

Ultrasound Guided Regional Anesthesia by Emergency Physicians for Hip Fractures Reduces Delirium

Sub Title: Stepped-Wedge Randomized Clinical Trial

Author List: Jacques S. Lee M.D. MSc., ^{a,b,c} Jordan Chenkin M.D. MEd., ^b Robert Simard M.D., ^{b,c} Tina Bhandari M.D., ^{b,c} Michael Y Woo M.D., ^{f,g} Jeffery J. Perry M.D. MSc., ^{f,g} Debra Eagles M.D., ^{f,g} Charles Wong M.D., ^h Andrew D. McRae M.D., Ph.D., ^h Eddy Lang M.D., ^h Joseph Newbigging M.D., ⁱ Marco L.A. Sivilotti M.D. MSc., ⁱ Ian Chernoff M.D., ^{a,b} Bjug Borgundvaag M.D., Ph.D., ^{a,b} Shelley L. McLeod PhD., ^{a,b} Donald Melady M.D., M.Sc., ^{a,b} Alex Kiss PhD., ^j and Marcel Émond M.D. PhD., ^{d,e}

Author Affiliations:

- a. Schwartz/Reisman Emergency Medicine Institute, Sinai Health, Toronto, Ontario, Canada.
- b. University of Toronto, Toronto, Ontario, Canada.
- c. Department of Emergency Service, Sunnybrook Health Sciences Center, Toronto, Ontario, Canada.
- d. Axe Santé des populations et pratiques optimales en santé, Centre de recherche du CHU de Québec-Université Laval, Québec, Canada.
- e. Département de médecine d'urgence, CHU de Québec-Université Laval, Québec, Canada.
- f. Department of Emergency Medicine, The Ottawa Hospital, Ottawa, Ontario, Canada.
- g. The University of Ottawa, Ottawa, Ontario, Canada.
- h. The University of Calgary, Calgary, Alberta, Canada.
- i. Queen's University, Kingston, Ontario, Canada.
- j. Department of Epidemiology and Biostatistics, Sunnybrook Research Institute, Toronto, Ontario, Canada.

Funding: This work was supported by the Canadian Institute for Health Research (MOP #142429).

Dr. Lee is funded by the Schwartz/Reisman Emergency Medicine Institute (SREMI) Inaugural Research Chair in Geriatric Emergency Medicine.

The authors have no conflicts of interest to declare.

This work was presented as the plenary abstract at the Canadian Association of Emergency Physicians meeting in Quebec City, QC in 2022 and was awarded the Grant Innes award as the top rated research abstract.

Corresponding author:

Jacques S. Lee MD, MSc

Inaugural Research Chair, Geriatric Emergency Medicine
Schwartz/Reisman Emergency Medicine Institute, Sinai Health
60 Murray St, 4th Floor, Room 4-017
Toronto, ON M5T 3L9
jacques.lee@sinaihealth.ca

Trial Registration: [clinicaltrials.gov NCT02892968](https://clinicaltrials.gov/NCT02892968)

URL: clinicaltrials.gov/study/NCT02892968?tab=results

Data Sharing: Data sharing will be made available on reasonable request to the corresponding author.

WORD COUNT: 3205/3500, including **one** figure and **three** tables and **one** supplementary table.

Background: Delirium complicates 500,000 hip fractures/year globally. Point-of-Care Ultrasound Guided Regional Anesthesia (POCUS-GRA) may reduce delirium, but it is rarely performed in emergency departments (ED).

Objectives: Measure the impact of a knowledge-to-practice intervention (KTP) on: 1) ED uptake of POCUS-GRA; 2) incidence of and days to delirium; 3) analgesic effectiveness, 4) safety and 5) procedure time.

Design: Multicentered, pragmatic, stepped-wedge cluster trial. The order in which ED physicians were trained at each site was randomized.

Setting: Seven academic EDs from three provinces in Canada.

Participants: We included patients ≥ 65 years with a hip fracture who were not anti-coagulated or delirious on ED arrival, and ED physicians who did not routinely performed POCUS-GRA.

Intervention: A two hour structured KTP training session, reminders and procedure bundles.

Main Outcome and Measures: Incidence of delirium within 7 days of ED presentation and days to delirium.

Results: We trained 208/213 (97.7%) ED physicians who assessed 694 eligible participants: 248 prior to training (control) and 446 after training (intervention). The KTP intervention increased blocks from 6/248 (2.4%) before to 229/446 (51.3%) after training. Adjusting for apriori confounders and clustering, the odds of delirium was reduced by 0.42, (95% CI: 0.35 – 0.50) and days to delirium was delayed by 22% (0.78, 95% CI: 0.65-0.95) in the intervention group. Blocks were effective, safe and quick.

Limitations: We enrolled only 96% of our sample size. Uptake of POCUS-GRA was 51.3%.

Conclusion and Relevance: Despite these limitations, our study significantly adds to the evidence that POCUS-GRA reduces incident delirium. Future work should evaluate strategies to optimize early, effective POCUS-GRA delivery to optimize pain control and improve delirium outcomes in this large and vulnerable population.

