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SCIENTIFIC ARTICLE

Perioperative lumbar plexus block and cardiac ischemia in patients with hip fracture: randomized clinical trial



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KEYWORDS

Hip fracture;
Analgesia;
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Abstract

Background: Perioperative myocardial ischemia is common among patients undergoing hip fracture surgery. Our aim is to evaluate the efficacy of perioperative continuous lumbar plexus block in reducing the risk of cardiac ischemic events of elderly patients undergoing surgery for hip fractures, expressed as a reduction of ischemic events per subject.

Methods: Patients older than 60 years, ASA II–III, with risk factors for or known coronary artery disease were enrolled in this randomized controlled study. Patients were randomized to conventional analgesia using opioid intravenous patient-controlled analgesia or continuous lumbar plexus block analgesia, both started preoperatively and maintained until postoperative day three. Continuous electrocardiogram monitoring with ST segment analysis was recorded. Serial cardiac enzymes and pain scores were registered during the entire period. We measured the incidence of ischemic events per subject registered by a continuous ST-segment Holter monitoring.

Results: Thirty-one patients (intravenous patient-controlled analgesia 14, lumbar plexus 17) were enrolled. There were no major cardiac events during the observation period. The number of ischemic events recorded by subject during the observation period was 6 in the lumbar plexus group and 3 in the intravenous patient-controlled analgesia group. This difference was not statistically significant ($p=0.618$). There were no statistically significant differences in the number of cases with increased perioperative troponin values (3 cases in the lumbar plexus group and 1 case in the intravenous patient-controlled analgesia group) or in terms of pain scores.

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Conclusions: Using continuous perineural analgesia, compared with conventional systemic analgesia, does not modify the incidence of perioperative cardiac ischemic events of elderly patients with hip fracture.

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PALAVRAS-CHAVE

Fratura do quadril;
Analgesia;
Bloqueio do plexo lombar;
Complicações cardiovasculares

Bloqueio perioperatório do plexo lombar e isquemia cardíaca em pacientes com fratura de quadril: ensaio clínico randomizado

Resumo

Justificativa: A isquemia miocárdica perioperatória é comum em pacientes submetidos à cirurgia de fratura de quadril. Nosso objetivo foi avaliar a eficácia do bloqueio perioperatório contínuo do plexo lombar na redução do risco de eventos cardíacos isquêmicos em pacientes idosos submetidos à cirurgia para fraturas de quadril, expresso como uma redução de eventos isquêmicos por indivíduo.

Métodos: Pacientes com mais de 60 anos de idade, ASA II–III com fatores de risco para ou com doença coronariana conhecida foram incluídos neste estudo controlado e randomizado. Os pacientes foram aleatorizados para analgesia convencional usando analgésicos opioides para administração de analgesia intravenosa controlada pelo paciente (Intravenous Patient-Controlled Analgesia – IVPCA) ou analgesia contínua com o bloqueio do Plexo Lombar (PL), ambas iniciadas no pré-operatório e mantidas até o terceiro dia de pós-operatório. Monitorização contínua de ECG com análise do segmento ST foi registrada. Enzimas cardíacas seriadas e escores de dor foram registrados durante todo o período. Medimos a incidência de eventos isquêmicos por indivíduo registrados com monitoração contínua do segmento ST via Holter.

Resultados: Trinta e um pacientes (IVPCA 14, PL 17) foram incluídos. Não houve eventos cardíacos sérios durante o período de observação. O número de eventos isquêmicos registrados por sujeito durante o período de observação foi de seis no grupo PL e três no grupo IVPCA. Essa diferença não foi estatisticamente significativa ($p=0,618$). Não houve diferenças estatisticamente significativas no número de casos com aumento dos valores de troponina no perioperatório (três casos no grupo LP e um caso no grupo IVPCA) ou em termos de escores de dor.

Conclusões: O uso da analgesia perineural contínua comparado ao da analgesia sistêmica convencional não modifica a incidência de eventos isquêmicos cardíacos no período perioperatório de pacientes idosos com fratura de quadril.

