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Peripheral Nerve Blocks and Potentially Attributable Adverse Events in Older People with Hip Fracture: A Retrospective Population-based Cohort Study

Natalie Melton, M.D., F.R.C.P.C., Robert Talarico, M.Sc.,
Faraj Abdallah, M.D., M.Sc., Paul E. Beaulé, M.D., F.R.C.S.C.,
Sylvain Boet, M.D., Ph.D., Alan J. Forster, M.D., M.Sc., F.R.C.P.C.,
Shannon M. Fernando, M.D., M.Sc., F.R.C.P.C.,
Allen Huang, M.D.C.M., F.R.C.P.C.,
Colin J. L. McCartney, M.B.Ch.B., Ph.D., F.R.C.A., F.C.A.R.C.S.I.,
F.R.C.P.C., Bradley Meulenkamp, M.D., F.R.C.S.C.,
Jeff Perry, M.D., M.Sc., C.C.F.P.-E.M.,
Barbara Power, M.D., F.R.C.P.C., Reva Ramlogan, M.D., F.R.C.P.,
Monica Taljaard, Ph.D., Peter Tanuseputro, M.D., M.H.Sc.,
F.R.C.P.C., Carl van Walraven, M.D., F.R.C.P.C.,
Duminda N. Wijeysundera, M.D., Ph.D., F.R.C.P.C.,
Daniel I. McIsaac, M.D., M.P.H., F.R.C.P.C.

EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Systematic reviews demonstrate that peripheral nerve blocks for hip fracture patients reduce pain and opioid consumption
- Although administrative data suggest that peripheral nerve blocks in this population may be associated with reduced length of stay and costs, the safety profile remains unknown

What This Article Tells Us That Is New

- Among 91,563 surgical and nonsurgical hip fracture patients in Ontario between 2009 and 2017, 17.1% (15,631) received a peripheral nerve block
- Administrative data demonstrate that 5.8% (5,321 of 91,563) of hip fracture patients experienced a nerve block–attributable adverse event (seizures, fall-related injuries, cardiac arrest, or nerve injury)
- Receipt of a nerve block was not associated with a higher rate of these adverse events (5.5% among patients receiving a block *vs.* 5.9% of patients without a block)

ABSTRACT

Background: Peripheral nerve blocks are being used with increasing frequency for management of hip fracture–related pain. Despite converging evidence that nerve blocks may be beneficial, safety data are lacking. This study hypothesized that peripheral nerve block receipt would not be associated with adverse events potentially attributable to nerve blocks, as well as overall patient safety incidents while in hospital.

Methods: This was a preregistered, retrospective population-based cohort study using linked administrative data. This study identified all hip fracture admissions in people 50 yr of age or older and identified all nerve blocks (although we were unable to ascertain the specific anatomic location or type of block), potentially attributable adverse events (composite of seizures, fall-related injuries, cardiac arrest, nerve injury), and any patient safety events using validated codes. The study also estimated the unadjusted and adjusted association of nerve blocks with adverse events; adjusted absolute risk differences were also calculated.

Results: In total, 91,563 hip fracture patients from 2009 to 2017 were identified; 15,631 (17.1%) received a nerve block, and 5,321 (5.8%; 95% CI, 5.7 to 6.0%) patients experienced a potentially nerve block–attributable adverse event: 866 (5.5%) in patients with a block and 4,455 (5.9%) without a block. Before and after adjustment, nerve blocks were not associated with potentially attributable adverse events (adjusted odds ratio, 1.05; 95% CI, 0.97 to 1.15; and adjusted risk difference, 0.3%, 95% CI, −0.1 to 0.8).

Conclusions: The data suggest that nerve blocks in hip fracture patients are not associated with higher rates of potentially nerve block–attributable adverse events, although these findings may be influenced by limitations in routinely collected administrative data.

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Globally, 18% of women and 6% of men will experience at least one hip fracture during their lifetime.[1,2] Hip fractures are also the most common indication for emergency surgery in older people.[3] Although age–adjusted rates of hip fractures have decreased over time, ongoing population aging means that the absolute number of hip fractures will continue to increase.[2]

Post–hip fracture medical and surgical complications are common, with more than 20% of hip fracture patients experiencing a serious in–hospital complication.[4,5] These early adverse events subsequently contribute to poor long-term outcomes. Approximately 25% of older people die in the year after their fracture, and survivors develop new disability at a rate of 32 to 80%.[4,5] Efforts are required to identify safe and effective treatments to improve care for hip fracture patients.