INTRODUCTION

There are approximately 1.5 million hip fractures each year globally, with an average cost estimated at \$43,669 U.S, representing global costs of over \$65 billion annually.^{1,2} Delirium complicates up to 62% of hip fractures, doubling mortality, extending hospital stays by 7.8 days, and increasing nursing care burden, nursing home admissions, and risk of dementia.³⁻⁶ Delirium can be life-altering as well –it has been shown to cause lasting psychological trauma to patients and their families.⁷

Previous research has shown that regional anesthesia provides better pain management for patients with hip fractures than parenteral opioid analgesics.^{8,9} These meta-analyses found moderate quality evidence that regional anesthesia independently reduces the risk, severity and duration of delirium, and that early administration of the intervention is critical.⁸⁻¹² Point-of-care ultrasound guided regional anesthesia (POCUS- GRA) allows direct visualization of neurovascular structures, and is considered by many to improve the safety and efficacy of regional anesthesia.¹³⁻¹⁶

To date, the adoption of POCUS-GRA by emergency department (ED) physicians has been low. We previously reported less than 5% of academic ED physicians routinely used any form of regional anesthesia for hip fractures.¹⁷ Inadequate training and perceived time to perform blocks were the most commonly identified barriers. To address these challenges, we developed a knowledge-to-practice (KTP) intervention to train and encourage ED physicians to perform POCUS-GRA.¹⁸

The primary objective of this study was to assess whether our KTP intervention increased the use of POCUS-GRA by ED physicians, and whether increased uptake impacted the incidence of and time to delirium in older people with hip fractures. Secondary outcomes included efficacy, safety of POCUS-GRA, and time to perform the block.

METHODS

Study Design

The **ED** **U**ltrasonographic **R**egional **A**nesthesia to **P**revent **I**ncident **D**elirium (EDU–RAPID) study was a pragmatic, multicenter, stepped-wedge, cluster randomized clinical trial.^{19,20} We enrolled physicians and patients with hip fractures at seven academic EDs in four provinces in Canada: Rockyview General Hospital; Kingston General Hospital, Mount Sinai Hospital, The Ottawa Hospital, Civic and General sites, and Hôpital Enfant-Jésus and Hôpital Saint-François d'Assise. Sunnybrook Health Sciences Center was the site of our feasibility study,¹⁸ and led training of other sites (see Table 3). We included emergency physicians who worked a minimum of four shifts per month, and who did not regularly perform POCUS-GRA (defined as ≥ 4 blocks in the year prior to enrollment). We included patients aged 65 years and older who underwent surgical fixation of a hip fracture, excluding those who were delirious on ED arrival, allergic to local anesthetic, on anticoagulants, reported minimal pain ($\leq 3/10$ on a 10-point numeric rating scale) at presentation, or had severe dementia defined as either non-verbal or too cognitively impaired to complete study interviews.

Description of KTP Intervention

The KTP intervention for this multicenter trial has been previously described.¹⁸ In brief, it included a two-hour training session with three stations: a phantom simulator station, a turkey thigh station, and ultrasonographic land marking on a live older patient model. Research assistants provided pre-assembled equipment bundles to facilitate POCUS-GRA in the ED, and sent out e-mail reminders to participating ED physicians.²¹ We used a “train-the-trainer” model to disseminate the KTP intervention to all participating sites. ED physicians needed to demonstrate competence by successfully completing a competency-based checklist. The coordinating center randomized the order in which physicians at each site received training using computer generated sequences. Each site trained 4-8 physicians at a time every 4 to 8 weeks until all eligible physicians completed training. Hip-fracture patients treated by an ED physician prior to training were allocated to the control group,

and patients treated after the physician completed training were allocated to the intervention group. Outcome assessors were blinded to whether the ED physician had been trained and whether a nerve block had been done. Reporting of this trial follows the CONSORT extension for reporting cluster randomized trials.¹⁹

Physician Data Collection

A data form was included in each procedure bundle. Physicians were trained to use the validated Confusion Assessment Method, short form, (CAM-S)^{22,23} and to document if the patient had delirium. Physicians also recorded the patient's self-reported pain severity on a 10-point numeric rating scale at baseline and 30 minutes post-procedure, any complications from a pre-specified list: minor (i.e. local hematomas), or serious (femoral artery or nerve puncture, hypotension, seizures, shortness of breath, anaphylaxis, or any other complication requiring treatment)²² and the time they started and completed the procedure.

Research Assistant Data Collection

All research assistants received standardize training for all study scales, including: the Short-Blessed Test of mental status^{24,25}; the Mini-Cognitive Test ²⁶administered with the CAM-S ^{22,23}; mobility status; Richmond Agitation Scale (RASS) scores²⁷; and pre-injury activities of daily living using the Older American Resources Scale (OARS).²⁸⁻³¹ Research assistants reviewed standardized simulated delirium cases and had to demonstrate competence and reliability with three live cases prior to independent assessments. All delirium outcomes were reviewed by the coordinating center to assure consistency across sites. Research assistants obtained consent to collect participant data after the participants' pain had been controlled, typically the next day.

Research assistants interviewed participants daily to assess delirium, and recorded the Mini-Cog²⁶ and RASS daily until discharge from hospital or the seventh post-operative day. They also conducted a chart review to verify physicians initial delirium assessment using a validated chart review tool³² and to assess for transient delirium occurring between daily interviews as recommended by the CAM-S training manual.²³ Research assistants were unaware of the randomization status of the ED physicians to minimize unblinding. In addition there was no evidence that a patient had received POCUS-GRA during interviews, the procedure was not routinely documented in the medical chart at participating sites, and research assistants were trained not to inquire whether the patient received a block and to report if they became unblinded.

Statistical Analysis

The intended unit of clustering was the physician and the unit of analysis was individual participant using intention-to-treat analysis (clinical trials.gov NCT02892968). The primary outcome was the proportion of patients with in-hospital delirium within seven days from the index admission, and proportional differences between the intervention and control groups were estimated using chi-square statistics with 95% confidence intervals (CIs).

