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A Population-based Comparative Effectiveness Study of Peripheral Nerve Blocks for Hip Fracture Surgery

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ABSTRACT

Background: Adverse outcomes and resource use rates are high after hip fracture surgery. Peripheral nerve blocks could improve outcomes through enhanced analgesia and decreased opioid related adverse events. We hypothesized that these benefits would translate into decreased resource use (length of stay [primary outcome] and costs), and better clinical outcomes (pneumonia and mortality).

Methods: The authors conducted a retrospective cohort study of hip fracture surgery patients in Ontario, Canada (2011 to 2015) using linked health administrative data. Multilevel regression, instrumental variable, and propensity scores were used to determine the association of nerve blocks with resource use and outcomes.

Results: The authors identified 65,271 hip fracture surgery patients; 10,030 (15.4%) received a block. With a block, the median hospital stay was 7 (interquartile range, 4 to 13) days *versus* 8 (interquartile range, 5 to 14) days without. Following adjustment, nerve blocks were associated with a 0.6-day decrease in length of stay (95% CI, 0.5 to 0.8). This small difference was consistent with instrumental variable (1.1 days; 95% CI, 0.9 to 1.2) and propensity score (0.2 days; 95% CI, 0.2 to 0.3) analyses. Costs were lower with a nerve block (adjusted difference, –$1,421; 95% CI, –$1,579 to –$1,289 [Canadian dollars]), but no difference in mortality (adjusted odds ratio, 0.99; 95% CI, 0.89 to 1.11) or pneumonia (adjusted odds ratio, 1.01; 95% CI, 0.88 to 1.16) was observed.

Conclusions: Receipt of nerve blocks for hip fracture surgery is associated with decreased length of stay and health system costs, although small effect sizes may not reflect clinical significance for length of stay.

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Many observational analyses and ongoing randomized trials have evaluated the potential value of neuraxial *versus* general anesthesia for hip fracture surgery
- The association between peripheral nerve blocks and outcomes after hip fracture surgery is less well studied

What This Article Tells Us That Is New

- Among elderly patients undergoing emergency hip fracture surgery in Ontario, Canada, peripheral nerve blocks may be associated with slightly decreased postoperative lengths of stay and health system costs
- The use of peripheral nerve blocks was not associated with a difference in postoperative pneumonia rates

Hip fractures are the most frequent indication for emergency surgery in older adults.[1] More than 300,000 hip fracture surgeries are performed annually in the United States,[2] more than 65,000 in the United Kingdom,[3] and more than 20,000 in Canada.[4] Individuals requiring hip fracture surgery are typically older and are often medically complex.[5,6] Mortality and adverse events are common after hip fracture surgery; one in five individuals experience a complication and 1-yr mortality rates exceed 25%.[7–9] Given the rapid aging of the population,[10,11] hip fractures will continue to be a significant contributor to adverse individual and population-level health outcomes. While many studies and reviews have evaluated the role of neuraxial *versus* general anesthesia in hip fracture care,[12–14] further anesthetic strategies to improve outcomes and decrease healthcare resource use after hip fracture surgery are urgently needed.

The advanced age and high baseline illness severity typical of hip fracture surgery patients may leave them vulnerable to adverse effects of systemic opioid analgesics, which are used to treat fracture- and surgery-related pain.[15,16] However, poorly treated acute pain is also associated with negative clinical outcomes.[16,17] Therefore, alternate analgesic strategies, such as peripheral nerve blocks, could help to improve postoperative clinical outcomes by decreasing requirements for systemic opioids and reducing opioid-related adverse effects. A recent Cochrane review that included 31 trials and 1,760 participants[18] found high-quality

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evidence that supports the efficacy of peripheral nerve blocks in improving acute pain scores; moderate-quality evidence supports the role of peripheral nerve blocks in decreasing pneumonia and time to first mobilization. Inadequate data were available to estimate the impact of peripheral nerve blocks on other outcomes. Evidence supporting the generalizability of these findings, as well as the population-level impact of peripheral nerve blocks on clinical outcomes or resource use after hip fracture surgery are lacking.

We hypothesized that older hip fracture surgery patients who receive a peripheral nerve block would be less likely to experience opioid-related adverse events, however, in-hospital use of these drugs and related adverse events are not routinely coded in population-level data. Therefore, we further hypothesized that decreasing opioid-related adverse events should translate into decreased resource use, such as shorter length of stay (a priority outcome for older people[19]) and lower healthcare costs (a secondary outcome). We also hypothesized that the odds of clinical outcomes validly available in population-level data, such as all-cause mortality and pneumonia, might also be lower when peripheral nerve blocks were used.