Multiple factors influence outcomes after hip fracture, including acute and chronic patient-level conditions, as well as perioperative processes of care. Anesthetic and analgesic care may have a substantial impact on hip fracture outcomes. While choice of primary anesthesia type may influence early recovery by decreasing venous

thromboembolic events, pulmonary complications, and length of stay, analgesic choices have stronger evidence of impacting outcomes.[6–8] Specifically, systematic reviews pooling moderate-to-high-quality evidence suggest that peripheral nerve blocks reduce pain and opioid consumption, improve mobility, and decrease pulmonary complications.[6] Population-based studies suggest that nerve blocks may reduce costs and length of hospital stay.[9] However, nerve blocks do have associated risks, especially in hip fracture patients who have many risk factors for nerve injury and systemic local anesthetic toxicity (which can lead to seizures and/or cardiac arrest).[10,11] In fact, case reports of nerve block–attributable deaths have been published.[12] Currently, the safety data from randomized trials are insufficient,[13] an issue that is further exacerbated by a lack of representativeness in randomized trial participants compared to the general population of hip fracture patients.

Population-based health administrative data can be a useful means to evaluate the safety of interventions that appear efficacious in randomized trials but may result in excess adverse outcomes when generalized.[14] Therefore, we undertook a retrospective population-based cohort study to compare the relative incidence of potentially nerve block–attributable adverse safety events (seizures, cardiac arrests, fall-related injuries, and nerve injury) and overall patient safety incidents between hip fracture patients who did or did not receive a nerve block. We hypothesized that hip fracture patients who received a nerve block, including those treated surgically and nonoperatively, would not be at greater risk of potentially nerve block attributable adverse events.

Materials and Methods

Design and Data Source

This was a population-based cohort study using linked health administrative data from the Canadian province of Ontario (population 14 million). Ontario residents are provided universal health insurance for hospital and physician services, which generates data that are collected using standardized formats and procedures by trained abstractors.[15,16] These data are housed at ICES (formerly known as Institute for Clinical Evaluative Sciences [Toronto, Ontario, Canada]), an independent research institute, where the episode of care can be recreated through deterministic linkage across data sets using an anonymized unique identifier. For this study, we created our analytic data set from the Discharge Abstract Database (information (including diagnoses and procedures) for all hospitalizations; the Registered Persons Database, which captures all deaths (including date) and sociodemographic information; the National Ambulatory Care Reporting System, which records all emergency department visits; the Ontario Health Insurance Claims Database, which records fee-for-service physician claims; the Ontario Drug Database, which records outpatient prescription drug receipt for residents over 65 yr of age; the Narcotics Monitoring System, which records receipt of all prescription opioids; the Ontario Laboratory Information System, which captures laboratory data from some regions of Ontario; and the Continuing Care Reporting System, which captures clinical and demographic information on residents receiving facility-based continuing care. Because these data are anonymized and routinely collected, the study was legally exempt from research ethics review. A protocol was registered at the Open Science Framework (osf.io/z2r95/ [last updated June 5, 2020; accessed May 31, 2021]) before analysis. Reporting followed relevant guidelines.[17,18]

Cohort

We identified all Ontarians 50 yr of age or older who presented to the hospital (2009 to 2017) with a hip fracture, using International Classification of Disease, Tenth Edition (ICD-10) code S72 (97% sensitive, 99% specific for hip fracture).[19] We created a patient-level cohort that included only the first hip fracture for any individual.

Exposure

We identified in-hospital nerve blocks using validated physician billing codes applied to ICES data (appendix; positive likelihood ratio, 16.8; negative likelihood ratio, 0.03).[20] Because some emergency physicians are not on a direct fee-for-service contract (which may limit their billing accuracy), we also identified nerve blocks provided in the emergency department from the National Ambulatory Care Reporting System record (Supplemental Digital Content table 1, http://links.lww.com/ALN/C641); reabstraction studies of emergency department procedure codes demonstrate 97.7% agreement.[21] Although this approach allowed us to identify that a block was provided, codes do not differentiate between anatomic locations or approaches (*i.e.*, plexus *vs.* fascial plane or landmark *vs.* ultrasound–guided).

Our main exposure was receipt of any nerve block *versus* no nerve block, but we also identified a count of total blocks provided during the index hospitalization for each participant (if a participant had a block identified from both billing codes and the emergency department record on the same day, we attributed that block to the emergency department to avoid double counting).

Confounders

Additional variables were collected to account for possible confounding. These included year of admission and preadmission factors (age, sex, long-term care residence, rural *versus* urban residence, neighborhood income quintile, resource utilization band (a measure of predicted future healthcare resource use based on previous health services utilization[22]), previous acute hospitalizations and emergency department visits (within the year before fracture), validated 1-yr mortality risk score,[23] frailty status,[24] and Elixhauser comorbidities (based on a 3-yr lookback period)[25]). Surgical *versus* nonsurgical management was captured using validated procedure codes (Supplemental Digital Content table 2, http://links.lww.com/ALN/C641; agreement $\kappa = 0.95$; positive predictive value, 0.95).[19] For surgical patients, we captured the American Society of Anesthesiologists' status and the specific type of surgery performed. The year of surgery and the index hospital identifier were also collected. We also collected data that were available only for a subset of patients (*i.e.*, filling a preoperative opioid prescription for people having surgery in 2012 or later (from the Narcotics Monitoring System in the 90 days before admission) or filling an anticoagulant, antiplatelet, antipsychotic, opioid benzodiazepine, or dementia medication prescription for those over 65 (from the Ontario Drug Database), and preoperative serum creatinine, hemoglobin, sodium, and potassium (as not all health regions in Ontario consistently report lab data to ICES). All confounders were prespecified based on clinical and epidemiologic knowledge of factors that may influence receipt of a nerve block and occurrence of an attributable safety outcome, acknowledging that not all confounders have proven associations with both our exposure and outcomes. Therefore, we erred on the side of adjusting for any factor that we postulated could be a direct confounder or an important proxy for an unmeasured confounder.