We expected clustering by physician to be an inherent feature of the data, and order of training was randomized at each site. However 37% of ED physicians only cared for one trial-eligible patient during the study period, precluding cluster analysis based on physician. We observed significant variance in delirium rates across sites from 1.5% to 41.1% (Table 3, see “Limitations” below). In addition, site start dates were not randomized - enrollment began when research staff were recruited and trained. Accordingly, we accounted for clustering by site in our analysis using a generalized estimating equation (GEE) model with a compound symmetry correlation structure, using a logit link function and a binomial distribution to adjust for the correlation among observations taken from the same site for our primary outcome, incidence of delirium. We controlled for imbalances between

groups that might exist despite cluster randomization for the following confounders identified *a priori* from existing systematic literature reviews: age, sex, time to surgery, baseline cognitive impairment, dehydration and iatrogenic complications.³³ We used a GEE model with a log link function and a Poisson distribution for the co-primary outcome, days to delirium.

Nerve block effectiveness

We measured the proportion of blocks that could be considered “effective” based on existing literature³⁴ and consensus among our study team as being a 50% relative reduction from initial pain score at 30 minutes post-block. We also collected data on mean morphine milligram equivalents for opioids given in the ED from the medical records.

Sample Size Calculation

Sample size was based on the primary outcome, the risk of incident delirium within seven days. We expected each physician to treat four to six patients. Assuming 144 participating physicians and an intraclass correlation coefficient of 0.01 to 0.04, at the point at which half of the physicians have been trained, a sample size of 720 to 840 patients would provide 80% power with an alpha of 0.05 to detect an absolute difference in delirium risk of 7.6% to 8.0%.

Ethics

The study was approved by the Research Ethics Board (REB) at all participating centers. Eligible ED physicians provided informed consent prior to enrollment and randomization. All REBs waived the requirement for patient informed consent prior to use of POCUS-GRA as approaching a patient for consent while they were still in pain might not be fully informed and voluntary. Instead, participating ED physicians explained the risks and benefits of the procedure to patients and obtained consent for

the procedure as per their routine. Research assistants subsequently sought informed consent from potential participants for administration of study-related questionnaires and access to their medical records. We used the Adamis method to assess capacity.³⁵ We obtained written informed consent from substitute decision makers if patients lacked capacity.

Role of the Funding Source: This study was supported by the Canadian Institute for Health Research, institute of ageing (MOP #142429). Dr. Lee is funded by the Schwartz/Reisman Emergency Medicine Institute (SREMI) Inaugural Research Chair in Geriatric Emergency Medicine. The funders had no role in the study design, conduct or reporting of this trial.

RESULTS

Of 217 eligible physicians, 213 (98.1%) agreed to participate. Mean years of ED experience was 15.6 years and 31.3% were female. We were able to schedule and train 208/213 (97.7%) of participating ED physicians.

We screened 937 patients with hip fractures, of whom 205 (21.9%) were excluded, and 732 were randomized – 264 (36.0%) to the control group and 468 (64.0%) to the intervention group. A further 32 (4.4%) had missing outcome data and 6 (0.8%) withdrew (Figure 1). The remaining 694 participants were included in the analysis: 248 (35.7%) in the control and 446 (64.3%) in the intervention group. The mean age of participants was 81.0 years and 69.6% were female. Demographics of control and intervention patients are provided in Table 1 and those with and without delirium are provided in Table 2. Participants were enrolled at seven ED sites in four provinces (See Table 3). The number of physician participants per site varied from 12 to 51, and participants enrolled per site varied from 24 to 202.

Once trained, ED physicians attempted blocks on 237/446 (53.1%) intervention participants and completed 236/237 (99.6%) blocks. Among the 217/446 (48.7%) intervention participants who did not

have a block performed, reasons given included: too busy 74 (32.0%), difficult anatomy 38 (15.1%), patient or caregiver refused the procedure 10 (4.3%), physician forgot 9 (3.8%), other reason 4 (1.7) and no reason was given in 96 cases (41.6%). There were 6 protocol violations in the control group – participants in which a nerve-block was attempted by a physician prior to completing training (Figure 1).

Overall, 193/694 (27.8%) included hip fracture patients developed delirium – 77/228 (31.1%) in the control group and 116/446 (26.0%) in the intervention group (Table 1). In GEE intention to treat analysis adjusted for clustering by site and apriori confounders (see *statistical analysis* above), the odds of delirium among those in the treatment group was reduced by 0.42, (95% CI: 0.38 – 0.50, see Supplementary Table 4 for details of the model). This corresponds a reduction of the probability of delirium of 28% in the treatment group. The number needed to treat was seven. Days to delirium was analyzed using a Poisson regression model with the incidence rate ratio for the treatment group compared to control being 0.78 (95% CI 0.65-0.95). This indicates, comparing treatment to control, days to delirium were reduced by 22% (95% CI: 5% – 35%).

Of the 236 blocks completed in the intervention group, pain effectiveness data were available for 186 (78.8%) participants. The mean pain score at 30 minutes post block fell by 3.1 points from a baseline of 5.5 on a 10-point pain scale, and 107/186 (57.5%) experienced an effective block with 50% reduction in pain. Mean morphine milligram equivalents were lower in the intervention group (7.0, 95% CI 1.3 to 20 MME) compared to the controls (7.6, 95% CI 2.0 to 20 MME), although the 95% CIs overlap.