Materials and Methods

Design and Setting

Following protocol registration (osf.io/ts658/), we conducted a population-based cohort study in Canada's most populous province (Ontario; more than 13 million inhabitants), which provides universal physician and hospital health insurance coverage. Healthcare data in Ontario are collected using standardized methods and are stored at ICES.[20] For the current study, data were linked deterministically using encrypted, patient-specific identifiers across the following databases: the Discharge Abstract Database (acute care hospitalization details including diagnoses, procedures and length of stay); the Ontario Health Insurance Plan (physician service claims); the National Ambulatory Care Reporting System (all emergency and outpatient care); the Continuing Care Reporting System (long-term and respite care); the Ontario Drug Benefits Database (prescription drug claims for residents greater than or equal to 65 yr); and the Registered Persons Database, which captures all death dates for residents of Ontario. Because data used for this study were routinely collected and deidentified, it was legally exempt from research ethics review.

Cohort

We identified all Ontario residents age 66 yr or older on the day of their hip fracture surgery using Canadian Classification of Interventions codes for hip fracture surgery (diagnostic code S72 for hip fracture plus an emergency hospital admission that included procedural codes 1VA53, 1VA74, 1VC74, or 1SQ53).[21] Reabstraction studies demonstrate high levels of agreement when identifying hip fracture surgery patients ($\kappa = 0.95$; positive predictive value, 0.95 [95% CI, 0.94 to 0.97]).[22] This was a patient-level analytic data set and included surgeries occurring from January 1, 2011 to December 31, 2015. Use of this start date placed all data after an update to peripheral nerve block physician billing codes that occurred in 2008. Data from 2008 to 2009 were excluded to allow normalization of billing code use, while instrumental variable analysis required a 1-yr lookback, making 2011 the earliest available start date. The end date reflects the most recent availability of complete data.

Exposure

We identified peripheral nerve blocks 1 day before, on the day of, or 1 day after, surgery using Ontario Health Insurance Plan physician billing codes (G260: major plexus block [could include 3-in-1 block, lumbar plexus, or sacral plexus block]; G060: major peripheral nerve block [could include fascia iliaca or femoral nerve block]; G061: minor peripheral nerve block [could include block of terminal branches, such as lateral femoral cutaneous]; G279: percutaneous nerve block catheter) that have been validated against a clinical reference to demonstrate their accuracy (positive likelihood ratio, 16.83; negative likelihood ratio, 0.03; sensitivity, 97%; specificity, 94%) for correctly identifying the true presence (or absence) of a peripheral nerve block.[23] Peripheral nerve blocks were coded as provided or not provided based on the presence (or absence) of a billing code within one day of surgery.

Outcomes

Our primary outcome was postoperative length of stay, measured from the Discharge Abstract Database as the number of days from surgery to hospital discharge.[22] Our secondary resource use outcome was 30-day health system costs (calculated from the day of surgery to 30 days after surgery from the perspective of the healthcare system). We used patient-level validated costing algorithms,[24,25] standardized to 2016 Canadian dollars. This approach includes all direct costs (those where costs are directly and specifically available and attributable to the patient such as physician service claims, diagnostic and laboratory testing, pharmaceuticals, equipment or medical devices, home care) and indirect costs (*i.e.,* health system utilization of inpatient and outpatient hospital care, emergency care, inpatient rehabilitation, complex continuing care, and long-term-care, calculated by accounting for an individual's resource intensity weight, case-mix group and duration of care) to the health system. This approach includes the cost of surgery but lacks the granularity to specifically account for materials such as regional anesthesia supplies (the anesthesiologist's fee for placing the peripheral nerve block is included). Patient costs incurred outside of those covered by the health system are not accounted for. Clinical outcomes were in-hospital pneumonia, identified using validated *International Classification of Diseases, Tenth Revision* codes J10 through J18, flagged as arising during hospitalization from the index the Discharge Abstract Database,[26] and 30-day all-cause mortality (from the Discharge Abstract Database and Registered Persons Database). *Post hoc* we identified discharge disposition from the Discharge Abstract Database, which was categorized as institutional (nursing home, continuing care facility, rehabilitation) *versus* home (back to prefracture place of residence).

Covariates

We measured baseline covariates that we postulated—based on clinical and epidemiologic knowledge—could influence receipt of a peripheral nerve block, as well as outcome risk. Demographics were identified from the Discharge Abstract Database and from the Canadian Census. Standard methods were used to identify Elixhauser comorbidities using *International Classification of Diseases, Tenth Revision* codes from the Discharge Abstract Database in in the 3 yr preceding surgery.[27] Preoperative residence in a long-term care facility was identified from the Continuing Care Reporting System. We calculated each individuals' hospital-patient one-year mortality risk score.[28] Prescription drugs in the 6 months before surgery were identified (opioids, anticoagulants, antiplatelet agents, antipsychotics, benzodiazepines, and dementia medications). The Johns Hopkins Adjusted Clinical Groups system was used to identify healthcare resource utilization bands and frailty-defining diagnoses.[29] The specific surgical procedure, and a unique identifier for each hospital, was recorded from the Discharge Abstract Database. We identified the year of surgery as a potential confounder as, in 2013, evidence-based provincial recommendations[30] for hip fracture care were published that recommended nerve block use. We also identified whether each patient was admitted to a trauma service (as opposed to an orthopedic surgery admission) by identifying the specialty of the physician service listed as most responsible for the admission in the Discharge Abstract Database.