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Introduction

Even under the best conditions, hip fractures are associated with high complication rates.^{1,2} Different interventions have been implemented to reduce this risk: fast-track surgical scheduling to facilitate mobilization,³ antibiotic therapy⁴ and antithrombotic prophylaxis to decrease the incidence of pneumonia and pulmonary thromboembolism. Perioperative cardiac ischemic events, however, still represent a problem in search of a solution.⁵

From a pathophysiological standpoint, the hip fracture acts as an initial injury, triggering a myriad of systemic disorders, such as pain and stress response. Both may represent relevant causal factors for myocardial ischemia and major cardiovascular events: perioperative myocardial ischemia occurs in 35% of elderly patients undergoing hip

fracture surgery, and cardiovascular events are sources of perioperative morbidity and mortality in these patients.⁶ Myocardial infarction and heart failure are the main causes of inpatient mortality.

Previous studies have evaluated the use of perioperative continuous epidural analgesia administered right after admission in these patients⁷ demonstrating a significant reduction in the amount of cardiac ischemic events, both in the appearance of cardiovascular complications during perioperative period.

The use of perioperative analgesia using peripheral nerve blocks has been suggested as a cost-efficient alternative to manage pain in these patients.⁸ Continuous lumbar plexus blockade is an analgesic alternative more localized and with fewer complications than the epidural technique, when used both for primary hip arthroplasty and surgery of fractured

patients, offering an analgesia equivalent to an epidural technique.⁹

No studies have addressed the effect of continuous perineural analgesia on the incidence of adverse cardiac events during the perioperative period.

The main objective was to evaluate the efficacy of perioperative continuous lumbar plexus block in reducing the risk of cardiac ischemic events of elderly patients undergoing surgery for hip fractures, expressed as a reduction of ischemic events per subject registered by a 3 day continuous ST-segment Holter monitoring. As secondary outcomes, we reported the effect of the analgesic technique upon postoperative pain scores, cardiac adverse events and length of stay.

Materials and methods

The study was approved by the Institutional Review Board, Escuela de Medicina, Pontificia Universidad Católica de Chile, and retrospectively registered at Clinical Trials website (ClinicalTrials.gov identifier: NCT01961895). After written informed consent, we enrolled patients older than 60 years, admitted to the Emergency Department (ED) with the diagnosis of a traumatic hip fracture with less than 48 h of evolution, and had either known Coronary Artery Disease (CAD) or risk factors for it. History of CAD was defined as history of myocardial infarction, stable chronic angina, or evidence of CAD (documented by scintigraphic, angiographic or echocardiographic studies). Patient with at least two independent predictors of perioperative cardiac adverse event (age ≥ 68 , body mass index $\geq 30 \text{ kg}\cdot\text{m}^{-2}$, active congestive heart failure, previous cardiac intervention, cerebrovascular disease, and hypertension)¹⁰ were included in our study.

We excluded patients receiving orthopedic treatment, evidence of cognitive deterioration, dementia or delirium, patients with non-sinus rhythm or conduction abnormalities (complete left- or right-bundle branch blocks, atrio-ventricular blocks) in the ECG on admission, patients with pacemaker, history of coagulopathy, contraindication to regional anesthesia or analgesia, severe renal (creatinine levels $>2.0 \text{ mg / day}$) or hepatic dysfunction or known allergy to any of the drugs used in the study.

Description of the intervention

After the diagnosis of hip fracture was made at the Emergency Department (ED), those patients willing to participate were randomly allocated (1:1) using a table of computer-generated random numbers, to receive one of two interventions: Control Group (IVPCA), were the patients was started on an intravenous morphine Patient-Controlled Analgesia (PCA), programmed with no basal infusion, 1 mg demand bolus, and 8-min bolus lockout interval; Lumbar Plexus Group (LP), were patients received a continuous lumbar plexus blocks using electrical stimulation technique according to Capdevila et al.¹¹ A 18 gauge insulated Tuohy needle (B. Braun Medical, Bethlehem, Pennsylvania) connected to a nerve stimulator (Stimuplex Dig; B. Braun Medical) was advanced until obtaining quadriceps contraction with a current output of 0.5 mA, at 2 Hz frequency and a

pulse width of 0.1 ms. Twenty mL of bupivacaine 0.1% were administered in incremental doses through the needle. A 20G perineural catheter was caudally advanced 4 cm beyond the needle tip. Successful blockade was defined as loss of sensitivity to cold and pinprick in the cutaneous distribution of the femoral nerve within 20 min post bolus injection. Posteriorly, a continuous infusion of bupivacaine 0.1% was started using a PCA pump, programmed with a continuous infusion at $8 \text{ mL}\cdot\text{h}^{-1}$, 5 mL demand bolus and a 30 min bolus lockout time. All patients were instructed to use their respective PCA system to achieve an intensity of pain under 3 in a numeric rate score (NRS, 0=no pain, 10=worst possible pain). Additionally, all patients received intravenous NSAIDs (ketorolac, $0.5 \text{ mg}\cdot\text{kg}^{-1} \text{ q8h}$), and oral acetaminophen (500 mg q6h).