There were no serious adverse outcomes reported in the 236 blocks performed and only one (0.4%, 95% CI: 0.0-2.4%) minor complication (a hematoma at the injection site) that required no additional treatment. The time needed to perform blocks was recorded in 126/236 blocks performed

(53.4%) in the intervention group, with a median time to block of 15 minutes (IQR 12 to 20), and 90% of blocks were completed within 25 minutes.

DISCUSSION

This pragmatic trial of 694 participants demonstrated that a KTP intervention reduced the odds of delirium incidence by 0.42 and delayed time to delirium by 22%. By including only physicians who did not already routinely perform regional anesthesia, we confirmed the safety and effectiveness of early POCUS-GRA performed by ED physicians even during early uptake.

Our trial was inspired by two meta-analyses of the efficacy of regional anesthesia to reduce delirium.^{36,37} The authors concluded there was moderate-quality evidence for reduced delirium. However, there were only four randomized^{10,11,38,39} trials included, and one trial (n=338) contributed almost all (36/38) the cases of delirium.¹¹ Kim et. al.⁴⁰ published a meta-analysis after our trial was initiated that added seven randomized clinical trial with a total of 289 delirium cases. Overall delirium odds were reduced by one third in those randomized to receiving a block, however the 95% CI crossed 1.0 (0.36 to 1.22). No trials to date have evaluated the effectiveness of translation into practice of regional anesthesia for reducing delirium in patients with hip fractures.

With 193 cases of incident delirium, our trial substantively adds to the evidence base supporting the effectiveness of regional anesthesia in reducing delirium. We demonstrated the feasibility of training almost all ED physicians at multiple centers to perform safe and effective POCUS-GRA. Only one minor complication occurred out of 236 blocks performed, and 58% of blocks were highly effective, resulting in a 50% reduction in initial pain. Our KTP intervention improved block uptake from 2.4% to 51.3%. Early regional anesthesia is now accepted as a Healthy Quality Ontario standard⁴¹ and in 2023 the Australian and New Zealand Hip Fracture Registry (ANZHFR) reported that 87%

of older hip fracture patients in the registry received early regional anesthesia.⁴² The additional evidence provided by this study that regional anesthesia reduces incident delirium by over 50% challenges decision makers to answer the questions: why is it not standard of care in their jurisdiction? what they are doing to change this?

Limitations

A significant limitation of this pragmatic trial was that we enrolled 694/720 patients, short of the prespecified sample size (96.4%) as we terminated enrollment after 841 apparently eligible patients were enrolled. However, 109 participants had been misclassified as eligible in our database, and a further 38 withdrew or had missing outcome data. Post-hoc analysis demonstrates our trial was sufficiently powered to exclude a difference in odds of delirium of 0.52 to 0.54, corresponding to a reduction of delirium rates of 8.5 to 9.5% between intervention and control groups. Being under-powered is a conservative bias. Given that we demonstrated an odds reduction of 0.42 corresponding to a 28% reduction in delirium in the treatment group, the impact of our premature termination appears to be limited. However, the marginal reduction in the odds of days to delirium onset may have been due to being slightly under powered.

The fact that we were unable to use physicians as unit of analysis as originally intended, because 38% of physicians only treated one eligible participant during the study, is another limitation. We therefore accounted for clustering by site instead of physicians given the large between-site variability in delirium incidence.

Another limitation is the fact that one site had an extremely low delirium rate (1.5%) compare to all other sites (24.4 to 41.1%). We believe this may in part be due to a lower rate of obtaining informed consent from substitute decision makes for patients with cognitive impairment at this site as only 1.5% of enrolled patients had baseline cognitive impairment at this site compared to 9.6% at all other sites. In addition, this site only enrolled 66/694 subjects (9.6%). However, we cannot exclude

the possibility of differential measurement of delirium outcomes at this one site. Misclassification of delirium outcomes due to poor sensitivity at this site would bias the results towards the null. Thus we do not believe this limitations detracts from our conclusion that the treatment reduced delirium.

A clinical trial where randomization occurred at the individual level would have better isolated a causal link between POCUS-GRA and lower delirium and our team had considered both designs. However, the chosen design was superior for testing the KTP intervention and to limit the risk of contamination within physicians. Obtaining informed consent from older people suffering from a hip fracture to participate in a trial where the most effective form of analgesia might be randomly withheld was also felt to be ethically questionable.

Even in expert hands, POCUS-GRA with femoral nerve blocks will not always be effective to control the pain of hip fractures due to variations in individual innervation anatomy plus variability in fracture site (e.g. intra-capsular vs. extracapsular). Blocks in this study resulted in a greater than 50% reduction in pain for the majority of patients, however there was significant room for improvement in the effective block rate. Again, this element of our pragmatic trial introduces a conservative bias. Improving the proportion of effective blocks may have further reduced delirium.

Another limitation is missing data for secondary outcomes collected by the participating ED physicians including the change in pain scores following POCUS-GRA. ED physicians recorded an initial and 30-minute pain score in 78.8% of cases. While it would have been prohibitively expensive to have research assistants on duty at participating centers 24/7, having research assistants collect secondary outcome on purposefully sampled patients across all sites might have been feasible.

Future trials should explore methods for improving the uptake and effectiveness of POCUS-GRA. On average, POCUS-GRA takes only 15 minutes to perform, but this may be perceived by some emergency physicians as being too long on a busy shift. Ordering parenteral opioids takes far less time for physicians, shifting the burden onto nursing staff. Our trial supports future trials to explore the

impact of improved block effectiveness on delirium risk. This may include training innovations to improve block quality, duration and uptake, and/or exploring new POCUS-GRA approaches. In addition, fascia iliaca, pericapsular nerve group (PeNG) block and supra-inguinal approaches have been shown to produce superior analgesia to femoral nerve blocks.^{43,44} Finally, collaborations between the ED, anesthesia, orthopedics and perioperative medicine departments are needed to promote not only prompt, effective analgesia on ED arrival, but also ongoing attention to pain control and prevention of delirium throughout the care trajectory for all persons with hip fracture.