Outcome

Our primary outcome was a composite of potentially nerve block–attributable safety events, using validated administrative codes identifying the occurrence of any cardiac arrest (ICD-10 type 2 codes I47.2, I49.0, I46.0, I46.1, I46.9, or flag for heart resuscitation [positive predictive value, 88%]),[26] seizure (ICD-10 type 2 codes G40.6, G40.5, G40.8, G40.9, or G41.X [positive predictive value, 94%]),[27] fall-related injury (ICD-10 type 2 codes starting with T0, T1, T8, T9 or

T79, S12, S22, S32, S42, S52, S62, S72, S82, S92, T02, T08, T10, or T12 [sensitivity, 96%; specificity, 91%]),[28] or possible nerve injury (physician billing codes G455/G456 or G466/G457 for nerve conduction study; 88 to 95% agreement)[29] (Supplemental Digital Content table 3, http://links.lww.com/ALN/C641). The composite was used as a primary approach due to the low expected incidence of each component. We also collected each individual component of the composite outcome to assess whether each was associated with exposure in a directionally congruent manner. Because there is no widely accepted definition of nerve block–related adverse events, we also studied a secondary outcome defined as any in-hospital safety incident. This outcome was based on a validated set of ICD-10 patient safety indicators (hospital acquired infections, decubitus ulcers, endocrine or metabolic complications, venous thromboembolism, cardiac complications, respiratory complications, hemorrhagic events, drug-related adverse events, adverse events related to fluid management, complications directly related to surgery, traumatic injuries arising in the hospital, anesthesia-related complications, delirium, central nervous system complications, gastrointestinal complications, severe events threatening to life; Supplemental Digital Content table 4, http://links.lww.com/ALN/C641) developed by a team of experts in patient safety and health data to identify adverse outcomes potentially related to in-hospital patient safety.[30,31]

Anticipated Sample Size and Missing Data

We estimated that we would identify approximately 10,000 hip fractures per year; however, estimating the expected number of nerve block–attributable adverse safety outcome was difficult. Assuming cardiac arrest would be the most common component of the composite (~0.5% of admissions), we estimated that we would have at least 450 outcomes, which conservatively supports 45 degrees of freedom for modeling. Our prespecified approach to missing data was to use multiple imputation if greater than 1% of participants had missing covariate data or complete case analysis if less than 1% had missing covariate data. All analyses were conducted using a two-sided significance threshold of $P < 0.05$; sensitivity analyses were exploratory, and we did not prespecify multiplicity adjustment.

Analysis

All analyses employed SAS, version 9.4 for Windows (SAS Institute, USA). Descriptive statistics (proportions for categorical variables, means, and SDs for normally distributed continuous variables, and median and interquartile ranges for skewed continuous variables [with distributions visually inspected for normality]) were compared between exposure levels using absolute standardized differences.

To address our first objective, we estimated the incidence proportion (per person) of the primary outcome and each of its components, generating 95% CI using Wilson's

method. We then estimated the unadjusted and adjusted association of nerve block receipt with the primary outcome using logistic regression. Adjusted models accounted for each hospital as a random intercept along with prespecified covariates (see parameterizations Supplemental Digital Content table 5, http://links.lww.com/ALN/C641). The adjusted model was also used to estimate the absolute risk difference and 95% CI *via* bootstrap resampling across replicates generated with replacement; 1,000 replicates were planned, but computational limitations required decreasing the number of replicates to 400.[32] The secondary outcome was analyzed as described for the primary.

Sensitivity Analyses

To test the robustness of our primary outcome, we ran our primary outcome analysis again with the following alterations: (1) additionally adjusting for filling a preoperative opioid prescription (limited to the subgroup admitted in 2012 or later); (2) additionally adjusting for filling a potentially confounding drug prescription in the subgroup of patients over 65 (anticoagulants, antiplatelet agents, antipsychotics, benzodiazepines, opioids, and dementia medications); (3) adjusting for laboratory values in the subgroup with available data (as three-knot restricted cubic splines, serum creatinine, hemoglobin, sodium, and potassium); (4) changing the exposure from a binary variable to a three-level categorical (no nerve block, single nerve block [emergency department record only], and single nerve block [non–emergency department record only]); and (5) changing the exposure from a binary variable to a three-level categorical (0, 1, and 2 or more) variable representing the total count of blocks received.