On admission to the ED, a complete history and physical exam was performed, followed by an electrocardiogram (ECG) and plasma Troponin I (Tnl). At the time of randomization, a continuous 12 lead Holter monitor (NorthEast Monitoring®, Boston, USA) was initiated, and continued until the third postoperative day. The information was stored in digital format (flashcard) and further analyzed using the Holter 5.0 software (NorthEast Monitoring®, Boston, USA) which performed an evaluation of the 12 lead ECG every 60s throughout the entire period in which the patient was monitored. The time of each ischemic episode, its number and duration during the ECG monitoring was registered. A cardiologist, blind to group allocation and clinical condition of the patient, performed all the ECG analyses.

Serial ECGs and troponin levels were performed daily until the third postoperative day, or more frequently, depending on the suspicion of myocardial ischemia.

All cardiovascular medications were continued until the day of the surgery. All patients entered an early surgical Management Protocol including geriatric assessment and rapid optimization of fitness for surgery.⁵

In order to perform the surgical procedure, all patients received spinal anesthesia with 15 mg of isobaric 0.5% bupivacaine and standardized sedation with propofol in continuous infusion. If hypotension occurred (defined as a 20% decrease from baseline), lactated Ringer's solution and phenylephrine IV bolus were given. After surgery, all patients were transferred to the Post-Anesthesia Care Unit (PACU).

The analysis of ST-segment was evaluated a posteriori, by a cardiologist blind to the study group. Criteria for myocardial ischemia in the ST-segment Holter were divided into: major criteria, any ST segment depression greater than 0.1 mV in two or more continuous leads persisting for at least a minute or any ST segment up sloping greater than 0.2 mV in two or more contiguous leads persisting for at least a minute; and minor criteria, appearance of polymorphic ventricular arrhythmias, premature polymorphous ventricular complex or transient ventricular conduction delays.

Statistical analysis

Based on the study by Scheinin et al.,⁷ who reported a mean count of 4.7 ischemic episodes per patient/per day (λ_0 based on 85 h of follow-up) in elderly patients with traumatic hip fracture treated with perioperative parenteral opioid analgesia for pain control, and assuming that each

ischemic event follows a Poisson distribution, a sample size of 39 person-days of observation in each group is needed for detecting a minimum difference in the incidence rate of 30%, with a power of 90% and an α level of 0.05. We planned to enroll 17 patients per arm (51 person-days of observation) to allow for possible dropouts.

We tested normality using the Shapiro–Wilk test. The analysis of the primary outcome – ischemic episodes per patient/per day – was performed using Poisson regression with robust standard errors (similar unconditional mean and variance of the outcome). The model was adjusted for the number of Independent Predictors of Cardiovascular Adverse Events (IPCAE).¹⁰ We used unpaired Student's *t*-test or Wilcoxon rank sum test for between group comparisons, as appropriate. Chi-squared test and Fisher's exact test were used for inferences on proportions. A two-sided *p*-value less than 0.05 were considered significant. Analyses were performed using R statistical programming language, version 3.0.3 (R: A language and environment for statistical computing: <http://www.r-project.org>).

Results

We were able to enroll a total of 31 patients in a 2-year period, representing 42 and 51 person-days of observation for the LP and IVPCA group, respectively. All received their assigned study treatment (Fig. 1). Both groups were similar with respect to patient characteristics, as it is shown in Table 1.

During the 3-day period of ST monitoring, a total of 9 ischemic events were recorded, 6 in the LP group and 3 in the IVPCA group (Table 2). No difference in the incident rate between groups was observed, based on the adjusted Poisson regression ($p=0.401$). The predicted number of events for group IVPCA was 0.12 and 0.21 for L, holding IPCAE at its median. Also no difference was observed in the number of cases with increased troponin values during the perioperative period: 3 cases in the LP group and 1 case in the IVPCA group. The difference of median and IQR (median [IQR]) of the values for each group were not statistically significant (LP group: 0 [0;0], max value: 2.15 ng.mL⁻¹, IVPCA group 0 [0;0], max value: 0.187 ng.mL⁻¹).