Sample Size

This was a population-based study; therefore, all eligible members of the Ontario population were included. All tests of significance were two-tailed with alpha = 0.05.

Missing Data

No exposure, outcome, or covariate data was missing.

Statistical Analysis

All analyses were performed using SAS 9.4 (SAS Institute, USA). Baseline covariate data was compared between those with and without a peripheral nerve block using absolute standardized differences; values greater than 0.10 were considered to represent substantial imbalance.[31]

Unadjusted outcome rates were compared between exposure levels. Because our length of stay and cost distributions were skewed, but our regression approach is based on transformed mean values, we reported summary statistics using both means and SD and medians and interquartile ranges. Our primary adjusted analysis used multilevel, multivariable, generalized linear regression with a log link and γ response distribution (which is recommended for surgical data to account for the skewed length of stay distribution).[32] Cost data were analyzed in the same manner as length of stay.[33] When exponentiated, the β coefficient from a log-γ model can be interpreted as the ratio of means. A generalized linear model with a logit link and binomial distribution (*i.e.,* logistic regression) was used for mortality and pneumonia. Differences in continuous outcomes (length of stay, costs) on the absolute difference scale were calculated using predicted outcome estimates from the adjusted model, generated across 1,000 bootstrap samples (created using 1:1 resampling with replacement).[34] The median, 97.5th and 2.5th percentiles of the bootstrap distribution were used to define the effect size and 95% CI.

All adjusted regression models used generalized estimating equation methods to account for clustering of patients in hospitals, and included the exposure of interest (peripheral nerve block), age (restricted cubic spline with five knots), biologic sex (binary), neighborhood income quintile (five-level categorical variable), rurality (binary), procedure (categorical), hospital-patient one-year mortality risk score (continuous linear), each Elixhauser comorbidity (binary), each specified drug class (binary), year of surgery (categorical), resource utilization band (categorical), frailty (binary), and preoperative long-term care residence (binary).

Prespecified Sensitivity Analyses

Two prespecified additional approaches were used to analyze the association of receipt of peripheral nerve block with length of stay. Because even with a robust set of measured confounders, unmeasured differences between patients who did or did not receive a peripheral nerve block could still exist and influence outcome, our first approach was to account for the likely presence of unmeasured confounding variables using an instrumental variable analysis (Supplemental Digital Content 1, http://links.lww.com/ALN/C47). First, we performed a Durbin–Wu–Hausman test of endogeneity to evaluate whether unmeasured confounding may be present.[35–37] Next, we performed the instrumental variable analysis, which leverages a source of natural variation (sometimes called quasi-randomization) to help block the influence of unmeasured variables, while adjusting for measured confounders. A common type of instrumental variable is called the hospital preference instrumental variable, which has been used in previous studies in perioperative medicine.[38] This approach assumes that the local practice pattern (in our case the proportion of hip fracture patients at each participant's hospital who received a peripheral nerve block in the year before each participant's surgery) influences receipt of the intervention (*i.e.,* the peripheral nerve block), without otherwise influencing the outcome. This approach is built on three key assumptions: (1) patients who happen to receive care at a hospital that provides a high proportion of peripheral nerve blocks to its hip fracture patients is more likely to receive a peripheral nerve block than someone who presents to a low peripheral nerve block–use hospital, regardless of their personal characteristics; (2) going to a high peripheral nerve block use hospital does not influence outcome, except through receipt of a peripheral nerve block; and (3) going to a high peripheral nerve block use hospital is not influenced by a patient's unmeasured characteristics. The first two assumptions are verifiable by looking at the strength of correlation between the instrumental variable and receipt of a peripheral nerve block (which should be strong) and with outcome (which should be negligible). The last assumption is not directly verifiable, although determining that measured patient characteristics between high and low peripheral nerve block–use hospitals are similar supports the validity of the assumption, as does content knowledge, like the fact that a patient requiring emergency surgery is unlikely to choose their hospital based on regional anesthesia practice.[39] The second additional approach was a propensity score matched analysis (Supplemental Digital Content 2, http://links.lww.com/ALN/C47).

Subgroup Analyses

We tested for the presence of effect modification for length of stay by adding the following prespecified multiplicative interaction terms to the primary adjusted regression model: (1) peripheral nerve block × chronic obstructive pulmonary disease (as regional anesthesia techniques may be more effective in people with respiratory disease[40]); (2) peripheral nerve block × sex (as sex and gender based analyses are recommend in health services research[41]); (3) peripheral nerve block × dementia (as opioids are associated with delirium in older hospitalized patients[42]); (4) peripheral nerve block × frailty (as individuals with frailty are vulnerable to adverse health outcomes[43]); (5) peripheral nerve block × preoperative opioid prescription (as peripheral nerve blocks may be particularly beneficial in individuals with preexisting chronic pain[44]). *Post hoc* we tested a peripheral nerve block × trauma admission interaction term. Where an interaction term had a *P* value less than 0.05, we calculated the effect estimate at each level of the effect-modifying variable.