CONCLUSIONS

Widespread training of ED physicians with limited prior experience in use of POCUS-GRA in a multicenter national setting was feasible and resulted in effective, safe and rapid analgesia for older people with hip fractures. Uptake of the procedure improved from 2.4% to 51.3%, and this reduced the incidence of delirium by 58%. Future research is needed to identify strategies to improve POCUS-GRA uptake and efficacy by ED physicians, and to assess the impact of policy and quality improvement initiatives on delirium outcomes in this vulnerable population.

ACKNOWLEDGMENTS

Funding Source: This work was funded by the Canadian Institute of Health Research, Institute of Ageing.

Dr- Jacques S. Lee is supported by the Inaugural Research Chair in Geriatric Emergency Medicine at the Schwartz/Reisman Emergency Medicine Institute, Sinai Health, Toronto, Ontario, Canada.

Sponsors Role:

The funder, CIHR, had no role in preparation of this manuscript.

Contributions:

JSL is the principal author, had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. He conceived and designed the study, obtained research funding, supervised the conduct of the data collection, prepared the manuscript and is responsible for the paper overall.

MÉ, JP, MS and JC also contributed to the conception and obtaining funding for the study.

TB, RS, JC, MÉ, CT, JP, DE, MW, DE, AM, EL, CW, JN, BB, SLM, DM, and IC all substantially contributed to design, data collection, interpretation of data and manuscript drafting and revisions.

AK substantially contributed to the design, analysis, interpretation and revision of the manuscript. All authors approved the final version of the manuscript.

REFERENCES

1. Johnell O, Kanis JA. An estimate of the worldwide prevalence, mortality and disability associated with hip fracture. *Osteoporos Int*. 2004;15(11):897-902.
2. Williamson S, Landeiro F, McConnell T, et al. Costs of fragility hip fractures globally: a systematic review and meta-regression analysis. *Osteoporos Int*. 2017;28(10):2791-2800.
3. Edlund A, Lundstrom M, Lundstrom G, Hedqvist B, Gustafson Y. Clinical profile of delirium in patients treated for femoral neck fractures. *Dement Geriatr Cogn Disord*. 1999;10(5):325-329.
4. Inouye SK. Delirium in older persons. *N Engl J Med*. 2006;354(11):1157-1165.
5. McCusker J, Cole M, Dendukuri N, Han L, Belzile E. The course of delirium in older medical inpatients: a prospective study. *J Gen Intern Med*. 2003;18(9):696-704.
6. McCusker J, Cole M, Abrahamowicz M, Primeau F, Belzile E. Delirium predicts 12-month mortality. *Arch Intern Med*. 2002;162(4):457-463.
7. Duppils GS, Wikblad K. Patients' experiences of being delirious. *J Clin Nurs*. 2007;16(5):810-818.
8. Abou-Setta A, Beaupre L, Jones C, et al. *Pain Management Interventions for Elderly Patients with Hip Fracture*. Rockville (MD): Agency for Healthcare Research and Quality; May 2011.
9. Abou-Setta AM, Beaupre LA, Rashiq S, et al. Comparative Effectiveness of Pain Management Interventions for Hip Fracture: A Systematic Review. *Ann Intern Med*. 2010.
10. Monzon DG, Iserson KV, Vazquez JA. Single fascia iliaca compartment block for post-hip fracture pain relief. *J Emerg Med*. 2007;32(3):257-262.
11. Mouzopoulos G, Vasiliadis G, Lasanianos N, Nikolaras G, Morakis E, Kaminaris M. Fascia iliaca block prophylaxis for hip fracture patients at risk for delirium: a randomized placebo-controlled study. *J Orthop Traumatol*. 2009;10(3):127-133.
12. Fletcher AK, Rigby AS, Heyes FL. Three-in-one femoral nerve block as analgesia for fractured neck of femur in the emergency department: a randomized, controlled trial. *Ann Emerg Med*. 2003;41(2):227-233.
13. Akhtar S, Hwang U, Dickman E, Nelson BP, Morrison RS, Todd KH. A brief educational intervention is effective in teaching the femoral nerve block procedure to first-year emergency medicine residents. *J Emerg Med*. 2013;45(5):726-730.
14. Barrington MJ, Uda Y. Did ultrasound fulfill the promise of safety in regional anesthesia? *Current opinion in anaesthesiology*. 2018;31(5):649-655.
15. Haines L, Dickman E, Ayvazyan S, et al. Ultrasound-guided fascia iliaca compartment block for hip fractures in the emergency department. *J Emerg Med*. 2012;43(4):692-697.
16. Marhofer P, Schrogendorfer K, Wallner T, Koinig H, Mayer N, Kapral S. Ultrasonographic guidance reduces the amount of local anesthetic for 3-in-1 blocks. *Reg Anesth Pain Med*. 1998;23(6):584-588.
17. Haslam L, Lansdown A, Lee J, van der Vyver M. Survey of Current Practices: Peripheral Nerve Block Utilization by ED Physicians for Treatment of Pain in the Hip Fracture Patient Population. *Canadian geriatrics journal : CGJ*. 2013;16(1):16-21.
18. Lee J, Bhandari T, Simard R, et al. Point of Care Ultrasound-Guided Regional Anesthesia in Older ED Patients with Hip Fractures: A Study to Test the Feasibility of a Training Program and Time Needed to Complete Nerve Blocks by ED Physicians after Training. *BMJ Open*. 2021;In Press.
19. Hemming K, Taljaard M, Grimshaw J. Introducing the new CONSORT extension for stepped-wedge cluster randomised trials. *Trials*. 2019;20(1):68.
20. Hussey MA, Hughes JP. Design and analysis of stepped wedge cluster randomized trials. *Contemporary clinical trials*. 2007;28(2):182-191.
21. Lee J, Bhandari T, Simard R, et al. Point-of-care ultrasound-guided regional anaesthesia in older ED patients with hip fractures: a study to test the feasibility of a training programme and time needed to complete nerve blocks by ED physicians after training. *BMJ Open*. 2021;11(7):e047113.
22. Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegel AP, Horwitz RI. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *Ann Intern Med*. 1990;113(12):941-948.