There were no major adverse cardiac events (acute heart failure, or non-fatal/fatal myocardial infarction) in the 3-day period of ST monitoring.

There were no statistically significant differences between the groups in terms of pain scores during the perioperative period (Fig. 2).

The mean length of stay was 7.6 ± 2.6 days in the group lumbar plexus and 8.2 ± 3.2 days in the group IVPCA ($p=0.574$). There were no differences in the incidence of adverse events during the perioperative period among groups.

Discussion

Our data suggests that the incidence of cardiac ischemic events during the perioperative period of elderly patients with hip fracture is not modified by the use of continuous perineural analgesia through lumbar plexus catheters, compared with conventional systemic intravenous analgesia.

Pain caused by hip fractures has been associated to adverse outcomes, including delirium or cardiovascular complications. The increased sympathetic tone secondary to pain during the perioperative period could increase the risk of sub-endocardial ischemia and therefore, to cause post-operative cardiac complications.^{12,13} Adequate pain control could decrease the risk of cardiac ischemia.

Previous studies have reported an overall incidence of perioperative myocardial ischemia of 31%. Most of these episodes were silent, but constitute a strong predictor of cardiovascular morbidity: patients with perioperative myocardial ischemia had a significantly greater relative risk to develop an adverse cardiac event postoperatively.¹⁴

Our study reported a 29% of incidence of perioperative myocardial ischemia, similar to previous studies. The occurrence of myocardial ischemia was not associated to significant cardiac complications in the perioperative period, probably due to our small sample size.

A systematic review and meta-analysis evaluating the effect of nerve blocks (neuraxial and perineural) in pain scores during the perioperative period after hip fractures was published by Parker et al. in 2002.¹⁵ The study concluded that using nerve blocks reduced significantly the pain experienced after hip fractures, compared with standard systemic analgesia. The effect of these interventions upon other outcomes, such as mortality or cardiovascular complications, indicates a general absence of differences between nerve blocks and the control groups. Specifically, studies evaluating the effect of peripheral nerve blocks upon the risk of any cardiac complication do not currently exist. There are only two studies assessing the effect of epidural blocks on any cardiac complication.^{7,16} Only one of them demonstrated a significant clinical reduction of major cardiac complications for those patients allocated to receive the epidural blocks.¹⁶

A recent systematic review and meta-analysis conducted by Guay et al. in 2017¹⁷ focused on the use of peripheral nerves blocks as perioperative analgesia, solely or as a supplement to general anesthesia for hip fracture surgery in the elderly patients. Our study was included in the systematic review as an abstract. The study demonstrated that peripheral nerve blocks reduce pain on movement within 30min after block placement, reduced risk for pneumonia, decreased time to first mobilization and cost reduction of the analgesic regimen (even using just single shot blocks).

To the best of our knowledge, this is the first study evaluating the effect of perioperative analgesia using perineural catheters in the risk of cardiac ischemia and major cardiovascular complications. The negative results obtained by our study in terms of reduction of the incidence of ischemia should be analyzed with caution. One of the main differences of our study compared with previous ones is the fact that the systemic scheme of analgesia provided considered intravenous morphine administered using a patient controlled analgesia (PCA) system. Previous studies evaluating pain scores and cardiovascular complications in patients with perioperative epidurals used intramuscular opioids given q6h.^{7,16} Both studies reported significantly less pain for the epidural groups in the postoperative period. Matot et al.¹⁶ found a statistically significant difference favoring the epidural group during the preoperative period in terms of dynamic pain scores.