Post Hoc Sensitivity Analyses

Following completion of our primary analyses, we performed several *post hoc* analyses to test assumptions in our primary analysis. First, because death in-hospital could decrease length of stay in a biased manner, we repeated the primary analysis limited to individuals discharged alive from hospital. Next, because neuraxial (*vs.* general) anesthesia is a regional anesthesia technique associated with decreased length of stay but is a covariate that could precede receipt of a peripheral nerve block (therefore acting as a confounder), we repeated the primary analysis with the addition of a reviewer-recommended categorical variable representing receipt of a neuraxial anesthetic (spinal or epidural), general anesthetic, or combined general and neuraxial anesthesia. Peer reviewers also recommended that we perform a fixed effects regression analysis with a hospital identifier entered as a categorical variable (as opposed to accounting for each hospital using a clustered, generalized estimating equation approach as we did in our primary analysis; Supplemental Digital Content 3, http://links.lww.com/ALN/C47).

Results

We identified 65,271 hip fracture surgery patients; 10,030 received a peripheral nerve block (15.4%). Of people with a peripheral nerve block, 62.2% were billed as a plexus block and 37.8% as a major nerve block, and no one had a minor block billed as the sole peripheral nerve block; only 0.6% of patients had a continuous catheter inserted. Standardized differences for all measured covariates suggested non-substantial differences between exposure groups except for a larger proportion peripheral nerve block receivers being from a nonrural residence and having surgery in 2015 (table 1). *Post hoc* we identified that 9,054 (13.9%) patients were admitted to a trauma service.

Peripheral Nerve Blocks and Postoperative Length of Stay

The mean and median postoperative length of stay for people who received a peripheral nerve block were 11.5 ± 17.7 and 7 (interquartile range, 4 to 13) days; for people without a peripheral nerve block the mean and median length of stay were 12.5 ± 19.0 and 8 (interquartile range, 5 to 14) days. Before covariate adjustment, receipt of a peripheral nerve block was associated with a decrease in length of stay (1-day decrease; ratio of means, 0.92; 95% CI, 0.90 to 0.94). After multilevel multivariable adjustment, receipt of a peripheral nerve block remained associated with decreased length of stay (0.6-day decrease; 95% CI, 0.5 to 0.8; ratio of means, 0.96; 95% CI, 0.93 to 0.99). The fully-adjusted regression model is presented in table 2.

The proportion of hip fracture patients who received a peripheral nerve block at each participant's hospital in the year before the index surgery met the two verifiable assumptions required for a valid instrumental variable: (1) it was strongly associated with receipt of a peripheral nerve block (*F*-statistic, 45.5); and (2) it was uncorrelated with length of stay (correlation coefficient, −0.02). Measured covariate data for patients at high *versus* low (cut off greater than 8% *vs.* less than or equal to 8%) peripheral nerve block–use hospitals is provided in the Supplemental Digital Content (http://links.lww.com/ALN/C47), showing that

Table 1. Baseline Characteristics of Study Population by Peripheral Nerve Block Status