Results

We identified 91,563 hip fracture patients from 2009 to 2017; 15,631 (17.1%) received a nerve block. Age, sex, and frailty status were similar between exposure levels, while nerve blocks were more common in patients who had surgery and use increased over the study period (table 1). Only 171 nerve blocks (1.1%) were documented in the emergency department record only; 544 (3.5% with any block) received two nerve blocks, and 19 (0.1%) received three or four during the index admission. No exposure or outcome data were missing; 400 (0.4%) participants had any missing covariate data; therefore, complete case analysis was used.

Potentially Nerve Block–Attributable Safety Events

The potentially nerve block–attributable safety event composite occurred in 5,321 of the 91,563 included patients (5.8%; 95% CI, 5.7 to 6.0). In patients with a block, 866 of 15,631 (5.5%) had a potentially nerve block–attributable safety event compared to 4,455 of 75,932 (5.9%) without a block. Table 2 provides a breakdown by nerve block receipt

status, as well as by each component of the composite. Fall-related injuries were the most common component, whereas seizures were rare.

On an unadjusted basis, there was no association between potentially nerve block–attributable safety events and nerve block receipt (odds ratio, 0.94; 95% CI, 0.87 to 1.01; $P = 0.112$). After multilevel, multivariable adjustment, there remained no evidence of association (odds ratio = 1.05; 95% CI, 0.97 to 1.15); the adjusted model predicted observed outcome rates close to the line of ideal calibration across the risk spectrum (Supplemental Digital Content table 5, http://links.lww.com/ALN/C641) and had a c-statistic of 0.71. The adjusted absolute risk difference was 0.3% (95% CI, –0.1 to 0.8)

Sensitivity Analyses

A full summary of results of sensitivity analyses is provided in figure 1. Receipt of multiple nerve blocks was associated with an increase in the odds of potentially nerve block–attributable safety events; nerve blocks documented in the emergency department record were also associated with increased rates of adverse outcomes. Additional adjustment for prefracture filling of opioid prescriptions, filling prescriptions for potentially confounding other medications, and laboratory values did not change the direction, size, or significance of the primary finding substantively. All models specified for sensitivity analyses had c-statistics of 0.71.

Secondary Outcomes

The incidence of any patient safety indicator event was 19,394 (25.5%) for patients without a nerve block and 3,670 (23.5%) for those with a nerve block (unadjusted odds ratio, 0.89; 95% CI, 0.86 to 0.93). After multilevel, multivariable adjustment, receipt of a nerve block was not associated with occurrence of any patient safety indicator events in hospital (odds ratio, 0.99; 95% CI, 0.94 to 1.03; $P = 0.557$).

Discussion

In this retrospective, population-based study, we found no evidence that receipt of a nerve block was associated with increased odds of potentially nerve block–attributable adverse events in hip fracture patients. We also found no association between receipt of a nerve block and any occurrence of patient safety incidents. However, future study is required to evaluate provision of nerve blocks in non–operating room locations and where multiple nerve blocks are provided during the same admission.

Moderate to severe pain is common after hip fracture.[33] However, achieving safe and effective pain relief is well described as a substantial challenge because of the vulnerable nature of hip fracture patients. These sources of vulnerability place hip fracture patients at risk of adverse events due to undertreated pain and the systemic effects of analgesics.[2,34,35] To date, systematic review of randomized trials and

Table 1. Cohort Characteristics by Nerve Block Status

	No Nerve Block (n = 75,932)*	Nerve Block (n = 15,631)*	Absolute Standardized Difference
Age	81 (SD 10)	81 (SD 10)	0.00
Female	69.8	70.3	0.01
Neighborhood income quintile			
Lowest quintile	23.6	24.6	0.02
2	20.9	23.0	0.05
3	19.3	18.4	0.02
4	18.1	17.2	0.02
Highest quintile	17.7	16.3	0.04
Rural residence	13.9	10.6	0.10
Frailty Index score	0.24 (SD 0.08)	0.23 (SD 0.08)	0.01
Resource utilization band			
Lowest two quintiles	1.5	1.6	0.01
3	13.3	13.5	0.01
4	24.3	25.3	0.02
Highest quintile	60.9	59.6	0.03
Preadmission nursing home	17.0	15.9	0.03
ASA score			
I to II	7.7	5.0	0.11
III	38.5	38.5	0.00
IV or V	42.0	49.2	0.14
No surgery	11.7	7.3	0.15
Acute hospitalization of less than 1 yr	25.0	24.0	0.02
Number of emergency department visits in less than 1 yr			
None	39.3	41.9	0.05
One	28.1	27.9	0.00
Two or more	32.6	30.2	0.05
Diabetes with complications	14.1	14.4	0.01
Diabetes without complications	13.2	13.5	0.01
Heart failure	11.7	10.7	0.03
Hypertension without complications	40.1	39.0	0.02
Hypertension with complications	1.2	1.0	0.02
Chronic pulmonary disease	11.8	10.8	0.03
Dementia	11.6	11.5	0.00
Cerebrovascular disease	5.4	4.7	0.03
Chronic renal disease	4.2	4.0	0.01
Dialysis	1.4	1.4	0.00
Primary cancer	7.4	7.0	0.02
Metastatic cancer	2.0	1.7	0.02
Peripheral vascular disease	2.5	2.3	0.01
Liver disease	1.3	1.0	0.03
Peptic ulcer disease	1.5	1.4	0.01
Rheumatic disease	1.0	0.7	0.03
Hemiplegia or hemiparesis	0.9	0.7	0.02
Atrial fibrillation or flutter	8.9	8.0	0.03
Venous thromboembolism	0.7	0.6	0.01
Cardiac valve disease	3.3	3.3	0.00
Disease of the pulmonary circulation	2.3	2.1	0.01
Coagulopathy	2.7	2.3	0.03
Obesity	1.0	0.8	0.02
Weight loss	3.4	3.0	0.02
Blood loss anemia	17.9	16.6	0.03
Deficiency anemia	0.6	0.6	0.00
Alcohol abuse	3.2	2.6	0.04
Drug abuse	0.6	0.5	0.01
Psychoses	0.9	0.9	0.00
Depression	4.4	3.9	0.03
Year of admission			
2009	10.9	7.4	
2010	11.1	9.0	0.07
2011	11.1	8.9	0.07
2012	11.4	9.7	0.06
2013	11.8	10.7	0.03
2014	11.6	10.2	0.04
2015	10.6	13.4	0.09
2016	11.0	14.0	0.09
2017	10.5	16.8	0.18