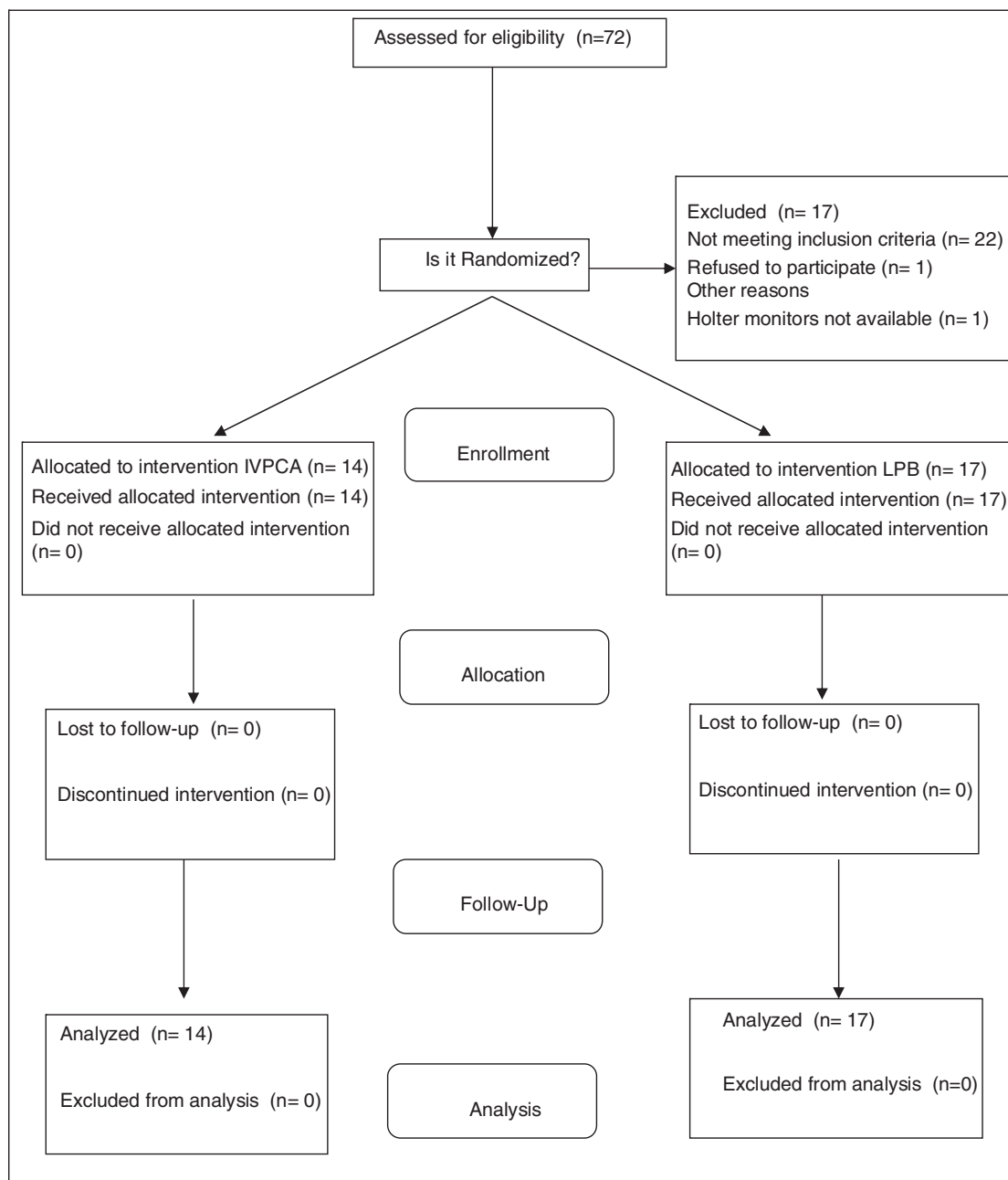


Figure 1 Consort diagram.

Likewise, other authors have demonstrated that using single injection fascia iliaca compartment blocks resulted in better pain control after admission to the emergency department, compared with intramuscular morphine.¹⁸

One interpretation of this discrepancy is that the quality of analgesia could be better in our study using a PCA scheme, compared with IM opioids. Accordingly, no pain differences were observed associated with less cardiovascular events. In favor of this interpretation, evidence does exist demonstrating that analgesic treatment with continuous IV. Infusion of sufentanil reduces the pain and severity of ischemic episodes after myocardial re-vascularization.¹⁹

Pain control has always been an issue in patients suffering from hip fractures. The analgesic therapy used in these cases is commonly seemed inadequate for the levels

of perceived pain, leaving most of the patients experiencing severe pain.²⁰ Using peripheral nerve blockade has been associated with reductions not only in postoperative pain intensity,²¹ but also in delirium, and length of hospital stay by some studies.²⁰ The use of regional anesthetic and analgesic techniques could reduce postoperative mortality. Foss et al. however has demonstrated that the vast majority of postoperative mortality is dependent on the pre-fracture morbidity and restrictions in level of active care. This potential impact of anesthetic/analgesic technique could be evident if subgroup analyses are performed in large numbers of patients.²

Several studies have demonstrated a critical role of insufficient analgesia as a promoter of adverse outcomes, particularly in terms of cognitive dysfunction.