	Peripheral Nerve Block (n = 10,030)	No Peripheral Nerve Block (n = 55,241)	ASD*
Demographics			
Age at surgery (yr; mean ± SD)	79 ± 13	78 ± 14	0.07
Female	7,015 (69.9)	37,581 (68.0)	0.04
Income quintile			
1 (lowest)	2,178 (21.7)	12,167 (22.0)	0.01
2	2,216 (22.1)	11,069 (20.0)	0.05
3	1,985 (19.8)	10,912 (19.8)	0.00
4	1,913 (19.1)	10,633 (19.3)	0.01
5 (highest)	1,738 (17.3)	10,460 (18.9)	0.04
Rural	1,019 (10.2)	7,826 (14.2)	0.12
Year of surgery			
2011	1,640 (16.4)	10,587 (19.2)	0.07
2012	1,839 (18.3)	11,205 (20.0)	0.04
2013	2,070 (20.6)	11,571 (21.0)	0.01
2014	1,949 (19.5)	11,365 (20.6)	0.03
2015	2,532 (25.3)	10,693 (19.4)	0.14
Comorbidities			
Alcohol abuse	283 (2.8)	2,031 (3.7)	0.05
Atrial arrhythmia	835 (8.3)	4,783 (8.7)	0.01
Blood loss anemia	1,673 (16.7)	10,241 (18.5)	0.05
Cardiac valve disease	321 (3.2)	1,829 (3.3)	0.01
Coagulopathy	223 (2.2)	1,492 (2.7)	0.03
Chronic obstructive pulmonary disease	1,104 (11.0)	6,574 (11.9)	0.03
Cerebrovascular disease	458 (4.6)	2,726 (4.9)	0.01
Disease of pulmonary circulation	216 (2.2)	1,387 (2.5)	0.02
Dementia	1,780 (17.8)	9,944 (18.0)	0.01
Depression	460 (4.6)	2,729 (4.9)	0.01
Deficiency anemia	56 (0.6)	352 (0.6)	0.00
Diabetes mellitus without complications	1,377 (13.7)	7,505 (13.6)	0.00
Diabetes mellitus with complications	1,450 (14.5)	7,668 (13.9)	0.02
Dialysis	166 (1.7)	803 (1.5)	0.02
Drug abuse	68 (0.7)	477 (0.9)	0.02
Heart failure	2,142 (21.4)	11,601 (21.0)	0.01
Hemiplegia	72 (0.7)	479 (0.9)	0.02
Hypertension without complications	4,002 (39.9)	23,202 (42.0)	0.04
Hypertension with complications	95 (1.0)	493 (0.9)	0.01
Liver disease	125 (1.3)	815 (1.3)	0.00
Malignancy	630 (6.3)	3,687 (6.7)	0.02
Metastases	180 (1.8)	1,127 (2.0)	0.00
Obesity	128 (1.3)	886 (1.6)	0.03
Peptic ulcer disease	139 (1.4)	852 (1.4)	0.00
Peripheral vascular disease	231 (2.3)	1,328 (2.4)	0.01
Psychoses	91 (0.9)	560 (1.0)	0.01
Renal disease	408 (4.1)	2,259 (4.1)	0.00
Rheumatic disease	96 (1.0)	701 (1.3)	0.03
Venous thromboembolism	67 (0.7)	436 (0.8)	0.01
Weight loss	338 (3.4)	1,857 (3.4)	0.00
Frail	6,050 (60.3)	33,621 (60.9)	0.01
Hospital One-year Mortality Risk score (mean ± SD)	37 ± 6	37 ± 7	0.01
Medications			
Anticoagulant	1,240 (12.4)	7,258 (13.1)	0.02
Antiplatelet agent	797 (8.0)	4,074 (7.4)	0.02
Antipsychotic	1,165 (11.6)	5,891 (10.7)	0.03
Benzodiazepine	1,771 (17.7)	9,328 (16.9)	0.02
Opioid	2,228 (22.2)	12,233 (22.1)	0.00
Dementia medication	755 (7.5)	4,228 (7.8)	0.01
Healthcare resource use			
Long-term care facility	1,571 (15.7)	8,383 (15.2)	0.01
Resource utilization band			
2 (lowest)	205 (2.0)	1,220 (2.2)	0.01
3	1,370 (13.7)	7,587 (13.7)	0.00
4	2,465 (24.6)	13,097 (23.7)	0.02
5 (highest)	5,990 (59.7)	33,337 (60.4)	0.01
Procedure			
Implantation of internal device, pelvis	16 (0.2)	147 (0.3)	0.02
Implantation of internal device, hip joint	3,449 (34.4)	20,914 (37.9)	0.07
Fixation, hip joint	2,233 (22.3)	10,403 (18.8)	0.09
Fixation, femur	4,332 (43.2)	23,777 (43.0)	0.00

All column values indicate n (%) unless otherwise indicated.

*Values greater than 0.10 indicate a substantial difference.

ASD, absolute standardized difference.