23. Inouye S. The Short Confusion Assessment Method (Short CAM): Training Manual and Coding Guide. In: Boston: Hospital Elder Life Program.; 2014.
24. Barbic D, Kim B, Salehmohamed Q, Kemplin K, Carpenter CR, Barbic SP. Diagnostic accuracy of the Ottawa 3DY and Short Blessed Test to detect cognitive dysfunction in geriatric patients presenting to the emergency department. *BMJ Open*. 2018;8(3):e019652.
25. Katzman R, Brown T, Fuld P, Peck A, Schechter R, Schimmel H. Validation of a short orientation-memory concentration test of cognitive impairment. *American Journal of Psychiatry*. 1983;140:734-739.
26. Borson S, Scanlan J, Brush M, Vitaliano P, Dokmak A. The Mini-Cog: A cognitive 'vital signs' measure for dementia screening in multi-lingual elderly. *International journal of geriatric psychiatry*. 2000;15(11):1021-1027.
27. Sessler CN, Gosnell MS, Grap MJ, et al. The Richmond Agitation-Sedation Scale: validity and reliability in adult intensive care unit patients. *Am J Respir Crit Care Med*. 2002;166(10):1338-1344.
28. McCusker J, Cole MG, Dendukuri N, Belzile E. The delirium index, a measure of the severity of delirium: new findings on reliability, validity, and responsiveness. *J Am Geriatr Soc*. 2004;52(10):1744-1749.
29. Katzman R, Brown T, Fuld P, Peck A, Schechter R, Schimmel H. Validation of a short Orientation-Memory-Concentration Test of cognitive impairment. *Am J Psychiatry*. 1983;140(6):734-739.
30. Carpenter CR, Bassett ER, Fischer GM, Shirshekan J, Galvin JE, Morris JC. Four sensitive screening tools to detect cognitive dysfunction in geriatric emergency department patients: brief Alzheimer's Screen, Short Blessed Test, Ottawa 3DY, and the caregiver-completed AD8. *Acad Emerg Med*. 2011;18(4):374-384.
31. Katz S. Assessing self-maintenance: activities of daily living, mobility, and instrumental activities of daily living. *J Am Geriatr Soc*. 1983;31(12):721-727.
32. Inouye SK, Leo-Summers L, Zhang Y, Bogardus ST, Jr., Leslie DL, Agostini JV. A chart-based method for identification of delirium: validation compared with interviewer ratings using the confusion assessment method. *J Am Geriatr Soc*. 2005;53(2):312-318.
33. Inouye SK, Viscoli CM, Horwitz RJ, Hurst LD, Tinetti ME. A predictive model for delirium in hospitalized elderly medical patients based on admission characteristics. *Ann Intern Med*. 1993;119(6):474-481.
34. Lee JS, Hobden E, Stiell IG, Wells GA. Clinically important change in the visual analog scale after adequate pain control. *Acad Emerg Med*. 2003;10(10):1128-1130.
35. Adamis D, Martin FC, Treloar A, Macdonald AJ. Capacity, consent, and selection bias in a study of delirium. *J Med Ethics*. 2005;31(3):137-143.
36. Ritcey B, Pageau P, Woo MY, Perry JJ. Regional Nerve Blocks For Hip and Femoral Neck Fractures in the Emergency Department: A Systematic Review. *CJEM*. 2016;18(1):37-47.
37. Monzon DG, Vazquez J, Jauregui JR, Iserson KV. Pain treatment in post-traumatic hip fracture in the elderly: regional block vs. systemic non-steroidal analgesics. *Int J Emerg Med*. 2010;3(4):321-325.
38. Foss NB, Kristensen MT, Kristensen BB, Jensen PS, Kehlet H. Effect of postoperative epidural analgesia on rehabilitation and pain after hip fracture surgery: a randomized, double-blind, placebo-controlled trial. *Anesthesiology*. 2005;102(6):1197-1204.
39. Graham C, Baird K, McGuffie A. a pilot randomized control trial of 3-in-1 femoral nerve block and intravenous morphine as primary analgesia for patients presenting to the emergency department with a fractured hip. *Hong Kong J Emerg Med*. 2008;15(4):205-211.
40. Kim CH, Yang JY, Min CH, Shon HC, Kim JW, Lim EJ. The effect of regional nerve block on perioperative delirium in hip fracture surgery for the elderly: A systematic review and meta-analysis of randomized controlled trials. *Orthop Traumatol Surg Res*. 2022;108(1):103151.
41. Ontario HQ. Quality Statement 3: Multimodal Analgesia. <https://www.hqontario.ca/Evidence-to-Improve-Care/Quality-Standards/View-all-Quality-Standards/Hip-Fracture/Quality-Statement-3-Multimodal-Analgesia>. Published 2024. Accessed.
42. (ANZHFR) AaNZHFR. Australian and New Zealand Hip Fracture Registry (ANZHFR) Annual Report. 2023.
43. Lin DY, Morrison C, Brown B, et al. Pericapsular nerve group (PENG) block provides improved short-term analgesia compared with the femoral nerve block in hip fracture surgery: a single-center double-blinded randomized comparative trial. *Reg Anesth Pain Med*. 2021;46(5):398-403.