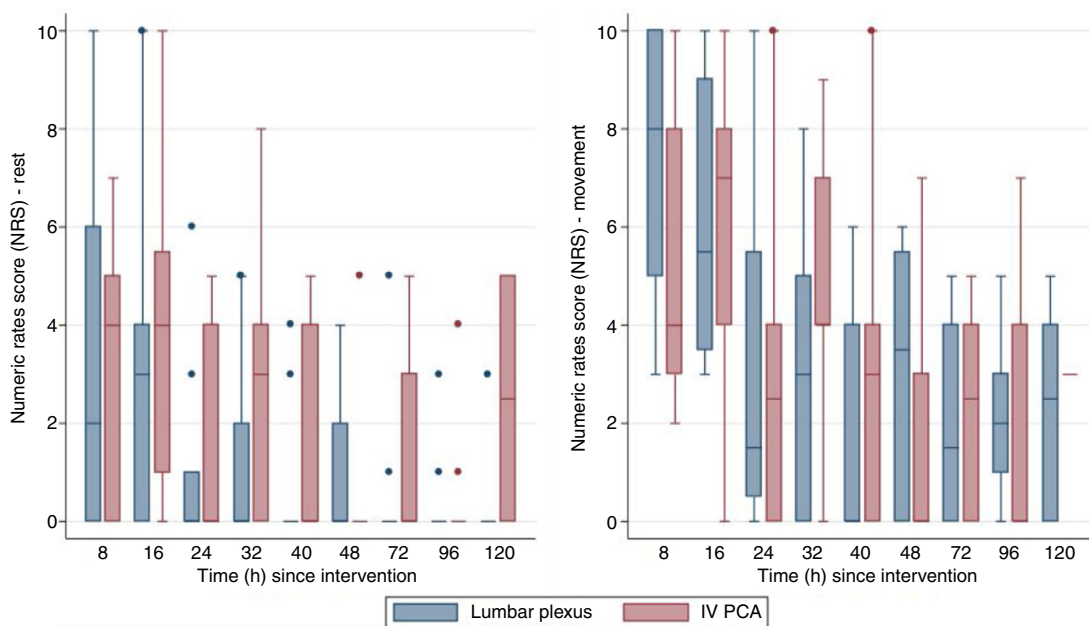


Figure 2 Pain scores, expressed as numeric rate scores (NRS) static and dynamic, during the perioperative period.

Table 1 Patients' characteristics.

	LPB (n = 17)	IVPCA (n = 14)
Age (years)	81.8 ± 8.9	80.1 ± 12.3
Gender (M/F)	4/13	3/11
Weight (kg)	62.2 ± 13.5	67.4 ± 12.6
Height (cm)	159.3 ± 10.0	161.6 ± 10.6
ASA (II/III)	13/4	10/4
Previous myocardial infarction, n (%)	1 (5.8)	2 (14.2)
Angina pectoris, n (%)	1 (5.8)	1 (7.1)
History of CHF, n (%)	3 (17.6)	2 (14.3)
Hypertension, n (%)	15 (88.2)	13 (92.9)
Current smoking, n (%)	3 (17.6)	1 (7.1)
Cholesterol (240 mg.dL ⁻¹), n (%)	1 (5.8)	2 (14.2)
Diabetes mellitus, n (%)	3 (17.6)	4 (28.6)

Table 2 Ischemic events during the 3-day period of ST monitoring.

	Day 1	Day 2	Day 3	Total events
LP group	2	3	1	6
IVPCA group	1	1	1	3

No difference in the incident rate between groups was observed (adjusted Poisson regression $p = 0.401$).

