, the sam-



ple obtained was insufficient to perform a subgroup analysis. Variables such as quadriceps strength, falls, length of hospital stay, time to start assisted walking were not evaluated.

A randomized, multicenter clinical trial is recommended to help determine whether PENG blockade is superior when performed in association with LFCN compared to PENG alone or with FNB.

### Conclusions

The PENG block, despite being a recently described block, is a very safe technique that could be associated with a more complete sensory analgesia of the hip compared to FNB with or without association of LFCN, decreasing opioid requirements in the first 12 POP hours. In addition, with a lower rate of motor block reported in the literature, which makes it an ideal alternative, favoring a much faster recovery and early start of rehabilitation with less risk of falls.

### Author contribution

Andrés Fabricio Caballero-Lozada contributed to the concept, design, definition of intellectual content, literature search, clinical studies, data acquisition, data analysis, statistical analysis, manuscript preparation, manuscript editing and manuscript review.

Claribel Olave contributed to the definition of intellectual content, literature search, clinical studies, data acquisition, data analysis, statistical analysis, manuscript preparation, manuscript editing and manuscript review.

Diana Carreño-M contributed to the definition of intellectual content, literature search, clinical studies, data acquisition, data analysis, statistical analysis, manuscript preparation, manuscript editing and manuscript review.

Andrés Velásquez: contributed to the definition of intellectual content, literature search, clinical studies, data acquisition, data analysis, statistical analysis, manuscript preparation, manuscript editing and manuscript review.

This manuscript has been read and approved by all the authors. All the requirements for authorship have been met, and each author believes that the manuscript represents honest work.

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### Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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