44. Kumar K, Pandey RK, Bhalla AP, et al. Comparison of conventional infrainguinal versus modified proximal suprainguinal approach of Fascia Iliaca Compartment Block for postoperative analgesia in Total Hip Arthroplasty. A prospective randomized study. *Acta Anaesthesiol Belg.* 2015;66(3):95-100.

Figure 1. CONSORT diagram.

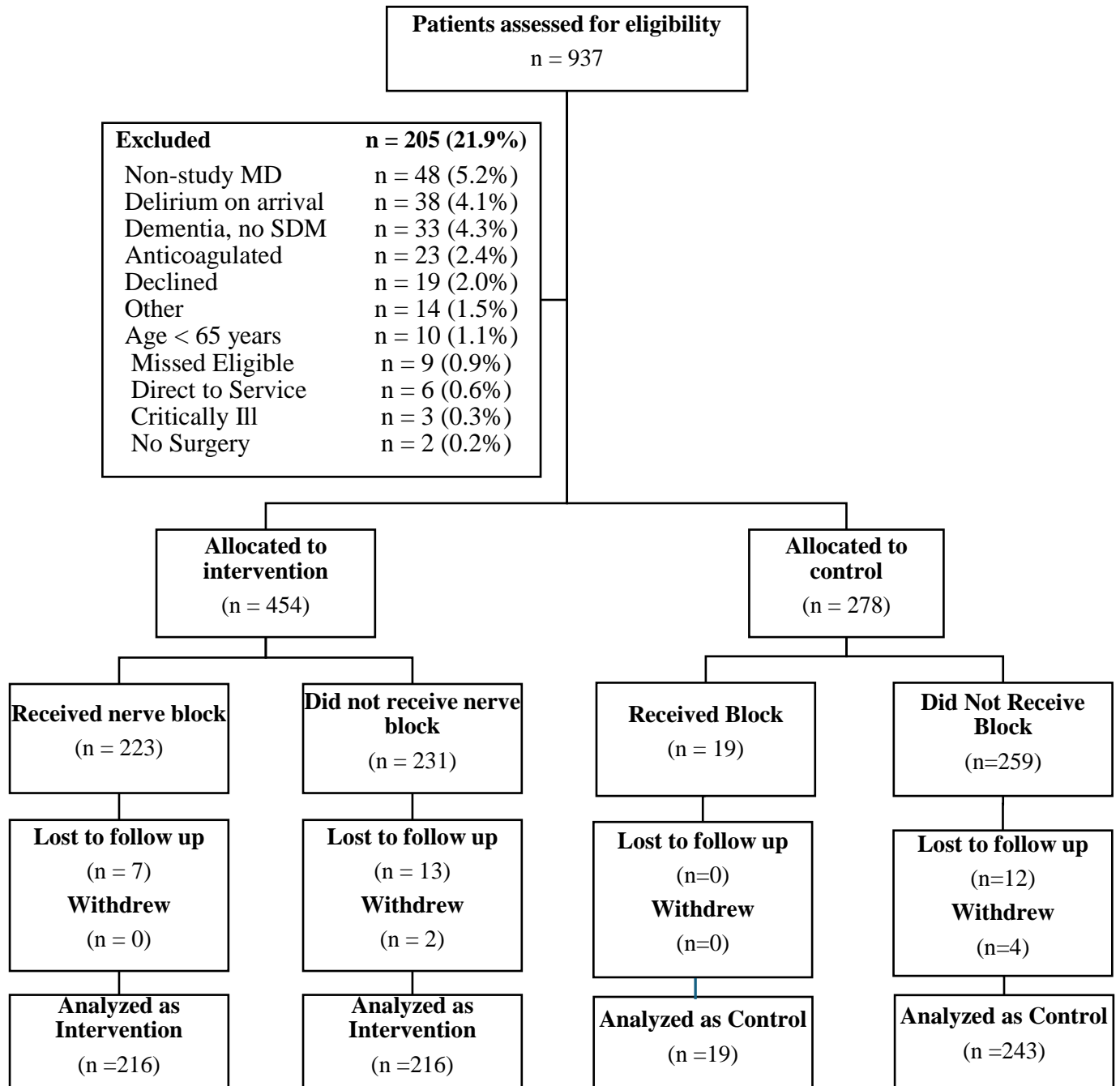


Table 1: Baseline characteristics of participants in intervention and control groups.