*Column values represent percentages with each characteristic, unless otherwise specified.

ASA, American Society of Anesthesiologists.

**Table 2.** Incidence of Potentially Attributable Adverse Events

	No Nerve Block (n = 75,932)		Nerve Block (n = 15,631)	
	n	%*	n	%*
Composite†	4,455	5.9 (5.7–6.0)	866	5.5 (5.2–5.9)
Cardiac arrest	778	1.0 (1.0–1.1)	137	0.9 (0.7–1.0)
Fall-related injury	3,414	4.5 (4.4–4.7)	682	4.4 (4.1–4.7)
Seizure	22	0.03 (0.02–0.04)	‡	0.02 (0.01–0.06)
Nerve injury	420	0.6 (0.5–0.6)	73	0.5 (0.4–0.6)

*95% CI provided in parentheses and calculated using Wilson's method. †Composite represents the incidence of any of cardiac arrest, fall-related injury, seizure, or nerve injury. ‡Not reportable because of cell size less than 6.

population-based studies both suggest benefits from nerve blocks for hip fracture patients, including improved pain control and mobility and reduced complications, length of stay, and healthcare costs.[9,13] However, randomized trials, primarily designed for questions of efficacy, do not typically address safety concerns in an adequate manner.[36] Whereas the review of Guay *et al.*[6] did not identify safety issues, the majority of data available related only to changes in vital signs in immediate proximity to block placement. Furthermore, trial populations and processes may not reflect routine practice. In the setting of hip fractures, the largest trials included in systematic reviews had younger populations with more males and less renal dysfunction and had much closer monitoring practices than the general population, which was further reflected in highly selective inclusion criteria

leading to low proportions (13%) of screened patients being enrolled.[6,9,37] Therefore, as utilization of nerve blocks in hip fracture care increases,[38,39] the safety of vulnerable older patients must be carefully considered.

In the current study using routinely collected data, we found that most safety events potentially attributable to nerve blocks were rare overall and unlikely to be associated with nerve blocks, especially as 95% CIs included the null value and did not include even a moderate effect size.[40,41] In-hospital cardiac arrests, seizures, and investigations related to possible nerve injury each had well under 1% incidence. However, injuries related to falls were present in 5% of records, further highlighting the risk of falls in older patients[42] and the need to decrease in-hospital falls through improvements in systems of care. Furthermore, more than
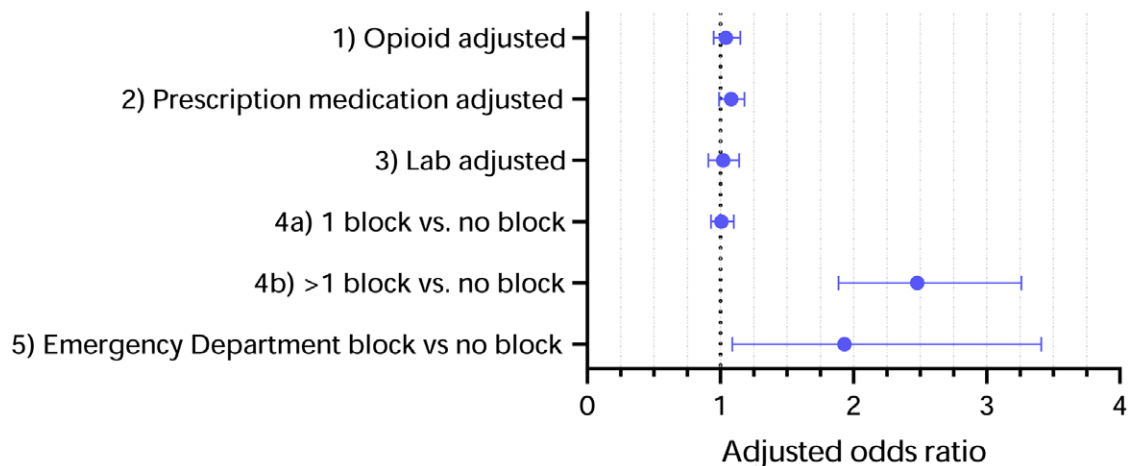
Fig. 1. Forest plot of adjusted odds ratios from sensitivity analyses examining association between nerve blocks and the composite of fall-related injuries, seizures, cardiac arrest. or nerve injury: (1) adjusted for filling a preoperative opioid prescription (n = 48,391 without a block *vs.* n = 11,269 with a block); (2) adjusted for filling a prescription (anticoagulants, antiplatelet agents, antipsychotics, benzodiazepines, opioids, or dementia medications) in people more than 65 yr old (n = 68,243 without a block *vs.* 14,257 with a block); (3) adjusted for lab values (creatinine, hemoglobin, sodium, or potassium; n = 75,932 without a block *vs.* 15,631 with a block); (4a) one block received during the hospitalization *versus* none (n = 75,932 without a block *vs.* n = 15,068 with one block); (4b) more than one block received during the hospitalization *versus* none (n = 75,932 without a block *vs.* n = 563 with more than one block); and (5) nerve block in the emergency department *versus* no block (n = 75,932 without a block *vs.* n = 171 with a block in the emergency department).