Undertreated pain and inadequate analgesia appear to be risk factors for delirium in older adults. Opioids per se, with the exception of meperidine, do not cause delirium, and avoiding them is associated with a nine-fold risk of developing it among cognitively intact adults.²²

In our study, although there is a tendency toward a better pain control in the group receiving regional analgesia, there are no statistically significant differences among the

groups, resulting in adequate levels of analgesia, independently from the type of analgesia the patients received. Our main aim was the risk of cardiac ischemia, based on previously reported data using neuraxial analgesia compared with systemic one. One of the main drawbacks of these previous studies was the fact that the type of systemic analgesia was suboptimal, using intramuscular opioids. Pain evaluation was a secondary outcome. The fact that we did not find any differences in terms of pain scores between the groups could be due to the fact that the study is underpowered to find differences on that secondary outcome. Cumulative evidence from most recent reviews provides consistent evidence that regional nerve blocks can effectively reduce pain associated with hip fracture, providing rapid-onset, site-specific analgesia that is more effective than standard systemic analgesia alone.

Our study has several limitations. One of the most important is that due to the nature of the intervention (lumbar plexus catheter versus intravenous PCA), it was not conducted in a blinded fashion. This lack of blinding potentially could affect the reporting of clinical events. The main outcome, however, was the occurrence of myocardial ischemia in the ST-Holter monitor. An independent researcher, blinded to the patients' allocation, adjudicated these events, reducing the risk of bias. The same occurs with other secondary outcomes, such as cardiac enzymes.

Probably one of the main reasons why no differences were observed between groups is the risk of selection bias. A proper evaluation of pain scores and correct use of the intravenous PCA requires an adequate cognitive status of the patients. We decided therefore to exclude those patients with any cognitive impairment. Using regional analgesia using continuous perineural infusions in patients with cognitive impairment, who cannot use an intravenous PCA with morphine, potentially could be a better option in terms of adequate analgesia, compared with standard

techniques. Further research should evaluate this alternative and its impact upon outcomes such as cardiovascular complications or mortality on that specific subgroup of patients, using nonverbal pain assessment scales specifically developed for this purpose.²³

The procedure requires a highly trained operator; in special considering that patients' positioning to perform the block is more complex due to the fracture. A simpler alternative approach could be using fascia iliaca catheters. Those kind of nerve blocks are easier to perform, they do not require any special positioning, and can be performed under ultrasonographic guidance, potentially increasing the success of the technique and decreasing potential complications. Indeed, there are previous studies reporting the effect of fascia iliaca catheters upon pain scores during the postoperative period. Those studies did not demonstrate any effect of the technique on pain relief, compared with standard systemic analgesia. The main difference with our protocol is the fact that those studies considered the postoperative period only.²⁴ One of the main reasons for us to prefer lumbar plexus blocks was the fact that the puncture site and insertion of the catheter is safely away from the surgical area, allowing to maintain the catheters' position during the entire perioperative period.

Although nerve blockades are commonly performed by most of the practicing anesthesiologists, many clinicians do not perform them routinely because they believe the additional time, effort, and supervision required may outweigh the benefits.²⁵

Conclusions

The incidence of cardiac ischemic events during the perioperative period of elderly patients with hip fracture is not modified by the use of continuous perineural analgesia, compared with conventional systemic analgesia. Better pain control using intravenous patient controlled analgesia with morphine provides an adequate pain relief when used in cognitively intact older patients.

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Conflicts of interest

The authors declare no conflicts of interest.