| | Intervention Group n=446 | Control Group n=248 | All Patients n=694 |
|--|---|-----------------------------------|-----------------------------------|
| Female, n (%) | 300 (67.3%) | 183 (73.8%) | 483 (69.6) |
| Age in Years Median (IQR)* n with data (%) | 81.0 (73.0- 88.0) 446 (100%) | 82.0 (75.0 – 88.0) 248 (100%) | 81.0 (74.0 – 88.0) 694 (100%) |
| Short Blessed Test Median, (IQR) n with data (%) | 5.0 (2.0 – 10.0) 437 (98.0) | 6.0 (2.0- 10.0) 246 (99.2%) | 6.0 (2.0 – 10.0) 683 (98.4%) |
| Pre-Block Pain Score Median (IQR) n with data (%) | 6.0 (2.0 – 10.0) 274 (61.4%) | 5.0 (3.0 – 8.0) 185 (74.6%) | 6.0 (3.0 – 8.0) 459 (66.1%) |
| Post-Block Pain Score Median (IQR) n with data (%) | 2.0 (0.0 – 4.0) 184 (41.3%) | 4.0 (2.0 – 6.0) 2 (0.8%) | 2.0 (0.0 – 4.0) 186 (26.8%) |
| Activities of Daily Living Median (IQR) n with data (%) | 14.0 (12.0 – 14.0) 443 (99.3) | 13.0 (12.0 – 14.0) 243 (98.0%) | 13.0 (12.0 – 14.0) 686 (98.8%) |
| Instrumental Activities of Daily Living Median (IQR) n with data (%) | 13.0 (10.0 – 14.0) 442 (99.1%) | 13.0 (10.0-14.0) 240 (96.8%) | 13.0 (10.0 – 14.0) 682 (98.3%) |
| Days to Surgery Median (IQR) n with data (%) | 1.0 (1.0-2.0) 446 (100%) | 1.0 (1.0-2.0) 248 (100%) | 1.0 (1.0-2.0) 694 (100%) |
| | | | |
| No Delirium Risk Factors | 154 (34.5%) | 80 (32.3%) | 234 (33.7%) |
| Dehydration (Urea/Creatinine Ratio \geq 0.1) | 115 (27.8%) | 69 (27.8%) | 184 (26.5%) |
| Cognitive Impairment (Short Blessed Test Score $>4/28$) | 233 (52.2%) | 131 (52.8%) | 364 (52.5%) |
| Iatrogenic Complication | 18 (4.0%) | 10 (4.0%) | 28 (4.0%) |
| Delirium | 116 (26.0%) | 77/228 (31.1%) | 193 (27.8%) |

*IQR = interquartile range.

Table 2: Baseline characteristics of participants by delirium.

| | No Delirium 501 | Developed Delirium 193 | All Patients N = 694 |
|---|-----------------------------------|-----------------------------------|-----------------------------------|
| Female, n (%) | 358 (71.5%) | 125 (64.8%) | 483 (69.6%) |
| Age in Years Median (IQR) n with data (%) | 80.0 (73.0-87.0) 501 (100%) | 80.0 (73.0 – 87.0) 193 (100%) | 81.0 (74.0 – 88.0) 693 (99.8%) |
| Short Blessed Test Median, (IQR) n with data (%) | 4.0 (0.0 – 8.0) 494 (98.6%) | 10.0 (6.0 – 15.0) 189 (97.9%) | 6.0 (2.0 – 10.0) 683 (98.4%) |
| Pre-Block Pain Score Median (IQR) n with data (%) | 6.0 (3.0 – 8.0) 333 (66.5%) | 5.5 (3.0 – 8.0) 126 (65.3%) | 6.0 (3.0 – 8.0) 459 (66.1%) |
| Post-Block Pain Score Median (IQR) n with data (%) | 2.0 (0.0 – 4.0) 136 (27.1%) | 2.0 (0.0 – 5.0) 50 (25.9%) | 2.0 (0.0 – 4.0) 186 (26.8%) |
| Activities of Daily Living Median (IQR) n with data (%) | 14.0 (13.0 – 14.0) 496 (99.0%) | 13.0 (11.0 – 14.0) 190 (100%) | 13.0 (12.0 – 14.0) 686 (98.8%) |
| Instrumental Activities of Daily Living, Median (IQR) n with data (%) | 13.0 (11.0-14.0) 494 (98.6%) | 11.0 (7.0 – 13.0) 188 (98.9%) | 13.0 (10.0 – 14.0) 682 (98.3%) |
| Days to Surgery Median (IQR) n with data (%) | 1.0 (1.0-2.0) 501 (100%) | 1.0 (1.0-2.0) 193 (100%) | 1.0 (1.0-2.0) 694 (100%) |
| No Delirium Risk Factors | 205 (40.9%) | 29 (15.0%) | 234 (33.7%) |
| Dehydration (Urea/Creatinine Ratio \geq 0.1) | 133 (26.6%) | 51 (26.4%) | 184 (26.5%) |
| Cognitive Impairment (Short Blessed Test Score $>4/28$) | 212 (42.3%) | 152 (78.8%) | 364 (53.5%) |
| Iatrogenic Complication | 18 (3.6%) | 10 (5.2%) | 28 (4.0%) |

Table 3: Number of physicians, patients and delirium incidence at each site.

| Site | Participating MDs | Site Patients n (% of total) | Delirium Cases n | Site Delirium Rate (%) |
|---------------|------------------------------|---|---------------------------------|---------------------------------------|
| Site 1 | 12 | 24 (3.5%) | 6 | 25.0% |
| Site 2 | 22 | 202 (29.1%) | 55 | 28.2% |
| Site 3 | 32 | 66 (9.5%) | 1 | 1.5% |
| Site 4 | 51 | 103 (14.8%) | 40 | 38.8% |
| Site 5 | 46 | 95 (13.7%) | 39 | 41.1% |
| Site 6 | 27 | 41 (5.9%) | 10 | 24.4% |
| Site 7 | 23 | 163 (23.5%) | 42 | 25.8% |
| Total | 213 | 694 | 193 | |