25% of patients experienced at least one patient safety incident overall based on a validated definition derived from diagnostic codes identified by patient safety experts to be attributable to quality of care.[30,31] This further highlights the vulnerability of hip fracture patients and the need to improve the quality of care and resultant outcomes that they experience. Finally, although exploratory, our data did identify associations between nerve blocks and attributable adverse events in certain circumstances. Specifically, people receiving multiple nerve blocks during their admission had a 2.5-fold increase in their odds of a potentially attributable safety event, whereas blocks that were documented only in the emergency department were associated with a 1.9-fold increase. These results must be cautiously interpreted because we found only 171 blocks documented in the emergency department and 563 patients who received more than one block. Such individuals may have unmeasured characteristics could lead to residual confounding and potentially biased results. The results of our sensitivity analyses serve primarily as a call for future research as underlying mechanisms are biologically plausible but underrepresented in these secondary analyses. For example, a patient may be at greater risk of local anesthetic exposure or nerve issues with multiple blocks,[10,11] and there is the possibility of less monitoring in a non–operating room setting.[12]

Strengths and Limitations

This study, and these findings, should be appraised in consideration of their strengths and limitations. First, our study used routinely collected health administrative data, which were not initially collected for research purposes. Although the population-based nature of these data supports the generalizability of our findings and directly aligns with our study's objectives, certain biases could be present. Although our exposures and outcomes have been previously validated, differing billing and documentation practices in Ontario emergency departments could have led to misclassification of nerve block procedures provided in this setting. Additionally, nerve block billing codes have specifically been validated in shoulder surgery; although we have no reason to believe accuracy would differ substantively in hip fracture and overall physician billing codes in Ontario have been found to be highly accurate,[43] misclassification was possible. Although limiting our cohort to people 50 yr or older increases the likelihood of isolated fragility fractures, it is possible that some blocks were placed for analgesia related to other fracture locations in the case of multiple sites of injury. Specifically, we were unable to ascertain the specific anatomic location of each block, whether it was a plexus or fascial plane technique, or whether ultrasound was used to guide nerve block placement. Furthermore, our potentially nerve block–attributable adverse events definitions relied on administrative data codes, which typically capture only events substantial enough to be documented in the medical record and do not provide a specific date of occurrence,

only that the event arose after admission. This means that temporal misclassification is possible (i.e., an event could have occurred before a block was placed), which would bias our findings away from the null. Less severe events may have been missed but could still be relevant to decision making and care planning. Our outcome was a composite that had a single event (fall-related injuries) that was of much higher incidence than the other components. However, analysis of each component of the composite separately did not suggest a differential effect. Any observational study is also at risk of confounding and indication bias. We used a robust set of prespecified covariates along with multilevel modeling to adjust for measurable confounders and completed a variety of sensitivity analyses to test the role of different high-priority confounders; the results of these analyses were consistent and support the robustness of our findings. Finally, we cannot assess the degree to which our findings would generalize to health systems that are substantially different than Ontario's.

Conclusions

In older adults admitted to the hospital with hip fracture, we found no evidence to suggest that provision of peripheral nerve blocks is associated with increased risk of potentially attributable adverse events.

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Competing Interests

The authors declare no competing interests.

Correspondence

Address correspondence to Dr. McIsaac: Department of Anesthesiology, Ottawa Hospital, University of Ottawa, 1053 Carling Avenue, Room B311, Ottawa, Ontario K1Y

4E9, Canada. dmcisaac@toh.on.ca. This article may be accessed for personal use at no charge through the Journal Web site, www.anesthesiology.org.