References

1. Roche JJW, Wenn RT, Sahota O, et al. Effect of comorbidities and postoperative complications on mortality after hip fracture in elderly people: prospective observational cohort study. *BMJ*. 2005;331:1374.
2. Foss NB. Mortality analysis in hip fracture patients: implications for design of future outcome trials. *Br J Anaesth*. 2004;94:24–9.
3. Shiga T, Wajima Z, Ohe Y. Is operative delay associated with increased mortality of hip fracture patients? Systematic review, meta-analysis, and meta-regression. *Can J Anaesth*. 2008;55:146–54.
4. Southwell-Keely JP, Russo RR, March L, et al. Antibiotic prophylaxis in hip fracture surgery: a metaanalysis. *Clin Orthop Relat Res*. 2004;179–84.
5. Liu J, Ahn J, Elkassabany NM. Optimizing perioperative care for patients with hip fracture. *Anesthesiol Clin*. 2014;32:823–39.
6. Huddleston JM, Gullerud RE, Smither F, et al. Myocardial infarction after hip fracture repair: a population-based study. *J Am Geriatr Soc*. 2012;60:2020–6.
7. Scheinin H, Virtanen T, Kentala E, et al. Epidural infusion of bupivacaine and fentanyl reduces perioperative myocardial ischaemia in elderly patients with hip fracture – a randomized controlled trial. *Acta Anaesthesiol Scand*. 2000;44:1061–70.
8. Abou-Setta AM, Beaupre LA, Jones CA, et al. Pain management interventions for hip fracture. Rockville, MD: Agency for Healthcare Research and Quality; 2011.
9. Türker G, Uçkunkaya N, Yavaşcağlı B, et al. Comparison of the catheter-technique psoas compartment block and the epidural block for analgesia in partial hip replacement surgery. *Acta Anaesthesiol Scand*. 2003;47:30–6.
10. Kheterpal S, O'Reilly M, Englesbe MJ, et al. Preoperative and intraoperative predictors of cardiac adverse events after general, vascular, and urological surgery. *Anesthesiology*. 2009;110:58–66.
11. Capdevila X, Macaire P, Dadure C, et al. Continuous psoas compartment block for postoperative analgesia after total hip arthroplasty: new landmarks, technical guidelines, and clinical evaluation. *Anesth Analg*. 2002;94:1606–13.
12. Landesberg G, Luria MH, Cotev S, et al. Importance of long-duration postoperative ST-segment depression in cardiac morbidity after vascular surgery. *Lancet*. 1993;341:715–9.
13. Fleisher LA, Nelson AH, Rosenbaum SH. Postoperative myocardial ischemia: etiology of cardiac morbidity or manifestation of underlying disease? *J Clin Anesth*. 1995;7:97–102.
14. Marsch SC, Schaefer HG, Skarvan K, et al. Perioperative myocardial ischemia in patients undergoing elective hip arthroplasty during lumbar regional anesthesia. *Anesthesiology*. 1992;76:518–27.
15. Parker MJ, Griffiths R, Appadu B. Nerve blocks (subcostal, lateral cutaneous, femoral, triple, psoas) for hip fractures. *Cochrane Database Syst Rev*. 2002;CD001159.
16. Matot I, Oppenheim-Eden A, Ratrot R, et al. Preoperative cardiac events in elderly patients with hip fracture randomized to epidural or conventional analgesia. *Anesthesiology*. 2003;98:156–63.
17. Guay J, Parker MJ, Griffiths R, et al. Peripheral nerve blocks for hip fractures. *Cochrane Database Syst Rev*. 2017;5:CD001159.
18. Foss NB, Kristensen BB, Bundgaard M, et al. Fascia iliaca compartment blockade for acute pain control in hip fracture patients: a randomized, placebo-controlled trial. *Anesthesiology*. 2007;106:773–8.
19. Mangano DT, Siliciano D, Hollenberg M, et al. Postoperative myocardial ischemia therapeutic trials using intensive analgesia following surgery. The Study of Perioperative Ischemia (SPI) Research Group. *Anesthesiology*. 1992;76:342–53.
20. Rashiq S, Vandermeer B, Abou-Setta AM, et al. Efficacy of supplemental peripheral nerve blockade for hip fracture surgery: multiple treatment comparison. *Can J Anaesth*. 2013;60:230–43.
21. Roberts HC, Eastwood H. Pain and its control in patients with fractures of the femoral neck while awaiting surgery. *Injury*. 1994;25:237–9.

22. Morrison RS, Magaziner J, Gilbert M, et al. Relationship between pain and opioid analgesics on the development of delirium following hip fracture. *J Gerontol A Biol Sci Med Sci*. 2003;58:76–81.
23. Warden V, Hurley AC, Volicer L. Development and psychometric evaluation of the Pain Assessment in Advanced Dementia (PAINAD) scale. *J Am Med Dir Assoc*. 2003;4:9–15.
24. Cuvillon P, Ripart J, Debureaux S, et al. Analgésie postopératoire par cathéter fémoral après fracture du col du fémur chez la personne âgée: étude prospective randomisée. *Annales Françaises d’Anesthésie et de Réanimation*. 2007;26:2–9.
25. Abou-Setta AM, Beaupre LA, Rashiq S. Comparative effectiveness of pain management interventions for hip fracture: a systematic review. *Ann Intern Med*. 2011;155:234–45.