Table 2. Adjusted Regression Model for Length of Stay

	RoM	95% CI
Covariate		
Peripheral nerve block *vs.* none	0.96	0.93–0.99
Year of surgery		
2015	Ref	1.00–1.00
2014	1.08	1.04–1.12
2013	1.10	1.06–1.15
2012	1.16	1.11–1.21
2011	1.20	1.13–1.27
Age linear segment	0.99	0.98–0.99
RCS segment 1	1.02	1.01–1.02
RCS segment 2	0.90	0.84–0.96
RCS segment 3	1.31	1.05–1.63
Rural (*vs.* not rural)	1.25	1.17–1.33
Neighborhood income quintile		
1 (lowest)	1.04	1.01–1.08
2	1.03	1.00–1.06
3	1.03	0.99–1.07
4	1.02	0.99–1.05
5 (highest)	Ref	1.00–1.00
Comorbidities		
Alcohol abuse (*vs.* not/none)	0.99	0.93–1.05
Atrial arrhythmia (*vs.* not/none)	0.91	0.87–0.95
Blood loss anemia (*vs.* not/none)	1.17	1.14–1.20
Cardiac valve disease (*vs.* not/none)	0.97	0.92–1.02
Cerebrovascular disease (*vs.* not/none)	0.90	0.85–0.95
Chronic obstructive pulmonary disease (*vs.* not/none)	0.96	0.93–0.99
Coagulopathy (*vs.* not/none)	1.05	0.99–1.11
Deficiency anemia (*vs.* not/none)	1.04	0.92–1.18
Dementia (*vs.* not/none)	1.14	1.09–1.18
Depression (*vs.* not/none)	1.19	1.12–1.27
Diabetes mellitus without complications (*vs.* not/none)	0.95	0.91–0.98
Diabetes mellitus with complications (*vs.* not/none)	1.03	1.00–1.07
Dialysis (*vs.* not/none)	1.18	1.06–1.33
Disease of pulmonary circulation (*vs.* not/none)	1.16	1.09–1.23
Drug abuse (*vs.* not/none)	0.97	0.84–1.11
Frail (*vs.* not/none)	1.57	1.50–1.65
Heart failure (*vs.* not/none)	1.07	1.04–1.11
Hemiplegia (*vs.* not/none)	1.09	0.98–1.22
Hypertension without complications (*vs.* not/none)	0.95	0.93–0.98
Hypertension with complications (*vs.* not/none)	0.92	0.83–1.03
Liver disease (*vs.* not/none)	0.90	0.83–0.98
Malignancy (*vs.* not/none)	0.87	0.83–0.91
Metastases (*vs.* not/none)	0.94	0.88–1.01
Obesity (*vs.* not/none)	1.22	1.14–1.30
Peptic ulcer disease (*vs.* not/none)	0.98	0.91–1.06
Peripheral vascular disease (*vs.* not/none)	0.94	0.88–1.01
Psychoses (*vs.* not/none)	1.40	1.19–1.64
Renal disease (*vs.* not/none)	0.88	0.83–0.94
Rheumatic disease (*vs.* not/none)	0.89	0.81–0.98
Venous thromboembolism (*vs.* not/none)	1.03	0.91–1.16
Weight loss (*vs.* not/none)	1.16	1.09–1.23
Hospital One-year Mortality Risk score (per 1-unit increase)	1.03	1.02–1.03
Healthcare resource use		
Long-term care before admission	0.63	0.61–0.66
Resource utilization band		
2 (lowest)	0.72	0.66–0.79
3	0.80	0.76–0.85
4	0.85	0.83–0.87
5 (highest)	Ref	1.00–1.00
Medications		
Anticoagulant (*vs.* not/none)	1.03	1.00–1.06
Antiplatelet agent (*vs.* not/none)	0.95	0.92–0.98
Antipsychotic (*vs.* not/none)	1.01	0.97–1.06
Benzodiazepine (*vs.* not/none)	0.97	0.94–1.00
Opioid (*vs.* not/none)	0.95	0.93–0.97
Dementia medication (*vs.* not/none)	0.92	0.87–0.98
Procedure		
Implantation of internal device, hip joint	1.08	0.92–1.27
Fixation, hip joint	0.96	0.93–0.98
Fixation, femur	0.95	0.92–0.97
Implantation of internal device, pelvis	Ref	1.00–1.00

RCS, restricted cubic spline; Ref, reference; RoM, ratio of means.

only having surgery in 2015 was substantively different between groups (more common in high peripheral nerve block–use hospitals). The Durbin–Wu–Hausman test was significant ($P < 0.0001$), supporting the role of an instrumental variable analysis. Following two-stage residual inclusion analysis, receipt of a peripheral nerve block was associated with a 1.05-day decrease in length of stay (95% CI, 0.87 to 1.19; ratio of means, 0.77; 95% CI, 0.73 to 0.82).

We successfully matched 8,261 (82.4%) peripheral nerve block patients to a similar patient without a peripheral nerve block. Following matching, receipt of a peripheral nerve block was associated with a 0.2-day (95% CI, 0.2 to 0.3) decrease in length of stay.

Effect Modifiers

Significant effect modification was identified between receipt of a peripheral nerve block and frailty ($P = 0.041$) and age ($P < 0.0001$). The association of peripheral nerve blocks with length of stay was greater in people without frailty (ratio of means, 0.93; 95% CI, 0.89 to 0.97) than in people with frailty (ratio of means, 0.97; 95% CI, 0.94 to 1.01). The association of peripheral nerve block with length of stay was stronger at younger ages (fig. 1). No significant effect modification was found between receipt of a peripheral nerve block and chronic obstructive pulmonary disease, sex, history of dementia, or trauma admission.

Peripheral Nerve Blocks and Secondary Outcomes

In the 30 days after surgery, peripheral nerve blocks were associated with a decrease in health system costs before and after covariate adjustment (greater than $1,400; table 3). There was no unadjusted or adjusted difference in the odds of mortality or pneumonia between people with or without a peripheral nerve block (table 3).