References

1. Number, percentage and average acute length of stay for top 10 high-volume inpatient surgeries by province/territory, HMDB, 2015–2016. Ottawa, Canada, 2017. Available at: https://www.cihi.ca/en/quick-stats. Accessed November 2, 2020.

2. Brauer CA, Coca-Perraillon M, Cutler DM, Rosen AB: Incidence and mortality of hip fractures in the United States. JAMA 2009; 302:1573–9

3. Canadian Institute for Health Information: Number of surgical discharges. Available at: https://www.cihi.ca/en/access-data-and-reports. Accessed May 31, 2021.

4. Hannan EL, Magaziner J, Wang JJ, Eastwood EA, Silberzweig SB, Gilbert M, Morrison RS, McLaughlin MA, Orosz GM, Siu AL: Mortality and locomotion 6 months after hospitalization for hip fracture: Risk factors and risk-adjusted hospital outcomes. JAMA 2001; 285:2736–42

5. Eastwood EA, Magaziner J, Wang J, Silberzweig SB, Hannan EL, Strauss E, Siu AL: Patients with hip fracture: Subgroups and their outcomes. J Am Geriatr Soc 2002; 50:1240–9

6. Guay J, Parker MJ, Griffiths R, Kopp S: Peripheral nerve blocks for hip fractures. Cochrane Database Syst Rev 2017; 5:CD001159

7. Guay J, Parker MJ, Gajendragadkar PR, Kopp S: Anaesthesia for hip fracture surgery in adults, Cochrane Database of Systematic Reviews. Edited by Guay J. Chichester, United Kingdom, John Wiley & Sons, Ltd., 2016

8. Malhas L, Perlas A, Tierney S, Chan VWS, Beattie S: The effect of anesthetic technique on mortality and major morbidity after hip fracture surgery: A retrospective, propensity-score matched-pairs cohort study. Reg Anesth Pain Med 2019; 44:847–53

9. Hamilton GM, Lalu MM, Ramlogan R, Bryson GL, Abdallah FW, McCartney CJL, McIsaac DI: A population-based comparative effectiveness study of peripheral nerve blocks for hip fracture surgery. Anesthesiology 2019; 131:1025–35

10. El-Boghdadly K, Pawa A, Chin KJ: Local anesthetic systemic toxicity: Current perspectives. Local Reg Anesth 2018; 11:35–44

11. Sondekoppam RV, Tsui BC: Factors associated with risk of neurologic complications after peripheral nerve blocks: A systematic review. Anesth Analg 2017; 124:645–60

12. Death after Fascia Iliaca Block (FIB). London, UK, Royal College of Emergency Medicine, 2018. Available at: https://www.rcem.ac.uk/docs/Safety Resources + Guidance/Feb FIB Alert.pdf. Accessed May 31, 2021.

13. Guay J, Parker MJ, Griffiths R, Kopp S: Peripheral nerve blocks for hip fractures. Cochrane Database Syst Rev 2017; 5:CD001159

14. Juurlink DN, Mamdani MM, Lee DS, Kopp A, Austin PC, Laupacis A, Redelmeier DA: Rates of hyperkalemia after publication of the Randomized Aldactone Evaluation Study. N Engl J Med 2004; 351:543–51

15. About ICES, ICES website. Available at: https://www.ices.on.ca/About-ICES. Accessed May 31, 2021.

16. Vision and Mandate, Canadian Institute for Health Information website. Available at: https://www.cihi.ca/en/about-cihi/vision-and-mandate. Accessed November 2, 2020.

17. Elm E von, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP: Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. BMJ 2007; 335:806–8

18. Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM; RECORD Working Committee: The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement. PLoS Med 2015; 12:e1001885

19. Juurlink DN, Croxford R, Chong A, Austin P, Tu J, Laupacis A: Canadian Institute for Health Information Discharge Abstract Database: A validation study – ICES Investigative Report June 2006. Ottawa, Canada, Canadian Institute for Health Information, 2006

20. Hamilton GM, Ramlogan R, Lui A, McCartney CJL, Abdallah F, McVicar J, McIsaac DI: Peripheral nerve blocks for ambulatory shoulder surgery: A population-based cohort study of outcomes and resource utilization. Anesthesiology 2019; 131:1254–63

21. CIHI Data Quality Study of Ontario Emergency Department Visits for Fiscal Year 2004–2005: Executive Summary. Ottawa, Canada, Canadian Institute for Health Information, 2007. Available at: https://secure.cihi.ca/free_products/vol1_nacrs_executive_summary_nov2_2007.pdf. Accessed November 2, 2020.