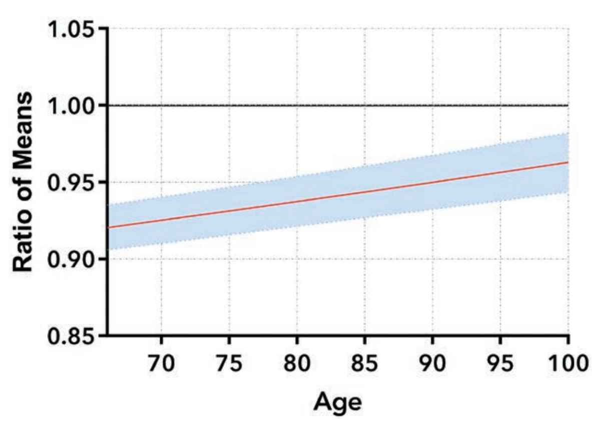

Fig. 1. Effect modification by age on the association of peripheral nerve blocks with length of stay. This figure demonstrates the effect size (*red line*) and 95% CI (*shaded area*) for receipt of a nerve block with length of stay at each age between 66–100 yr. The *solid black line* at 1.0 represents the null value for the association; values where the *line* and *shaded area* are below the *black line* represent a significant association. These values were calculated using the primary adjusted multilevel regression model for length of stay.

Post Hoc Sensitivity Analyses

In the analysis limited to people who were discharged alive from hospital, the adjusted ratio of means for length of stay was 0.95 (95% CI, 0.92 to 0.98). In the analysis that included anesthesia type as a categorical variable, the adjusted ratio of means from the regression model was 0.96 (95% CI, 0.93 to 0.99); when this categorical anesthesia type was used in the IV analysis, the peripheral nerve block–attributable decrease in length of stay was estimated to be 1.0 day (95% CI, 0.9 to 1.2). When the hospital identifier was entered into our primary adjusted regression model as a categorical fixed effect, the ratio of means was 0.97 (95% CI, 0.95 to 0.99). There was no significant adjusted difference in the odds of institutional discharge between people with and without a peripheral nerve block (odds ratio, 0.97; 95% CI, 0.89 to 1.09).

Discussion

In this population-based cohort of older people having emergency hip fracture surgery, the receipt of a peripheral nerve block was associated with a small decrease in length of postoperative hospital stay (that was statistically significant, but of questionable clinical significance) and decreased health system costs (approximately 5% lower). These findings were consistent across a variety of analytic approaches, including instrumental variable and propensity score analyses and are consistent with the positive effects of peripheral nerve blocks previously described in a systematic review of small randomized trials.[18] Given the increasing number of older people in Western populations, these findings are promising, however, the effect sizes varied notably (largest upper confidence limit, 1.2 days; smallest lower confidence limit, 0.2 days). This suggests that future multicenter randomized trials are likely required to provide more definitive causal data and should include patient-centered outcomes.

Hip fractures are the most common surgical indication for hospitalization in older people, and although rates of hip fracture are decreasing, the aging of the population means that hip fractures will continue to be a major driver of emergency healthcare utilization by older adults.[1,2,45] Additionally, the comorbidity burden of older people who experience a hip fracture is increasing,[2] leaving many hip fracture patients vulnerable to the adverse effects of systemic analgesic therapies.[15,16] A recent Cochrane review found that peripheral nerve blocks may offer advantages in hip fracture patients, with high quality evidence supporting a clinically relevant decrease in pain on movement immediately after block placement (–3.4 on a 10-point scale), and moderate evidence of decreased time to first mobilization

Table 3. Unadjusted and Adjusted Secondary Outcomes

Outcomes	Peripheral Nerve Block (n = 16,162)	No Peripheral Nerve Block (n = 6,499)	Crude Effect Estimate† (95% CI)	Adjusted Effect Estimate*† (95% CI)
30-day health system costs, mean ± SD	$20,158 ± $21,746	$22,221 ± $30,186	0.91 (0.89–0.92)	0.95 (0.92–0.98)
30-day mortality, n (%)	685 (6.8)	3,683 (6.7)	0.94 (0.89–1.00)	0.99 (0.89–1.11)
In-hospital pneumonia, n (%)	245 (2.4)	1,492 (2.7)	0.90 (0.79–1.04)	1.01 (0.88–1.16)

*All adjusted analyses included: age, neighborhood income quintile, rurality, procedure, Hospital One-Year Mortality score, each Elixhauser comorbidity, each specified drug class, year of surgery, resource utilization band, frailty, and long-term care residence;

†Effect estimate for costs is a ratio or means, for mortality and pneumonia an odds ratio.

(11 h shorter), reduced rates of pneumonia (relative risk, 0.41), and lower analgesic costs.[18] However, despite the large number of hip fracture surgeries that occur each year, findings from the Guay *et al.*'s Cochrane review were limited; most were small and single center and few reported key outcomes. For example, only three studies (total n = 131) evaluated pneumonia, and only two studies (total n = 155) evaluated time to mobilization.