22. The Johns Hopkins ACG System. Available at: https://www.hopkinsacg.org/applications/#impact. Accessed May 16, 2021.

23. Walraven C van, McAlister FA, Bakal JA, Hawken S, Donzé J: External validation of the Hospital-patient One-year Mortality Risk (HOMR) model for predicting death within 1 year after hospital admission. CMAJ 2015; 187:725–33

24. McIsaac DI, Wong CA, Huang A, Moloo H, van Walraven C: Derivation and validation of a generalizable preoperative frailty index using population-based health administrative data. Ann Surg 2019; 270:102–8

25. Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi JC, Saunders LD, Beck CA, Feasby TE, Ghali WA: Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care 2005; 43:1130–9

26. Bruin ML De, Hemel NM van, Leufkens HGM, Hoes AW: Hospital discharge diagnoses of ventricular arrhythmias and cardiac arrest were useful for epidemiologic research. J Clin Epidemiol 2005; 58:1325–9

27. Kee VR, Gilchrist B, Granner MA, Sarrazin NR, Carnahan RM: A systematic review of validated methods for identifying seizures, convulsions, or epilepsy using administrative and claims data. Pharmacoepidemiol Drug Saf 2012; 21 Suppl 1:183–93

28. Brand CA, Sundararajan V: A 10-year cohort study of the burden and risk of in-hospital falls and fractures using routinely collected hospital data. Qual Saf Health Care 2010; 19:e51

29. Williams J, Young W: Appendix: A summary of studies on the quality of health care administrative databases in Canada. 1996. Available at: https://www.ices.on.ca/Publications/Atlases-and-Reports/1996/Patterns-of-health-care-2nd-ed. Accessed May 31, 2021.

30. Southern DA, Burnand B, Droesler SE, Flemons W, Forster AJ, Gurevich Y, Harrison J, Quan H, Pincus HA, Romano PS, Sundararajan V, Kostanjsek N, Ghali WA: Deriving ICD-10 codes for patient safety indicators for large-scale surveillance using administrative hospital data. Med Care 2017; 55:252–60

31. McIsaac DI, Hamilton GM, Abdulla K, Lavallée LT, Moloo H, Pysyk C, Tufts J, Ghali WA, Forster AJ: Validation of new ICD-10-based patient safety indicators for identification of in-hospital complications in surgical patients: A study of diagnostic accuracy. BMJ Qual Saf 2020; 29:209–16

32. Austin PC, Laupacis A: A tutorial on methods to estimating clinically and policy-meaningful measures of treatment effects in prospective observational studies: A review. Int J Biostat 2011; 7:6

33. Morrison SR, Magaziner J, McLaughlin MA, Orosz G, Silberzweig SB, Koval KJ, Siu AL: The impact of post-operative pain on outcomes following hip fracture. Pain 2003; 103:303–11

34. Morrison RS, Magaziner J, Gilbert M, Koval KJ, McLaughlin MA, Orosz G, Strauss E, Siu 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

35. Mangoni AA, Jackson SH: Age-related changes in pharmacokinetics and pharmacodynamics: Basic principles and practical applications. Br J Clin Pharmacol 2004; 57:6–14

36. Ioannidis JP, Lau J: Completeness of safety reporting in randomized trials: An evaluation of 7 medical areas. JAMA 2001; 285:437–43

37. Morrison RS, Dickman E, Hwang U, Akhtar S, Ferguson T, Huang J, Jeng CL, Nelson BP, Rosenblatt MA, Silverstein JH, Strayer RJ, Torrillo TM, Todd KH: Regional nerve blocks improve pain and functional outcomes in hip fracture: A randomized controlled trial. J Am Geriatr Soc 2016; 64:2433–9

38. Neuman MD, Rosenbaum PR, Ludwig JM, Zubizarreta JR, Silber JH: Anesthesia technique, mortality, and length of stay after hip fracture surgery. JAMA 2014; 311:2508–17

39. Evans B, Brown A, Bulger J, Fegan G, Ford S, Guy K, Jones S, Keen L, Pallister I, Rees N, Russell I, Seagrove A, Snooks H: 74 Paramedics' experiences of administering fascia iliaca compartment block to patients with suspected hip fracture. BMJ Open 2018; 8:A28

40. Man-Son-Hing M, Laupacis A, O'Rourke K, Molnar FJ, Mahon J, Chan KB, Wells G: Determination of the clinical importance of study results. J Gen Intern Med 2002; 17:469–76

41. Chen H, Cohen P, Chen S: How big is a big odds ratio?: Interpreting the magnitudes of odds ratios in epidemiological studies. Commun Stat Simul Comput 2010; 39:860–4

42. Memtsoudis SG, Danninger T, Rasul R, Poeran J, Gerner P, Stundner O, Mariano ER, Mazumdar M: Inpatient falls after total knee arthroplasty: The role of anesthesia type and peripheral nerve blocks. Anesthesiology 2014; 120:551–63

43. Williams J, Young W: Appendix: A summary of studies of health care administrative databases in Canada, Patterns of Healthcare in Ontario: The ICES Practice Atlas. Edited by Goel V, Williams J, Anderson G, Blackstein-Hirsch P, Fooks C, Naylor C. Ottawa, Canada, Canadian Medical Association, 1996