Findings from our study build on Guay *et al.*'s Cochrane review, as the beneficial patient-level impacts of peripheral nerve blocks identified in randomized trials appear to translate into beneficial health system outcomes at a population level, including more than 7,000 potential hospital days saved per year if applied across 13,000 surgeries annually. Causally, improved pain control and earlier ambulation could translate into earlier discharge readiness and decreased healthcare resource use. The potential causality (*i.e.,* internal validity) of our findings are further supported by the minimal differences in patient characteristics between individuals who received a peripheral nerve block and those who did not, as well as by the consistency of the directional effect across three different analytic approaches, including an instrumental variable analysis (which may address issues of unmeasured confounding more effectively than traditional methods in observational research[46,47]). The fact that effect sizes differed between each approach likely reflects the slightly different question addressed by each analysis.[34,48,49] Our primary approach (*i.e.,* regression analysis) provides an estimate of average treatment effect; in other words, what would happen if the entire population received a peripheral nerve block compared to no one receiving a nerve block. In contrast, the instrumental variable analysis provides a local average treatment effect estimate (*i.e.,* what is the treatment effect in people who were eligible and willing to have or not have a peripheral nerve block). In this case, this local average treatment effect cannot be extrapolated to the types of patients who would never receive a peripheral nerve block (such as someone with an absolute contraindication or totally unwilling to have a peripheral nerve block), or someone who would almost always receive a peripheral nerve block. However, in the setting of a peripheral nerve block for hip fracture surgery the local average treatment effect may be practice- and policy-relevant as very few absolute contraindications to peripheral nerve blocks exist, and few patients would always be expected to receive a peripheral nerve block. Finally, the propensity score matched analysis provides an estimate of the average effect of treatment in the treated, which reflects the impact of a peripheral nerve block in the subset of the population who actually received a block. The positive impact of peripheral nerve blocks was also reflected in an estimated reduction in health system costs of greater than $1,400 CAD per patient. Considering that more than 13,000 hip fractures per year are treated surgically on Ontario, these savings could translate into more than $18 million dollars in yearly health system savings.

The inconsistency between our findings related to pneumonia (no decrease in the odds of pneumonia after receipt of a peripheral nerve block) and systematic review findings (decreased pneumonia risk with a peripheral nerve block) must also be considered and could reflect numerous issues. First, across the three trials included in the Cochrane review, only 25 pneumonias were identified.[50–52] A single study drove results with a control group respiratory infection rate of 43%.[50] Therefore, these findings may be fragile.[53] Furthermore, these three trials were conducted between 1980 and 2003, and may not reflect contemporary practice. Finally, although the pneumonia definition used has been validated,[26] misclassification bias is always a risk in observational research. Whether the causal pathway involves other postulated benefits of peripheral nerve blocks, such as early mobilization or reduced incidence of delirium, these outcomes cannot be accurately captured in administrative data. Specifically, functional data are not routinely captured and diagnostic codes for delirium suffer from substantial misclassification bias.[54,55] Therefore, prospective multicenter trials are needed to address patient-centered outcomes and to elucidate specific causal pathways.

Strengths and Limitations

Our findings should be considered in the context of the study's strengths and limitations. First, as an observational study, we could only estimate an association (as opposed to causation) between peripheral nerve blocks and outcomes. We also used health administrative data that were not initially collected for research purposes and are therefore at risk of misclassification bias. However, our exposure and outcome variables have been validated and demonstrate a high level of accuracy relative to clinical data. We were not able to capture outcomes considered as typical opioid-related adverse events (*e.g.,* nausea, pruritis, respiratory depression), therefore our findings provide no insights into how peripheral nerve blocks impact these relatively common clinical outcomes. We did not capture postdischarge opioid use either. Our adjusted analyses included a large set of measurable postulated confounding variables, accounted for clustering at the hospital level, and had consistent results across analytic approaches. Furthermore, while observational research is at risk of unmeasured confounding, our instrumental variable analysis (which can help to account for unmeasured confounders) estimated a larger treatment effect than our regression-based analysis. We were unable to account for exactly what type of peripheral nerve block was placed (*e.g.,* fascia iliac *vs.* femoral), how successful each peripheral nerve block placement was in establishing effective analgesia, or whether adjuncts (such as local anesthesia additives or additional analgesics like intrathecal opioids) were provided; therefore, our effect estimates reflect a pragmatic (as opposed to explanatory) research question.[56] We also limited our analyses to perioperative blocks (within 1 day of surgery); therefore, the role of blocks placed on arrival in the emergency department were not captured. We must also acknowledge that small differences in length of stay may not be as relevant at the individual patient level as at the health system level. Finally, the external validity of these results beyond Ontario will require confirmation in future research.

Conclusions

In a population-based cohort study of older people having emergency hip fracture surgery, receipt of a peripheral nerve block was consistently associated with reduced postoperative length of stay and reduced health system costs. These findings suggest that peripheral nerve blocks could contribute to improved population-level health system outcomes for hip fracture surgery patients. An appropriately powered multicenter trial will be required to estimate a causal relationship with patient-centered outcomes.

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Competing Interests

The authors declare no competing interests.

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